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CAN ARTICULATION INDEX BETTER ESTIMATE SPEECH INTELLIGIBILITY ON ADULT COCHLEAR IMPLANT USERS COMPARED TO AIDED PURE TONE THRESHOLDS?

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ABSTRACT

Introduction and objective: Aided pure-tone audiometry is often performed on cochlear implant (CI) users to evaluate speech sound accessibility. This study examines the relationship of speech recognition thresholds (SRT) of CI users using 1) Bisyllabic Malay Speech Audiometry (BMSA) and 2) Malay Matrix Sentence Test (MMST) with pure-tone audiometry aided thresholds (PTA_{AT}) as well as the articulation index (AI). **Methods**: In this cross-sectional study, SRT measurements for all three speech tests were collected from nineteen (average device age of 4.2 ± 3.7 years) post-lingual adult CI users. Participants had a median age of 37 years old (IQR = 17.5) and PTA_{AT} of 34 dB HL (IQR = 5.5). **Results:** Median SRT of BMSA and MMST were 45 dB SPL (IQR = 7.5 dB) and -4 dB SNR (IQR = 4.9 dB SNR), respectively. Spearmen's rank-order correlation revealed no statistically significant correlations between average PTA_{AT} and the SRT of BMSA ($r_s(19) = 0.396$, $p = 0.09$) and MMST ($r_s(19) = 0.135$, $p = 0.582$). Spearmen's rank-order correlation also revealed no statistically significant correlations between average AI and the SRT of BMSA ($r_s(19) = -0.169$, $p = 0.489$) and MMST ($r_s(19) = 0.035$, $p = 0.887$). **Conclusion:** Both PTA_{AT} and AI are poor estimators of speech perception abilities with and without competing noise. Speech tests should be routinely performed on CI users as neither aided thresholds nor AI are reliable measures of speech-sounds accessibility.

KEYWORDS: Articulation index (AI), Aided pure tone thresholds, Speech Recognition Threshold (SRT), Cochlear Implant (CI).

INTRODUCTION

Cochlear implant users are routinely evaluated with speech perception testing because one of the primary aims of cochlear implantation is to improve understanding of speech. An ideal test would be reliable and highly sensitive to different conditions, for example, tests that are typically done in quiet such as the AB words list (Boothroyd, 1968) or the Hearing in Noise Test (Nilsson et al., 1994) and the Quick SIN (Killion et al., 2004) for testing speech perception in background noise. It is understood that many CI users achieve excellent speech understanding in acoustically quiet conditions however they are likely to exhibit poor speech perception abilities in presence of background noise (Fetterman & Domico, 2002). An important contributing factor to this poor speech-in-noise performance is the limited transmission of low-frequency sound information through the implants or reduced spectral resolution from limited number of electrodes (Spriet et al., 2007). There are pre-, per- and post-operative factors that could affect speech perception performance; keen readers may refer to Lazard et al., (2012) and Blamey et al., (2012) for further reading on this topic.

A study by Ali et al., (2017) revealed that 62.24 % of audiologist in Malaysia either never or seldom perform speech audiometry in their practice. This would suggest dependency on the pure tone audiogram to interpret a patient's ability to hear speech sounds or reliance on disability type questionnaires (Goh et al., 2018; Rajan Devesahayam et al., 2018). The use of pure tone thresholds is especially problematic to make assumptions about hearing speech sounds particularly in noise as discussed in Killion & Niquette, (2000). Another method of using audiometric data to estimate accessibility to speech sounds is called the articulation index (AI). Using AI supposedly allows better representation of speech sounds between octave frequencies of 250 Hz to 6000 Hz because pure-tone thresholds are often averaged within a smaller range of octave frequencies to accommodate for easy calculations. AI can be easily measured based on complete audiograms using the count-the-dot method (Mueller & Killion, 1990) and is a known measure used for evaluating hearing aid performance (Fabry

& Van Tasell, 1990). This study aims to evaluate the applicability of using AI to estimate speech perception performance as compared to average pure tone thresholds.

METHODS AND MATERIALS

This is a quasi-experimental cross-sectional study using convenience sampling. Nineteen post lingual MED-EL™ CI users aged between 21 and 60 years old with median age of 37 years old (IQR = 17.5) were involved in this study. Three participants were bilateral CI users and two were bimodal users however, only data using unilateral CI were used for each participant. In terms of device experience, implant usage ranged between 0.6 to 15 years with median of 3 years (IQR = 3.7) of experience. Inclusion criteria for participants include native Malay speakers, normal pre-implant temporal bone anatomy on the implant side, free from surgical complications and more than 8 active electrode channels.

Participants were tested in an audiometric cabin at the Hearlife Hearing Care Centre in Kuala Lumpur. Average aided hearing thresholds of 500, 1000, & 2000 Hz (PTA_{AT}) were recorded using the MAICO MA 42 two-channel diagnostic audiometer (MAICO Diagnostics GmbH, Berlin, Germany). The AI was calculated using the count-the-dot method and was verified by 2 audiologists. The speech recognition thresholds were recorded for each participant using two speech tests; the BMSA which is a test in quiet (SRT) and the MMST which is a test with competing speech-shaped background noise (SRTn). The MMST was recorded using a closed-set test format measured using the adaptive step approach. Additionally, the maximum score was also recorded for the BMSA (MS). The BMSA was presented via the audiometer whereas the MMST was presented using a Windows™ PC using an external Creative X-Fi 2.1 SoundBlaster sound card (Sound Blaster X-Fi Surround 5.1 Pro, Creative Labs, Singapore). Free-field sound samples were delivered via the PreSonus Eris® E3.5 Powered Studio Monitors (PreSonus Audio Electronics Inc, USA). One training list was conducted for every subject for the MMST prior to data collection to reduce the procedural training effect of the test.

RESULTS

Data were analysed using the open source JASP statistical software version 0.18.1.0. (JASP, University of Amsterdam). The normality of the data was investigated using the Shapiro-Wilk Test Multivariate analysis for normality which revealed the distribution for $PTA_{AT,}$ AI, SRT and SRTn departed significantly from normality where, $W = 0.809$ p value < 0.01. Based on this outcome, the non-parametric test Spearman Rank Order Correlation was used to investigate the relationships between $PTA_{AT,}$ AI, SRT and SRTn.

The median PTA_{AT} was 34 dB HL (IQR = 5.5) with the worst average hearing thresholds recorded at 45 dB HL. The median AI was 0.43 (IQR = 0.19) with the lowest AI of 0.11 from a participant with a PTA_{AT} of 43 dB HL and highest AI of 0.8 from a participant with PTA_{AT} of 24 dB HL. In terms of speech perception scores, the median SRT of BMSA and MMST were 45 dB SPL (IQR = 7.5 dB) and -4 dB SNR (IQR = 4.9 dB SNR), respectively. Figures 1 and 2 shows the boxplots and jitter elements of the $PTA_{AT,}$ AI, SRT and SRTn.

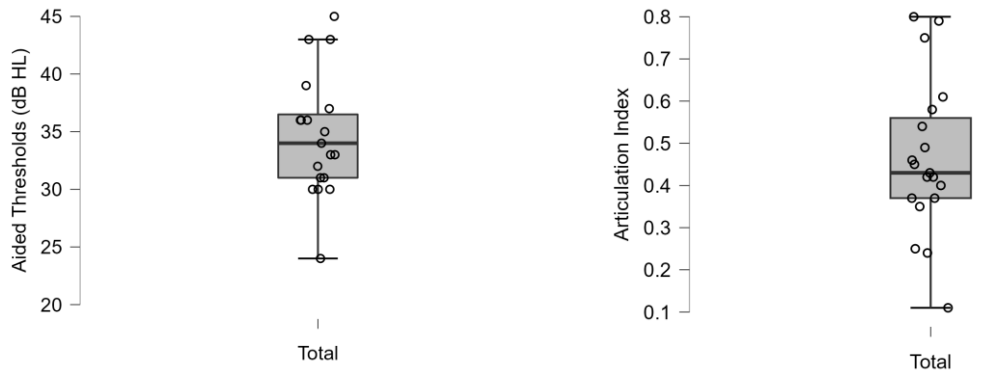


Figure 1: Distribution of average aided hearing thresholds of 500, 1000 & 2000 Hz (PTA_{AT}) and articulation index (AI) (n=19)

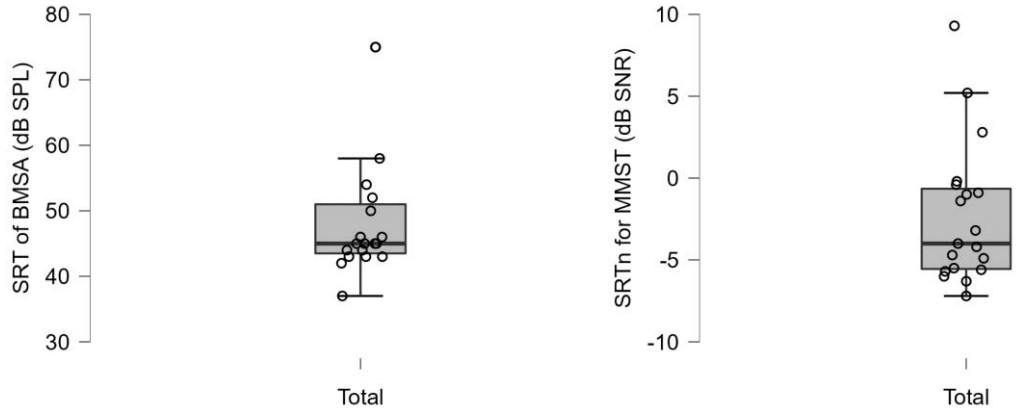


Figure 2: Distribution of speech recognition thresholds for BMSA (SRT in dB SPL) and the MMST (SRTn in dB SNR) (n=19)

We also recorded the maximum scores obtainable by the participants using the BMSA. The median maximum score using the BMSA was 87.5 dB HL (IQR=16.25) with two participants obtained the maximum score of 100% and the lowest score recorded was 45%. The distribution of the BMSA maximum score is shown in Figure 3.

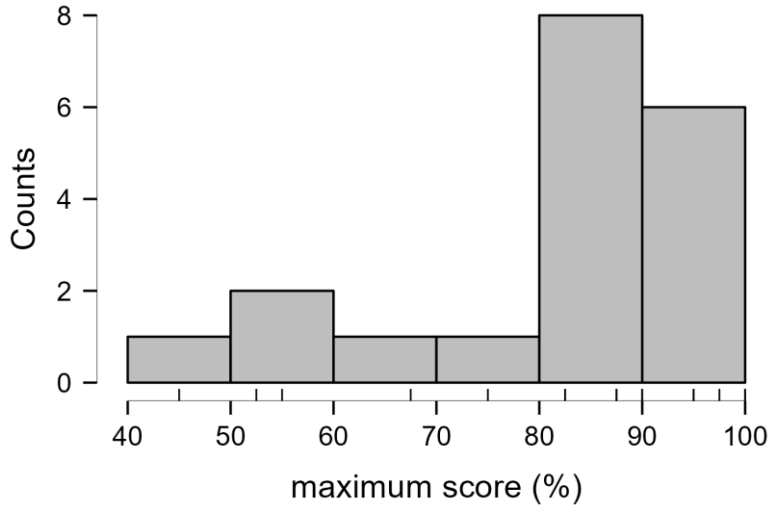


Figure 3: Histogram showing the distribution of maximum score using the BMSA.

To investigate the relationship between factors, the Spearmen's rank-order correlation was performed. Firstly, there was a statistically significant and strong negative correlation between the PTA_{AT} and AI, where $r_s(19) = -0.91$, $p_{value} < 0.01$. The test also showed that the two speech tests performed had no statistically significant correlations where, $r_s(19) = 0.262$, $p_{value} = 0.297$. Additionally, correlation analysis revealed a statistically insignificant correlation between the maximum score and SRT of BMSA where, $rs(19) = -0.24$, $p_{value} = 0.371$. The correlation plots between the AI and PTA_{AT} as well as the speech recognition thresholds of BMSA and MMST is shown in the Figure 4 below.

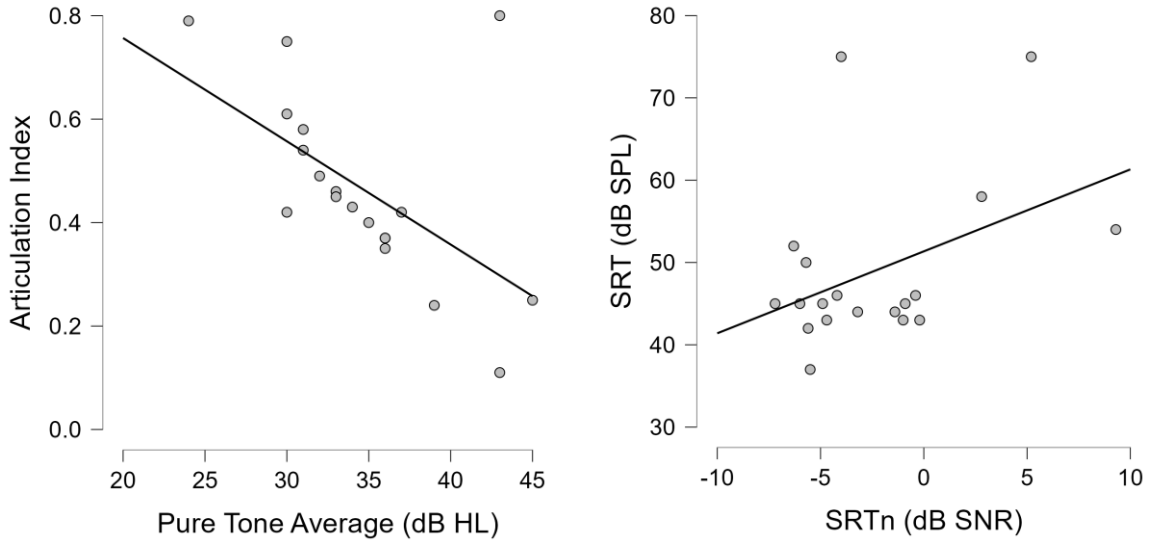


Figure 4: Correlation plots between articulation index (AI) and pure tone average (PTA_{AT}) and Speech recognition thresholds of BMSA (SRT) and MMST (SRTn)

Figure 5 shows the correlation plots between PTA_{AT} and AI and the two speech tests. The PTA_{AT} and AI did not show statistically significant correlations between the two speech tests. Spearmen's rank-order correlation revealed PTA_{AT} and the SRT of BMSA of $r_s(19) = 0.396$, $p_{value} = 0.09$ and PTA_{AT} and

MMST of $r_s(19) = 0.135$, $p_{value} = 0.582$. Spearmen's rank-order correlation revealed AI and the SRT of BMSA of $r_s(19) = -0.169$, $p_{value} = 0.489$) and AI and the MMST of $r_s(19) = 0.035$, $p_{value} = 0.887$.

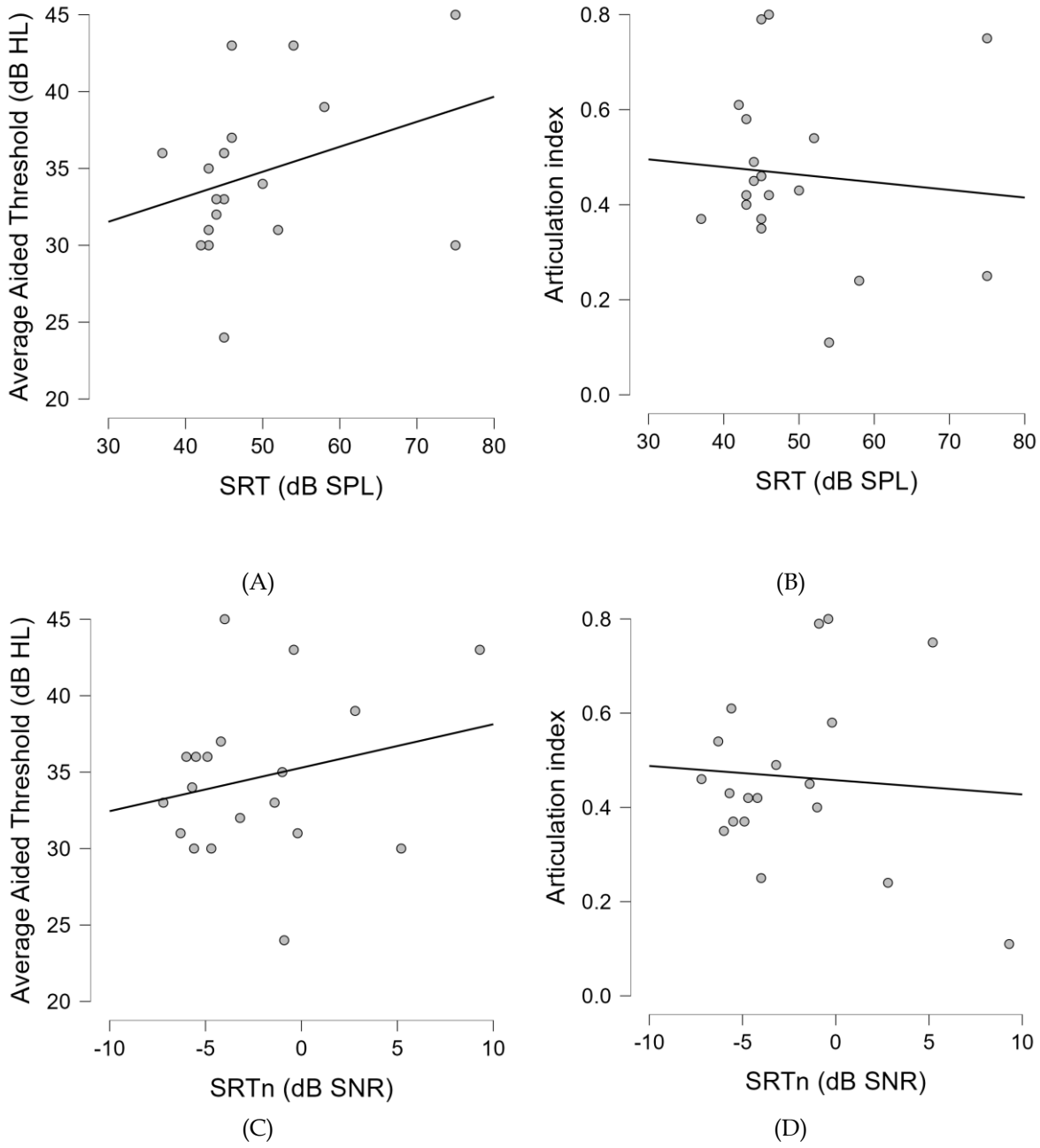


Figure 5: (A) Relationship between average aided thresholds (PTA_{AT}) and speech recognition thresholds using BMSA (SRT), (B) Relationship between articulation index (AI) and speech recognition thresholds using BMSA (SRT), (C) Relationship between average aided thresholds (PTA_{AT}) and speech recognition thresholds using MMST (SRTn), (D) Relationship between articulation index (AI) and speech recognition thresholds using MMST (SRTn)

DISCUSSION

As expected, the AI value and PTA_{AT} revealed a strong inverse correlation between the factors as the values from AI were derived from the level of aided hearing thresholds obtained from the participants. Despite this significant correlation, close inspection of the data showed that for two participants with same average aided hearing thresholds of 43 dB HL had largely different AI values (0.4 and 0.8) assigned to them. This is due to the fact that the AI is also dependent on the level and the configuration of hearing loss. Hearing loss that is predominantly high frequency would lead to lower AI scores as 74% of the assigned dots are allocated to hearing above 1000 Hz (Pavlovic, 1987).

This study confirms findings from previous studies where CI users showed predictably good speech intelligibility in quiet (Dowell et al., 1987; Fetterman & Domico, 2002). Seventy-four percent (n=14) participants scored a maximum score of 80% to 100% on the BMSA test which suggests good speech perception in acoustically favourable conditions for most users. For the BMSA, we found that the suprathreshold speech perception did not correlate with listening to speech at threshold levels. This pattern is consistent with the other correlation tests for the AI and PTA_{AT} with the SRT of BMSA. The difference in performance between threshold is most likely due to signal processing factors specifically the varying amount of effective frequency bands that could be used to code speech (Shannon et al., 1995). The findings in this study also suggests that threshold values are inadequate to assume speech intelligibility in quiet. Therefore, in order to get best results from CI users in acoustically quiet environments, speech signals need to be adequately audible. For speech perception in noise, both PTA_{AT} and AI were found to be not correlated to the SRTn in the MMST. This is also consistent with previous findings as CI users are inclined to show poorer speech perception in noise compared to in-quiet tests (Fetterman & Domico, 2002 & Dowell et al., 1987).

Speech intelligibility for both tests used in this study was independent of the average aided pure tone thresholds or its derivatives such as the AI. This is a logical outcome as pure tone hearing is primarily dependent on peripheral hearing abilities whereas speech perception is dependent on individual cognitive abilities (Moore & Shannon, 2009). Therefore, clinician must not be too dependent on aided audiograms to assume accessibility to speech sounds. Performing speech tests both in quiet and in noise would give in-depth understanding of individual CI user abilities. Clinicians can record and understand about at-threshold and -suprathreshold speech listening abilities as well as the effects of implant device configuration and sound pre-processing strategies.

LIMITATION OF STUDY

Despite the findings from this study, we would like to highlight areas that are known to have direct effect on the speech intelligibility of CI users but was not considered in the analysis. For example, the effect of pre-implant residual hearing (Cullen et al., 2004), duration without aided hearing (Blamey et al., 1992) and duration of implant use (Cesur et al., 2020)was not investigated.

CONCLUSION

Both PTA_{AT} and AI were found to be poor estimators of speech intelligibility in both in-quiet and in-noise speech tests. Speech testing should be repeatedly conducted on CI users before and after implantation to objectively observe progress with the device.

DECLARATION OF INTEREST

We would like to acknowledge the research grant sponsorship by the MED-EL Malaysia Sdn. Bhd., registered under IIUM Research Management Centre (SPP21-060-0060)

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MENTAL HEALTH STATUS AND SOCIAL COMMUNICATION SKILLS AMONG ADULTS SUSPECTED WITH ATTENTION DEFICIT HYPERACTIVITY DISORDERS (ADHD) SYMPTOMS

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ABSTRACT

Introduction: To date, limited epidemiological data are available concerning the impact of attention deficit hyperactivity disorders (ADHD) and mental health issues on the social communication skills of adults in Malaysia. It is crucial to comprehend the relationship between ADHD symptoms and how they may affect individuals' mental health status and social communication skills. **Objective:** The aims of the current study are to ascertain the prevalence of undergraduate students suspected of having ADHD, experiencing depression-anxiety-stress, and exhibiting poor social communication skills. Furthermore, this study seeks to compare the mental health status and social communication skills of adults with and without ADHD symptoms. Additionally, this study also aims to examine the relationships between mental health status, ADHD symptoms, and social communication skills among undergraduate students in higher education institutions. **Method:** A cross-sectional study design was utilized among undergraduate students at one of the universities in Pahang. The study subjects were recruited through snowball sampling and data collection was conducted over a period of approximately three months. A total of 186 participants completed self-reported demographic information, self-rating questionnaires, including the Depression Anxiety and Stress Scale 21 (DASS-21), Adult ADHD Self-Report Scale (ASRS v1.1) and Conversational Skills Rating Scale (CSRS), via an online questionnaire platform (Google Forms). **Results:** It was found that 39% of undergraduate students are suspected to have ADHD symptoms. A high prevalence of depression, anxiety, and stress, at 69.0%, 75.9%% and 49.7%, respectively, was also observed. Significant differences ($p<0.05$) were found in depression-anxiety-stress and social communication skills between students with and without ADHD symptoms. There were low to moderate correlations, ranging from -0.08 to 0.61, between communication skills, mental health domains, and ADHD subdomains. **Conclusions:** ADHD symptoms, mental health status, and social communication skills between undergraduate students with and without ADHD symptoms were statistically different. There were significant associations between ADHD symptoms, depression, anxiety, and stress. However, only a weak association was revealed between ADHD symptoms and social communication skills among undergraduate students in Pahang.

KEYWORDS: ADHD, stress, anxiety, depression, social communication

INTRODUCTION

Attention Deficit Hyperactivity Disorder (ADHD) in childhood is known to often persist into adulthood (Weiss & Hechtman, 1993). The pooled prevalence of adult ADHD has increased from 5.29% in 2007 to 6.76% in 2021 (Song et al., 2021; Polanczyk et al., 2007). The rising percentage in the prevalence of adult ADHD may indicate the seriousness of this condition. According to Kooij et al. (2010), many adults with ADHD are underdiagnosed and do not receive proper treatment for several reasons. Firstly, there may be a lack of information about the disorder. Next, it is common for adults with ADHD to cope with their symptoms by adjusting their behaviours. Lastly, comorbid psychiatric conditions may mask the ADHD symptoms (Kooij et al., 2010).

Generally, individuals with ADHD are more likely to experience other mental health problems (Mayo Clinic, 2019; Centers for Disease Control and Prevention, 2021). It is quite common for people with ADHD to also have anxiety, depression, conduct disorder, substance abuse, and sleeping problems (Harpin, 2005). Individuals with ADHD may exhibit issues such as difficulty in paying attention, hyperactivity, impulsive behaviour, or a combination of these three symptoms (American Psychiatric Association, 2013). However, the symptoms of ADHD in the adult population may not be as distinct as ADHD symptoms in children, which may explain cases of misdiagnosis and underdiagnosis of ADHD in adults (Ginsberg et al., 2014).

A study mentioned that the executive functions of the brain such as judgment, decision-making, initiative, memory, and the ability to complete complex tasks, are disrupted in individuals with ADHD (Wilens and Spencer, 2010). Therefore, ADHD in adults can lead to various problems, including low confidence and self-esteem, poor academic or work outcomes, and unstable relationships (Kim et al., 2016; Watters et al., 2017). Moreover, their social communication skills may be impaired, as they often find speech, social, and executive function skills challenging. The affected components of speech, social skills, and executive functions among adults with ADHD fall within the scope of practice of speech language pathologists (James (2017).

Furthermore, it was found that the quality of life in adults with ADHD is lower than that of those without ADHD (Pinho et al., 2017). For example, one study concluded that college students with ADHD behave similarly to other working adults with ADHD and have a lower quality of life than students without ADHD (Pinho et al., 2017). In another study, it was found that these students appeared to be more depressed and anxious, easily frustrated, and inclined to suppress their emotions. They also experience difficulty in achieving excellent academic performance and maintaining positive relationships with their friends (Kim et al., 2016). These negative impacts of ADHD may raise concerns regarding mental health problems among the students.

Several studies have examined the prevalence of ADHD, comorbid depression, stress, and anxiety, as well as their associations with ADHD amongst university students outside of Malaysia (Shen et al., 2020; Salla et al., 2019; Panevska et al., 2015). However, little epidemiological data are available concerning the influence of ADHD and comorbid mental health issues on social communication skills among adults in Malaysia. Therefore, the aims of this study are as follows: (1) to determine the prevalence of undergraduate students suspected with ADHD, depression-anxiety-stress, and poor social communication skills, (2) to identify differences in mental health status and social communication skills between adults with and without ADHD symptoms, and (3) to examine the association between mental health status, ADHD symptoms, and social communication skills among undergraduate students in Pahang.

METHODOLOGY

Study Design

This cross-sectional study protocol was approved by the International Islamic University Malaysia (IIUM) Research Ethics Committee (IREC 2022 - KAHS/DASLP/11). It was conducted at one of the higher education institutions in Pahang, using an online platform (i.e., Google forms). All participants have signed the informed consent form to enrol in the study.

Subjects

The study subjects were undergraduate students who were taking any bachelor's degree in the selected institution.

The inclusion criteria for the subjects:

1. Undergraduate students from all years, faculties and courses who are willing to participate in the study.

The exclusion criteria for the subjects:

1. Undergraduate students who refuse and are not willing to participate due to personal reasons.
2. Undergraduate students who are involved in pre-testing and pilot study.

Sample Size Calculation

To examine the mean difference between two independent groups utilizing a two-tailed test with a significance level ($\alpha = 0.05$) and medium effect size ($d=0.50$), a priori power analysis was conducted using G*Power3 (Faul et al., 2007). The analysis indicated that this study necessitated a sample of 128 participants, distributed equally into two groups ($n=64$ for each), to achieve a statistical power of 0.80. A total of 187 undergraduate students consented to participate in this research.

Instrumentation

In this study, the researchers administered an online questionnaire using Google Forms to collect data from the participants. The questionnaire included sections for obtaining participants' informed consent form, gathering socio demographic information, and administering the following self-reported scales: the Depression, Anxiety and Stress Scale - 21 (DASS-21) Questionnaire (21 items) (Henry & Crawford, 2005), the Adult ADHD Self-report Scale (ASRS v1.1) Symptom Checklist Questionnaire (18 items) (Kessler et al., 2005) and Conversational Skills Rating Scale-Rating of Self Form (CSRS) Questionnaire (25 items) (Spitzberg & Adam, 2007).

In the case of the DASS-21, responses were recorded on a 4-point Likert scale, ranging from 0 ("did not apply to me at all") to 3 ("applied to me very much"). The ASRS v1.1 employed a 5-item Likert scale to gauge the frequency of symptoms occurrence, with responses ranging from 0 ("never") to 4 ("very often"). Lastly, the CSRS questionnaire utilized a 5-point continuum to assess competence, encompassing the following categories: inadequate, fair, adequate, good, and excellent. English as the language of choice for all sections of the questionnaire.

Reliability Measurement

As the DASS-21 questionnaire is widely employed within the adult population in Malaysia, this study did not assess its. Nevertheless, previous research has reported that the DASS-21 demonstrates internal consistency and concurrent validity within acceptable to excellent ranges for both its overall and its

subscales, aligning with findings from the original version of the DASS-42 questionnaire. Specifically, reported Cronbach's alpha value for the overall scale was 0.93, while for the depression, anxiety, and stress subscales, they were 0.91, 0.85, and 0.86, respectively (Noorlila et al., 2018; Antony et al., 1998).

In this study, as the ASRS v1.1 and CSRS are not yet widely utilised within the Malaysian population, we conducted an analysis to examine their internal reliability. This analysis involved calculating the Cronbach's Alpha (α) coefficient for the overall items in both questionnaires. This analysis yielded an excellent Cronbach's Alpha (α) value of 0.906 for the 18 items in ASRS v1.1 questionnaire., Furthermore, acceptable α values were observed for its individual domains, specifically inattention (9 items) with a value of 0.85, motor hyperactivity-impulsivity (5 items) at 0.77, and verbal hyperactivity-impulsivity (4 items) with a value of 0.76.In addition, Cronbach's alpha (α) value for the 25 items in the CSRS questionnaire was also excellent at 0.908. These results affirm the excellent reliability of both questionnaires, supporting their suitability for use in this study.

Validity Measurement

Face validity testing for both ASRS v1.1 and CSRS questionnaires was conducted during the pre-testing phase. In this process, a group of undergraduate students from various universities in Malaysia (n=10) were engaged. Evaluation was based on four key domains, namely readability (comprehensibility), feasibility (suitability), clarity of language, and layout and style, with scoring determined by 'Yes' (1 point) and 'No' (0 points) (Venkitachalam, 2015). Participants were tasked with scoring the items in both questionnaires across these domains, with a criterion proposed by Jusoh (2020) that items scoring 90% or above were considered acceptable.

For ASRS v1.1 questionnaire, this study revealed that all four pre-testing domains achieved acceptability, with a perfect score of 100% in readability, feasibility, clarity of words and layout and style. Meanwhile, in the case of the CSRS questionnaire, the pre-testing scores were also deemed acceptable, with a 100% score for feasibility, and layout and style. The scores for comprehensibility and clarity of language were 98.80% and 97.60%, respectively. As reported by the participants, the time required to complete both the ASRS v1.1 and CSRS questionnaires averaged five minutes, a duration considered not unduly protracted. All participants confirmed that all items were clear and easily understood. Consequently, no further revision to the items were deemed necessary.

Statistical Analysis

Descriptive analysis of the data was done by computing SPSS version 12.0. To assess the normal distribution of continuous data, the Skewness and Kurtosis test was employed. The results indicated that all continuous data conformed to a normal distribution, as evidenced by Z values falling the range of -3.00 to 3.00. Consequently, parametric tests were applied for data analysis. An independent sample 'T' test was utilized to discern differences in mental health status and social communication skills between adults with and without ADHD symptoms. The relationships between variables were measured using Pearson correlation coefficients. All statistical analyses were performed using SPSS (Version 12.0; IBM, Inc., Chicago, Illinois), with a significance level set at 0.05 (two-tailed).

RESULTS

In this study, a total of 187 responses were obtained during the research period. Demographic characteristics of the participants are presented in Table 1. Of the 187 participants, 82.4% were female, with the majority falling within the 21 to 25 years age range (90.4%). Students from all years of study were invited to participate in the research; however, Year 4 students constituted the largest percentage of participants (46.1%). Regarding Cumulative Grade point average (CGPA), 66.3% of the students achieved

a CGPA between 3.50 and 4.00. Approximately 46.0% of the students reported a family income exceeding RM5000. The majority of the participants also disclosed no family history of mental illnesses (92.0%), current non-smoking status (97.9%), non-use of drugs (98.4%), and abstinence from alcohol (100%). During the data collection period, a small proportion of participants (18.2%) reported having utilised counselling services offered by their institution.

Table 1: Demographic Characteristics of the Participants (N=187)

Variable	Percentage (%)	Frequency (n)
Gender		
Male	17.6	33
Female	82.4	154
Age		
15-20	7.5	14
21-25	90.4	169
25-30	1.6	3
>30	0.5	1
Year of Study		
Year 1	8.6	16
Year 2	14.4	27
Year 3	26.2	49
Year 4	47.1	88
Year 5	3.7	7
CGPA		
3.50-4.00	66.3	124
2.00-3.49	33.2	62
<2.00	0.5	1
Family income		
>RM5000	46.0	86
RM2501-RM5000	27.8	52
RM1500-RM2500	10.2	19
<RM1500	16.0	30
Family history of mental disorder		
Yes	8.0	15
No	92.0	172
Smoking status		
Yes	2.1	4
No	97.9	183
Drugs usage		
Yes	1.6	3
No	98.4	184
Alcohol usage		
Yes	0	0
No	100	187

Utilised counselling services offered by the institution		
Yes	18.2	34
No	81.8	153

This study aimed to determine the prevalence of adults suspected of having ADHD, depression, anxiety, stress, and poor social communication skills among undergraduate students in Pahang. The investigation revealed that 39% of the participants (73 out of 187) were suspected of having ADHD. Among the 73 subjects suspected of having ADHD, 9 were male, and 33 were female. The frequencies of depression, anxiety and stress among university students were 69.0%, 75.9%% and 49.7%, respectively. In terms of communication skills, 7 out of 187 participants (3.74%) scored as having poor communication skills, while the remaining respondents scored in the range of good to excellent.

The mean scores for depression, anxiety, and stress in this study were 7.27, 7.16 and 8.21, respectively. The study's findings indicate the prevalence of depression in the following categories: normal (31%), mild (17.1%), moderate (25.7%), severe (12.8%), and extremely severe (13.4%). The prevalence of anxiety was distributed as normal (24.1%), mild (16%), moderate (17.1%), severe (12.8%), and extremely severe (30%). Meanwhile, the prevalence of stress was observed within the range of normal (50.3%), mild (15%), moderate (13.3%), severe (15.5%), and extremely severe (5.9%). Detailed information on the levels of depression, anxiety, and stress can be found in Table 2.

Table 2: Levels of Depression, Anxiety and Stress among The Participants

Variable	Levels	Percentage (%)	Frequency (n)
Depression	Normal	31.0	58
	Mild	17.1	32
	Moderate	25.7	48
	Severe	12.8	24
	Extremely Severe	13.4	25
Anxiety	Normal	24.1	45
	Mild	16.0	30
	Moderate	17.1	32
	Severe	12.8	24
	Extremely Severe	30.0	56
Stress	Normal	50.3	94
	Mild	15.0	28
	Moderate	13.3	25
	Severe	15.5	29
	Extremely Severe	5.9	11

The independent 'T' test statistical analysis was carried out to compare the mental health status and social communication skills in adults with and without ADHD. The statistical analysis revealed significant two-tailed results with p-value less than 0.05 (p=0.000 - 0.01) for all variables, and a 95%

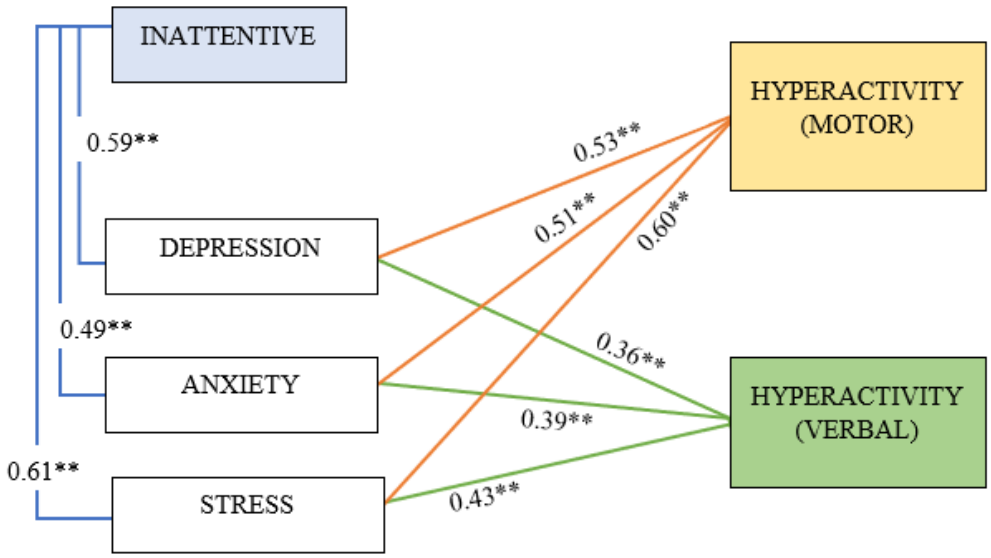
confidence interval was applied. Therefore, we can infer that significant differences exist in depression-anxiety-stress, and social communication skills between adults with and without ADHD symptoms.

Table 3: Independent 'T' Test of Differences of Mental Health Status and Social Communication Skills among Students with and without ADHD

Domain	Mean Difference	Std. Error Difference	Degree of Freedom (df)	Sig. (2-tailed)
Total depression score	-4.662	0.654	185	0.000
Total anxiety score	-3.287	0.642	185	0.000
Total stress score	-4.503	0.630	185	0.000
Total communication score	6.378	1.966	185	0.001

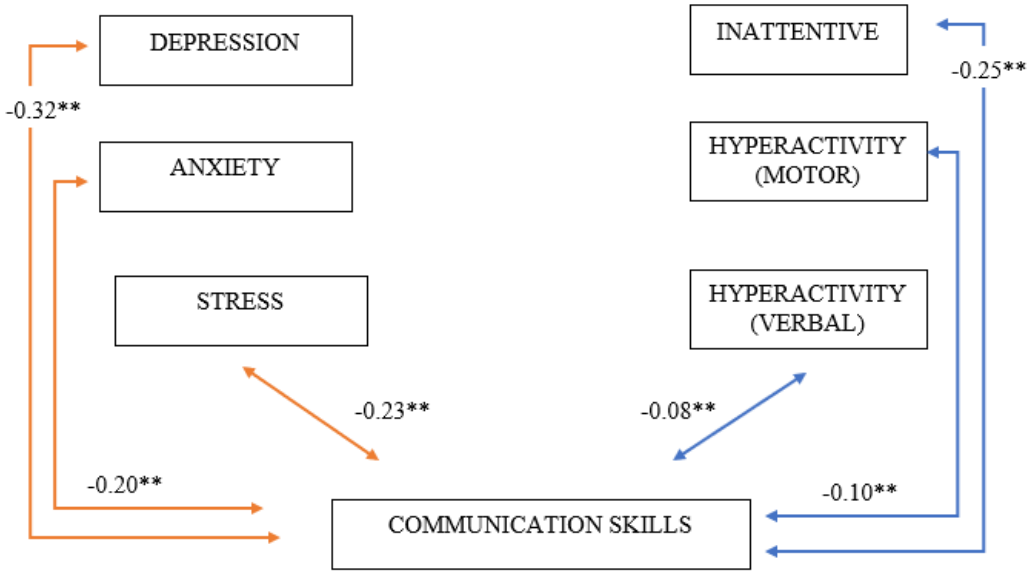
Given the normal distribution of data for the variables, Pearson product-moment correlation coefficient analysis was employed to measure the relationships between mental health status, ADHD symptoms, and social communication skills. The correlation coefficients (*r*) values were interpreted according to the established guidelines for correlation coefficient ranges (Ratner, 2009 as cited in Sharif, 2019).

Figure 1 presents the correlation coefficients (*r*) between ADHD subdomains and mental health status, with r-values falling within the range of low to moderate, specifically ranging from 0.36 to 0.61. Moreover, Figure 2 illustrates the correlation coefficients (*r*) between communication skills and mental health domains, as well as communication skills and ADHD subdomains, with r-values spanning from -0.08 to -0.32, with most values suggesting a weak negative correlation. All the correlation coefficients were significant at the 0.01 confidence level (two-tailed). In summary, these results affirm that a significant association between the ADHD sub-domains and mental health domains.



NOTE: **Correlation is significant at the 0.01 level (2-tailed)

Figure 1: ***Correlation Coefficients between ADHD Sub-domains and Mental Health Domains***



NOTE: **Correlation is significant at the 0.01 level (2-tailed)

Figure 2: ***Correlation Coefficients between ADHD Sub-domains, Mental Health, and Communication Skills***

DISCUSSION

In this study, the prevalence of undergraduate students suspected of having ADHD is 73 out of 187 students, accounting for 39.0% of the sample. A prior study found that approximately 15.9% of university students exhibited ADHD symptoms (Roshani et al., 2020). Moreover, globally, 6.76% of adults are documented to experience ADHD symptoms, with the pooled prevalence of ADHD among adults showing an increase from 2006 to 2021 (Song et al., 2021; Polanczyk et al., 2007). However, the proportion of undergraduate students with symptomatic ADHD in this study is surpasses the reported statistics, suggesting a higher prevalence. The upward trend may be attributed to the underdiagnosis of ADHD among adults. Individuals with ADHD symptoms might not recognise their condition as such and instead consider these symptoms as typical aspects of daily life. Factors contributing to the underdiagnosis of ADHD among adults may include a lack of information about the disorder, adults' adaptive coping mechanisms, and the presence of comorbid psychiatric (Kooij et al., 2010).

The prevalence of mildly to extremely severe depression, anxiety, and stress among undergraduate students was found to be 69%, 75.9% and 49.7%, respectively, suggesting relatively high levels of these mental health challenges among undergraduate students in Pahang. A comparable study conducted in Pakistan, which examined the mental health status of undergraduate students, reported that 75% of the students were experiencing depressive symptoms, 88.4% exhibited anxiety symptoms, and 84.4% reported experiencing stress (Asif et al., 2020). In Malaysia, undergraduate students have also been reported to experience varying degrees of depression and anxiety, largely attributed to the COVID-19 pandemic (Sundarasen et al., 2020; Woon et al., 2021). Several factors may contribute to the elevated levels of depression, anxiety, and stress among undergraduate students in Malaysia. For instance, prior research has suggested that higher levels of anxiety and stress among university students could be linked to disruption and delays in academic programs (Islam et al., 2020). With Malaysia experiencing multiple Movement Control Orders (MCO) since the onset of the COVID-19 pandemic, this may have intensified feelings of anxiety, depression, and stress among students. In light of these findings, it becomes essential for the university authorities to play a pivotal role in safeguarding the psychological and mental well-being of students through various means and platforms.

This study also observed significant differences in mental health status and social communication skills between adults with and without ADHD symptoms. This aligns with prior research indicating disparities in brain development, structure, and function between the two groups (ADHD and without ADHD) (American Academy of Child and Adolescent Psychiatry, 2017; Hoogman et al., 2017). The distinct characteristics of the ADHD brain can have substantial impacts on thinking, behaviour, and emotions. Consequently, adults with ADHD symptoms often encounter considerable challenges in their daily lives as these aspects are affected. In line with our hypothesis, a study revealed that the quality of life in adults with ADHD is lower compared to those without ADHD (Pinho et al., 2017). Besides, ADHD symptoms have implications for the psychosocial domain, potentially leading to diminished self-confidence and self-esteem among adults with ADHD symptoms (Watters et al., 2017). For instance, a study was conducted to examine the ability of adults, particularly undergraduate students with varying levels of ADHD symptoms, to take their conversational partner's perspective. The results implied that individuals with more severe ADHD symptoms exhibited decreased ability to consider their conversational partner's perspective when formulating responses. Furthermore, the study emphasized that successful communication necessitates significant cognitive and attention resources, including short term memory and the ability to resist the urge to respond inappropriately (Lin et al., 2010; Nilsen et al., 2013). Given that individuals with high self-reported ADHD symptoms encounter challenges with these skills, experts are keen on investigating how these issues may affect more intricate social interactions. Therefore, these findings contribute to the existing body of evidence illustrating distinctions between adults with and without ADHD symptoms.

Our study also identified a moderate positive correlation ($0.3<r<0.7$) between ADHD symptoms, including inattentive, motor hyperactivity, verbal hyperactivity, and mental health status, encompassing

depression, anxiety, and stress. These findings align with previous studies that has consistently reported the common co-occurrence of ADHD in the adult population with various psychiatric disorders, including mood disorders, depressive and anxiety disorders, substance use disorders, and personality disorders (Ginsberg et al., 2014; Katzman et al., 2017). Moreover, high prevalence of comorbid psychiatric disorders has been observed in adults with ADHD (Pehlivanidis et al, 2020), underscoring the existence of overlapping symptoms between ADHD and other concurrent psychiatric conditions. Among the subdomains of ADHD, inattentiveness and motor hyperactivity exhibited particularly high r-values ($r>0.5$) in their association with depression, anxiety, and stress, signifying a significant and moderate level of correlation with these three mental health domains in our study. A similar study reported noteworthy associations between anxiety, depression, inattention, and hyperactivity (Shen et al., 2020). These findings are valuable for informing clinical diagnosis and treatments approaches to the patients. Providing clinical diagnosis and tailored treatment programs tailored to individual patients can be challenging. Katzman et al. (2017) have noted that the Canadian ADHD Resource Alliance (CADDRA) guidelines recommend that when ADHD coexists with other psychiatric disorders in adults, the primary treatment should target the most impairing condition. Thus, the early identification and treatment of ADHD and its comorbidities can potentially alter the trajectory of the psychiatric morbidity later in life.

Furthermore, this study reveals a weak negative correlation ($-0.3<r<0$) between ADHD symptoms, encompassing inattentiveness, motor hyperactivity, and verbal hyperactivity, and social communication skills. These results contrast with the assertions made in previous studies that have linked ADHD to both speech and language issues as well as mental health and behavioural challenges (Cantwell, Baker, & Mattison, 1979, 1981; Chess & Rosenberg, 1974; Love & Thompson, 1988; Trautman, Giddan, & Jurs, 1990 as cited in Damico et al., 2010). Nonetheless, upon closer examination of the data, it is noteworthy that 5 out of 7 students (71.4%) who scored poorly in communication skills are suspected of having ADHD. This suggests a potential vulnerability for individuals experiencing ADHD symptoms in terms of their social communication abilities. Previous research has proposed that individuals with more severe ADHD symptoms exhibit reduced abilities in using another person's perspective during communication to guide their responses (Nilsen et al., 2013). In essence, those with severe ADHD symptoms encounter greater difficulties in social communication. The contradictory results may be attributed to several factors. Firstly, the tools used to measure ADHD symptoms and social communication skills relied on self-reported assessments, which are susceptible to bias. Participants may opt for answers deemed socially acceptable rather than providing truthful responses, potentially leading to an inaccurate self-assessment. To address this, a combination of self-reporting and peer or observer-rated scales may offer a more comprehensive perspective and help validate the findings. Secondly, it is important to note that university students generally exhibit a high level of communication skills. Previous study highlighted that tertiary educational institutions play a significant role in enhancing communication skills (Sabbah et al., 2020). These institutions provide a range of opportunities for students to develop and refine their communication skills.

CONCLUSION

This study seeks to examine the prevalence of depression, anxiety, stress, and the occurrence of suspected ADHD among undergraduate students. The findings reveal that 39.0% of the participants are suspected of having ADHD, with a significant proportion of students experiencing high levels of depression, anxiety, and stress. However, a relatively small percentage (3.74%) of participants exhibit poor communication skills. Notably, only 18.2% of the students in the study reported seeking counselling services provided by the university. Moreover, this study corroborates the hypothesis, demonstrating statistically significant differences in ADHD symptoms, depression, anxiety, stress, and social communication skills between adults with and without ADHD symptoms. Besides, the findings indicate moderate associations between ADHD symptoms and depression, anxiety, and stress. However, a weaker association is observed between ADHD symptoms and social communication skills. These findings hold significant value in raising awareness about the need to address ADHD symptoms among adults, particularly university students.

Other than that, they underscore the importance of early diagnosis and intervention for promoting the mental health and overall well-being of students who may be experiencing symptoms of ADHD or other mental health issues.

LIMITATIONS OF THE STUDY AND FUTURE RECOMMENDATIONS

This study possesses several limitations that warrant acknowledgement. Firstly, the sample size, when compared to the overall population of undergraduate students, was relatively small. Besides, a substantial majority of the participants were female, resulting in an imbalanced gender ratio of approximately 8:2. Consequently, the findings derived from this study may be more representative of females, and their applicability to undergraduate students across Malaysia may be limited. Multiple factors could contribute to the skewed gender distribution in this study. National statistics from 2020 indicate a notably higher proportion of female students in public universities, with a female-to-male ration of 6:4 (Hirschmann, 2022). Other than that, this study utilized snowball sampling, which relies on existing participants to recruit future participants from their social networks. Therefore, a larger and more diverse sample, encompassing male students, may have been less inclined to participate after receiving invitations. Secondly, the tools employed in the study consisted of self-reported questionnaires, which can introduce self-reporting bias. Participants may not always provide completely honest responses, may face difficulties recalling information accurately, or may exhibit stigma towards mental health conditions (Althubaiti, 2016; Sartorius, 2007). Finally, it is important to acknowledge that the sample size was relatively small, and the findings should not be generalized. Moreover, the findings of this study do not provide sufficient evidence to establish causal relationships between the variables. Notwithstanding these limitations, the findings from this study can act as preliminary findings, offering a foundation for more comprehensive research in the future. Therefore, we encourage future researchers to adopt a mixed-methods approach that combines quantitative (e.g., self-reported and third-party reported questionnaires) and qualitative research (e.g., interviews) to delve deeper into the complexities of comorbidity between ADHD and mental health and its impact on social communication skills.

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ADAPTATION OF THE REVISED FIVE-TO-FIFTEEN (5-15R) QUESTIONNAIRE INTO MALAY-5-15R: PRELIMINARY FINDINGS

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ABSTRACT

Introduction: There is a limited number of teacher and parent-reported questionnaires available for screening developmental and behavioural issues in children and adolescents in the Malay language. Therefore, there is a need for research on the translation and development of such a survey, particularly in the Malay language, to enhance the treatment and intervention process by the related professionals. **Objective:** The aims of the current study are to translate and adapt the Revised Five-To-Fifteen (5-15R) questionnaire into the Malay language, creating the Malay-5-15R, and to examine the content validity of the Malay-5-15R for potential use as a parent-reported questionnaire for screening purposes. **Method:** The 5-15R questionnaire was translated into the Malay language through a cross-cultural adaptation and translation process. This process involved several stages, including: 1) forward translation; 2) synthesizing forward translation; 3) backward translation; 4) synthesizing backward translation; 5) expert committee review; and 6) finalization. **Results:** The initial version of the Malay-5-15R questionnaire demonstrated a high content validity index. The Malay-5-15R questionnaire was found to be culturally acceptable, with all 181 items from the original version retained within specified domains. Minor amendments were made to several items to improve the sentence structures and to ensure the questionnaire's clarity and understandability for the Malaysian population, especially Malay speakers. These improvements involved refining the phrases, providing examples and explanations, and correcting the grammatical aspects. **Conclusions:** Despite the preliminary findings of the adaptation process, the Malay-5-15R questionnaire has significant potential as a screening tool for the Malay-speaking population.

KEYWORDS: Five-to-Fifteen (FTF) questionnaire, 5-15R questionnaire, adaptation, development, children, behaviour

INTRODUCTION

Globally, among the questionnaires that commonly used by the parents and teachers for screening developmental and behavioural issues in children and adolescents, four well-established instruments are (1) the Five-To-Fifteen Revised (5-15R) questionnaire (Kadesjö et al., 2017), (2) the Child Behaviour Checklist (CBCL) (Achenbach, 1991), (3) the Behaviour Assessment System for Children (BASC) (Reynolds & Kamphaus, 1992), and (4) the Strengths and Difficulties Questionnaire (SDQ) (Goodman, 1997). Among these questionnaires, the 5-15R questionnaire, originally referred to as the Five to Fifteen (FTF) questionnaire (Kadesjö et al., 2004)), is widely utilised by researchers and clinician in clinical practice (Lindblad et al., 2011). This is because, it offers more comprehensive information on developmental and behavioural issues in children and adolescents, shedding light on various critical of their development.

The 5-15R questionnaire was developed by Scandinavian and Finnish research groups as a comprehensive screening tool for the assessment of neurodevelopmental-neuropsychiatric disorders and related conditions, such as attention deficit hyperactivity disorders (ADHD), autism spectrum disorders (ASD), oppositional defiant disorder (ODD), tic disorders, developmental coordination disorder (DCD), conduct disorder (CD), among others (Kadesjö et al., 2017). This questionnaire represents an enhanced and re-standardized iteration of the previously known FTF questionnaires (Kadesjö et al., 2004). Notably, the 5-15R questionnaire expands its utility by involving teachers in the data collection process and extends its applicability to individuals aged between 5 and 17 years (Kadesjö et al., 2017). f This instrument encompasses a total of 181 items, which are further categorised into eight subdomains, encompassing motor skills, executive functions (inclusive of ADHD symptoms following DSM-IV criteria), perception, memory, language, tic disorders, learning, social skills and autism, and emotional/behavioural problems (Lindblad et al., 2011).

Kadesjö et al. (2004) articulated the rationale behind the development of a questionnaire, which aimed to serve as a preliminary instrument for clinical assessment, particularly in cases involving ADHD or related conditions. In Denmark, healthcare practices also place significant emphasis on parental reports to gain insights into children's disabilities that impact their daily lives (Illum & Gradel, 2014). The original FTF questionnaire was initially designed as a parental screening tool. However, the revised version, known as 5-15R, accommodates input from teachers, facilitating the collection of information from both home and school environments. This multifaceted approach enables clinicians to access a more comprehensive understanding of children's behaviour, as perceived by multiple stakeholders in various contexts. Prior studies (Farooqi et al., 2013; Linblad et al., 2011) have indicated the value of considering both parental and teacher ratings to attain a comprehensive assessment of children's well-being.

The 5-15R questionnaire serves a versatile role, not limited to neurodevelopmental-neuropsychiatric disorders but extending to other conditions, such as Unilateral Cerebral Palsy (Forsman & Eliasson, 2016). Neurodevelopmental disorders primarily encompass conditions associated with the nervous system and brain function. Children with neurodevelopmental disorders often experience challenges in motor skills, behaviour, language and speech, memory, learning, or other neurological functions (Forsman & Eliasson, 2016). Symptoms and behaviours in these disorders can evolve as children age, although some disabilities may persist throughout life. Consequently, the diagnosis and treatment of neurodevelopmental disorders necessitate a comprehensive approach, combining professional therapies, pharmacological interventions, and home- and school-based programs. Speech-language therapists (SLTs) play a pivotal role in addressing speech and language issues within the spectrum of neurodevelopmental disorders. SLTs typically craft interventions based on thorough assessments across diverse areas and skills, including speech, language, pragmatics, social communication disorders, cognitive-communication disorders, and swallowing disorder) (American Speech-Language-Hearing Association [ASHA], n.d.), as well as the additional information from the observation, and parental reports (Ebert, 2017).

In addition to assessments by qualified professionals, parental perspectives, as gleaned from screening outcomes and reports, contribute significantly to early identification and intervention programs (Ebert, 2017). Parents naturally harbour considerable concerns and expectations regarding their children's well-being, especially concerning health, followed by academic and social performance. Professionals must acknowledge and address these parental concerns in their management strategies. Parental awareness of their children's developmental and behavioural issues can catalyse the early identification process by professionals, thus enabling timely and appropriate intervention or treatment programs (Breiner et al., 2016). The utilization of the 5-15R questionnaire empowers parents to articulate their concerns about their children's well-being to professionals, while simultaneously enabling professionals to gather essential information, aiding in the accurate diagnosis and formulation of tailored management plans for these children.

In the specific context of Malaysia, there exists a notable scarcity of parent-reported questionnaires or scales designed for the purpose of screening developmental and behavioural issues in children and adolescents. Malaysia, is nation renowned for its diverse cultural and linguistic landscape, encompasses a populace composed of various ethnic groups, each possessing distinct cultural heritages and languages such as Malay, Chinese, Indian, and indigenous peoples of Borneo. Malay, the official language of Malaysia, is employed in government affair, educational institutions, and media outlets. Among the few questionnaires that have been translated into Malay language, one noteworthy example is the Strengths and Difficulties Questionnaire (SDQ) developed by Robert Goodman in 1997. The SDQ represents a widely utilised psychological screening tool that aims to evaluate the emotional and behavioural well-being of children and adolescents. However, it is essential to note that the SDQ predominantly centres on the identification of potential emotional and behavioural challenges encountered by children and adolescents.

The selection of the 5-15R questionnaire in this study is underpinned by several compelling reasons. First, it offers a comprehensive evaluation, encompassing a wide array of aspects, transcending the exclusive focus on behaviour and emotion, as observed in instruments like the SDQ. This breadth is essential for a holistic understanding of children and adolescents, assessing not only behaviour and emotion but also their abilities in various domains, including motor skills, executive functions (which includes the evaluation of ADHD symptoms accordance with DSM-IV criteria), perception, memory, language, tic disorders, learning, social skills/autism, and emotional/behavioural problems (Lindblad et al., 2011). Second, the 5-15R questionnaire possesses the unique advantage of being applicable to both parents and teachers, allowing for the acquisition of complementary data pertaining to children's development and behaviours in home and school settings. Prior research studies (Farooqi et al., 2013; Linblad et al., 2011) have advocated for the amalgamation of information gathered from both parental and teacher ratings to obtain a comprehensive perspective on children's well-being. Furthermore, it finds utility within the domain of Speech-Language Therapy, with specific questions related to language and communication development, thus facilitating a comprehensive assessment of children's current performance. Third, the FTF questionnaire, currently known as 5-15R, exhibits sensitivity to sociodemographic variables, including gender, age, area of residence and parental education. This sensitivity positions the FTF questionnaire as an instrumental tool for delineating specific problem areas within the field of child neuropsychiatry (Bohlin & Janols, 2004). These findings were highlighted based on a study by Bohlin and Janols (2004) who conducted comparative analysis between the FTF questionnaire and CBCL with three primary aims; 1) to investigate the congruence of information obtained from these instruments in relation to the association between the problem scores with socio-demographic characteristics; 2) to establish a correlation between scores in certain domains of the FTF questionnaire and the three CBCL main scales (internalizing, externalizing and mixed problems); and 3) to evaluate the superordinate structure of the FTF subdomain scales through factor analysis (Bohlin & Janols, 2004).

As the 5-15R questionnaire is yet to be translated into Malay; a critical cross-cultural adaptation and translation process is imperative. This process is essential to enable the questionnaire's utilization within the Malay-speaking population as a screening tool for the early identification and intervention of

developmental and behavioural issues. The Malay version of the questionnaire holds the potential for widespread use not only within Malaysia but also in various parts of the Asia-Pacific region where Malay is employed in daily communication, including countries such as Brunei, Indonesia, and Singapore. Hence, as an initial exploratory study, the objective of this research encompasses two primary aims: 1) to undertake a cross-cultural translation and adaptation of the Five-To-Fifteen Revised (5-15R) questionnaire into the Malay language, resulting in the creation of the Malay-5-15R, and 2) to conduct a comprehensive examination of the content validity of the Malay-5-15R.

METHODOLOGY

Ethical considerations

Ethical clearance was granted by the International Islamic University Malaysia (IIUM) Research Ethics Committee (IREC) before the study was conducted. Every participant provided informed consent, receiving comprehensive information about the research process and the option to withdraw from the study at any point. They were guaranteed the confidentiality of their personal data, with exclusive access limited to the researcher.

Study Design

Adapting and translating a questionnaire for use in a different cultural or linguistic context is a critical step in ensuring the validity and reliability of the research instrument. Therefore, a cross-sectional study design was selected toto assess the characteristics, opinions, or behaviours of a specific population at a single point in time. This approach can help to determine the relevance and appropriateness levels of the questionnaire for the target audience.

Materials

In this study, the Five-To-Fifteen Revised (5-15R) questionnaire, developed by Kadesjö and colleagues in 2017, was utilised. The questionnaire comprises eight primary domains, further subcategorised into 22 subdomains. These subdomains encompass a wide range of aspects, including gross and fine motor skills, attention, hyperactivity-impulsivity, hypoactivity, planning or organizing, perception of space, time, and body, visual perception, speech, communication skills, memory, comprehension, reading or writing, mathematics, general learning, coping skills during learning, social skills, obsessive-compulsive behaviour and internalizing and externalizing behaviour (Lambek & Trillingsgaard, 2015). For the questionnaire responses, a scoring system featuring three levels is employed: 0 (indicating 'does not apply'), 1 (reflecting 'applies sometimes or to some extent'), and 2 (signifying 'definitely applies')

Methods

In order to enable the utilization of the 5-15R questionnaire within the Malay-speaking population, a cross-cultural translation and adaptation process was undertaken. This process adhered to the recommended guidelines outlined by Beaton et al. (2002) and World Health Organization (WHO) (2017). The translation and adaptation process consisted of several distinct stages: 1) forward translation; 2) synthesizing forward translation; 3) backward translation; 4) synthesizing backward translation; 5) expert committee review; 6) finalization.

Cross-Cultural Adaptation and Translation Procedures

The objective underlying the translation, adaptation, and validation of the 5-15R questionnaire was to produce a Malay version of the 5-15R, denoted as Malay-5-15R. This Malay version is intended to serve as an apt assessment and screening tool for utilization by the Malay-speaking population, particularly for parents, teachers, and related professionals.

Stage 1: Forward Translation

The forward translation process was carried out by two independent bilinguals with the goal of rendering the questionnaire into the target language, which is Malay, following established guidelines (Beaton et al., 2002; Hambleton, 2005). The 5-15R questionnaire was independently translated from English to the Malay language by two speech-language therapists possessing sound knowledge of developmental disorders in children. The first translator (T1) held an academic position in the field of speech-language pathology at IIUM Kuantan Campus, while the second translator (T2) worked as a clinician, specifically speech-language therapist, at IIUM Hearing and Speech Clinic, IIUM Kuantan Campus. Both translators were native speakers of Malay language and were bilingual in both Malay and English. The translators were instructed to focus on conceptual rather than literal translations and to employ natural and easily understandable language for the general population, adhering to guidelines set forth by the World Health Organization (2017). Given that both translators possessed similar undergraduate qualifications, the translation of the 5-15R questionnaire was conducted in a manner that preserved the conceptual integrity and content of the questionnaire while benefiting from distinct perspectives on the same contextual framework. This process yielded two forward-translated versions of the instrument, denoted as 5-15R (BM1) and 5-15R (BM2), derived from the translations by T1 and T2, respectively.

Stage 2: Synthesis of the Forward Translation

These two translated instruments, namely 5-15R (BM1) and 5-15R (BM2), were subsequently synthesized, summarized and compiled into a harmonized version of the forward-translated instrument (denoted as BM-H). The consolidation was achieved through consensus reached between both translators and the authors.

Stage 3: Backward Translation

The backward translation procedure involved two distinct translators tasked with independently translating the BM-H version back into English. This step constitutes a vital component of the validation process, aimed at ensuring that the translated version maintains fidelity to the original content and concepts (Beaton et al., 2002; Borsa et al., 2012). Both translators were proficient bilingual, being native speakers of Malay and English, who possessed no prior exposure to the 5-15R questionnaire. Notably, their academic backgrounds did not pertain to medicine or health sciences, a deliberate measure taken to mitigate potential information bias and the emergence of unforeseen interpretations of the questionnaire items (Beaton et al., 2002). For the backward translation phase, the participating translators were an English teacher at a secondary school (T3) and an English lecturer at the Centre of Foundation Study (CFS), IIUM Gambang (T4). Both translators had accrued over five years of teaching experience. It is pertinent to emphasize that during the backward translation, the translators were required to render the BM-H version back into English autonomously, refraining from any reference to the original version of the 5-15R questionnaire. This meticulous process yielded two distinct versions of the translated instrument, denominated as 5-15R (E1) and 5-15R (E2).

Stage 4: Synthesized of the Backward Translation

Both backward-translated versions (5-15R (E1) and 5-15R (E2)) were subsequently synthesized and revised by the translators in collaboration with the research team. The synthesis aimed to scrutinize any significant disparities in comparison to the original version of the 5-15R questionnaire, encompassing wording, concepts, and contextual aspects.

Stage 5: Expert Committee Review

The harmonized Malay-5-15R version (BM-H) underwent a rigorous review process led by an expert committee composed of five members with diverse academic backgrounds, encompassing expertise in three distinct areas: speech-language pathology (n=3), audiology (n=1), and psychiatry (n=1). This comprehensive approach was in accordance with the recommendation by Guillemin et al. (1993), which stipulated that an expert committee should comprise individuals proficient in the disease under investigation and the conceptual framework guiding the exploration. The review undertaken by the expert

committee embraced three primary facets: (1) an overarching evaluation of the questionnaire, (2) a qualitative assessment of content validity, and (3) a quantitative content validity analysis. Expert committee members were tasked with assessing the translated versions of the questionnaire (BM-H and E-H) alongside the original 5-15R questionnaire. This evaluation aimed to identify any discrepancies and verify the consistency of the translated versions in comparison to the original questionnaire. Next, the content validation encompassed qualitative considerations, involving recommendations related to wording, grammar, sentence structure. Additionally, a quantitative dimension was introduced, involving the computation of the Content Validity Index (CVI), comprising the Item-level CVI (I-CVI) and the overall scale-level CVI (S-CVI) (Waltz & Bausell, 1981). For I-CVI, the expert committee members were required to rate each item for intelligibility and relevance to the underlying concept using a 4-point Likert scale, ranging from not relevant (1 point) to highly relevant (4 points) (Davis, 1992). The I-CVI was subsequently computed using the formula for expert agreement, by summing the scores of 3 or 4 points provided by the expert committee members for each item and dividing by the number of experts. Regarding S-CVI, two calculation methods were employed: S-CVI/UA, computed as the items rated with scores of 3 or 4 by the expert committee divided by the total number of items (181), and S-CVI/Ave, which entailed summing the I-CVI scores and dividing by the total number of items (181).

Stage 6: Finalization

Following the completion of the content validation process and subsequent analysis, a conclusive deliberation was conducted to formalize the BM-H2 version as the preliminary Malay rendition of the 5-15R questionnaire, hereby denominated as Malay-5-15R.

Statistical Analysis

All data in this study were underwent a comprehensive descriptive analysis, encompassing both quantitative and qualitative approaches.

RESULTS

The initial version of the Malay-5-15R questionnaire was established subsequent to the conclusion of the cross-cultural translation and adaptation processes. Throughout the synthesis of the forward translation, a minor adjustment was introduced to three out of the 181 items, following discussion between both translators and the authors. These revisions were made to enhance the questionnaire's alignment with the Malaysian population by providing more pertinent examples and terminology. Detailed modifications to the items are documented in Table 1. The harmonized version, a culmination of these two translated versions (BM-H), was achieved following extensive discussion between the translators and the researchers. This phase focused on identifying any unsuitable translation choices and refining them to ensure accuracy and suitability. In the analysis of the synthesis of the backward translation, no significant disparities were identified between the translated version and the original version. Consequently, it can be inferred that the translated version maintains the same conceptual framework and contextual integrity as the original version.

In the context of the expert committee review, translated versions of the questionnaire (BM-H and E-H) were found to be generally satisfactory and closely aligned with the original version. Minor amendments were made exclusively to the BM-H version, primarily focusing on sentence structure, terminology selection, and the inclusion of culturally appropriate example that resonate with the Malaysian context. Qualitative content validity analysis identified a series of enhancements aimed at refining the structure and content of the questionnaire. These revisions encompassed the following aspects: 1) the addition of further explanations and examples; 2) refinement of phrases or sentences; 3) improvement in grammatical accuracy; and 4) alterations in word selections. Among the 181 items, a total of 33 were subject to these minor adjustments, following extensive deliberations among the expert committee members. Selected examples illustrating the qualitative content validity analysis of specific affected items in BM-H

(prior to its finalization into BM-H2) are detailed in Table 2. These enhancements were undertaken with the objective of achieving a high level of equivalency between the original and translated versions of the questionnaire, ultimately culminating in the creation of the second version of the Harmonized Malay-5-15R (BM-H2).

Table 1: Detailed Modifications to the Items of BM-H

Item No.	Original Version	BM-H	Remarks on Changes Made
Item 66	Difficulty remembering events that occurred some time ago, such as what happened on a trip, what **Christmas** presents he/she got etc	Kesukaran mengingat peristiwa yang berlaku suatu ketika dahulu, seperti apa yang berlaku ketika melancong, apa hadiah **hari jadi** yang dia dapat dan lain-lain	**Used different examples as the main celebration for the Malaysian population is not Christmas.**
Item 79	Difficulty finding words or explaining to other people, says: **"the, the, the ..."**	Kesukaran mencari perkataan atau menjelaskan kepada orang lain, berkata: **"itu, itu, itu… atau emm, emm, emm…"**	**Added examples that are usually used in real life.**
Item 90	Difficulty telling about experiences or situations so that the listener understands (e.g., what happened during the day or during the **summer vacation**)	Kesukaran menceritakan pengalaman atau situasi agar difahami oleh pendengar (contoh, apa yang berlaku pada siang hari atau **semasa cuti sekolah**)	**Used different examples as there is no summer vacation in Malaysia.**

Table 2: The Examples of Qualitative Content Validity Index Analysis of Several Items in BM-H

Item No.	Original Version	BM-H	BM-H2	Remarks on Changes Made
Item 12	Difficulty using knife and fork	Kesukaran menggunakan **pisau dan garfu**	Kesukaran menggunakan **pisau, sudu dan garfu**	**Added example**
Item 13	Difficulty buttoning or tying shoelaces	Kesukaran **membutang** atau mengikat tali kasut	Kesukaran **mengenakan butang** atau mengikat tali kasut	**Refined the phrases**
Item 27	Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (such as homework)	Sering mengelak, tidak suka, atau enggan melibatkan diri dalam tugasan yang memerlukan **usaha mental** yang berterusan (seperti kerja rumah)	Sering mengelak, tidak suka, atau enggan melibatkan diri dalam tugasan yang memerlukan **usaha mental (tumpuan pemikiran)** yang berterusan (seperti kerja rumah)	**Added further explanation of the phrases**
Item 40	Difficulty understanding consequences of own actions (e.g., climbs in dangerous places, careless in traffic)	Kesukaran memahami akibat daripada tindakan sendiri (contoh, memanjat di tempat berbahaya, **cuai di trafik**)	Kesukaran memahami akibat daripada tindakan sendiri (contoh, memanjat di tempat berbahaya, **tidak mematuhi aturan lalu lintas**)	**Refined phrases**

The quantitative content validity analysis employed a two-tiered approach, focusing on two distinct forms of Content Validity Index (CVI): Item-level CVI (I-CVI) and overall scale-level CVI (S-CVI) (Waltz & Bausell, 1981). In the present study, the I-CVI was computed for all 181 items, and the findings revealed that the I-CVI for most of the items (98.34%) was 0.80 or higher. Notably, except for items 4, 7 and 12, which exhibited an I-CVI of 0.60, the remaining items attained an I-CVI score of 0.80 or greater. The averages I-CVI (I-CVI/Ave) for the entire set of items was computed at 0.97, indicating a high degree of appropriateness for most items in the BM-H2 version. Moreover, the S-CVI/UA for the BM-H2 was calculated as 0.84, while S-CVI/Ave achieved a score of was 0.97. These values are indicative of the BM-H2 version's attainment of satisfactory scale-level content validity, as defined by the criteria established by Polit and Beck (2006). A comprehensive breakdown of the I-CVI and S-CVI calculations is presented in Table 3.

Table 3: The summary of quantitative content analysis of BM-H2

Items No.	Panel 1	Panel 2	Panel 3	Panel 4	Panel 5	Panels in Agreement	I-CVI
1–3, 5-6, 9-11, 15-20, 22-24, 28-39, 41-46, 48-72, 74-79, 81-85, 87-104, 106-109, 111-123, 125-127, 129-130, 133-134, 136, 138-143, 146-168, 170-171, 173, 176-181	√	√	√	√	√	5	1.00
80	√	**X**	√	√	√	4	0.80
8, 13, 21, 25, 40, 73	√	√	**X**	√	√	4	0.80
14	√	√	√	√	**X**	4	0.08
26, 27, 47, 86, 105, 110, 124, 128, 131, 132, 135, 137, 144, 145, 169, 172, 174, 175	√	√	√	**X**	√	4	0.08
4, 7	√	√	**X**	**X**	√	3	0.60
12	√	**X**	√	**X**	√	3	0.06
						Average I-CVI	0.97
Proportion relevant	1.00	0.99	0.96	0.89	1.00		

*Note: √ = rating of 3 or 4; **X** = rating of 1 or 2; BM-H2 = Second Version of the Harmonized Translation; I-CVI = Item Level-Content Validity Index*

Stage 6: Finalization

Following the completion of the content validation process and its accompanying analysis, a conclusive discussion was conducted with the objective of formalizing the BM-H2 version as the foundational Malay rendition of the 5-15R questionnaire, hereby referred to as Malay-5-15R. The domains and components within Malay-5-15R remained unaltered; however, select items underwent modifications to ensure alignment with the cultural and linguistic attributes of the Malaysian population.

DISCUSSION

The study was conceived with the intent to facilitate the cross-cultural translation and adaptation of the 5-15R questionnaire, originally in English, into the Malay language, thus rendering it accessible to the Malaysian population, particularly Malay-speaking population. The primary objective was to undertake a cross-cultural adaptation process to verify the congruence of the translated questionnaire's contents with the original version in terms of conceptual alignment. Additionally, the study sought to assess the appropriateness of the translated questionnaire for utilization by the Malaysian population, particularly parents and teachers, in terms of contextual relevance, conceptual alignment, and semantic equivalence of the questions.

Based on the findings, it can be generally inferred that the Malay-5-15R questionnaire demonstrated a notable degree of cultural acceptability. In essence, all 181 items from the original version were retained with only minor adjustments. These modifications were primarily aimed at enhancing sentence structures and ensuring the clarity and comprehensibility of the questionnaire for the Malaysian population. The refinement efforts encompassed fine-tuning phrasing, introducing illustrative examples and explanations, and rectifying grammatical aspects. Given the distinct linguistic and cultural contexts of the original and translated versions, these minor changes were essential to maintain conceptual and content equivalence, in alignment with the principles outlined by Guillemin et al. (1993). Notably, certain examples within the items underwent slight alterations to better align with the Malaysian population. For example, in Item 66, the reference to "Christmas celebration" was substituted with "birthday celebration", reflecting the more universal and culturally relevant nature of the latter within the Malaysian context, as opposed to the former. Similarly, Item 85, saw the transformation of English terms into Malay, such as "screwdriver" being changed to "*infrastruktur",* while still retaining the original item's conceptual and contextual integrity (i.e., complex word), thereby rendering it more pertinent for the Malaysian population, instead of opting for a literal translation, such as "*pemutar skru*".

The content validity analysis was conducted to measure the inclusiveness and representativeness of the content within the Malay-5-15R questionnaire. The findings from this analysis revealed that most items in the Malay-5-15R questionnaire exhibited high content validity, with the I-CVI values for each item and overall items ranging between 0.80 and 1. These values exceeded the recommended threshold of 0.79, as indicated by Abdollahpour et al. (2010), underscoring the translated version's strong alignment with the original context. However, three items, specifically Items 4, 7 and 12, yielded lower I-CVI values, each at 0.60. This discrepancy among the experts primarily revolved around sentence structure refinement, such as changing the word selection (e.g., Item 4: "*permainan sukan*" to "*sukan*") and incorporating culturally relevant examples (e.g., Item 12: "*Kesukaran menggunakan pisau dan garfu*" to "*Kesukaran menggunakan pisau, sudu dan garfu*"). Consequently, these items were amended by modifying their sentence structures in accordance with the recommendations put forth by the expert committee. The goal was to achieve a more refined sentence structure for these items, aligning them more suitably with the Malaysian population's linguistic nuances. Regarding the scale-level content validity for the BM-H2 version, the S-CVI/UA was calculated at 0.84, while the S-CVI/Ave yielded a score of 0.97. These values surpassed the thresholds proposed by Shi, Mo, and Sun (2012), where excellent content validity is indicated by an I-CVI of 0.78 or higher and S-CVI/UA and S-CVI/Ave of 0.8 and 0.9 or higher. Consequently, the content validity results affirm that the Malay-5-15R questionnaire exhibited strong comprehensiveness and was a representative instrument e for the study population.

The comparability of the CVI results for the Malay-5-15R version with prior studies is hindered by the absence of previously published studies that have conducted comprehensive CVI analyses on the original version of the FTF questionnaire and its revised counterpart, the 5-15R questionnaire. Notwithstanding, Kadesjo et al. (2004) have noted that the items in the FTF questionnaire were highly relevant and effectively covered each sub-domain. Several studies, including those by Korkman et al. (2004) and Bohlin & Janols (2004), have established the FTF questionnaire's commendable validity and reliability.

However, these studies do not offer explicit details regarding content validity or CVI. Consequently, the present study's findings concerning CVI represent pioneering efforts in quantitatively analysing content validity, potentially serving as a foundational reference for forthcoming research endeavours.

CONCLUSION

This study has ascertained that the Malay-5-15R questionnaire possesses commendable content validity, an essential psychometric property that establishes its readiness for application in the intended population. As a result, the Malay-5-15R questionnaire emerges as a valuable instrument for screening and assessing children aged 5 to 17 who confront neuropsychological challenges. The parental reports integrated into this questionnaire offer substantive insights into their children's behaviours and various dimensions. This, in turn, equips professionals with the necessary information to deliver comprehensive care for the managing these children within a holistic framework. The information gleaned from this questionnaire has the potential to enhance the comprehensive management of cases, including the identification of the appropriate professionals to engage in the child's care and the strategies these professionals can employ to enhance the child's quality of life. Furthermore, serving as a screening tool for parents, this questionnaire can also foster increased parental awareness and understanding of their children's behaviours, strengths, and areas requiring intervention. In doing so, it contributes to the early identification and intervention processes, thereby further supporting the child's well-being.

LIMITATIONS OF THE STUDY AND FUTURE RECOMMENDATIONS

This study entails several notable limitations that warrant acknowledgment. Firstly, it is essential to underscore that, at this stage, the Malay-5-15R questionnaire is not yet fully prepared for application within the target population, given that the adaptation process has been completed only up to the stage of content validation analysis. As such, future investigations should prioritize the comprehensive evaluation of the questionnaire's psychometric properties, with a particular emphasis on aspects such as reliability, test re-test reliability, construct validity, and divergent and convergent validity. This rigorous evaluation is vital to ascertain that the Malay-5-15R questionnaire is both reliable and valid for use within the designated population. Furthermore, it is worth considering that the current iteration of the questionnaire, while encompassing a multitude of items, retains its comprehensive approach to measuring various critical domains. Subsequent research endeavours may contemplate the possibility of revising the questionnaire to produce a condensed version that maintains its domain coverage and comprehensiveness while reducing the overall number of items. Such an adaptation aims to streamline the questionnaire, making it more time-efficient for parents to complete while still extracting the necessary information.

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KNOWLEDGE, ATTITUDE AND PRACTICES OF MALAY TRADITIONAL MEDICINE PRACTITIONERS TOWARDS COVID-19 PANDEMIC IN MALAYSIA

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ABSTRACT

Introduction: Restricted movement and preventive actions such as vaccination had been introduced in Malaysia to break the chain of transmission of the new coronavirus, COVID-19. These strategies, however, affected many sections of the society including Malay medicine practitioners. Malay medicine practitioners are important as they could also influence the response of the society towards health promotion by the mainstream modern medicine authority. This, however, depends on their own level of knowledge, attitude and practices concerning COVID-19 pandemic. **Methods**: A cross-sectional study using convenience sampling by online questionnaire was conducted among Malay traditional medicine practitioners in Malaysia. **Results**: This study showed that the level of knowledge was high (n=90, 89.1%) while the level of attitude was moderate (n= 66, 65.3%) and practice was moderate (n=55, 54.5%). Age and marital status were significantly associated with knowledge scores with the *p*-value of 0.001 and 0.010 respectively. None of the socio-demographic characteristic appeared to have an association with attitude and practice. Strong and significant correlation were found between knowledge and attitude (r = 0.230, p-value = 0.020), and attitude with practice (r = 0.395, p-value = 0.001) of the Malay traditional medicine practitioners concerning COVID-19. No correlation was found between knowledge and practice as p>0.05. **Conclusion**: The results would be useful for formulating policies that are suitable to this important and influential group of healthcare providers to reduce resistance and increase compliance to strategies concerning COVID-19 in society.

KEYWORDS: COVID-19, Malay traditional medicine, knowledge, attitude, practice.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) was defined as a respiratory infection caused by a novel coronavirus called Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). It first emerged in December 2019, in Wuhan city, Hubei Province, China (Wu et al., 2020). SARS-CoV-2, or COVID-19, belongs to the larger family of ribonucleic acid (RNA) viruses. This family of viruses lead to infections ranging from the common cold, to more serious diseases, such as Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV) (Zong et al., 2020). The main symptoms of COVID-19 had been identified as fever, cough, fatigue, myalgia, and shortness of breath. COVID-19 virus could be transmitted via respiratory droplet produced by infected person though coughing, talking and sneezing.

In Malaysia, the first case of COVID-19 was reported on 25 January 2020 (Chang et al, 2021). The number of cases increased until it passed the 500 mark on 16 March 2020. To curb its transmission, Malaysian authority had imposed Movement Control Order (MCO) on 18 March 2020. There are guidelines release from World Health Organization (WHO) in order to break the chain of transmission which includes protective measure by wearing a face mask, washing hands with soap or alcohol-based hand rubs and avoiding crowded places.

The traditional medicine practitioners in Malaysia were affected during this pandemic because they were only allowed to provide their service by following the Standard Operating Procedure (SOP) (Yusof, 2020). Many of their services such as the treatment of cupping, acupuncture, traditional massage and pre- and post-natal services, involved close contact between the practitioners and their patients which was prohibited during the outbreak (Chie, 2020). This severely limit their operations and made it difficult for them to treat patients. According to the Standard Operating Procedure (SOP), the patient also needs to set up an appointment before the treatment and this limit the number of patients that could be received per day (Yusuf, 2020). Some of the traditional medicine centres were forced to close even though they have the permission to open their premises as the cost of operation is higher than the revenue.

Traditional medicine practitioners are important people in society as they provide important medical service to the people, covering and providing more personalised attention that modern medical system may not be able to provide. The support that they provide also goes beyond medical support and include moral as well as spiritual engagements. Due to the personalised treatment and the development of trust in their service, they could influence patients sometimes more effectively than modern medical practitioners. The current study is performed to assess the knowledge, attitude and practice of traditional Malay medicine practitioners with regards to the pandemic of COVID-19. Most studies on COVID-19 in relation to traditional medicines were performed to assess the perception of user or patients towards the use of traditional medicine in treating COVID-19 (Alyami et al., 2020; Nguyen et al., 2020; Alotiby, 2021; Çetin, 2021; Leen et al., 2021) but none of these were conducted in Malaysia.

Nevertheless, there have been several studies on knowledge, attitude and practice of Malaysian society towards COVID-19. Some of these studies targets specific segments such as students (Mohd Zubir et al., 2021; Sazali et al., 2021; Ganaprakasam et al, 2021; Mohamad Aidid et al., 2022; Tan et al., 2022) and healthcare workers (Anuar et al., 2022) and food deliverers (Mohamad Saleh & Rahip, 2022), whereas others studied samples of the general Malaysia population (Azlan et al., 2020; Puwaneswarry et al., 2020; Abu Hasan et al., 2022; Chang et al., 2021; Syed Elias et al., 2022; Chai et al., 2022; Elias et al., 2021). The results are not easy to delineate since the studies were performed at different timepoints during the pandemic, on different sampling populations with different occupation and level of education, and conducted using different method of sampling. Hence, the outcome is varied with some studies showed that many Malaysians have high level of knowledge on COVID-19 (Azlan et al., 2020; Abu Hasan et al., 2022; Anuar et al., 2022; Mohamad Aidid et al., 2022; Tan et al., 2022; Syed Elias et al., 2022), where as other studies reported differently (Sazali et al., 2021). Some studies also reported that even when knowledge score is high, attitude and practice scores towards COVID-19 may be low (Sazali et al., 2021; Chai et al., 2022). Factors that may influence the

scores of knowledge, attitude and practice could be age group (e.g. older people scored higher than younger people) (Syed Elias et al., 2022), as well as monthly income, employment status, gender and race (Elias et al., 2021). At least one study, however, showed that some of these factors played no part in influencing the knowledge, attitude and practice of their sampling population (Tan et al., 2022). Worldwide, there have been very few studies conducted on the traditional medicine practitioners themselves as the main subjects in relation to COVID-19. Two published studies involved one study in Ethiopia (Asmelash et al., 2020) and another one in Bhutan (Gyeltshen et al., 2021) and none yet on traditional medicine practitioners in Malaysia in relation to COVID-19 (Ng, 2020).

MATERIALS AND METHODS

The research was designed as a cross-sectional study using convenience sampling and was conducted online from April to July 2021. The assistance of several associations of Malay Traditional Medicine registered under the Ministry of Health was officially sought after. This include *Gabungan Persatuan Pengamal Perubatan Tradisional Melayu Malaysia (GAPERA), MAMACARE (Postnatal Service), Persatuan Pengamal Urut Teraputik dan Penjagaan Melayu Malaysia* (PUTRAM), Heritage Association of Malay Massage (HAMA), and *Dar al-Syifa*. Ethical approval was submitted to and retrieved from the International Islamic University Malaysia Research Ethics Committee (IREC) IIUM/504/14/11/2/IREC-KAHS (DBMS). The study population initially included other ethnic groups prevalent in Malaysia such as the Indian and Chinese, however the final results were restricted to ethnic Malay traditional medicine practitioners as response from other ethnic groups was very low. Only those practitioners who are actively practicing with at least one year of experience were included.

The questionnaire was distributed to Malay traditional medicine practitioners either through the help of the associations' representative, or through contacts made via social media advertisements, or through direct contact. The questionnaire was divided into four parts namely Part A, B, C and D. Part A was on sociodemographic information of participants such as age, gender, religion, race, education, marital status, and income. Information on the involvement of the practitioners in their respective association, type of services being offered and working experiences, and source of their information on COVID-19 were also asked. Part B was focused on knowledge of COVID-19. It consists of 27 multiple choice questions concerning the clinical symptoms of COVID-19, route of transmission, preventive steps of COVID-19 transmission, association between vaccination, and use of traditional medicine related to COVID-19. Part C and D were regarding the attitude and practice of the traditional Malay medicine practitioners in relation to COVID-19. Likert scale was used in these two parts. There were 18 simple statements with choice of answer such as "strongly disagree", "disagree", "neutral", "agree" and "strongly agree". Besides, 19 easy statements were related to practice on impact of COVID-19 in the last part of the questionnaire consisting of various choice of answer: "never", "seldom", "sometimes", "often" and "always". The options scored marks ranked from 1 to 5 corresponding to "strongly disagree" for part C and "never" for part D, to "strongly agree" for part C and "always" for part D. The highest marks from each part indicated the higher level of knowledge, attitude and practice concerning COVID-19 outbreak among the respondents.

Statistical Analysis

The independent variables in this study were the socio-demographic data whereas the dependent variables were knowledge, attitude and practice towards COVID 19. The total score of responses was calculated and then categorised into low, moderate and high categories. Descriptive frequency table was used to analyse the sociodemographic characteristics of respondents in this study while Kruskal Wallis test was used to investigate the relationship between socio-demographic and knowledge, attitude and practice. The relationship between knowledge, attitude and practice was then analysed using the correlation test. As the distribution is non-parametric, Spearman correlation test was used in this study. The statistical significance was set at $p < 0.05$ for all tests mentioned above. All data was analysed using Statistical Package Software for Social Science (SPSS) version (IBM SPSS 20).

RESULTS AND DISCUSSIONS

A total of 115 respondents answered the questionnaires but 14 of them were excluded due to reasons such as not enough evidence of practicing traditional medicine. Hence, only 101 people were included during the final analysis. There were 14 socio-demographic variables including gender, religion, age, race, education, marital status, working sector, monthly income, working experiences, types of service, source of information, association, location of service and courses. The summary of socio-demographic characteristics among respondents in this study are illustrated in Table 1 and Table 2 below.

As shown in Table 1, most respondents were female traditional practitioners (n=72 or 71.3% of respondents) while male traditional practitioners numbers at 29 (28.7%). The respondents belong to four age-groups: 20-29 years old, 30-39 years old, 40-49 years old and 50 years old and above. The number of traditional practitioners for each category of age were 14 (13.9%), 29 (28.7%), 41 (40.6%) and 17 (16.8%) respectively. Nearly half of the respondents were from the age group of 40-49 years old (n=101, 40.6%). The respondents were all Muslim and Malay (n=101, 100%). Their educational level was categorised according to the highest qualification completed i.e. primary school, secondary school, Sijil Pelajaran Malaysia (Malaysian Education Certificate), Diploma, Degree, Master, and PhD. The frequency of respondents for each category of educational level was 2 (2.0%), 14 (13.9%), 32 (31.7%), 26 (25.7%), 19 (18.8%), 4 (4.0%), 2 (2.0%) and 2 (2.0%) respectively. Hence, most of respondents were SPM and diploma level-graduates with total number of 58 (57.4%). Most respondents, i.e. 78 (77.2%) of them, are married compared to the single and divorced/widowed categories at 11 (10.9%) and 12 (11.9%) respectively. It was also found that most respondents were self-employed (n=72; 71.3%) and most belongs to the B40 status (n=74; 73.3%). More than half of the respondents had more than five years of working experience (n=66, 65.3%) followed by less than 2 years (n=18; 17.8%) and between 2 to 5 years (n=17; 16. 8%).

Table 1 General sociodemographic profile of respondents

Characteristics		Frequency	Percentage
Gender	Male	29	28.7
	Female	72	71.3
Religion	Islam	101	100.0
Age	20-29 years old	14	13.9
	30-39 years old	29	28.7
	40-49 years old	41	40.6
	50 years and above	17	16.8
Education	Primary	2	2.0
	Secondary	14	13.9
	SPM	32	31.7
	Diploma	26	25.7
	Degree	19	18.8
	Master	4	4.0
	PHD	2	2.0
	Others	2	2.0

Marital status	Single	11	10.9
	Married	78	77.2
	Divorced/ Widow	12	11.9
Working sector	Government sector	12	11.9
	Private sector	17	16.8
	Self employed	72	71.3
Income	RM 0- RM 4849	74	73.3
	RM4850- RM 10959	18	17.8
	RM 10959 and above	9	8.9
Working experience	Less than 2 years	18	17.8
	2 to 5 years	17	16.8
	More than 5 years	66	65.3

The next part is regarding the traditional practitioners' services. There were 24 types of services offered by the traditional Malay medicine practitioners. Many respondents claimed expertise in more than one modality of treatments. However, the most often offered type of service was traditional massage at n=25, i.e. equivalent to 24.8%, followed by '*perubatan Islam*' (Islamic medicine) at the frequency of n=22, i.e. equivalent to 21.8%. "*Perbidanan & urutan tradisional*" or postnatal care and massage was also one type of service with quite a large number of respondents as the frequency was 13 (12%).

Table 2 illustrates the source of information regarding COVID-19 with social media-only emerged as the main source for most respondents (n=27; 26.7%) followed by social media + television + official website category (n=22; 21.8%). The social media + television + newspaper + website category also scored quite highly at n=20 corresponding to 19.8% of the respondents.

Table 2 Source of information regarding COVID-19 among Malay traditional medicine practitioners.

Source of information	**Number**	**Percentage**
Social media	**27**	**26.7**
Television	2	2.0
Official website	5	5.0
Social media, television, newspaper and official website	20	19.8
Social media, television, and official website	22	21.8
Social media, and television	9	8.9
Social media, and official website	10	9.9
Social media, official website and articles	1	1.0
Social media, websites and television	1	1.0
Social media, television and newspaper	1	1.0
Television and websites	1	1.0
Television, websites and newspaper	1	1.0

Regarding the involvement in association, 44% of the respondents did not involve in any association while the other 54% of respondents were involved in several different types of association in Malaysia (Figure 1). Location of service of traditional practitioners was also investigated in this study. Nearly half of traditional practitioners offered their service at both registered premise and home service (n=45) followed by home service only (n=36) and registered premises only (n=20) (Figure 9). Malay traditional medicine is the highest form practiced by Malay traditional medicine practitioners (80.2%), followed by '*perubatan Islam*' or Islamic medicine at 15.84%, and others at 0.99%.

Table 3 shows the data on knowledge regarding COVID-19. The questions consist of several elements including definition, main clinical symptoms, cause, risk factor, prevention, vaccination and SOPs on the COVID-19. The first question was on the definition of COVID-19. Majority of respondents managed to answer this question (n= 99; 98%). The second question was about clinical symptoms of COVID-19. Most of participants managed to answer accurately on the main clinical symptoms of COVID-19 which were fever (95%), fatigue (77.2%) and coughing (69.3%). However, 2% of the participants chose the "not sure" answer. Regarding the high mortality rate among chronic patients, most of the participants were able to answer correctly (n=98; 97%). For the two questions regarding the route of transmission of COVID-19, 34.7 % of respondents were able to answer correctly, while a significant number i.e. 35.6% respondents answered "not sure." Next, regarding the five different routes of transmission of COVID-19, the respondents were able to answer correctly for most of the options, except for the transmission via bodily fluid which was chose by most respondents. Next, there were six questions (i.e. questions 8-13) regarding the prevention of transmission of COVID-19. Majority of the respondents were able to answer with correct answer at the frequency of 98 (97%), 98 (97%), 88 (87.1%), 100 (99%), 101 (100%), 99 (98%), 97 (96%) and 100 (99%) respectively for each question. More than half of respondents were able to answer correctly regarding the vaccination of COVID-19. Lastly, almost all of the respondents (97%) knew the SOPs during COVID-19 pandemic.



Figure 1 Involvement in association among the respondents.

Table 3 Knowledge of respondents regarding COVID-19 (n= 101).

No	Statement	Yes (Freq %)	No (Freq %)	Not sure (Freq %)
1	Do you know what is COVID-19 pandemic?	**99 (98.0)**	0 (0)	2 (2.0)
2	The main clinical symptoms of COVID-19 are :			

	i. Fever	**96 (95.0)**	5 (5.0)	0 (0)
	ii. Fatigue	**78 (77.2)**	13 (12.9)	10 (9.9)
	iii. Coughing	**70 (69.3)**	17 (16.8)	14 (13.9)
	iv. Cold	93 (92.1)	**6 (5.9)**	2 (2.0)
4	COVID-19 can infect:			
	i. Baby	**97 (96.0)**	3 (3.0)	1 (1.0)
	ii. Elderly	**100 (99.0)**	1 (1.0)	0 (0)
	iii. Pregnant woman	**99 (98.0)**	2 (2.0)	0 (0)
5	Patient with chronic disease has high rate of mortality	**98 (97.0)**	2 (2.0)	1 (1.0)
6	Eating wild animals would result in the infection by the COVID-19 virus	30 (29.7)	**35 (34.7)**	36 (35.6)
7	Route of transmission of COVID-19 are:			
	i. Close contact	**93 (92.1)**	5 (5.0)	3 (3.0)
	ii. Sneezing	**100 (99.0)**	0 (0)	1 (1.0)
	iii. Coughing	**99 (98.0)**	0 (0)	2 (2.0)
	iv. Body's fluid	74 (73.3)	**12 (11.9)**	15 (14.9)
	v. Air borne	**85 (84.2)**	5 (5.0)	11 (10.9)
8	Prevention transmission of COVID-19 are			
	i. Face mask	**98 (97.0)**	3 (3.0)	0 (0)
	ii. Face shield	**98 (97.0)**	2 (2.0)	1 (1.0)
	iii. Glove	**88 (87.1)**	9 (8.9)	4 (4.0)
9	To prevent the infection by COVID-19, individuals should avoid going to crowded places.	**100 (99.0)**	1 (1.0)	0 (0)
10	Isolation of people who are infected with the COVID-19 virus are effective ways to reduce the spread of the virus.	**101 (100.0)**	0 (0)	0 (0)
11	Treatment of people who are infected with the COVID-19 virus are effective ways to reduce the spread of the virus	**99 (98.0)**	1 (1.0)	1 (1.0)
12	People who have contact with someone infected with the COVID-19 virus should be immediately isolated for 14 days in a proper place.	**97 (96.0)**	3 (3.0)	1 (1.0)
13	People with symptoms need to undergo swab test to detect COVID-19 virus	**100 (99.0)**	1 (1.0)	0 (0)
14	The is no cure treatment for	**54 (53.5)**	21 (20.8)	26 (25.7)

	COVID-19 currently			
15	Vaccine is the best preventative of COVID-19	**86 (85.1)**	7 (6.9)	8 (7.9)
16	Traditional complementary alternative medicine may help to treat symptoms of COVID-19	**37 (36.6)**	29 (28.7)	35 (34.7)
17	I know the Standard Operating Procedure (SOP) to open my service during COVID-19 pandemic.	**97 (96.0)**	2 (2.0)	2 (2.0)

Table 4 Attitude of respondents towards the impact of COVID-19 (n= 101) showing general positive receptiveness towards COVID-19 Standard Operational Procedure.

No	Statements	Strongly disagree (Freq%)	Disagree (Freq%)	Neutral (Freq%)	Agree (Freq%)	Strongly agree (Freq%)
1.	I believe in the existence of COVID-19 viruses.	5 (5.0)	0 (0)	27 (26.7)	**39 (38.6)**	30 (29.7)
2.	I feel COVID-19 is conspiracy and unnatural.	16 (15.8)	32 (31.7)	**34 (33.7)**	13 (12.9)	6 (5.9)
3.	COVID-19 is dangerous to human.	4 (4.0)	2 (2.0)	28 (27.7)	**36 (35.6)**	31 (30.7)
4.	COVID-19 definitely can infect huge number of people	4 (4.0)	1 (1.0)	28 (27.7)	33 (32.7)	**35 (34.7)**
5.	Washing hands is essential to protect myself from COVID-19	4 (4.0)	1 (1.0)	25 (24.8)	**36 (35.6)**	35 (34.7)
6.	It is important to keep my distance from others, to avoid spreading COVID-19	4 (4.0)	2 (2.0)	29 (28.7)	30 (29.7)	**36 (35.6)**
7.	I believe vaccine is the best cure treatment for COVID-19	5 (5.0)	3 (3.0)	32(31.7)	**35 (34.7)**	26 (25.7)
8.	Vaccine is essential					

	to all group of community in order to prevent the transmission	5 (5.0)	7 (6.9)	**33 (32.7)**	32 (31.7)	24 (23.8)
9.	I believe Traditional Complementary Alternative Medicine may help to treat COVID-19 patients.	5 (5.0)	14 (13.9)	**49 (48.5)**	20 (19.8)	13 (12.9)
10.	I feel herbal treatment may help to treat COVID-19 disease	6 (5.9)	12 (11.9)	**46 (45.5)**	21 (20.8)	16 (15.8)
11.	I feel Traditional Complementary Alternative Medicine should be given opportunity to help treat COVID-19 disease.	6 (5.9)	13 (12.9)	**43 (42.6)**	22 (21.8)	17 (16.8)
12.	I feel it is not appropriate to offer services during a pandemic.	16 (15.8)	28 (27.7)	**32 (31.7)**	19 (18.8)	6 (5.9)
13.	I believe my treatment service can spread COVID-19 virus	17 (16.8)	26 (25.7)	**30 (29.7)**	21 (20.8)	7 (6.9)
14.	I feel difficulties to generate income during COVID-19 pandemic	5(5.0)	11 (10.9)	**34 (33.7)**	26 (25.7)	25 (24.8)
15.	I feel Standard Operating Procedure (SOP) by provided authority is beneficial to prevent the transmission of the virus.	4 (4.0)	6 (5.9)	**39 (38.6)**	27 (26.7)	25 (24.8)
16.	I feel Standard Operating Procedure (SOP) provided by	24 (23.8)	33 (32.7)	**34 (33.7)**	6 (5.9)	4 (4.0)

	government are difficult.					
17.	I feel scanning QR code before entering the premise is important.	4 (4.0)	2 (2.0)	**34 (33.7)**	28 (27.7)	33 (32.7)
18.	Standard Operating Procedure (SOP) during COVID-19 pandemic limiting my treatment	4 (4.0)	11 (10.9)	**41 (40.6)**	33 (32.7)	12 (11.9)

Table 5 The practice of the respondents in response to COVID-19 (n= 101) showing general adherence to COVID-19 Standard Operation Procedure.

No	Statements	Never (Freq%)	Seldom (Freq%)	Sometimes (Freq %)	Often (Freq%)	Always (Freq%)
1.	I do go to crowded place	34 (33.7)	**44 (43.6)**	23 (22.8)	0 (0)	0 (0)
2.	I practice cultural behaviour such as shaking hands during COVID-19 pandemic	**58 (57.4)**	29 (28.7)	12 (11.9)	1 (1.0)	1 (1.0)
3.	I been practicing physical distancing	2 (2.0)	8 (7.9)	10 (9.9)	22 (21.8)	**59 (58.4)**
4.	Do you frequently washed your hands with soap and water especially after going to a public place?	3 (3.0)	2 (2.0)	11 (10.9)	27 (26.7)	**58 (57.4)**
5.	Do you use hand sanitizer when going to public place such as supermarket?	5 (5.0)	2 (2.0)	10 (9.9)	27 (26.7)	**57 (56.4)**
6.	I will advise my family members, friends and others to get COVID-19 vaccination	8 (7.9)	8 (7.9)	13 (12.9)	23 (22.8)	**49 (48.5)**

7. I give suggestion to use Traditional Complementary Alternative Medicine during COVID-19 pandemic to the government.	**47 (46.5)**	14 (13.9)	20 (19.8)	7 (6.9)	13 (12.9)
8. I follow the Standard Operating Procedure(SOP) by provided QR code, thermometer and hand sanitizer	4 (4.0)	6 (6.0)	14 (13.9)	16 (15.8)	**61 (60.4)**
9. I scan QR code before entering the premises	1 (1.0)	2 (2.0)	13 (12.9)	13 (12.9)	**72 (71.3)**
10. I scan patients' temperature before entering the premises	8 (7.9)	2 (2.0)	13 (12.9)	16 (15.8)	**62 (61.4)**
11. I operate when I am in red zone area	**74 (73.3)**	7 (6.9)	9 (8.9)	1 (1.0)	10 (9.9)
12. I do use hand sanitizer before the treatment	4 (4.0)	5 (5.0)	11 (10.9)	15 (14.9)	**66 (65.3)**
13. I do washing my hands after the treatment	4 (4.0)	3 (3.0)	9 (8.9)	16 (15.8)	**69 (68.3)**
14. I use glove during the treatment	7 (6.9)	3 (3.0)	18 (17.8)	16 (15.8)	**57 (56.4)**
15. I do other job to generate income during outbreak	22 (21.8)	8 (7.9)	18 (17.8)	45 (44.6)	**45 (44.6)**

Next, Kruskal-Wallis test was performed to measure the association of socio-demographic characteristics with knowledge, attitude and practice scores. Table 6 shows that there are significant association between age and marital status with knowledge regarding COVID-19 at the *p*-value of 0.001 and 0.010 respectively. However, there is no significant association between employment sector, working experience and gender with knowledge with p-value of 0.953, 0.211 and 0.129 respectively. Likewise, there is no significant association between all the socio-demographic characteristics with attitude and practice as shown in Table 7 and 8.

Table 6 Association between socio-demographic and knowledge showing the influence of age, marital status, employment sector, working experience and gender on the level of knowledge on COVID-19.

Variable	Knowledge Scores Mean (S.D)	*p*-value
Age		0.001**
20-29 years old	2.571 (0.514)	
30-39 years old	2.966 (0.186)	
40-49 years old	2.927 (0.264)	
50 years and above	2.941 (0.243)	
Status		0.010**
Single	2.636 (0.255)	
Married	2.936 (0.247)	
Divorced	2.833 (0.152)	
Employment		0.953
Government	2.917 (0.289)	
Private	2.882 (0.332)	
Self employed	2.889 (0.316)	
Working experience		0.211
Less Than 2 years	2.778 (0.4278)	
Two to five years	2.882 (0.332)	
5 years and above	2.924 (0.267)	
Gender		0.129
Male	2.966 (0.186)	
Female	2.861 (0.348)	

Table 7 Association between socio-demographic and attitude scores showing that none of the socio-demographic characteristics influences the attitude towards COVID-19.

Variable	Knowledge Scores Mean (S.D)	F	*p*-value
Age		0.310	0.845
20-29 years old	1.929 (0.475)		
30-39 years old	2.103 (0.558)		
40-49 years old	2.049 (0.590)		
50 years and above	2.059 (0.746)		
Status		0.685	0.705
Single	2.091 (0.539)		
Married	2.064 (0.610)		
Divorced	1.917 (0.515)		
Employment		0.055	0.584
Government	2.083 (0.669)		
Private	2.177 (0.728)		
Self employed	2.0139 (0.544)		
Working experience		0.068	0.831
Less Than 2 year	2.000 (0.485)		
Two to five years	2.000 (0.500)		
5 years and above	2.076 (0.640)		
Gender (t test)			0.510
Male	2.103 (0.772)	-	
Female	2.028 (0.503)	-	

Table 8 Association between socio-demographic and practice scores showing none of the socio demographic characteristics influencing practice scores

Variable	Practice Scores Mean (S.D)	*p*-value
Age		0.786
20-29 years old	2.286 (0.726)	
30-39 years old	2.172 (0.602)	
40-49 years old	2.098 (0.625)	
50 years and above	2.177 (0.809)	
Marital Status		0.775
Single	2.181 (0.751)	
Married	2.141 (0.618)	
Divorced	2.250 (0.866)	
Employment		0.863
Government	2.250 (0.622)	
Private	2.177 (0.728)	
Self employed	2.139 (0.657)	
Years of Working Experience		0.699
Less Than 2 years	2.056 (0.725)	
Two to five years	2.118 (0.781)	
5 years and above	2.197 (0.613)	
Gender		0.425
Male	2.241 (0.636)	
Female	2.125 (0.670)	

The results of correlation analysis shows that there is a positive correlation ($r = 0.230$; $p < 0.05$) between knowledge and attitude but no positive correlation ($r = 0.100$, $p > 0.05$) between knowledge and practice. There is significantly positive correlation ($r = 0.395$, $p < 0.05$) between attitude and practice.

Table 9 Correlation between knowledge and attitude, knowledge and practice, and attitude and practice in Malay traditional medicine practitioners towards COVID-19.

Knowledge and Attitude	r = 0.230	p = 0.02
Knowledge and Practice	r = 0.100	p = 0.46
Attitude and Practice	r = 0.395	p = 0.001

From our study, a total score obtained for knowledge was 89.1% indicating a good level of knowledge on COVID-19 among Malay traditional practitioners. Most of respondents were aware on the common clinical symptoms such as fever (95%), fatigue (77.2%), and coughing (69.3%). Most respondents knew the five examples of common route transmission i.e close contact (92.1%), sneezing (99.0%), coughing (98.0%), and airborne (84.2%), but many are not sure regarding transmission through body fluid (11.9%). A third of the respondents were also unsure regarding transmission of COVID-19 from animal to human whereas another one-third thought wrongly that this type of transmission is very likely to happen. Regarding the prevention of COVID-19, almost all respondents exhibited good awareness on the importance of preventive measures to be taken to stop the spread of COVD-19. Most respondents used a mix of channels to get their source of information, with social media being the favourite as alsmot all respondents chose an option that include social media as their main source of information. This is in line with widespread digital literacy in Malaysia in which, as of 2020, 98.6% of Malaysians found to own smartphones, with 89.6% of them are avid internet users whose major activities are engaging in scoial networking and finding information online (Department of Statistics, 2021). As this study had been conducted in April 2021, the sampling population already

had a year of experience in the pandemic. Hence, the overall excellent score for knowledge may be due to widespread educational campaign conducted by Malaysian health authority as well as enough exposure to information on COVID-19 among the sampling population.

Contradictory to the score level on knowledge section, the respondents moderate level of attitude towards COVID-19 as the score is only 65.3%. In terms of belief on the real existence of COVID-19, 38.6 % of respondents strongly opines that COVID-19 is real whereas 33.7% of respondents choose thought that COVID-19 is part of a conspiracy and not a naturally occuring pandemic. Only 35.6% agreed that COVID-19 is dangerous to human. This corresponds to the prevalent belief among some Malaysians that COVID-19 is a created fear, and data on COVID-19-related deaths was fabricated to increase sale of moden medicine and vaccination (Lee et al., 2022). Prevention steps such as washing hands and social distancing however are received well by the respondents but may be influenced by pre-existing knowledge on health and hygiene as all respondents are traditional medical practitioners themselves. 45.4% of respondents chose to be neutral when asked if they think traditional herbal preparation can help to treat COVID-19. Although most of the respondents woud have had some knowledge of medicinal herbs, their focus area of practice were massage and post-natal care and the herbal preparations that they used would be less on treating symptoms other than muscle complaints, hence the neutral answer. In addition, there was little to no research carried out using local traditional medicine in Malaysia and coverage over the use of other traditional medicine like the Chinese traditional medicine was likewise very low. There is a discernible 30% of respondents who always appear to be ambivalence in regards to questions on attitude which may indicate some level of resistance or indignant attitude towards COVID-19 preventive and treatment strategies. Although more than 90% agreed that regulations concerning COVID-19 were not very difficult to adhere to, more than 70% felt that it was difficult to them to generate income and 45% had to resort to other osurce of income.

Our finding also revealed a moderate level of practice at 54.5% score concerning COVID-19 among respondents. This means that although the respondents knew well about COVID-19 and have moderate level of attitude towards COVID-19 preventive measures, these may not be practiced. Only about 37 - 43.6% of respondents disclosed that they seldom or will not go to a crowded place during the pandemic. However, given that most respondents are from the lower-income group, they may have done this out of necessity to find extra work and alternative source of income. This is supported by 44.6% of respondents who answered that they had to switch to other profession to generate income during COVID-19 outbreak. Regarding vaccination, only 48.5 % respondents asnwered that they will always advise family, friends and other to get COVID-19 vaccination. Hence, there is quite a significant amount of resistance or hesitancy towards COVID-19 vaccination in this segment of Malaysian society. Slightly more than half of respondents (51.5%) said that they would not advised the community to use traditional medicine. Again, this is perhaps because of the lack of official data and personal experience on possible use of Malaysian herbal medicine to treat COVID-19. Adherence to COVID-19 prevention strategies is exhibited by 60.4% respondents who claimed to have followed the recommended SOPs by providing QR code, thermometer and hand sanitiser at their premises. 61.4% of respondents scanned patients' temperature before entering the premises, 65.3% used hand sanitiser before initiating treatment, 68.3% washed their hands after the treatment and 56.4% used glove during treatment. 73.3% of respondents also said that they would not operate if their locality has been declared a red zone.

In this study, knowledge scores appeared to be associated with age ($p< 0.005$). Middle age respondents i.e. 30-39 years old, had higher knowledge scores (mean= 2.966) in term of COVID-19's definition, clinical symptoms, prevention, vaccination and SOPs. The possible reason behind this finding might be because that age group is the most active phase, has a lot of family and financial responsibility to deal with and naturally had found more reason to equip themselves with accurate information as much as possible. Marital status also influence knowledge score significantly ($p< 0.05$) as married respondents were to have a higher knowledge scores (mean=2.936) compared to single (mean=2.636) and divorced group (mean=2.833). Again, this significant result could be related to their higher sense of responsibility.

In general, our data showed that despite having good knowledge on COVID-19, the scores on attitudes and practice among the Malay traditional practitioners were stil inadequate as of April 2021. This correlates with the finding on the larger Malaysian public at around the same time which exhibited sound knowledge but had negative attitudes and inadequate practices pertaining to COVID-19 during the pandemic (20). Contributing factors to this observation includes the implementation of the strict SOPs which had severely affected the lower income group as they were not able to work or move from one place to another, leading to resentment towards the SOPs. Also, vaccination against COVID-19 had just started in February 2021 but it met some mishaps in the initial stage of its implementation, thus earning some public mistrust and contributing to the lingering belief on conspiracy theory (29).

Our data revealed that Malay traditional medicine practitioners who were more knowledgeable towards COVID-19 were more likely to develop positive attitude such as acknowledging the danger of COVID-19. As these good attitudes correspond fairly well to knowledge score among Malay traditional medicine practitioners, this presented a clear and direct target for educational messaging, and if properly disseminated could have a substantial impact on improving the management of COVID-19. Although knowledge does not correlate directly to practice, it was found that as attitude does have a positive correlation to practice, ultimately the increase in knowledge will also results in better practice.

CONCLUSION

This study provided an interesting and rare insight into Malay traditional practitioners knowledge, attitude and practice towards modern public health policy and the impact of modern outbreak, in this case concerning COVID-19 outbreak in Malaysia. The Malay traditional medicine practitioners appeared to have means to keep themselves in tandem with current information of important diseases. They have positive attitudes towards modern strategies to tackle diseases and outbreak and if some of their concerns could be alleviated, may lead to higher scores for attitude and practice.

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ETHICS OF STUDY

Ethical approval number IIUM/504/14/11/2/IREC 2021-KAHS (DBMS) was granted by IIUM Research Ethical Committee. All information from respondents was kept as private and confidential matter.

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HEALTH RISK ASSESSMENT OF HEAVY METALS IN KUANTAN RIVER BASIN, PAHANG

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ABSTRACT

Introduction: Industrialisation, urbanisation, and nearby human activities can lead to heavy metal pollution in the Kuantan River basin, posing a health risk. **Objective:** This quantitative secondary data analysis study aimed to estimate the health risk assessment (HRA) of the arsenic (As), lead (Pb), cadmium (Cd) and mercury (Hg) in the Kuantan River basin. **Methods:** All the secondary data on heavy metals concentration, physicochemical parameters and rainfall were obtained from the Department of Environment (DOE) and the Meteorological Department (MET), respectively. In reducing the uncertainties in health risk estimation, the Monte Carlo simulation technique was used to estimate the Hazard Quotient, HQ and Lifetime Cancer Risk, LCR of studied heavy metals via ingestion and dermal absorption. Sensitivity analysis (SA) was used to measure the most influential parameters on the estimated risk. **Results:** The results demonstrated that in 2017, the ascending order of mean concentrations of heavy metals was Pb > As > Cd > Hg. However, from 2018 to 2021, Cd and Hg consistently fell below the detection limit, leaving Pb > As as the dominant heavy metals during this period. All mean HQ values of studied heavy metals did not exceed the acceptable limit of one for both ingestion and dermal uptake. The mean LCR values for As via ingestion and dermal exposure remained within acceptable limits (1×10^{-4}). However, in 2017, the mean LCR value for Cd through dermal uptake (1.40×10^{-4}) slightly exceeded the acceptable level. Meanwhile, the worst-case predicted values at the 95th percentile showed that the LCR values of As via ingestion route (all years), ranged from 1.48×10^{-4} to 2.98×10^{-4} and dermal uptake (except for 2019 and 2021), ranged from 3.80×10^{-3} to 1.99×10^{-4}, exceeded the acceptable limit. SA demonstrated that the concentration of As and Cd had the greatest influence on HRA via the ingestion pathway and dermal uptake in 2017. **Conclusion:** It indicates As and Cd potentially increasing the chance of developing cancer. This study will help individuals in high-risk heavy metal exposure areas be more cautious and aid authorities in mitigating contamination.

KEYWORDS: heavy metals, river water, hazard quotient, lifetime cancer risk, Monte Carlo simulation

INTRODUCTION

Over 700 substances have been identified as contaminants in the waters, with heavy metals posing the biggest threat to the environment and individuals due to their high toxicity and carcinogenicity (Ustaoglu and Aydin, 2020). It has been documented that in developing countries of Africa, Asia, and South America, river water often contains elevated heavy metal concentrations, exceeding global threshold limits (Zhou et al., 2020). Chromium (Cr), nickel (Ni), copper (Cu), zinc (Zn), cadmium (Cd), and lead (Pb) are examples of heavy metals that tend to exhibit greater persistence compared to organic contaminants (Lou et al., 2017), and some are able to accumulate and biomagnified. Therefore, long-term exposure to heavy metals, can exacerbate health issues and contribute to chronic conditions, with

unregulated heavy metal deposition in rivers, as noted by Liu & Ma (2019), posing significant health risks such as carcinogenic effects, neurological damage, impaired growth, and even fatalities.

Heavy metal pollution, originating from natural and human activities, is particularly prominent in Asian countries, primarily due to mining and manufacturing (Zhou et al., 2020). Malaysian rivers, including those in the Kuantan district, grapple with heavy metal contamination. Prior studies have identified elevated levels of copper (Cu), arsenic (As), iron (Fe), manganese (Mn), aluminum (Al), and magnesium (Mg) in various Malaysian rivers (Liang et al., 2020; Razak et al., 2021; Maharjan, Wong, and Rubiyatno, 2021). Rapid urbanisation and industrialisation in Kuantan, coupled with a high-density population, have led to concerns about heavy metal pollution. Recent reports indicate contamination of Tunggak and Balok rivers (Gebeng Rivers), Kuantan, with Cd, Co, Cu, Pb, Mn, and Ni from industrial sources (Islam et al., 2022). Kuantan's population, the largest among nine districts in Pahang, engages in land-use practices that may exacerbate heavy metal pollution in the rivers. Despite this, the water quality status of the Kuantan River basin has consistently been classified as slightly polluted from 2016 to 2020, according to data published by the Department of Environment (DOE, 2017-2020). This persistent pollution could pose health risks to individuals engaging in activities like swimming, fish consumption, or groundwater usage.

Health risk assessment (HRA) as suggested by the United States Environmental Protection Agency (US EPA) serves as a valuable tool for evaluating health risks in humans. There are numerous published studies on heavy metal contamination in water and their health risk assessment (Jin et al., 2015; Ustaoglu and Aydin, 2020; Islam et al., 2015; Fahimah et al., 2023; Adesiyan et al., 2018; Mahad et al., 2019). This study aimed to determine the hazard quotient (HQ) and lifetime cancer risk (LCR) of As, Cd, Pb and Hg in the Kuantan River basin coupled with the Monte-Carlo simulation technique in reducing the uncertainty of HRA (Liu et al., 2019; Jin et al., 2022), together with a sensitivity analysis to determine which parameters are the most influential on the health risk estimation's outputs. The identification of parameters with the greatest impact on health risk can guide related stakeholders in efficiently channeling their efforts and resources toward addressing these critical parameters.

MATERIALS AND METHODS

Study Design and Source of Data

Quantitative secondary data analysis was used as the study design for this research study. The term "secondary analysis" describes the method of using existing data from previous studies or primary data collected by other researchers or agencies to address new questions (Tripathy, 2013). The secondary data which is the concentration of As, Cd, Hg, and Pb in the Kuantan River basin were obtained from the Department of Environment (DOE) for HRA. Taking into account the influence of physicochemical parameters and rainfall, the data on dissolved oxygen (DO), biochemical oxygen demand (BOD), chemical oxygen demand (COD), suspended solids (SS), pH, and ammoniacal nitrogen (NH_3-N) from DOE for the Kuantan River basin were also obtained. Additionally, we sourced rainfall data for the Kuantan district from the Meteorological Department as supplementary information, as it may impact the measured levels of As, Hg, Cd, and Pb.

Study Area

The 87 kilometres long Kuantan River basin flows through the Kuantan district, which is in Pahang State's north-eastern region. Kuantan River basin was chosen due to the urbanisation and rapid development of industrial progress as it can increase the discharge of pollutants into the ecosystems. This is because there are many development areas near the Kuantan River basin including commercial, residential, lodging and chemical industries. There are 192 manual river water quality monitoring (MRWQM) stations and two automatic river water quality monitoring (CRWQM) stations located throughout the Kuantan River basin. The data obtained was based on these water quality monitoring stations. The selected rivers in the Kuantan River basin included rivers of Belat, Charu, Galing Besar, Galing Kecil, Kenau, Kuantan, Pandan, Pinang, Reman, Riau and Talam. The water monitoring stations in Kuantan River and Belat River were selected due to being the largest and second largest rivers in Kuantan respectively, with Belat River being a part of Kuantan River. Both rivers serve as the source of water supply for domestic, industrial, and agricultural usage. Additionally, the Kuantan River is near to Gebeng Industrial Estate as the water supply for industry purposes. Meanwhile, the Galing River (part of the Kuantan River) was chosen as it is located in the most urbanised area in Kuantan.

Health Risk Assessment

HRA of As, Cd, Hg, and Pb was observed via the two main exposure pathways: ingestion of water and dermal absorption through the skin. Hence, the average daily dose (ADD) for ingestion of water ($ADD_{ingestion}$) and dermal absorption (ADD_{dermal}) was required to be calculated using equations (1) and (2) suggested by EPA (1989) and had been used in the previous studies such as (Adesiyan et al., 2018; Jin et al., 2022; Liang et al., 2018; Ustaoğlu & Aydın, 2020). Both the $ADD_{ingestion}$ and ADD_{dermal} expressed in unit µg/kg/d.

$$ADD_{ingestion} = \frac{(C_{water} \times IR \times ABS_g \times EF \times ED)}{(BW \times AT)} \quad (1)$$

$$ADD_{dermal} = \frac{(C_{water} \times SA \times K_p \times ET \times EF \times ED \times CF)}{(BW \times AT)} \quad (2)$$

Where;

C_{water} = concentration of heavy metals in water
IR = ingestion rate
ABS_g = gastrointestinal absorption factor
ED = exposure duration
BW = body weight
CF = conversion factor
SA = surface area
K_p = dermal permeability coefficient
EF = exposure frequency
ET = exposure time
AT = averaging time

The calculation for non-carcinogenic and carcinogenic risk is required to evaluate HRA indicated by the Hazard Quotient (HQ) and Lifetime Cancer Risk (LCR), respectively. The ratio of the average daily dose for direct ingestion or dermal contact to the reference dose (RfD) is known as HQ calculated using the following equation below (3 & 4). Additionally, LCR indicates the carcinogen elements that can induce potential danger for humans. It is calculated with the following equation (5) where cancer slope factor (CSF) is required:

$$HQ_{ingestion} = \frac{ADD_{ingestion}}{RfD_{ingestion}} \quad (3)$$

$$HQ_{dermal} = \frac{(ADD_{dermal})}{(RfD_{dermal})} \quad (4)$$

$$LCR = ADD \times CSF \quad (5)$$

If HQ > 1, it indicates that heavy metal exposure has a negative impact on human health. Meanwhile, if HQ < 1, then there will be no adverse effects arising on human health (Ustaoglu and Aydin, 2020). There is a carcinogenic risk if LCR ≥ 10^{-4}, which indicates a high risk of developing cancer in humans (Ustaoglu and Aydin, 2020).

In estimating the Hazard Index (HI), the total of As, Pb, Cd, and Hg was computed to determine the impact of multiple heavy metals in the Kuantan River basin to the residents. HI was calculated using the USEPA guideline (Mohammadi et al., 2019; US EPA, 1991), as shown in equation (6) below:

$$HI = \sum_{HQ} = HQ_{As} + HQ_{Pb} + HQ_{Cd} + HQ_{Hg} \quad (6)$$

Monte Carlo simulation

Both Monte Carlo simulation and sensitivity analysis have been conducted by using Crystal Ball software (version 11.1.3.0.0; Oracle Corp., USA). Apart from that, HRA as a deterministic assessment commonly has uncertainty or variability characteristics that cause inaccuracies in the assessment results due to single-point input parameters. Therefore, a probabilistic method such as Monte Carlo analysis was carried out because it could produce a result that was more accurate by reducing uncertainties (Liu et al., 2019; Qu et al., 2018). In this study, iterations of 10,000 were applied to determine the ingestion and dermal risk associated with exposure to As, Hg, Cd and Pb. Additionally, the parameter used in the Monte Carlo simulation such as heavy metal concentration was defined as the log-normal distribution. Meanwhile, the parameters (IR, ED, BW, AT, SA, EF, ET, CF, K_p, R*f*D, ABS_g, CSF) that have fixed values were defined as uniform distributions. Moreover, the Monte Carlo technique can identify

the most influential parameter using sensitivity analysis (Liu et al., 2019). To identify the parameters influencing the uncertainty risk of HQ and LCR, the outcomes of the most influential parameters were presented in the rank correlation coefficient. This is because the correlation coefficient between each of the parameters and the value of risk will determine the sensitivity. Each element's contribution is bigger when it has a higher correlation coefficient since it contributes more to the outcomes (Qu et al., 2019).

RESULTS AND DISCUSSIONS

Concentration of heavy metals

Figure 1 below shows the mean for the concentration of studied heavy metals in the Kuantan River basin from 2017 to 2021. In 2017, the mean concentrations of the examined heavy metals followed the order Pb > As > Cd > Hg. However, from 2018 to 2021, Cd and Hg consistently were below the detection limit, with Pb > As emerging as the dominant heavy metals during this period. The figure shows the highest mean concentration of Pb recorded in 2019 (3.53×10^{-3} mg/L) and the highest mean concentration for As was reported in 2017 with 2.00×10^{-3} mg/L. In the year 2017, Cd and Hg were third (1.00×10^{-3} mg/L) and fourth-ranked (2.00×10^{-4} mg/L), respectively. However, the mean concentrations of Cd and Hg from 2018 to 2021 are unable to be analysed due to those two heavy metals below the detection limit (< 0.001 mg/L).

As and Pb were recorded as the highest and second-highest average concentrations over the subsequent five years. It can be associated with uncontrolled bauxite mining activities in Kuantan until it was banned in early 2016 (Abdullah et al., 2016). Apart from that, Abdullah et al. (2016) also stated the main contaminants of bauxite are Al and Fe but due to geological characteristics of the land and land-use activities, the other toxic metals such as As, Hg, Cd, Pb, Mn and Ni may deteriorate the quality of water when the natural ecosystem is aggressively discovered and excavated. Pb concentration peaked in 2019 meanwhile As in 2017. Although Pb is very little present on the earth's crust, it can be transported and dissolved in water (ATSDR, 2020). Moreover, there is a high possibility that Pb concentration may be high due to the municipal waste that may contain metal such as the usage of batteries or from the types of transport that use fuels containing Pb. This is because the major sources of Pb commonly come from paint, pesticides, fuels, batteries, industrial waste or fertilizers (Tadesse, Tsegaye & Girma, 2018).

Additionally, Kusin et al. (2016) stated, that an elevated concentration of As in the water can be associated with the leaching process of bauxite stockpiles that allows the heavy metals to enter the water directly. Since the mining operation was stopped in 2016, there is a high chance the high concentration of As in 2017 was caused by the leaching process. In addition, Cd, Hg and Pb concentration levels also showed approximately similar trends in 2017. Moreover, the previous studies found the elements of Cd, Hg and Pb in the soil particles (Ismail et al., 2018) and the Pb levels exceed the recommended value which is > 35 mg/kg in sediment (Kusin et al., 2018) in the vicinity of the Kuantan mining areas.

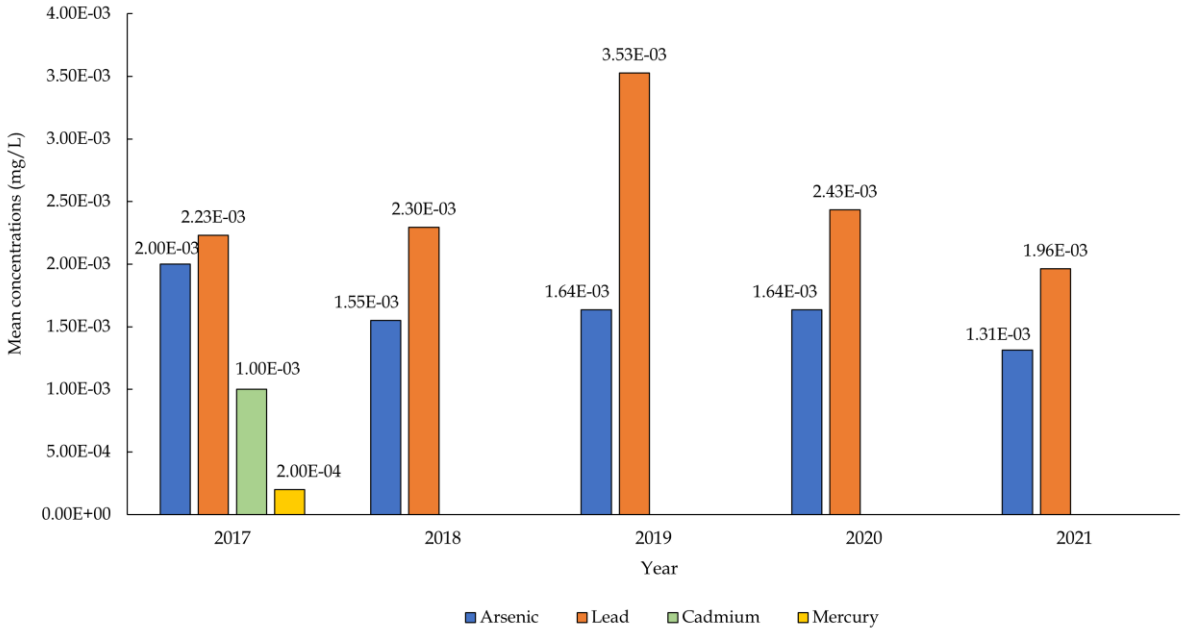


Figure 1 Mean concentrations of Arsenic (As), Lead (Pb), Cadmium (Cd) and Mercury (Hg) according to year from the Kuantan River

Further, the correlation between studied heavy metals, physicochemical properties and rainfall factors were observed. The influence of rainfall factor and suspended solid (SS) toward the elevation of As had statistically proved by the significant relationship between As and rainfall (p = 0.007) and between As and SS (p = 0.042) with both showing very high relationships (Figure 2). Rainwater has the ability to transport arsenic-bearing materials from an abandoned mine site into a river (Kusin et. al, 2018). Elevated levels of SS in a water body can lead to heavy metal precipitation within the SS, resulting in heavy metals settling as sediment, potentially causing adverse health effects, as discussed by Sujaul et al. (2013).

	As	Pb	Cd	Hg	DO	BOD	COD	SS	pH	NH_3-N	Rainfall
As	1	0.164	0.839	0.839	-0.017	0.676	0.643	0.891*	-0.690	-0.063	-0.968**
Pb		1	-0.240	-0.240	-0.081	-0.230	-0.394	0.445	0.480	0.733	-0.164
Cd			1	1**	0.124	0.871	0.780	0.734	-0.760	-0.464	-0.820
Hg				1	0.124	0.871	0.780	0.734	-0.760	-0.464	-0.820
DO					1	0.596	0.601	0.236	-0.367	-0.695	-0.231
BOD						1	0.932*	0.715	-0.802	-0.717	-0.784
COD							1	0.570	-0.947*	-0.783	-0.763
SS								1	-0.481	-0.033	-0.924*
pH									1	0.675	0.757
NH_3-N										1	0.209
Rainfall											1

* Correlation is significant at the 0.05 level (2-tailed) ** Correlation is significant at the 0.01 level (2-tailed)

Figure 2 Pearson correlation between studied heavy metals, physicochemical properties and rainfall factors (blue is positive and red is negative)

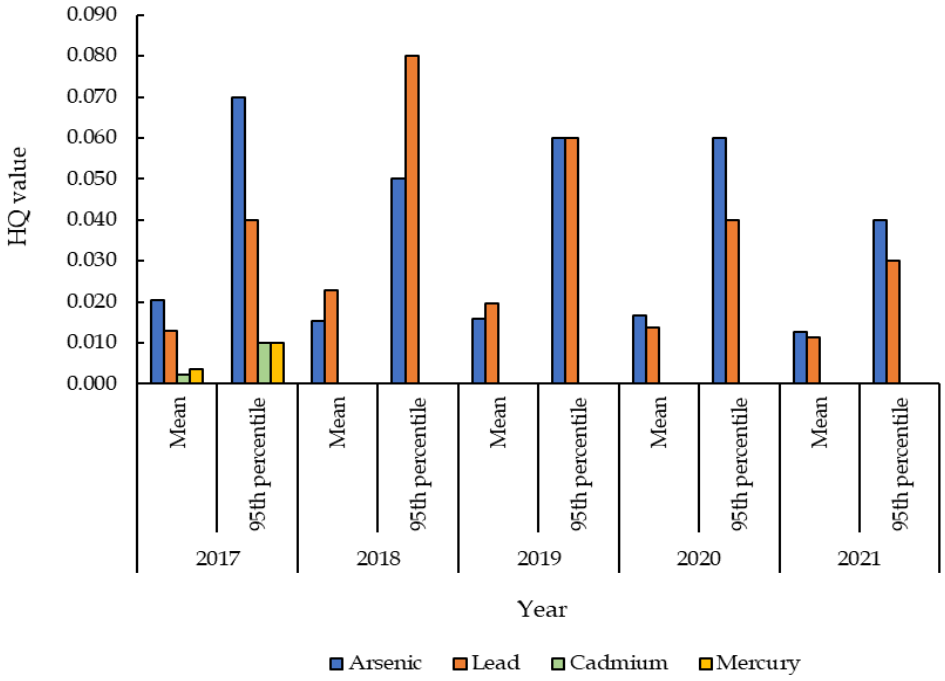
Meanwhile, the declining trend in heavy metals concentration of As and Pb in 2020 and 2021 can be associated with the implementation of the Movement Control Order (MCO) when the World Health Organization (WHO) declared the Coronavirus disease (COVID-19) outbreak as a global pandemic on 11th March 2020. Similarly, Malaysia has announced the COVID-19 lockdown starting on 18th March 2020 (Tang, 2022). According to Abdul Rahman & Abdul Halmi (2021), MCO has led to positive impacts on the environment due to restricted human movements, business or economic operations and anthropogenic activities. This is because anthropogenic activities contribute to the majority of water contamination.

Hazard Quotient

Figure 3 showed the results of HQ for both route of exposure, ingestion and dermal route of studied heavy metals. For ingestion route, the highest mean of HQ values of As and Pb were at 0.021 in 2017 and 0.023 in 2018, respectively. The mean HQ values were found to be at 0.004 for Hg and 0.002 for Cd in 2017. At 95th percentile, the highest HQ value of As was at 0.07 in 2017 and 0.08 in 2018, respectively. Hg and Cd possess a similar 95th percentile which is 0.01 in 2017.

Meanwhile, in 2017, the highest mean HQ for dermal uptake was found to be at 0.005 for As, while Pb reached its highest mean in 2019, also at 0.005. Estimated, Cd and Hg are in the third (0.020) and fourth-ranked (0.015) in terms of mean in 2017 respectively. The highest 95th percentile for As was reported at 0.02 in 2017 and Pb worst-case scenario' is at 0.02 in 2019. Both Cd and Hg showed similar 0.05 values which represents the 95th percentile in 2017. However, the mean and the 95th percentile for Cd and Hg were unable to be determined from 2018 - 2021 due to both heavy metals being below the detection limit (< 0.001 mg/L).

(a)



(b)

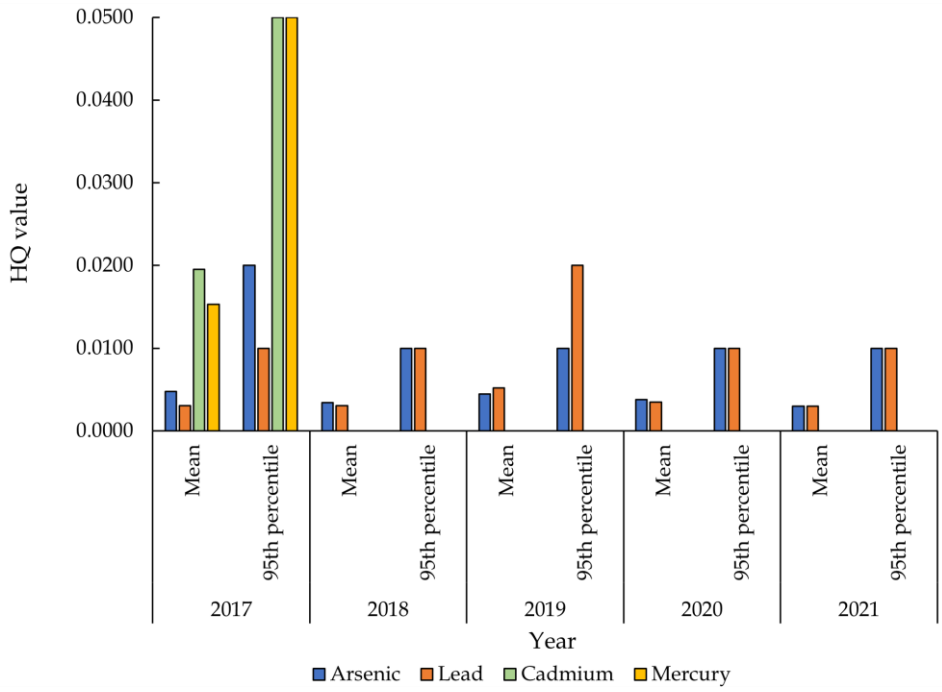


Figure 3 Result of Monte Carlo simulation of HQ via (a) ingestion and (b) dermal route according to year

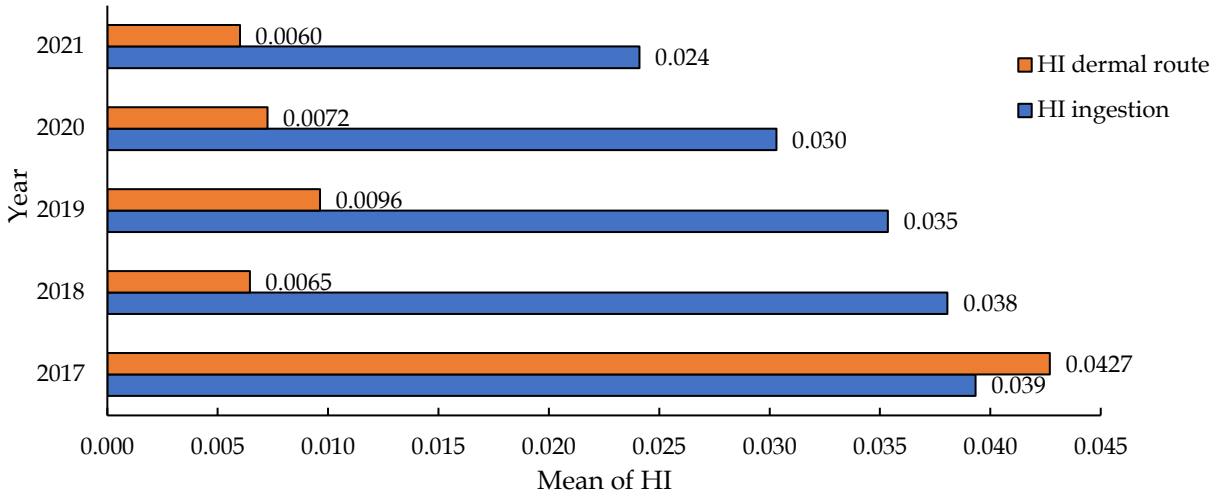
Hazard Index

The cumulative impact of multiple heavy metals was assessed using the Hazard Index (HI). The mean HI values for both oral and dermal intake ranged from 0.006 to 0.043 while at the 95th percentile, they varied between 0.020 and 0.130. The cumulative HQ values for heavy metals calculated were consistently below one, indicating adverse health effects are not likely associated with exposure to multiple heavy metals.

Both HQ values and HI for ingestion and dermal routes are below the maximum acceptable value established by the US EPA guidelines which are less than one, representing an unlikely risk of adverse health effects of As, Pb, Cd, and Hg to the residents along the Kuantan River basin, whether through oral or dermal exposure. Similar findings were observed from the previous studies conducted in the Kuantan River by Mahad et al. (2019), through the consumption of marine fish in Peninsular Malaysia

by Wan Azmi, Ahmad & Wan Mahiyuddin (2019), and in the Bertam River, Cameron Highlands by Razali et al. (2018).

(a)



(b)

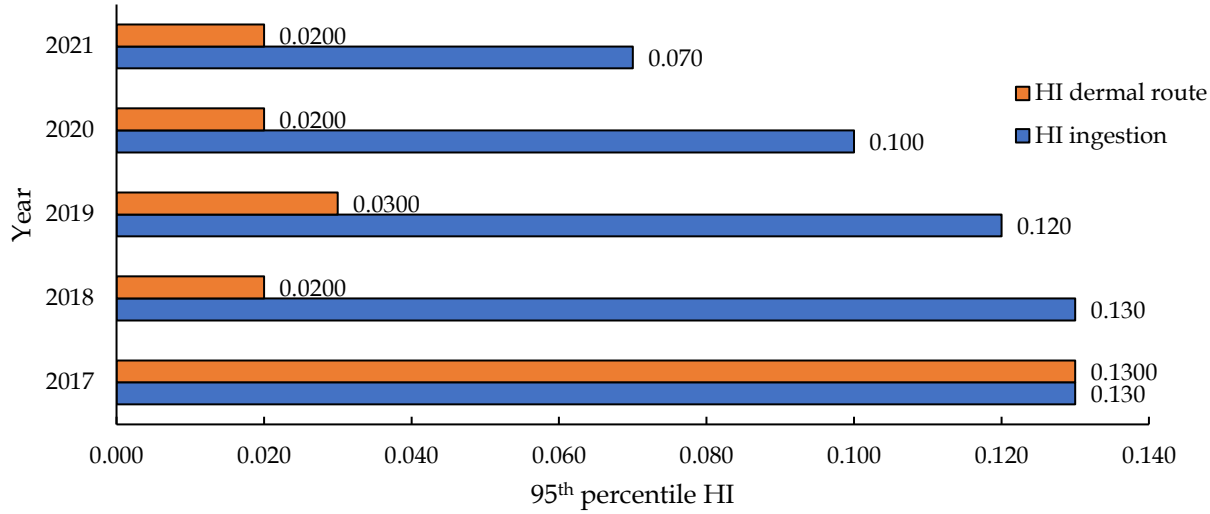


Figure 4 Results on (a) mean HI and (b) 95th percentile HI according to year

Lifetime Cancer Risk

LCR was determined only for As and Cd since both heavy metals are Group A or Class 1 human carcinogens (US EPA, 1998; IARC, 2012). Figure 5 demonstrates the mean LCR values via ingestion route across the five consecutive years were below the acceptable level of 1.00×10^{-4}, meanwhile, at the 95th percentile, the LCR values were beyond the acceptable level, which is represented by values of 2.98×10^{-4}, 2.75×10^{-4}, 1.97×10^{-4}, 1.99×10^{-4} and 1.48×10^{-4}, respectively. Cd recorded the mean and 95th percentile of LCR level at 2.97×10^{-6} and 5.64×10^{-6}, respectively which is below the value of 1×10^{-4}.

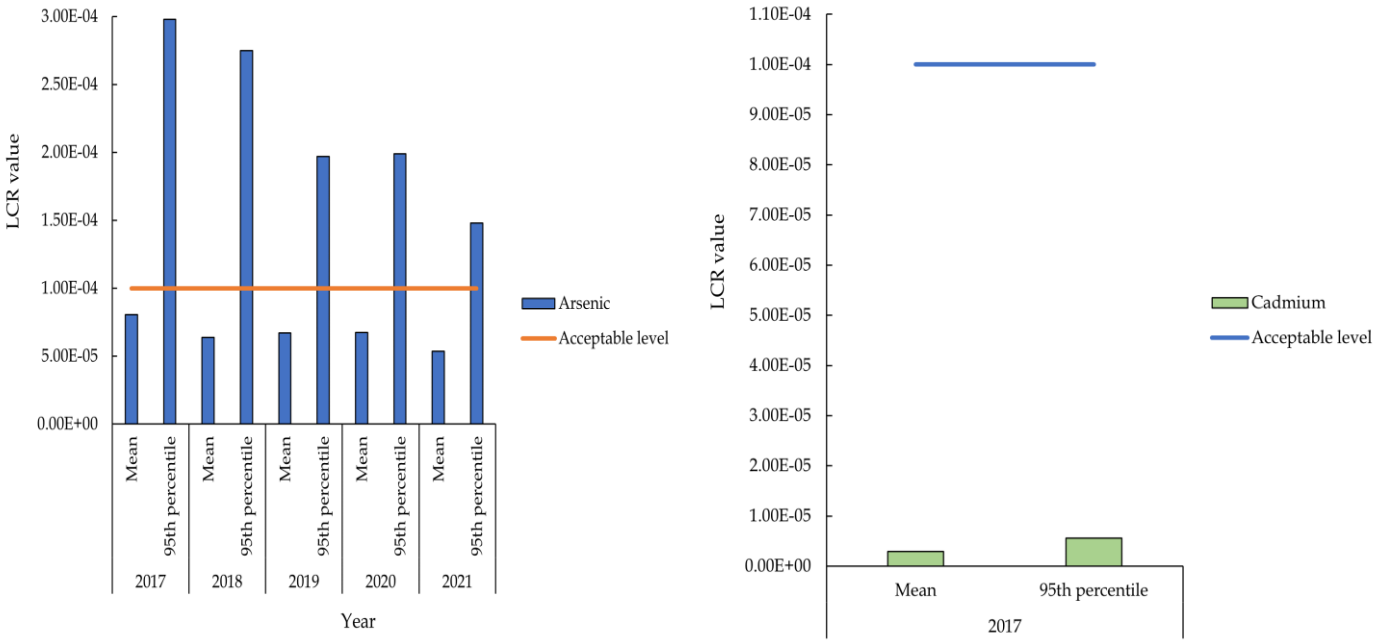


Figure 5 Result on Monte Carlo simulation of LCR via ingestion route according to year

The results of the mean of LCR due to dermal exposure to As and Cd are shown in Figure 6 below. The mean of LCR levels did not exceed the acceptable levels, however, among the five years, mean of LCR for As was highest at 3.72×10^{-5} in 2017 and lowest at 2.40×10^{-5} in 2019. Cd, on the other hand, recorded the reading of mean at 1.40×10^{-4} in 2017, which slightly exceeds the upper limit of 1×10^{-4}.

As reading for the 95th percentiles in all years shows that the readings exceeded the highest acceptable risk level of 1×10^{-4}, in which the values were 3.80×10^{-3}, 1.68×10^{-4}, 1.76×10^{-4} 1.99×10^{-4}, and 1.11×10^{-4}, respectively. Similarly, Cd also reported the same result when Cd's 95th percentile (5.70×10^{-4}) surpassed the upper limit which is 1×10^{-4} in 2017. However, in the following years starting from 2018 to 2021, the estimation of the LCR value and 95th percentile can be achieved for As only due to the Cd concentration in the water being below the detection limit (< 0.001 mg/L).

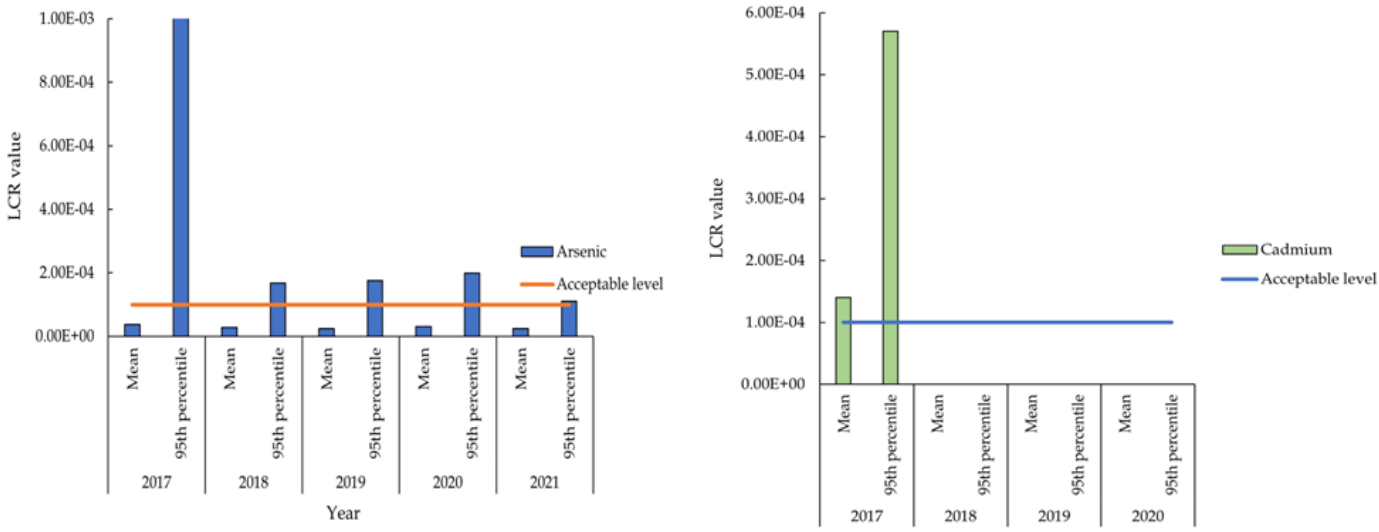


Figure 6 Result on Monte Carlo simulation of LCR via dermal route according to year

Carcinogenic risks, as defined by the EPA, refer to the increased likelihood of an individual developing cancer over their lifetime due to exposure to potential carcinogens (US EPA, 2023). The LCR values exceeding 1×10^{-4} are deemed unacceptable, as a carcinogenic risk at this level presents significant

health hazards requiring intervention and remediation due to its substantial impact on health (US EPA, 2012). This recent study highlights that As and Cd pose substantial cancer risks, primarily through dermal uptake from polluted rivers and potential oral exposure. In essence, individuals exposed to As and Cd face an increased likelihood of developing cancer over their lifetime, either through dermal contact (such as bathing) or by ingesting untreated water, which may originate from groundwater sources.

Accumulation of ingested arsenic can have a variety of negative effects on humans, including an increased risk of cancer, high blood pressure, dermal effects, diabetes, and peripheral neuropathy (Ustaoglu & Aydin, 2020). Cadmium is soluble in water, whereas insoluble forms are immobile but can deposit into the water and form sediment (ATSDR, 2012). Therefore, high dermal absorption of Cd might represent a potential threat such as '*itai-itai*' disease, hypertension, gastrointestinal upset, cardiovascular disease, severe rheumatoid disease and fragility of bone (Mahad et al., 2019; ATSDR, 2012). Contaminated water with high As and Cd is required to undergo the treatment of either conventional or extensive treatment technologies to assure the safety of the water.

Sensitivity Analysis via Ingestion Route

Figure 7 shows in 2017, the factor with the greatest significance for sensitivity analysis was the concentration of heavy metals in the water, with As having a value of 1 and Cd having a value of 0.98. Likewise, the concentration of heavy metals was the greatest impact parameter for sensitivity analysis from 2018 to 2021. This is because all the readings for the concentration of heavy metals are 1. The other parameters such as IR, BW, AT, CSF, ABS_g, ED, EF and *RfD* were less sensitive and varied from -0.01 to 0.02 over the duration of the five years. However, due to the fact that the majority of the concentration values were below the detection limit, Cd does not display the results on sensitivity from 2018 to 2021.

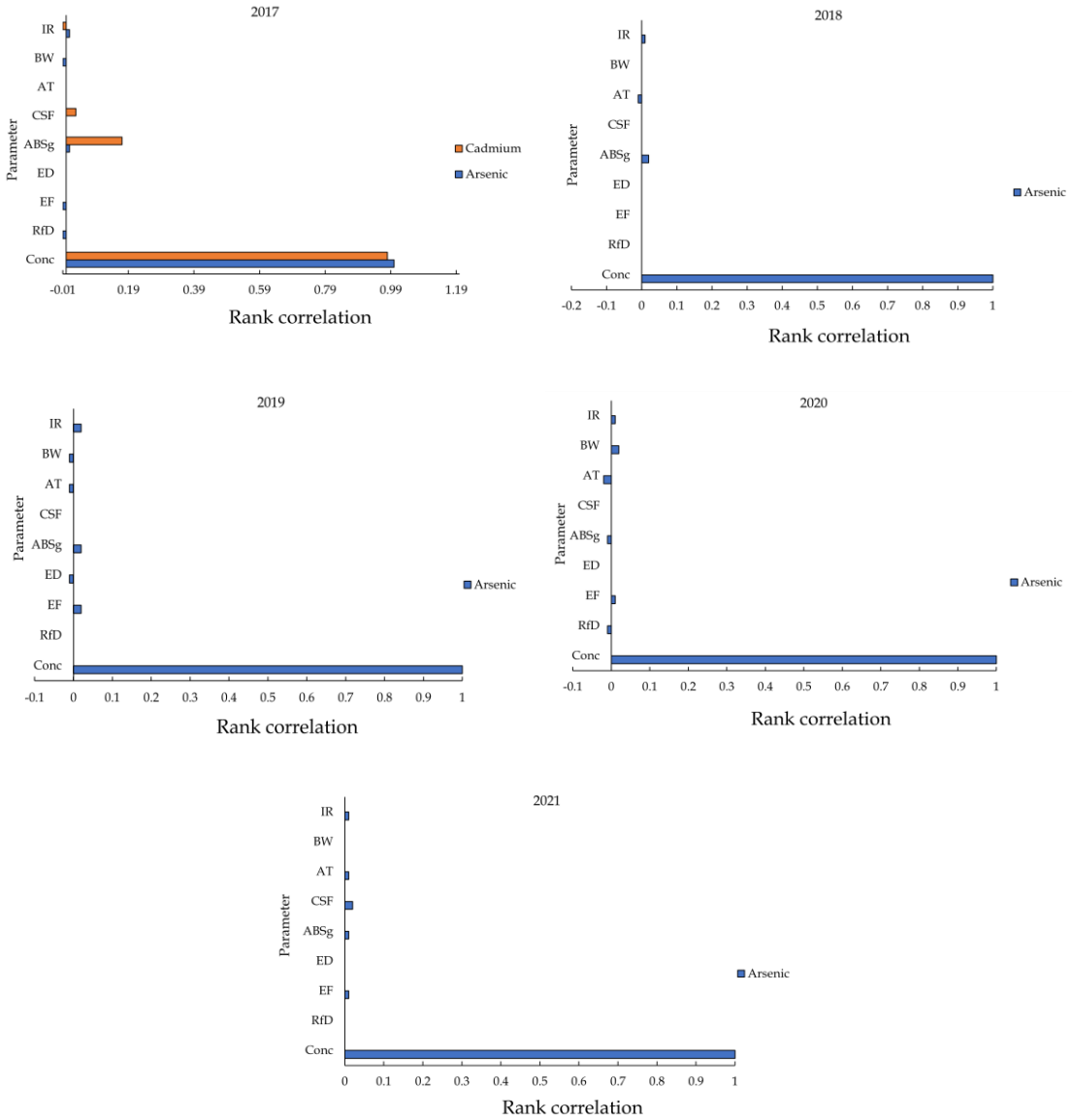


Figure 7 Sensitivity analysis result of As and Cd via ingestion route according to year

Sensitivity Analysis via Dermal Route

The sensitivity analysis results in Figure 8 indicate that the most significant parameter for arsenic (As) in 2017 was the concentration of heavy metals in water, with a value of 0.83. The parameter that significantly impacted Cd in 2017 was CF with a value of 0.56. The CF and the K_p both recorded the same value (0.56) in 2017 for As, CF is more significant than the K_p for Cd. CF parameter was analysed as a first ranked in 2018 to 2021 for As with values at 0.62, 0.70, 0.55, and 0.63, respectively. Meanwhile, the concentration value for Cd is below the detection limit (< 0.001 mg/L) during this period, hence the result of the sensitivity analysis was not estimated.

Sensitivity analysis was conducted to determine the most influential variable on the estimated risk. It is expected that the concentration of heavy metals in water is the most significant parameter reflected in the result of sensitivity analysis through the oral route. It reveals that toxic pollutants even at low concentrations can harm humans and deteriorate water quality. However, dermal uptake shows inverse results in which the CF had the highest impact except for As in 2017 which reported high heavy metal concentration as the most influential parameter.

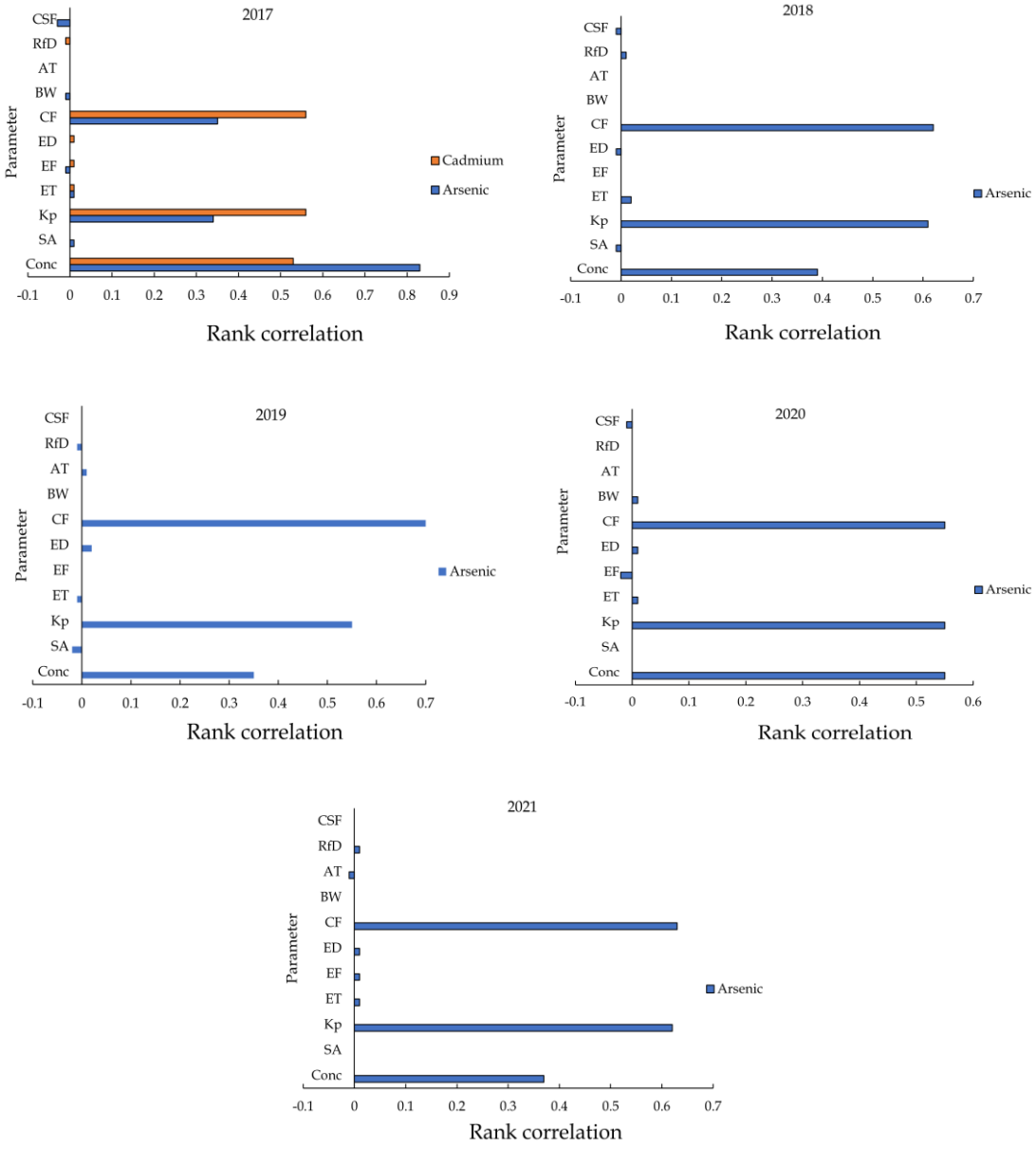


Figure 8 Sensitivity analysis result of As and Cd via dermal route according to year

CONCLUSION

LCR estimation indicated that Cd and As are the significant pollutants in the Kuantan River basin since they can increase the possibility of developing cancer in humans. These findings are crucial for both the environment and public health, highlighting the need for collaboration between the Department of Environment (DOE) and Ministry of Health (MOH) to mitigate heavy metal contamination. Strategic measures, increased monitoring, and public awareness campaigns are necessary to ensure water quality, especially for Kuantan's population, safeguarding their well-being and the aquatic ecosystem's sustainability.

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ANALYSIS OF PLANT INGREDIENTS IN REMEDIAL FORMULATIONS OF MALARIA IN MALAY MEDICAL MANUSCRIPTS

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ABSTRACT

Introduction: Malaria is an infectious disease caused by *Plasmodium* spp. The main treatment is artemisinin which was discovered after a massive study on Chinese medical manuscripts. However, artemisinin monotherapy is now challenged by antimalarial drug resistance and there are issues of relapse and failure when using artemisinin-based combination therapy (ACTs). Interestingly, traditional Malay medicine also provides numerous remedies to treat malaria, of which can be obtained from Malay medical manuscripts (MMM). Hence, this study aims to extract and analyse the formulations in MMM. **Methods:** Several terms referring to malaria were scanned throughout 10 MMM. The formulations were then extracted, and the ingredients were identified and compared to contemporary studies. **Results:** A total of 17 formulations were identified, comprising of 37 ingredients. Twenty-five of them were plant-based ingredients and were further analysed. The analysis revealed that 10 of the ingredients have been empirically demonstrated to possess pharmacological actions against malaria such as *Alpinia galanga, Syzygium aromaticum* and *Myristica fragrans*. Those plants had been shown to eliminate *Plasmodium* spp. in in vitro or in vivo experiments. Thirteen of the ingredients had been shown to have pharmacological actions that help relieve symptoms of malaria such as *Tabernaemontana corymbosa* that has anti-pyretic effect while the other two ingredients have not been reported in pharmacological studies. **Conclusion:** In short, the formulations mentioned in MMM have potential to be developed into accessible and affordable alternative malaria treatments due to its inhibitory and anti-plasmodial activity against *Plasmodium spp.*

KEYWORDS: Malay medical manuscript, malaria, *demam kura*, *Plasmodium*

INTRODUCTION

Malay manuscripts are written documents that originate from the Malay Archipelago that show information found by the populace in the past. The majority of the text has been passed down through the centuries and covers various disciplines including literature, medicine, religious texts, laws and legislation, and history. The Malay Archipelago is rich with its own knowledge of traditional medicine and it is recorded in the Malay medical manuscripts (MMM). Malay medical manuscripts are manuscripts containing information on medicinal practices and knowledge from the Malay Archipelago population that can be dated back to the 16th to the 18th century (Mohd Shafri, 2018a). In Malaysia, National Library of Malaysia has the highest collection of Malay manuscripts with approximately 4,884 copies as of in 2018 (National Library of Malaysia, 2018) and more than 100 copies are MMM (Mohd Shafri et al., 2021a).

Malay traditional medicine has the possibility to be a developed and recognised pharmacopeia considering that there is a significant number of MMM available. The current generation in Southeast Asia should be proud and make efforts to retrieve the valuable knowledge contained in MMM. Currently there are a few studies that have been done on the medical texts such as the works of Maidin & Mamat (2014), Mat Piah (2015) and Mohd Shafri (2021b). In MMM, various diseases are mentioned such as typhoid fever, tuberculosis, sinus, psoriasis and malaria.

Malaria is a disease that is frequently mentioned in MMM and it is still prevalent in hyper endemic countries. The disease is still considered as one of the most infectious vector-borne diseases worldwide caused by the parasitic *Plasmodium* protozoa and transmitted by the bites of female *Anopheles* mosquitoes (Talapko et al., 2019). It can present in complicated presentations that can progress to death within days or even hours (Buck & Finnigan, 2021). The discovery of artemisinin from *Artemisia Annua* tree that was recorded in a medical manuscript in 2nd Century BC China by Tu Youyou has led to development of antimalarial drug. The use of artemisinin in combination therapy, the Artemisinin-Combination Therapy (ACT), give rise to malarial treatment that could efficiently eliminate the *Plasmodium* parasite (Tse et al., 2019). However, due to the reports of treatment failure and the increasing antimalarial resistance such as the case reported in the Great Mekong (World Health Organization, 2021), there are initiatives for researchers to find another approach in combating antimalarial infection. Therefore, the objective of the study is to gather remedial formulations for malaria disease from MMM and conduct a comparative analysis with the contemporary studies on the herbs extracted from the MMM to identify the scientific evidence supporting the herbs' uses in treating Malaria.

METHODOLOGY

Selection of Manuscripts

The transliterated manuscripts were chosen if it contains any information on malaria. Keywords or term used for the screening of manuscripts are malaria, *demam kura, demam, hummā al-nāfid, humma al-thani, humma al-ghibb* or *hummā al-rib'* (Mohd. Shafri, 2018b).

Extraction & Classification of Data

The data extraction process was done by extracting information of several categorisation that include name of manuscripts, malaria term used in manuscripts, formulation number, formulation type, and materials from the formulation in the manuscripts.
Formulation number was assigned to formulations with no designated formulation number in the format of "YYYY.XX.YY", for which:

YYYY indicates the manuscript designated catalogue number.
XX indicates the order of the formulation was found in the manuscript.

YY indicates the page number the formulation was stated in the manuscript or transliterated book.

If there is no designated catalogue number, the first letter of the first and second words of the book title were utilised instead. Example of the first formulation number from the manuscript of *Rumah Ubat Di Pulau Penyengat* would be presented as RU.01.41. Plant-based materials from the formulations were further classified and scientific names were searched in various sources, i.e., Dewan Bahasa dan Pustaka (2017), Mat Piah & Mustapha (2019), Mamat et al. (2015), and online resources for botany, i.e., https://www.nparks.gov.sg/, https://mybis.gov.my/one/, and https://www.kew.org/.

Comparative Analysis of Manuscript Content

The extracted contents were analysed by comparing with contemporary studies on the treatment formulations and natural products. The search was carried out using Google Scholar using specific keywords. The keywords used for literature search were the scientific/vernacular name of plant, malaria, antimalaria, antimalarial resistance, *Plasmodium*, medicinal uses and pharmacology, any combination together with the use of Boolean operators, i.e., AND, OR, NOT.
The pharmacological actions that were screened in the studies to determine if a particular ingredient has any relation to treating malaria, are anti-plasmodial, antimalarial, anti-parasite, antioxidant and antipyretic. Any mention of treatment of fever and jaundice were also noted as symptoms reliever for malaria. If there was any scientific evidence in the literature in treating malaria, the article would be chosen for further reading.

RESULTS AND DISCUSSIONS

Malay medical manuscripts are the world heritage and not only the physical manuscript is valuable, what is more important is the content inside them. They can be sources for drug development especially in the current era where new diseases emerge and even some of the existing diseases are still not having effective treatment or at the risk of facing antimicrobial resistance. The latter is true for malaria where resistance is currently reported for the ART. Therefore, there is a need to look back into ancient medicine, specifically MMM, to find potential alternative treatment for malaria.

Selection of Manuscripts

Nine manuscripts and transliterated manuscripts were screened in the initial stage and only six contain the keywords and hence, were selected; *Al-Rahmah Fi al-Tibb wa al-Hikmah* (transliterated edition by Mohd Shafri & Muhammad Yahya, 2017), *Rumah Ubat Pulau Penyengat* (transliterated edition by Mohd Shafri, 2018a), *Tayyib al-Insan Fi Tibb al-Insan* (transliterated edition by Mohd Shafri, 2018b), *Kitab Tib* MSS 2515 (transliterated edition by Mat Piah & Baba, 2014), and *Warisan Perubatan Melayu* (transliterated edition by Ahmad, 2005) and MSS 4837 (unpublished).

Extraction of Data

From the transliterated manuscripts, 17 remedial formulations for malaria were extracted. The information extracted are the name of manuscripts, malaria term used in manuscripts, formulation number, formulation type, and materials from the formulation in the manuscripts. The extracted data is presented in the Table 1.

Table 1: Extracted information of Malaria formulations in Malay medical manuscript.

Manuscript	Term used in Manuscript (*Malay*/ English)	Formulation Number	Formulation (*Malay*/ English)	Materials (*Malay*/ English/ *Scientific name*)
MSS 4837	*Demam Kura* Spleen fever	4837.042.068	*Daun terung asam, Garam siam sedikit. giling lumat-lumat, perah, ambil airnya dan minum pagi sebelum basuh muka. Baiknya kita minum itu seruas jari manis kita. Buat demikian tiga pagi. Kalau muntah juga, jangan berhenti di dalam tiga pagi.* Borneo sour eggplant leaves, a little bit of Siamese salt, grind well, squeeze the paste to get the liquid part. Drink in the morning before washing the face. The best is to drink about one phalanx of our ring finger for three mornings. If the patient vomits, do not stop at least for three mornings.	*Daun terung asam* Borneo sour eggplant *Solanum lasiocarpum* *Garam siam* Siamese salt
MSS 2515	*Sehari demam sehari tiada sebab bertambah penyakit safrawi* Intermittent fever because increased *safrawi* disease.	2515.01.98	*Akan ubatnya minum air limau hantu dan sakar pagi belum makan nasi; maka ia muntah setelah itu maka makan tepung jerubah yang direndamkan dan tepung gandum yang direndamkan dengan sakar; maka makan tiga pagi; jika tiada baik maka makan pecahar yang menghilangkan penyakit itu; maka afiat.* The remedy is to drink the squeezed juice of key lime and sugar in the morning before eating rice. After the patient vomits, then eat rice flour and wheat flour that have been soaked with sugar. Eat it for three mornings. If there is no improvement, then eat the laxative that will remove the disease. Then you will recover.	*Air limau hantu* Key lime squeeze *Citrus aurantiifolia* *Sakar* Sugar *Tepung jerubah* Rice flour *Oryza sativa* *Tepung gandum* Wheat flour *Triticum spp.* *Pecahar* Laxative
Al-Rahmah fi al-Tibb wa al-Hikmah	*Humma Al-ghabb* Tertian fever	AF.01.171	*Diminum air buah limo, ertinya air buah mentul daripada sukkar pada pagi- pagi qadar tiga hari. Tiap kali diminum akan dimuntah akan dia. Bermula makanan tatkala dimakan ubat ini roti tepung jagung dan sukkar, dan roti tepung gandum yang sudah terkhamir, dimakan dia dengan kuah daging anak hayam.* Drink key lime squeeze with sugar for about three mornings. The patient will vomit after every drink. At the beginning of the treatment, eat this formulation: bread	*Air buah limo mentul* Key lime *Citrus aurantifolia* *Sukkar* Sugar *Roti tepung jagung* Bread made from corn flour *Zea mays*

			made from corn flour and sugar, and bread made from fermented wheat flour, eat it with the gravy chick curry.	*Roti tepung gandum yang terkhamir* Bread made from fermented wheat flour *Triticum spp.*
				Kuah daging anak hayam Gravy of chick curry *Gallus gallus*
	Humma al-thani Intermittent fever (every 24 hours and subsides with a full body chill)	AF.02.172	*Cuka pagi-pagi, minum qadar three hari jua.* Vinegar in the morning, drink for around three days.	*Cuka* Vinegar
	Humma al-rib' Quartan fever	AF.03.173	*Air susu lembu atau kerbau yang baharu diperah dicampur dengan minyak sapi yang sudah ditanak dan air madu yang sudah ditanak hingga hilang kubohnya.* Take fresh cow or buffalo milk, mix with cooked ghee and honey water that has been cooked until the foam disappears.	*Air susu lembu* Cow milk
				Air susu kerbau Buffalo milk
				Minyak sapi Ghee
				Air madu Honey water
		AF.04.174	*Diminum minyak lenga yang baharu diperah pagi-pagi qadar tiga hari, dan tiap-tiap hari diminum qadar (teks hilang) wiqyah atau empat wiqyah nescaya hilang lerai.* Drink cold-pressed sesame oil for about three mornings. Drink it every day of the amount about (missing text) *wiqyah* or four *wiqyah*, then the fever will go away.	*Minyak lenga* Sesame oil *Sesamum indicum*
Rumah Ubat Di Pulau Penyengat	*Demam Kura* Spleen fever	RU.01.35	*Minyak halia. Satu camca minyak halia dan satu camca air panas.* Ginger oil. One tablespoon of ginger oil and and one tablespoon of hot water.	*Minyak halia* Ginger oil *Zingiber officinale*
		RU.02.41	*Rebus Qaranful (Cengkih). Bungkus direbus dengan air sejuk satu gelas setengah, bila susut setengah gelas angkat. Sejukkan, minum itu air pagi dengan petang.* Boil cloves. Wrap the cloves and boil with one and half cups of water until the water decreases to half a cup. Cool it down, drink it in the morning and evening.	*Cengkih* Clove *Syzygium aromaticum*

		RU.03.43	*Buah halia. Tiga butir pagi dan tiga butir petang.* Ginger *ma'jun.* Eat three *ma'jun* in the morning and evening.	*Ma'jun Halia* Ginger electuary *Zingiber officinale*
Tayyib al-Ihsan fi Tibb al-Insan	*Humma al-ghibb* Tertian fever	TA.01.145	*Diminum air limau lima (limau nipis) dengan sukkar pada pagi -pagi dan muntah ia dan makanannya sagun-sagun dhurah dan tepung gandum yang dimasamkan dan kuah anak ayam tiga hari maka jika tiada hilang maka hendaklah diminum pecahar (ubat pencuci perut) safra (hempedu).* Drink key lime squeeze with sugar in the morning and the patient will vomit. Then eat *sagun-sagun* (a type of delicacy) made from sorghum and made from fermented wheat flour and gravy of chick dish for three days. If there is no improvement, then drink laxative for *safra* (remedy for cleaning the bowel).	*Air limau nipis* Key lime squeeze *Citrus aurantiifolia* *Sukkar* Sugar *Dhurah* Sorghum *Sorghum bicolor* *Tepung gandum* Wheat flour *Triticum spp.* *Pecahar safra* Laxative for *safra*
		TA.02.146	*Minum air limau lima tujuh biji besar dengan sukkar bagi orang yang kuasa atas minumannya.* Drink the squeeze of approximately 5-7 big-sized key limes with sugar, only for those who can bear the formulations.	*Air limau* Key lime squeeze *Citrus aurantiifolia* *Sukkar* Sugar
	Humma al-thani Intermittent fever (every 24 hours and subsides with a full body chill)	TA.03.146	*Diminum cuka tiap-tiap hari pagi-pagi dan makanannya muzawwarat (makanan berasaskan tumbuh-tumbuhan untuk orang sakit, lebih mudah dihadam) tiga hari.* Drink vinegar every morning and the food is *muzawwarat* (vegetarian dishes for sick people, easier to digest) for three days.	*Cuka* Vinegar
	Humma al-rib Quartan fever	TA.04.147	*Diminum air susu lembu serta minyak sapi dan manisan lebah dan meninggal ia akan yang lainnya mujarrab.* Drink cow milk with ghee and honey and it will be significantly effective.	*Air susu lembu* Cow milk *Minyak sapi* Ghee *Manisan lebah* Honey
	Humma al-nafid	TA.05.147	*Muntah ia dengan cuka dan manisan lebah tiga hari atau tujuh hari pada pagi-pagi kemudian isti'mal ia akan sharab asali iaitu*	*Cuka* Vinegar

	Fever with symptoms of ague fit or fever paroxysm		*diambil manisan lebah yang suci daripada buihnya dan dibubuh di dalam tiap-tiap seratl daripadanya satu dirham mustaki dan satu dirham lada hitam dan satu dirham halia dan disejukkan dia dan diisti'malkan dia dan makanannya tepung gandum yang halus bersih dan kuah daging kibash yang dimasukkan dengan baharat.* Drink vinegar and honey for three or seven mornings and the patient will vomit. Then take pure honey without foam and place every one *ratl* of honey with one *dirham* of terebinth tree bark, one *dirham* of peppercorn, one *dirham* of ginger. Cooled it down and use it and eat it with fined wheat flour and sheep broth that has allspice mixed in with.	*Manisan lebah* Honey *Mustaki (getah kayu)* Terebinth tree bark *Terebinthe pistache* *Lada hitam* Black pepper *Piper nigrum* *Halia* Ginger *Zingiber officinale* *Tepung gandum* Wheat flour *Triticum spp.* *Daging kibash /kambing biri-biri* Sheep flesh *Baharat* Allspice - *Lada hitam, buah pelaga, kulit kayu manis, cengkih, ketumbar, jintan putih, buah pala, paprika* - Black pepper, cardamom, cinnamon, clove, coriander, cumin, nutmeg, paprika. - *Piper nigrum, Amomum spp., Cinnamon zeylanicum, Syzygium aromaticum, Corriandrum sativum, Foeniculum vulgare, Myristica fragrans, Capsicum annuum.*
Warisan Perubatan Melayu	*Demam Kura* Spleen fever	WP.01.27	*Ambil akar susun kelapa berat tiga timbang, lempoyang berat dua timbang, lengkuas berat setimbang, bawang putih berat setimbang, lada sulah berat setimbang, kapur batu berat setimbang, dan cabai berat setimbang; maka sekalian ramuan itu giling lumat-lumat dengan air limau nipis. Maka rebus dengan air tiga bahagi, beri tinggal sebahagi, hingga hendak*	*Akar susun kelapa* Rosebay root *Tabernaemontana corymbosa* *Lempoyang* Bitter ginger *Zingiber zerumbet*

	menghancurkan ubat yang digiling itu sekadar dapat diminum jua. Sudah itu ambil besi tiga bilah, bakar pada api; kemudian celupkan pada ubat itu yang sudah diisi dalam cawan. Beri minum orang sakit itu berulang-ulang. Take Rosebay root (three portions), bitter ginger (two), galangal (one), garlic (one), white pepper (one), limestone (one) and chilli pepper (one), grind everything into a paste with key lime squeeze. Boil with three parts of water until left with one part of the water and the formulation is dissolved and palatable to drink. Take three metal blade and heat it on fire, then dip the hot metal into the medicine mixture that has been filled into a cup.	*Lengkuas* Galangal *Alpinia galanga* *Bawang putih* Garlic *Allium sativum* *Lada sulah* White pepper *Piper nigrum* *Kapur batu* Limestone *Calcium carbonate* *Cabai* Chilli pepper *Capsicum frutescens* *Air limau nipis* Key lime squeeze *Citrus aurantiifolia*
WP.02.27	*Ambil buah lakum yang masak, makan sebiji-sebiji pagi petang setiap hari, selama tiga hari.* Take ripe threeleaf cayratia fruits, take one fruit in the morning and in the evening every day for three days.	*Buah lakum* Threeleaf cayratia *Cayratia trifolia*
WP.03.27	*Ambil daun keduduk segenggam erat, daun gandarusa segenggam erat, bawang putih seulas, dan lada tujuh butir; sekalian itu pipis lumat-lumat, airnya cuka; beri minum sebanyak dua ruas jari selama tiga pagi; hampasnya ditempelkan betul-betul pada tempat kura itu.* A handful of strait rhododendron's leaves, a handful of leaves of willow-leaved justicia, a clove of garlic, seven black peppers. Grind everything with vinegar. Drink an amount of about two phalanges for three mornings. Take the residual paste and fix it at the area of the swollen spleen.	*Daun keduduk* Stratis rhododendron *Melastoma malabathricum* *Daun gandarusa* Willow-leaved justicia *Justicia gendarussa* *Bawang putih* Garlic *Allium sativum* *Lada* Black pepper *Piper nigrum* *Cuka* Vinegar

Classification of Data

Thirty-seven materials were identified from the extracted remedial formulations, of which 25 are plant-based materials. These materials are tabulated in Table 2. The table also includes the scientific names, plant parts used in the formulations, formulation number, and the frequency of mentions in manuscripts and formulations. The results show that key lime has been frequented the most in terms of number of manuscripts (four mentions) followed by clove, ginger, black/white pepper and wheat flour (two each). Key lime is also the most repeated ingredient in terms of number of formulations (five times) and followed by black/white pepper (four); ginger and wheat flour (3 each), and garlic and clove (two each).

Table 2: List of Identified Plant-Based Materials.

Plant Name	Scientific Name	Parts of Materials Used	Formulation Number	Frequency	
				Manuscript	Formulation
Air limau nipis, Air limau hantu	*Citrus aurantiifolia*	Fruit/ Juice	2515.01.98, AF.01.171, TA.01.145, TA.02.146, WP.01.27	4	5
Akar susun kelapa	*Tabernaemontana corymbosa*	Root	WP.01.27	1	1
Bawang putih	*Allium sativum*	Bulb	WP.01.27	1	2
Biji jintan	*Foeniculum vulgare*	Seeds	TA.05.147	1	1
Buah keduduk	*Melastoma mala-bathricum*	Leaf	WP.03.27	1	1
Buah lakum	*Cayratia trifolia*	Fruit	WP.02.27	1	1
Buah pala	*Myristica fragrans*	Seeds	TA.05.147	1	1
Buah pelaga	*Amomum spp.*	Seeds	TA.05.147	1	1
Cabai	*Capsicum frutescens*	Fruit	WP.01.27	1	1
Cengkih	*Syzygium aromaticum*	Flower	RU.02.41, TA.05.147	2	2
Daun gandarusa	*Justicia gendarussa*	Leaf	WP.03.27	1	1
Daun terung asam	*Solanum lasiocarpum.*	Leaf	4837.042.068	1	1
Dhurah	*Sorghum bicolor*	Seeds/ Grain	TA.01.145	1	1
Halia	*Zingiber officinale*	Not specified – Possibly Rhizome, Oil	TA.05.147, RU.01.35, RU.03.43	2	3
Ketumbar	*Corriandrum sativum*	Seeds	TA.05.147	1	1
Kulit kayu manis	*Cinnamon zeylanicum*	Bark	TA.05.147	1	1

Lada, Lada hitam, Lada sulah	*Piper nigrum*	Seeds	TA.05.147	2	4
Lempoyang	*Zingiber zerumbet*	Fruit	WP.01.27	1	1
Lengkuas	*Alpinia galanga*	Fruit	WP.01.27	1	1
Minyak lenga	*Sesamum indicum*	Oil	AF.04.174	1	1
Mustaki (getah kayu)	*Terebinthe pistache*	Wood latex/ resin	TA.05.147	1	1
Paprika	*Capsicum annuum*	Fruits	TA.05.147	1	1
Roti tepung jagung	*Zea mays*	Root	AF.01.171	1	1
Tepung gandum	*Triticum spp.*	Grain	TA.01.145, TA.05.147, 2515.01.98,	2	3
Tepung jerubah	*Oryza sativa*	Grain	2515.01.98	1	1

Comparative Analysis

Comparative analysis was performed by comparing the plant-based materia medica from the remedial formulations with contemporary scientific literature. The analysis shows that 11 or 44% of the plants-based materials play significant roles in relation to reduce, eradicate or manage the malaria infections in patients while 12 either have antipyretic and/or antioxidant pharmacological properties that can help reduce the symptoms, and 2 did not have any scientific evidence. The comparative analysis is presented in Table 3.

Table 3: Table of Comparative Analysis of Plant-based Materials.

Formulation Number	Vernacular Name	Scientific Name	Scientific Literature Evidence
TA.05.147	Cinnamon bark (*Kulit kayu manis*)	*Cinnamomum zeylanicum*	Antiparasitic effect by inhibition of heme bio-crystallization (Attieh et al., 2015) and enoyl-ACP reductase anzyme activity (Nkanwen et al., 2013).
TA.05.147, RU.01.35, RU.03.43	Ginger (*Halia*)	*Zingiber officinale*	Exhibit inhibitory effects on the malarial parasite's replication. (Biruksew et al., 2018).
WP.01.27	Garlic (*Bawang putih*)	*Allium sativum*	Contain allicin that inhibits the CAC1 cysteine proteases falcipain 2, rhodesain, cathepsin B and L in the low micromolar range. Potent antiparasitic activity (Coppi et al., 2006).
WP.01.27	Galangal (*Lengkuas*)	*Alpinia galanga*	Contain anti-plasmodial components and antioxidant activity that contribute to the antimalarial activity (Al-Adhroey et al., 2010).
TA.05.147	Nutmeg (*Buah pala*)	*Myristica fragrans*	Exhibit antioxidant properties. Potent antimalarial activity against *Plasmodium.* (Thiengsusuk et al., 2013)
TA.05.147	Cardamom (*Buah pelaga*)	*Amomum spp.*	Contain terpene endoperoxide, specifically cardamom peroxide, which exhibited strong inhibition of *Plasmodium falciparum.* (Hu et al., 2018)
WP.01.27	Chilli Pepper (*Cabai*)	*Capsicum frutescens*	Anti-plasmodial and antioxidant activity (Habte & Assefa, 2020).
RU.02.41, TA.05.147	Clove (*Cengkih*)	*Syzygium aromaticum*	Inhibitory effects against *P. falciparum* (Batiha et al., 2020a, Dantata & Hotoro, 2020).
TA.05.147	Black pepper/ peppercorn (*Lada hitam*)	*Piper nigrum*	Antimalarial Activity of Piperine cause changes in parasite morphology (Thiengsusuk et al., 2018).
WP.01.27	Bitter Ginger (*Lempoyang*)	*Zingiber zerumbet*	Antimalarial activity and cytotoxicity by inhibiting *Plasmodium* propagation (Sriphana et al., 2013, Yob, et al., 2010).
WP.02.27	Threeleaf cayratia (*Buah lakum*)	*Cayratia trifolia*	Antimalarial activity on *P. berghei* (Alkandahri et al., 2020)

2515.01.98, AF.01.171, TA.01.145, TA.02.146, WP.01.27	Key lime (*Limau nipis,*)	*Citrus aurantiifolia*	Enhance malarial clearance but does not have antimalarial effect on its own. (Adegoke et al., 2011; Shija et al., 2020).
WP.03.27	Willow-leave Justica (*Daun gandarusa*)	*Justicia gendarussa*	No study on anti-plasmodial activity found. Relieves fever and contain high antioxidant properties (Shinwari et al., 2020).
WP.01.27	Great Rosebay (*Akar susun kelapa*)	*Tabernaemontana corymbosa*	No study on anti-plasmodial activity found but have antiparasitic properties. Treat ailments such as fever, and jaundice (Abubakar & Loh, 2016).
4837.042.068	Borneo sour eggplant (*Daun terung asam*)	*Solanum lasiocarpum.*	No study on anti-plasmodial activity found. Contain high antioxidant activity (Soon & Ding, 2021).
TA.01.145	Grain sorghum (*Dhurah*)	*Sorghum bicolor*	No study on anti-plasmodial activity found.
WP.03.27	Straits Rhododendron (*Buah keduduk*)	*Melastoma malabathricum*	No study on anti-plasmodial activity found. Relieve fever and have antioxidant properties (Joffry et al., 2012).
TA.05.147	Cumin/ fennel seeds (*Biji jintan*)	*Foeniculum vulgare*	No study on anti-plasmodial activity found. Antipyretic and antioxidant properties (Badgujar et al., 2014).
AF.04.174	Sesame oil (*Minyak lenga*)	*Sesamum indicum*	No study on anti-plasmodial activity found. Sesamol contain anti-inflammatory and antioxidant properties (Wu et al., 2019).
TA.05.147	Terebinth tree (*Mustaki*)	*Terebinthe pistache*	No study on anti-plasmodial activity found. Compounds in resin used to treat fever due to its antipyretic activity (Bozorgi, et al., 2013).
TA.05.147	Cayenne (*Paprika*)	*Capsicum annuum*	No study on anti-plasmodial activity found. Capsicum has antioxidant properties (Batiha et al., 2020b, Sanati et al., 2018).
AF.01.171	Corn flour (*Tepung jagung*)	*Zea mays*	No study on anti-plasmodial activity found. Contains highly antioxidant secondary metabolites (Okokon et al., 2017).
TA.01.145, TA.05.147, 2515.01.98,	Wheat (*Tepung gandum*)	*Triticum spp.*	Not found
2515.01.98	Fermented Rice Flour (*Tepung jerubah*)	*Oryza sativa*	Not found

In a study by Al-Adhroey et al. (2010), the extract of *A. galanga* rhizome was demonstrated to suppress the activity of early infection of *Plasmodium* parasite and cure the infected mice up to 65-67% effectiveness at a dose of 400 mg/kg when compared to the negative control. It is postulated the antiplasmodial activity is contributed by terpenoid and flavonoid. Meanwhile, Thiengsusuk et al. (2018) reported that the exposure of piperine (alkaloid that can be found in *P. nigrum*) to *P. falciparum* in vitro showed a morphological change of the parasite that affects and slows down its growth until it undergoes death after eight-hour exposure. Other than that, *M. fragrans* was reported by the same research group, Thiengsusuk et al. (2013), to exhibit potent antimalarial activity in an in vitro experiment using parasite culture, with an IC_{50} of less than 10 mg/ml.

As for *Amomum spp.*, Hu et al. (2018) mentioned that cardamom contains cardamom peroxide which is a terpene endoperoxide that exhibits a strong inhibitory activity towards *P. falciparum*, however the pharmacological mechanism is unclear. Besides, Habte & Assefa (2020) revealed that *C. frutescens* extract suppresses the percentage of parasitaemia in infected up to 93.29% when. On the other hand, *S. aromaticum* was shown to possess inhibitory effect on *P. falciparum* at 50 mg/ml concentration (Dantata & Hatoro (2020). *Z. officinale* or ginger has been revealed by Biruksew et al. (2018) that its extract displays a notable chemo-suppression and suggested that it has an inhibitory effect on *Plasmodium* parasite replication, which may be due to the evenly spread active compounds found in the ginger extracts.

As for cinnamon, Nkanwen et al. (2013) discovered that the dicholomethane/methanol extract can inhibit the activity of *P. falciparum* enoyl-ACP reductase enzyme in vitro up to 33%. The enzyme is found in the parasite and it synthesises fatty acids which are crucial for membrane formation and survival. By inhibiting the enzyme, it may inhibit the growth of the parasite. Apart from that, the invasion of the parasite causes haemolysis, releasing free iron that is toxic towards *Plasmodium*. The parasite avoids this by detoxifying the free iron by bio-crystallisation into β-hematin. Hence, the inhibition of hematin bio-crystallisation by cinnamon water may result in toxicity to the parasite and this action is similar to chloroquine (Attieh et al., 2015).

Z. zerumbet essential oil contains a bioactive compound called zerumbone (Yob et al., 2011). Based on the study done by Sriphana et al. (2012), zerumbone was shown to exhibit antimalarial activity against *P. falciparum*. However, it also shows a high cytotoxicity towards cancer cell line. Thus, zerumbone could cause harm towards the human cells but the compound shows a potential alternative antimalarial drug. Lastly, *A. sativum* extract contains a compound allicin that is produced when the cloves is crushed. Coppi et al. (2006) reported that allicin is a cysteine protein inhibitor which can inhibit the erythrocytic stage and sporozoites invasions of the *Plasmodium*, which subsequently decreases parasitaemia. Based on the previous contemporary studies on these 11 plants and frequency of mentions of the ingredients, these four plants shall be prioritised in the effort of searching for potential therapeutic plants for malaria. They are ginger (mentioned in two manuscripts and three formulations), garlic (one manuscript and two formulations), clove (two manuscripts and two formulations), and black/white pepper (2 manuscripts and four formulations)

From the 25 plant-based material identified, 56% or 14 of the materials were found to not have any literature evidence on its pharmacological actions against the parasite. However, this does not mean the plant's medicinal values is dismissed. This may be attributed to low priority, low interest or lack of awareness regarding the plant. Further research should be done on the plant's pharmacological action against the *Plasmodium* parasite to ascertain whether it will truly aid in treating patients with malaria. In addition, not all materials in a formulation can be assumed to have therapeutic effects towards malaria. In modern pharmacology, some excipients are added with active ingredient to make a dosage form. Similarly, some materials in the formulations function as stabilisers for the formulation, e.g., lime juice maybe added to control the pH, sugar maybe added to mask bitter or sour taste, and flour maybe added to increase viscosity of a formulation.

Despite the lack of scientific literature evidence of not possessing any anti-plasmodial activity, 12 out of 25 plant-based materials were observed to have antioxidant properties and/or antipyretic properties. The plants stated to have antioxidant properties in literature were implied to have anti-plasmodial

activity as it can counteract the oxidative damages caused by the parasite (Builders et al., 2014). Meanwhile antipyretics are properties that can help to relieve fever, which is a clinical manifestation of malaria (Buck & Finnigan, 2021).

CONCLUSION

Malaria is a disease that has existed in the Malay Archipelago since the 16th century. In several Malay medical manuscripts, the remedial formulations for antimalarial drugs used during the olden times were able to be found. Seventeen formulations of remedies with 37 unique materials were extracted from the manuscripts and compared to contemporary literature. Eleven have supportive evidence while 14 are yet to be researched with regards to their scientific evidence of their antimalarial use. The plants that have the most potential to be developed for antimalaria are *Z. officinale*, *A. sativum*, *S. aromaticum*, and *P. nigrum*.

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KNOWLEDGE, ATTITUDE AND PRACTICE ABOUT SKIN CANCER AND ITS PREVENTION AMONG IIUM KUANTAN UNDERGRADUATE STUDENTS

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ABSTRACT

Introduction: The worldwide incidence of skin cancer has been rising for the past decades that at least two million of non-melanomas and 100,000 of melanomas occur every year. In Malaysia, there are 212 deaths related to skin cancer that were reported in 2018. Skin cancer is mainly caused by the exposure to ultraviolet light that most undergraduate students in IIUM Kuantan are exposed to as they commute to teaching and learning venue. The Malaysian Meteorological Department reported that the east coast region receives 50% sunny weather yearly as compared to other parts of Malaysia. Hence, the main objective of this research was to assess the level of knowledge, attitude and practice about skin cancer and its prevention among IIUM Kuantan undergraduate students. **Methods:** A cross-sectional study using convenience sampling method was conducted to collect data from 129 respondents. The questionnaire was adapted and modified before being distributed through Google form to the participants. **Results:** Overall, the level of knowledge, attitude and practice about skin cancer and its prevention among IIUM Kuantan undergraduate students was moderate. Mann-Whitney test and Kruskal-Wallis test performed revealed a significant association of level of knowledge between gender ($p = 0.020$) and exposure to direct sunlight ($p = 0.050$). Similarly, a significant association was observed in attitude as well as practice of skin cancer prevention between gender ($p<0.001$). Spearman correlation showed a positive correlation between knowledge and attitude and attitude and practice about skin cancer and its prevention. **Conclusion:** IIUM Kuantan undergraduate students have a moderate level for knowledge, attitude and practice about skin cancer and its prevention. There was an association of level of knowledge with gender and exposure to direct sunlight. However, only gender associate with the level of attitude and practice. This study found a positive correlation between knowledge and attitude and attitude and practice. This research is expected to provide more insight into overall awareness regarding skin cancer among the IIUM Kuantan undergraduate students which might serve as a benchmark for more related research in the future.

KEYWORDS: skin cancer, knowledge, attitude, practice, Malaysia

INTRODUCTION

Skin cancer does not receive a lot of attention like other types of cancers. In the past decades, the worldwide incidence of skin cancer has shown a rising trend, and it is estimated that between 2-3 million non-melanomas and approximately 132,000 melanomas occur every year (*World Health Organization*, 2017). In 2003-2005, Malaysia National Cancer Registry Report reported that skin cancer is the tenth common type of cancers in Malaysia which represent about 2.6% of all cancer cases while prostate gland cancer ranked ninth (National Cancer Registry Report, 2019). However, it is believed that this data is poorly reported because according to Dermatology Clinic, Hospital Kuala Lumpur in its reports from 2006-2014 revealed that basal cell carcinoma is the highest reported skin cancer case which is about 34.9% of cases (Mohd Affandi, 2021). Nevertheless, recent data published in 2018 by WHO reported that about 212 of total deaths related to skin cancers in Malaysia.

Malaysia was one of the countries that was mostly sunny and receives 2200 hours of sun per year. The Malaysian pose a high risk of developing skin cancer especially in the east coast region of Malaysia that receives on average 2530 hours of sun per year (Al-Naggar, 2013). According to the Malaysian Meteorological Department (*Weather Atlas*, n.d.), Kuantan, which is the main city of Pahang on the east coast, receives on average 3.6 hours to 9.7 hours of sunshine per day in a year, while the UV index throughout the year is between 11 to 12. The UV index "indicate the amount of skin-damaging UV rays reaching the Earth's surface during the day" (*Ultraviolet (UV) radiation*, 2019), which the value of more than 6 is considered as high and protection against the sun is needed. The annual average of high temperature was reported between 28.9 ^{o}C to 32.8 ^{o}C. Therefore, this present study is aimed at conducting assessment on knowledge, attitude, and practice regarding skin cancer and its prevention among the undergraduate students of one of the universities in Kuantan, Pahang, which is in the east coast region of Malaysia.

International Islamic University Malaysia (IIUM) Kuantan is a public university located in Kuantan, Pahang. It consists of six kulliyyah which are Kulliyyah of Allied Health Sciences (KAHS), Kulliyyah of Medicine (KOM), Kulliyyah of Pharmacy (KOP), Kulliyyah of Nursing (KON), Kulliyyah of Dentistry (KOD), and Kulliyyah of Science (KOS). Approximately, there are more than 3000 students in the IIUM Kuantan which includes undergraduate and postgraduate students. Kuantan is the capital state of Pahang located on the east coast of Peninsular Malaysia. The majority of IIUM Kuantan students study sciences, allied health, pharmacy, dentistry, nursing, and medicine. They regularly traveled to class under direct sun by means of walking and riding motorcycles as well as participated in many outdoor activities. Hence, this research is expected to provide more insight into overall awareness regarding skin cancer among the IIUM Kuantan undergraduate students in terms of their knowledge, attitude, and practice of its prevention, which might serve as a benchmark for more related research in the future.

MATERIAL AND METHODS

Study Design and Area

A quantitative based cross-sectional study was conducted using an online survey to assess the level of knowledge, attitude and practice of skin cancer and its prevention among IIUM Kuantan undergraduate students. Google form was distributed among IIUM Kuantan undergraduate students to collect the data from the respondents. The study was conducted from October 2021 until May 2022.

Sample Size

A single proportion formula was used to determine the sample size. The sample size was calculated with 0.09 precision, 95% Confidence Interval and 50% population with good knowledge level toward skin cancer.

Sample size, $n = (\frac{Z\alpha/2}{\Delta})^2 \, p(1-p)$

$Z_{\alpha/2} = 1.96$ (for 95% Confidence Interval (CI))

p = estimate 50% of population with good knowledge level, 0.5

Δ = level of precision, 0.09

Sample size calculation:

$n = (\frac{1.96}{0.09})^2 \, 0.5(1-0.5)$

$= 119 + 10\%$ (non-response rate)

$= 129$

Approximately 10% of respondents were expected to drop out from the study, thus, the minimum required sample size for this study was 129.

Sampling Method

A non-random convenience sampling was employed to recruit the subjects for this study. This method was chosen to recruit the subjects which were among IIUM Kuantan undergraduate students who were willing to answer the survey. In addition, this method is affordable, easy and less time consuming. Due to time constraints, convenience sampling method can help to collect data in a short time.

Inclusion Criteria

All male and female undergraduate students of IIUM Kuantan from year 1 to year 5.

Exclusion Criteria

Students who cannot read and understand English were excluded from the study as the questionnaire was designed in English only. Besides, postgraduate students were excluded from this study.

Data Collection

The data was collected from 17th March 2022 until 23rd April 2022 through Google form that was distributed to the Year 1 until Year 5 students of IIUM Kuantan from all kulliyyah. Consent form has been obtained at the beginning of the online survey.

Questionnaire and Pilot Study

In this study, the questionnaire was adapted and modified from previous published studies (Alamri et al., 2015; Al-Naggar, 2013; Nguyen et al., 2020; Pinos-León et al., 2021) to fit the suitability of the IIUM Kuantan students. The first section of the questionnaire comprises of demographic information, whereas the second section covered on knowledge about skin cancer and its prevention with total of 16 items that covers question regarding the type, risk factors and preventive measures of skin cancer. This section included

questions with 'Yes', 'No', and 'Maybe' options. One mark was given to correct answer and zero mark was given to false and unsure answers. The third section was on attitude towards skin cancer and its prevention. Five-point Likert's scale was used for this section which consists of 'Strongly Disagree', 'Disagree', 'Neutral', 'Agree', and 'Strongly Agree'. Each response was graded from one to five, starting from Strongly Disagree to Strongly Agree. However, for negative statements, the score was reversed. The fourth section was regarding the practice of skin cancer prevention. This section was assessed using a four-point Likert scale which are 'Never', 'Rarely', 'Sometimes', and 'Always'. The marks for each option were graded from one to four, starting from Never to Always. Then, a pilot study was done among 15 respondents. The purpose of the pilot study was to test the reliability of the questionnaire. Internal consistency of the questionnaire was determined by looking at Cronbach's alpha value. The value of more than 0.7 is considered as reliable. The items were analyzed using Statistical Package for Social Sciences (SPSS) version 26.

Data Analysis

Descriptive frequency was used to identify the level of knowledge, attitude and practice about skin cancer and its prevention among IIUM undergraduate students. While Mann-Whitney U test and Kruskal-Wallis test were used to investigate the association between the demographic information such as age, gender, year of study, kulliyyah, family income and duration of exposure to sunlight per day with the level of knowledge, attitude and practice about skin cancer and its prevention. Spearman correlation was used to evaluate the correlation between the level of knowledge, attitude and practice about skin cancer and its prevention among IIUM Kuantan undergraduate students.

RESULTS AND DISCUSSIONS

Sociodemographic Characteristics of Respondents

A total of 129 undergraduate students of IIUM Kuantan participated in this study. There were six sociodemographic characteristics which include gender, age, kulliyyah, year, family's income, and exposure to direct sunlight per day, which were tabulated in Table 1 in terms of their frequency and percentage. The female respondent was more than male with 76% and 24% respectively. Majority of respondent is 19-21 years old (51.2%). All six kulliyyah responded to the survey but most of the respondent was from Kuliyyah of Allied Health sciences (40.3%). The student of year 3 was the the highest that responded to the survey followed by year 2 and year 1 with 32.6%, 31% and 23.2% respectively. Nevertheless, 48.8% of respondent receive 20-30 minute whereas 34.9% of them receive more than 40 minutes of exposure to the sunlight.

Table 1 Sociodemographic data of the respondents (n = 129)

Sociodemographic Characteristics	Frequency	Percentage (%)
Gender		
Male	31	24.0
Female	**98**	**76.0**
Age		
19 – 21 years old	**66**	**51.2**
22 – 24 years old	59	45.7
25 – 27 years old	4	3.1

Kulliyyah		
Kulliyyah of Allied Health Sciences	**52**	**40.3**
Kulliyyah of Dentistry	8	6.2
Kulliyyah of Medicine	14	10.9
Kulliyyah of Nursing	19	14.7
Kulliyyah of Pharmacy	20	15.5
Kulliyyah of Sciences	16	12.4
Year		
Year 1	30	23.2
Year 2	40	31.0
Year 3	**42**	**32.6**
Year 4	15	11.6
Year 5	2	1.6
Exposure to direct sunlight per day		
Less than 10 minutes	21	16.3
20 - 30 minutes	**63**	**48.8**
More than 40 minutes	45	34.9

Note: The total of the highest frequency from each category is highlighted in bold.

Scores for Knowledge, Attitude and Practice about Skin Cancer and its Prevention

Table 2 depicts the categories of score for knowledge, attitude, and practices along with their frequency and percentage. The result shows that the knowledge, attitude and practice about skin cancer and its prevention among IIUM Kuantan undergraduate students were moderate. From the table, more than half of the respondents possessed a moderate knowledge score (n = 70, 54.2%). For the attitude section, most of the respondents obtained a moderate score (n = 78, 60.5%). Lastly, for the practice section, only twelve percent of them achieve a good practice score (n = 16, 12.4 %).

Table 2: Categories of score for knowledge, attitude and practice about skin cancer and its prevention (n = 129)

Categories	Frequency	Percentage (%)
Knowledge		
Poor	25	19.4
Moderate	**70**	**54.2**
Good	34	26.4
Attitude		
Poor	8	6.2
Moderate	**78**	**60.5**
Good	43	33.3
Practice		
Poor	37	28.7
Moderate	**76**	**58.9**
Good	16	12.4

Note: The total of the highest frequency for each category is highlighted in bold.

Level of Knowledge about Skin Cancer and its Prevention

Table 3 illustrates the distribution of knowledge about skin cancer and its prevention. Most of the respondents answered correctly for most of the questions. However, there were only three questions that have the highest frequency of 'Not sure' option which were questions number 13, 14 and 15.

Table 3: Distribution of knowledge about skin cancer and its prevention (n = 129)

Statement	True freq. (%)	False freq. (%)	Not sure freq. (%)
1. Ultraviolet rays from sun cause sun tan.	**93 (72.1)**	1 (0.8)	35 (27.1)
2. Sun exposure can cause freckles.	**88 (68.2)**	15 (11.6)	26 (20.2)
3. Sun exposure can cause wrinkles on face.	**91 (70.5)**	11 (8.5)	27 (20.9)
4. Sun exposure can cause skin cancer.	**121 (93.8)**	2 (1.6)	6 (4.7)
5. Sun exposure can cause dry skin.	**116 (89.9)**	6 (4.7)	7 (5.4)
6. Sun exposure can cause aging.	**98 (76.0)**	7 (5.4)	24 (18.6)
7. Sun exposure can cause spots.	**97 (75.2)**	6 (4.7)	26 (20.2)
8. Sun is harmful to dark skin compared to fair skin. #	2 (1.6)	**114 (88.4)**	13 (10.1)
9. Sun is harmful to fair skin compared to dark skin.	**107 (82.9)**	8 (6.2)	14 (10.9)
10. Sunscreen do not protect from ultraviolet radiation. #	3 (2.3)	**109 (84.5)**	17 (13.2)
11. Melanoma is the most dangerous type of skin cancer.	**63 (48.8)**	8 (6.2)	58 (45.0)
12. Severe sunburns during childhood does not increase the chance of getting skin cancer. #	13 (10.1)	**60 (46.5)**	56 (43.4)
13. The number of moles of a person has is an important risk factor for developing melanoma.	42 (32.6)	26 (20.2)	**61 (47.3)**
14. There are two main types of skin cancer: melanoma and non-melanoma.	55 (42.6)	8 (6.2)	**66 (51.2)**
15. Skin cancer is common in Malaysia. #	26 (20.2)	48 (37.2)	**55 (42.6)**

16. Skin cancer can cause death.	**77 (59.7)**	9 (7.0)	43 (33.3)

Note: The total of highest frequency for each category is in bold. Negative items are denoted with (#)

Level of Attitude about Skin Cancer and its Prevention

The attitude level was assessed by 7 items that covers skin cancer and its prevention. This section also combines both positive and negative statements with the purpose to reduce bias. The analyses were tabulated in Table 4, which depicts the distribution of attitude about skin cancer and its prevention. Most of the respondents are strongly agree regarding the statement "I always use sunscreen when doing outdoor activities". Besides, majority of respondents agree on statements "Sunscreen is expensive", "I am concerned about the exposure to sun can give me cancer", and "My skin will age quickly if I am expose to the sun" with the percentage of 33.3%, 43.4%, and 41.1% respectively. For statements "Sunscreen is harmful because it contains chemical substances" and "It is unnecessary to apply sunscreen during cloudy day", most of them are disagree with the statement. Finally, almost 40% of the respondents give a neutral response for statement "I think my occupation increases the risk of skin cancer".

Table 4 Distribution of attitude about skin cancer and its prevention (n = 129)

Statements	Strongly disagree freq. (%)	Disagree freq. (%)	Neutral freq. (%)	Agree freq. (%)	Strongly agree freq. (%)
1. I always use sunscreen when doing outdoor activities.	11 (8.5)	11 (8.5)	16 (12.4)	40 (31.0)	**51 (39.4)**
2. Sunscreen is expensive.	2 (1.6)	24 (18.6)	35 (27.1)	**43 (33.3)**	25 (19.4)
3. Sunscreen is harmful because it contains chemical substances. #	31 (24.0)	**60 (46.5)**	36 (27.9)	2 (1.6)	0 (0.0)
4. It is unnecessary to apply sunscreen during cloudy day. #	32 (24.8)	**59 (45.7)**	14 (10.9)	13 (10.1)	11 (8.5)
5. I am concerned about the exposure to sun can give me cancer.	2 (1.6)	6 (4.7)	19 (14.7)	**56 (43.4)**	46 (35.7)
6. My skin will age quickly if I am expose to the sun.	1 (0.8)	4 (3.1)	30 (23.3)	**53 (41.1)**	41 (31.8)

7. I think my occupation increases the risk of skin cancer.	17 (13.2)	40 (31.0)	**50 (38.8)**	5 (3.9)	17 (13.2)

Note: The total of highest frequency for each category is in bold. Negative items are denoted with (#)

Level of Practice about Skin Cancer Prevention

The practice level was assessed by 8 items that covers regarding the practice of skin cancer prevention. Table 5 illustrates the distribution of practice about skin cancer prevention. As can be seen from the table, majority of the respondents always apply sunscreen when doing outdoor activities, wear clothing that covers most part of the body and go in the shade to prevent from skin cancer. Besides, the highest frequency of 'never' option can be seen on two items, which are regarding the application of sunscreen when stay at home and wearing sunglasses, which accounted for 34.1% and 43.4% respectively. Furthermore, 16.3% of the respondents always use umbrella during hot day and only 7.8% of the respondents always wear hat when going out.

Table 5 Distribution of practice about skin cancer prevention (n = 129)

Statements	Never freq. (%)	Rarely freq. (%)	Sometimes freq. (%)	Always freq. (%)
1. Apply sunscreen when doing outdoor activities	10 (7.8)	12 (9.3)	37 (28.7)	**70 (54.3)**
2. Apply sunscreen every 4 hours a day	42 (32.6)	**43 (33.3)**	36 (27.9)	8 (6.2)
3. Apply sunscreen when stay at home	**44 (34.1)**	41 (31.8)	27 (20.9)	17 (13.2)
4. Wear clothing that covers most part of the body	4 (3.1)	6 (4.7)	25 (19.4)	**94 (72.9)**
5. Wear sunglasses	**56 (43.4)**	48 (37.2)	17 (13.2)	8 (6.2)
6. Use umbrella during hot day	15 (11.6)	**54 (41.9)**	39 (30.2)	21 (16.3)
7. Wear hat when going out	40 (31.0)	**41 (31.8)**	38 (29.5)	10 (7.8)
8. Go in the shade	11 (8.5)	15 (11.6)	41 (31.8)	**62 (48.1)**

Note: The total of highest frequency for each category is highlighted in bold.

Association of Sociodemographic Characteristics with Knowledge

Table 6 shows the outcome of the tests that have been conducted on gender, age, kulliyyah, year and duration of exposure to direct sun per day. Mann-Whitney U test revealed that there was a statistically significant difference in terms of knowledge between male and female ($p = 0.020$). However, Kruskal-Wallis test revealed that there was no significant difference in terms of knowledge between age ($p = 0.514$), kulliyyah ($p = 0.220$) and year ($p = 0.736$).

Table 6 Association between sociodemographic characteristics with knowledge (n = 129)

Variable	Mean	Median	p-value
Gender			
Male	9.68	10.00	0.020*
Female	11.01	11.00	
Age			
19 – 21 years old	10.97	11.00	
22 – 24 years old	10.37	11.00	0.514
25 – 27 years old	10.75	11.00	
Kulliyyah			
Kulliyyah of Allied Health Sciences	10.90	11.00	
Kulliyyah of Dentistry	9.63	10.50	
Kulliyyah of Medicine	8.38	10.00	0.220
Kulliyyah of Nursing	11.32	12.00	
Kulliyyah of Pharmacy	11.40	12.00	
Kulliyyah of Sciences	9.44	10.00	
Year			
Year 1	10.67	10.00	
Year 2	10.95	11.00	
Year 3	10.21	11.00	0.736
Year 4	11.27	12.00	
Year 5	11.50	11.50	
Exposure to direct sunlight	10.81	11.00	
Less than 10 minutes	10.17	10.00	0.050*
20 – 30 minutes	11.36	12.00	
More than 40 minutes			

Note: (*) p-values is statistically significant

Association of Sociodemographic Characteristics with Attitude

Table 7 presents the outcome of the tests that have been conducted on gender, age, kulliyyah, year and duration of exposure to direct sun per day. Mann-Whitney U test revealed that there was a statistically significant difference in terms of attitude between male and female ($p < 0.001$). However, Kruskal-Wallis

test revealed that there was no significant difference in terms of attitude between age (p = 0.441), kulliyyah (p = 0.529), year (p = 0.559) and exposure to direct sunlight (p = 0.172).

Table 7 Association between sociodemographic characteristics with attitude (n = 129)

Variable	Mean	Median	p-value
Gender			
Male	24.04	22.00	<0.001*
Female	26.66	27.00	
Age			
19 – 21 years old	25.85	27.00	
22 – 24 years old	25.47	25.00	0.441
25 – 27 years old	25.50	26.00	
Kulliyyah			
Kulliyyah of Allied Health Sciences	25.87	27.00	
Kulliyyah of Dentistry	24.25	24.00	
Kulliyyah of Medicine	25.64	26.50	
Kulliyyah of Nursing	26.16	26.00	0.529
Kulliyyah of Pharmacy	25.80	25.00	
Kulliyyah of Sciences	25.00	25.00	
Year			
Year 1	24.87	26.00	
Year 2	26.50	27.00	0.559
Year 3	25.60	25.50	
Year 4	25.40	25.00	
Year 5	24.50	24.50	
Exposure to direct sunlight			
Less than 10 minutes	24.57	26.00	
20 – 30 minutes	25.19	25.00	0.172
More than 40 minutes	26.29	27.00	

Note: (*) p-value is statistically significant

Association of Sociodemographic Characteristics with Practice

Table 8 depicts the outcome of the tests that have been conducted on gender, age, kulliyyah, year and duration of exposure to direct sun per day. Mann-Whitney U revealed that there was a statistically significant difference in terms of attitude between male and female (p <0.001). However, Kruskal-Wallis revealed that there was no significant difference in terms of attitude between age (p = 0.508), kulliyyah (p = 0.654), year (p = 0.141) and exposure to direct sunlight (p = 0.198).

Table 8 Association between sociodemographic characteristics with practice (n = 129)

Variable	Mean	Median	p-value
Gender			
Male	18.06	18.00	<0.001*
Female	21.65	22.00	
Age			
19 – 21 years old	21.17	21.00	
22 – 24 years old	20.34	20.00	0.508
25 – 27 years old	21.25	20.00	
Kulliyyah			
Kulliyyah of Allied Health Sciences	21.27	21.00	0.654
Kulliyyah of Dentistry	20.75	22.00	
Kulliyyah of Medicine	19.57	20.50	
Kulliyyah of Nursing	21.05	23.00	
Kulliyyah of Pharmacy	20.55	20.00	
Kulliyyah of Sciences	20.31	19.00	
Year			
Year 1	20.57	20.00	0.141
Year 2	22.03	22.00	
Year 3	20.26	20.00	
Year 4	19.80	19.00	
Year 5	18.00	18.00	
Exposure to direct sunlight			
Less than 10 minutes	19.71	19.00	
20 – 30 minutes	19.63	20.00	0.198
More than 40 minutes	20.26	22.00	

Note: (*) p-value is statistically significant

Correlation between Knowledge, Attitude and Practice about Skin Cancer and Its Prevention

Table 9 shows the result that showed a moderately positive correlation between knowledge and attitude (r = 0.318) as well as attitude and practice (0.457). The p-value suggests that there is a statistically significant correlation between knowledge and attitude (p = 0.001) as well as attitude and practice (p <0.001).

Meanwhile, there was a weak positive correlation between knowledge and practice (r = 0.105). Besides, there is no statistically significant correlation between knowledge and practice (p = 0.611). Figures 1, 2, and 3 illustrate the correlation between knowledge and attitude, knowledge and practice and attitude and practice about skin cancer and its prevention among IIUM Kuantan undergraduate students.

Table 9 Correlation between knowledge, attitude and practice about skin cancer and its prevention (n = 129)

Variables	Correlation coefficient, r	p-value
Knowledge and attitude	+0.318	0.001**
Knowledge and practice	+0.105	0.611
Attitude and practice	+0.457	<0.001**

Note: positive r-value show positive correlation; (**) p-value is statistically significant (<0.05)

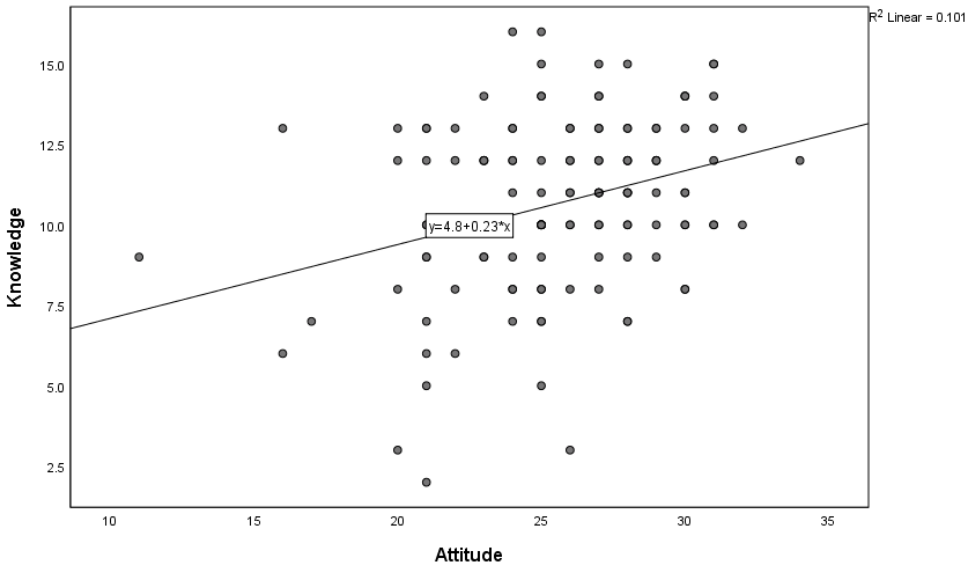


Figure 1 Correlation between knowledge and attitude about skin cancer and its prevention among IIUM Kuantan undergraduate students

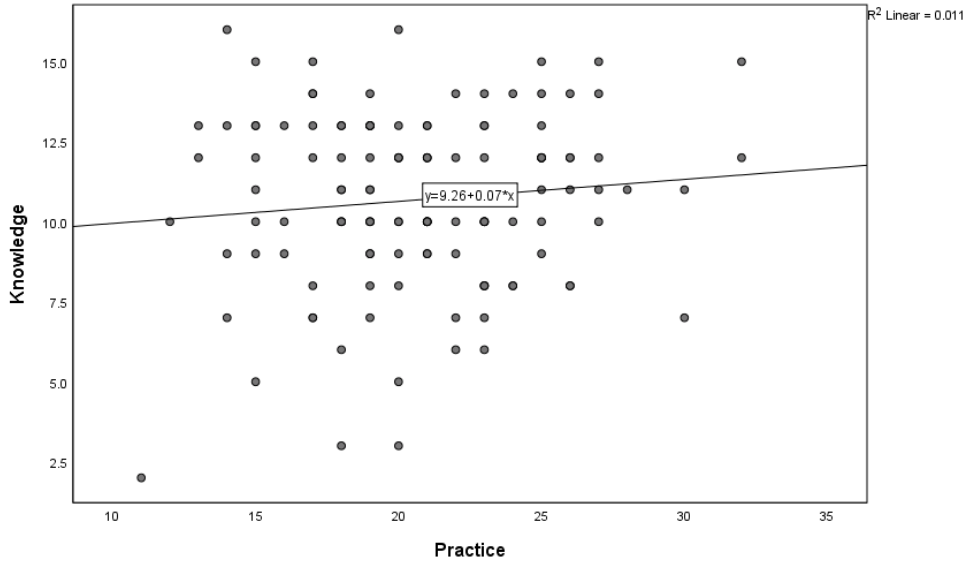


Figure 2 Correlation between knowledge and practice about skin cancer and its prevention among IIUM Kuantan undergraduate students

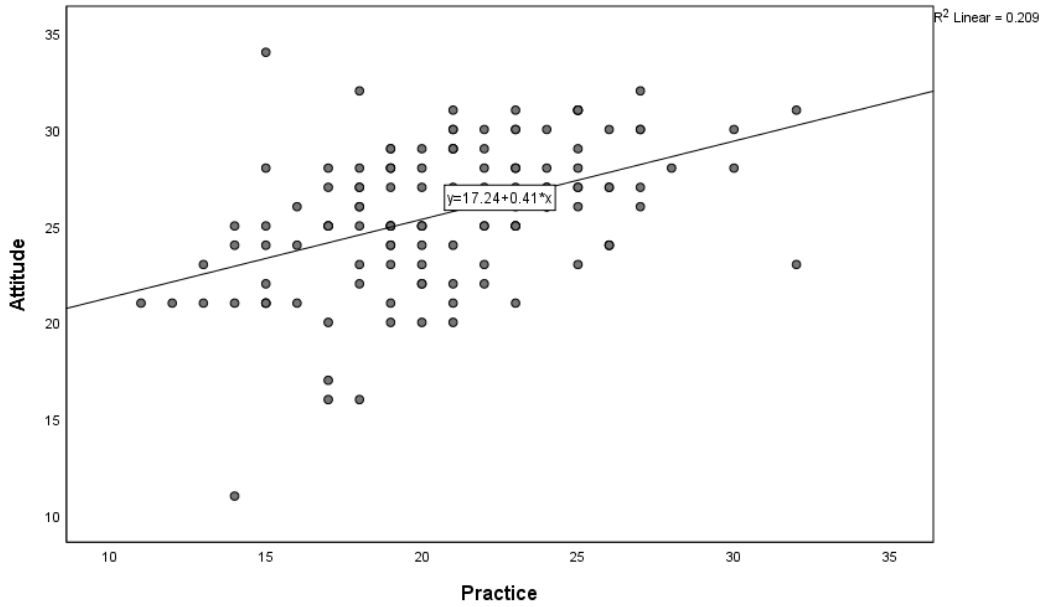


Figure 3 Correlation between attitude and practice about skin cancer and its prevention among IIUM Kuantan undergraduate students

Level of Knowledge about Skin Cancer and its Prevention

The results of the study revealed that majority of the respondents were well informed regarding the type, risk factors and preventive measures of skin cancer. A total of 70 out of 129 respondents (54.3%) possessed a moderate level of knowledge about skin cancer and its prevention. 26.4% obtained a good level of knowledge and another 19.4% had poor knowledge.

Most of the respondents managed to answer correctly regarding the negative effects of sun exposure such as freckles (68.2%), wrinkles (70.5%), skin cancer (93.8%), dry skin (89.9%), aging (76.0%) and spots (75.2%) (Table 3). From the result, it can be said that almost all respondents knew that skin cancer is associated with sun exposure. Similarly, a study by Pinos-León et al. (2021) revealed that about 72% of respondents reported knowing the association between the development of skin cancer and sun exposure. However, these findings contradict with a study by Alamri et al. (2015) which revealed that 83.4% of respondents did not aware that sun exposure is the risk factor for skin cancer.

Despite the low incidence of skin cancer in Malaysia, IIUM Kuantan undergraduate students can achieve a moderate level of knowledge about skin cancer and its prevention. This finding might be influenced by their background of study which most of them are in the health sciences field. This is supported by a study from Nguyen et al. (2020) that reported education influences the level of knowledge regarding skin cancer.

Level of Attitude about Skin Cancer and its Prevention

The results of the study revealed that more than half (60.5%) of respondents have a moderate attitude, 33.3 % of good attitude and 6.2% of poor attitude regarding skin cancer and its prevention. This result was noticeably better than the previous study by Şenel & Süslü (2015), which disclosed that the attitude among the studied population was generally unsatisfactory.

Approximately 70% of the respondents always apply sunscreen when going for outdoor activities (Table 4). Similar study that was conducted among doctors and pharmacists revealed that about 87.5% of

respondents agree that sunscreen should be applied when going for outdoor activities (Low et al., 2021). According to Whiteman et al. (2019), the best protection during outdoor activities is sunscreen. When going for outdoor activities, we are more likely to be exposed to the damaging UV rays. Most studies agree that the function of sunscreen is to prevent the damaging effects of sunlight (Awadh et al., 2016; Ibrahim et al., 2021). Therefore, by applying sunscreen, it can protect our skin from the risk of skin cancer.

Level of Practice about Skin Cancer and its Prevention

The results of the study illustrated that the majority of the respondents (58.9%) achieved a moderate level of practice while a good level of practice has the least percentage (12.4%) (Table 5). This result was way better compared to study by Al Naggar (2012) which reported poor conduct of skin cancer preventive measures among university students.

The fact that more than half of the respondents (54.3%) apply sunscreen when going for outdoor activities was a pleasant finding. The percentage reported from this study was found to be slightly higher than several previous studies as they revealed that 43.5% (Al Naggar, 2012), 41% (Awadh et al., 2016), 42.6% (Nguyen et al., 2020), and 31.5% (Low et al., 2021) of the respondents use sunscreen as a practice of skin cancer preventions. However, another study conducted by Al-Atif (2021) reported that 82% of the Saudi Arabia population use sunscreen as a preventive measure. The difference regarding the usage of sunscreen could be due to the difference in target population.

Besides, only 6.2% of them reapply sunscreen every 4 hours a day. Reapplying sunscreen is necessary to keep your skin protected. Furthermore, Hung et al. (2022) revealed that the usage of sunscreen was associated with a lower prevalence of skin cancer. Another epidemiological study suggested that the usage of sunscreen can prevent squamous cell carcinoma and decrease the number of moles that are known to be one of the risk factors for skin cancer. Also, it was found that the regular application of sunscreen could reduce the risk of skin cancer (Green et al., 2011). In terms of application of sunscreen when staying at home, it is reported that most of them (34.1%) never apply sunscreen when staying at home (Table 5). As UV radiation can pass through windows, it is important to apply sunscreen when staying indoors. However, through this study, it is revealed that majority of them were not aware of the importance of applying sunscreen when staying indoors.

Association of Sociodemographic Characteristics with Knowledge

In terms of knowledge, the results showed a significant difference in knowledge between gender ($p = 0.020$). Females had higher knowledge ($\bar{X} = 11.01$) compared to male ($\bar{X} = 9.68$). The possible reason behind this finding is that majority of the respondents were female (76.0%). In general, the number of female students in the Kuantan campus is higher than the number of male students, which leads to higher response from female students to participate in this study. This finding is in line with a previous study by Alamri et al. (2015) where the knowledge about skin cancer among females ($\bar{X} = 9.9$) is slightly higher than male ($\bar{X} = 9.6$). However, another study conducted by Pinos-León et al. (2021) found no differences in terms of knowledge level between male and female.

Moreover, there was a significant difference in terms of knowledge between exposure to direct sunlight ($p = 0.050$). Different duration of exposure to direct sunlight might lead to the differences in terms of knowledge in which those who are exposed to direct sunlight for more than 40 minutes had the highest knowledge ($\bar{X} = 11.36$) compared to those who exposed for less than 10 minutes ($\bar{X} = 10.81$) and 20 – 30 minutes ($\bar{X} = 10.17$) (Table 6). The difference in duration of exposure to the sun could be due to the fact that students are actively involved in outdoor activities such as physical exercise and jogging in the evening. However, there was no information between the association of level of knowledge about skin cancer and its prevention and exposure to direct sunlight found in previous studies that related to skin cancer.

Meanwhile, Kruskal-Wallis test had revealed that age, kulliyyah and year do not show any association in terms of knowledge level.

Association of Sociodemographic Characteristics with Attitude

Regarding the association of sociodemographic characteristics with attitude level, only gender shows a significant difference in terms of attitude level (p = <0.001). In this study, it shows that females have a higher attitude about skin cancer and its prevention ($\bar{X}$ = 26.66) compared to male ($\bar{X}$ = 24.04). Evidence from a study by Pinos-León et al. (2021) revealed that female respondents were more likely to have good attitudes compared to male respondents. This could be due to the high level of awareness related to sun protection among females compared to male (Low et al., 2021). Another study stated that attitudes about skin cancer were associated with gender, education level, and family income (Nguyen et al., 2020). However, this study showed there was no association in terms of attitude level between year of study (p = 0.559). Meanwhile, the study on the level of attitude about skin cancer and its prevention for exposure to direct sunlight was not found in previous studies that related to skin cancer. Hence, the findings revealed that only gender is associated with the level of attitude.

Association of Sociodemographic Characteristics with Practice

In terms of practice, there was an association found between male and female with practice level (p = <0.001). In this study, females had a higher practice level ($\bar{X}$ = 21.65) compared to male ($\bar{X}$ = 18.06). This finding coincides with a finding from another study which reported that females are 1.68 times more likely to obtain a higher score in practice than male (Pinos-León et al., 2021). This could be caused by the nature of females, who are always concerned about beauty and grooming, hence consistently applying sunscreen to improve their cosmetic look (Rajagopal et al., 2021). Nevertheless, there were no associations found between other sociodemographic characteristics such as age, kulliyyah, year and exposure to direct sunlight regarding attitude level. This finding contradicts a study by Al Naggar (2012) which revealed that gender, age, educational background and family income significantly influenced the level of practice. Study by Al Naggar (2012) also reported that the practice of skin cancer prevention increased with age. From this study, although there was no association in terms of practice with age, it can be seen that the eldest age group, 25 – 27 years old, had a slightly better practice level ($\bar{X}$ = 21.25) compared to younger group, 19 – 21 years old ($\bar{X}$ = 21.17) and 22 – 24 years old ($\bar{X}$ = 20.34). The study on level of practice about skin cancer prevention for exposure to direct sunlight was not found in previous studies that related to skin cancer.

Correlation between Knowledge, Attitude and Practice about Skin Cancer and Its Prevention

As can be seen from Table 6, the findings showed that there was a statistically significant correlation between knowledge and attitude (r = 0.318, p = 0.001) as well as attitude and practice (r = 0.457, p = <0.001). This suggests that an increase in knowledge contributes to the increase in attitude and good attitude level result in good practice on skin cancer prevention. However, there was no correlation found between knowledge and practice (p = 0.611). Hence, knowledge level does not have an impact on the practice levels among IIUM Kuantan undergraduate students. The predictor factor might be due to less awareness regarding the benefits of skin cancer prevention practices on oneself.

CONCLUSIONS

In conclusion, more than half of IIUM Kuantan undergraduate students achieved a moderate level for knowledge, attitude and practice about skin cancer and its prevention. Nearly 55% presented a moderate knowledge level, about 60.5% achieved a moderate attitude level, and almost 60% showed a moderate attitude level about skin cancer and its prevention. Next, there was an association in terms of knowledge between gender and exposure to direct sunlight. Besides, only gender is associated with the level of attitude

and practice. In terms of correlation between knowledge, attitude and practice, this study found that there was a positive correlation between knowledge and attitude and attitude and practice. By conducting this study, IIUM Kuantan undergraduate students' awareness regarding skin cancer was determined and their awareness can be increased by promoting them to regularly practice the use of sunscreen as it is one of the most convenient preventative measures of skin cancer.

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KNOWLEDGE AND CONCERNS ON INFERTILITY AND ASSISTED REPRODUCTIVE TECHNOLOGY AMONG GRADUATING STUDENTS OF KAHS AT IIUM KUANTAN

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ABSTRACT

Introduction: Infertility is a disease that is common in one in six people today. One of the ways to reduce the rate of infertility is perhaps by raising basic knowledge and awareness especially in the young adults, as they will most likely embark on family life following completion of their studies. This study aimed to investigate the knowledge on infertility and assisted reproductive technology including the association to the level of physical, emotional and economical concerns on in vitro fertilization and intracytoplasmic sperm injection infertility treatments among graduating students of the Kulliyyah of Allied Health Sciences at International Islamic University Malaysia in Kuantan. **Methods**: The sample of the study consisted of 124 graduating students with a breakdown of 102 females and 22 males. The sampling method used in this research was purposive sampling. Online survey data from respondents were run in SPSS version 26. **Results**: It was found that the score of knowledge of infertility and assisted reproductive technology and the score of concerns on in vitro fertilisation and intracytoplasmic sperm injection procedures among these students were of a good level, being more than 80% achievement. However, there were no differences observed in the knowledge and awareness on infertility and assisted reproductive technology ($p=0.813$), as well as concerns on in vitro fertilisation and intracytoplasmic sperm injection procedures ($p=0.264$) between male and female students. A positive correlation was shown between knowledge of infertility and assisted reproductive technology and concerns on in vitro fertilisation and intracytoplasmic sperm injection procedures ($\rho=+0.249$, $p=0.005$,). **Conclusion**: The graduating students of the Kulliyyah of Allied Health Sciences at IIUM have adequate knowledge of infertility and assisted reproductive technology but concerns regarding related treatment procedures seemed substantial. These findings indicate that implementing an awareness program could be advantageous for individuals who are at a stage where they are considering starting a family.

KEYWORDS: infertility, assisted reproductive technology, *in vitro* fertilisation, intracytoplasmic sperm injection, concerns

INTRODUCTION

Infertility is the inability to achieve pregnancy or to conceive after one year or longer of unprotected sex, as defined by the World Health Organization (WHO) (WHO, 2020). In its new report on infertility prevalence estimates, WHO reported that globally, one in six people have experienced infertility in some stage of their lives (WHO, 2023). Couples believe themselves infertile when their partners did not achieve successful pregnancy after a year of unprotected sexual intercourse (Maheshwari, 2020) and this mindset may lead to stress and disturbance to mental health consequently affecting daily lives and reproductive capacity. According to Department of Statistics Malaysia, live births rate in the country for the last two years was the lowest in a decade. It was also mentioned that the total fertility rate (TFR) in Malaysia continued to decline over three decades, from 4.9 children per woman in 1970 to approximately 1.7 children in 2020 (Department of Statistics Malaysia, 2021). Migration and mortality notwithstanding, a TFR of 2.1 children per woman is an indicator of a stable population but as a whole, fertility rate reflects the economic and social status of a country and is an important element of population growth (OECD, 2023). Multiple factors influence the TFR of countries across the world and various correlations have been shown towards level of education, religiosity, contraception prevalence rates, gross domestic product as well as family planning programs (Götmark and Andersson, 2020).

Assisted Reproductive Technology (ART) is one of the mainstays of infertility treatments and this includes procedures such as in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI). IVF was introduced in the early 1960s and this procedure is a process of fertilisation in which an egg is combined with sperm in a laboratory dish. Three decades after the birth of the IVF method, another type of ART was established mainly to treat severe cases of male infertility. This is known as intracytoplasmic sperm injection (ICSI), where a single sperm is injected directly into the cytoplasm of an egg (Wennerholm & Bergh, 2020). IVF and ICSI involve many steps from collection of gametes to in vitro fertilization process and especially the selection of the most viable embryo or sperm for transfer or injection into the oocyte, all in the hope to provide couples with healthy live offspring (Woodward, 2018).

In this era where information is at our fingertips, it is expected that adults, especially married couples, are aware and have at least some basic knowledge regarding ART. Nevertheless, it is unfortunate that not everyone has an equal level of understanding about ART and available fertility services due to lack of awareness. There is heterogeneity in fertility awareness and it has been suggested that fertility programmes in family planning settings, target men and people with low education (Pedro, et al., 2018). It is also believed that it serves the best interests of graduating students entering married life following graduation to be aware of infertility issues as well as available infertility treatments in order to better prepare themselves. Improving their level of knowledge regarding IVF and ICSI may be of assistance in achieving successful pregnancy should they choose to have a family. Hence, this research aims to focus on knowledge and awareness of infertility and ART, alongside procedures of IVF and ICSI, among graduating students of the Kulliyyah of Allied Health Sciences (KAHS) at the International Islamic University Malaysia (IIUM) of Kuantan campus.

MATERIALS AND METHODS

Study population

This study was designed based on cross-sectional study methods. Purposive sampling was done to identify the available respondents among the male and female graduating students (fourth year) of KAHS at IIUM Kuantan. Participants that are married and fourth-year students who were not graduating at the time of the research due to study extension or insufficient credit hours were excluded from participation. A total of 124 respondents participated in this research. Ethical approval of this research had been obtained from the IIUM Research Ethics Committee (IREC) (ID: IREC 2022-KAHS/DBMS/5).

Development and validation of questionnaire

The questionnaire consists of four sections as follows.

Section A	Consent
Section B	Socio-demographic (2 questions)
Section C	Knowledge on infertility and ART (10 questions)
Section D	Concerns on IVF and ICSI treatments (8 questions)

Answer options for knowledge and concerns sections included 'yes', 'no' and 'not sure'. Content validity of the questionnaire had been checked through ratings by experts (n=4; S-CVI=0.8), followed by a pilot study (n=16) to assess consistency and reliability of the content and items. The Cronbach's Alpha test of the pilot study gave values of 0.73 for the section on knowledge on infertility and ART and 0.70 for concerns on IVF and ICSI treatments.

The data from the target group was collected by using an online survey. Basic questions such as the definitions, causes and treatments were self-developed to assess participant's knowledge regarding infertility and ART including adapted from themes in the study by Peddie et al. (2005). Questions in the section on concerns were adapted from an online forum that discussed the physical, emotional and financial concerns regarding infertility treatments (Kaliarnta et.al, 2011).

Scoring systems

Table 1 is used as the scoring system for each response. All items in the questionnaire are true statement questions except for question no. 8 in section D for aspect of concerns.

Level of knowledge and concerns were evaluated based on the percentage of marks gained and later categorised into three groups which were good (or substantial), moderate and poor (or low) using modified Bloom's cut off point as adapted from Ramli et al. (2018) (Table 2).

Table 1 Categorisation for level of knowledge on infertility and ART and level of concerns on IVF and ICSI

Response	Score
Section C: Knowledge	
Correct statement:	
Yes	3
Not Sure	2
No	1
False statement (No false statement in this section)	
Section D: Concerns	
Correct statement:	
Yes	3
Not Sure	2
No	1
False statement (For statement question no. 8):	
Yes	1
Not Sure	2
No	3

Table 2 Categorisation for level of knowledge on infertility and ART and level of concerns on IVF and ICSI

Percentage (%)	Total scores on knowledge	Total scores on concerns	Scoring level indicator
80-100	25 - 30	20 -24	Good/Substantial
60-79	19 - 24	15 -19	Moderate
≤ 59	0 - 18	0-14	Poor/Low

Statistical analysis

This study was a quantitative study and since both independent and dependent variables were nominal, non-parametric testing was used. The non-parametric tests used included descriptive statistics, Spearman's Correlation Coefficient and Mann Whitney test. The tests were run in the Statistical Package for Social Sciences (SPSS) software version 26. Details are as follows.

Data analysis	Test / Scoring used
Level of knowledge on infertility and ART	Descriptive statistics and Mann-Whitney test
Level of concerns on IVF and ICSI	
Comparison of responses between male and female respondents	Median ± IQR
Association between the level of knowledge of infertility and ART with the level of economical, physical and emotional concerns on IVF and ICSI	Descriptive statistics and Spearman's Correlation Coefficient test

RESULTS AND DISCUSSIONS

Characteristic of respondents

Frequency and proportion of respondents showed responses from 102 female and 22 male students (Table 3).

Table 3 Gender of respondents (n=124)

Gender	Frequency	Percentage (%)
Male	22	17.7
Female	102	82.3

Level of knowledge on infertility and ART and concerns on IVF and ICSI

Table 4 shows the category of knowledge scores on infertility and ART, together with scores for concerns on IVF and ICSI, including its frequency and percentage for each category. Ten statement questions about knowledge of infertility and ART were included in the questionnaire, and one hundred percent of the respondents scored in the good knowledge category. Eight statement questions were included in the questionnaire for concerns on IVF and ICSI treatments. 82.3% of respondents scored in the substantial category for concerns while 17.7% indicated moderate concern for the said infertility treatments. None of the respondents scored poor or low in both categories.

Table 4 Categories of Knowledge of Infertility and ART and Concerns of IVF and ICSI

Categories	Frequency	Percentage (%)
Knowledge Score		
Good / Substantial	124	100
Moderate	0	0
Poor / Low	0	0
Concerns Score		
Good / Substantial	102	82.3
Moderate	22	17.7
Poor / Low	0	0

Knowledge on infertility and ART

Aspects of knowledge such as definition of related terms, risk factors and common infertility treatments have been assessed by ten questions that are all correct statements. Data have been analysed by using descriptive statistics. The distribution of knowledge on infertility and ART based on items in the statement questions and frequency of answers are as presented in Table 5. Most respondents indicated good knowledge on the subject matter. Following determination of scores, the association of knowledge of infertility and ART between male and female respondents indicated a *p*-value of 0.813 as shown in Table 6.

Table 5 Overall distribution of knowledge of infertility and assisted reproductive technology (ART) among graduating students of KAHS, IIUM (n= 124)

Statement Questions	Frequency of Answers		
	Yes (%)	No (%)	Not Sure (%)
1) Infertility is the inability to get pregnant (conceive) after one year (or longer) of unprotected sex.	123 (99)	1 (1)	0 (0)
2) Both male and female infertility are the possible causes of inability to conceive a child.	117 (94.4)	3 (2.4)	4 (3.2)
3) Abnormal sperm function, injury at scrotum/testicles, immature sperm and unhealthy diet and lifestyle are some of the possible causes of male infertility.	124 (100)	0 (0)	0 (0)
4) Polycystic ovary syndrome (PCOS), ovulation disorders, endometriosis and unhealthy diet and lifestyle are some of the possible causes of female infertility.	123 (99)	0 (0)	1 (1)
5) There are prescribed medications to treat infertility.	96 (77.4)	0 (0)	28 (22.6)
6) There are surgeries to treat infertility.	93 (75)	1 (0.8)	30 (24.2)
7) *In vitro* fertilization (IVF) is a process of fertilisation in which an egg is combined with sperm in a laboratory dish.	113 (91.1)	0 (0)	11 (8.9)
8) Intracytoplasmic sperm injection (ICSI) is a process where a single sperm is injected directly into the cytoplasm of an egg.	77 (62.1)	0 (0)	47 (37.9)

9) There is a high risk of getting IVF and ICSI, including multiple births, congenital deformity and chromosomal abnormalities.	89 (72)	1 (0.8)	34 (27.4)
10) There are fertility centres in Malaysia that help to assist couples or individuals, who want to become parents but for medical reasons have been unable to achieve this goal via the natural course.	41 (33)	3 (2.5)	80 (64.5)

Table 6 Comparison of level of knowledge on infertility and assisted reproductive technology (ART) between male and female graduating students of KAHS, IIUM (n=124)

Gender	n	Score on Knowledge (Median ± IQR)	*p*-value
Male	22	60.89	0.813
Female	102	62.85	

Concerns on *in vitro* fertilization (IVF) and intracytoplasmic sperm injection (ICSI)

Eight statement questions were used to assess concerns regarding common infertility treatments specifically IVF and ICSI. The statement questions included were based on economic concern (1 question), physical concern (1 question) and on emotional concerns (6 questions). All of the questions under this aspect are correct statements except for statement question no. 8. Distribution of findings are presented in Table 7.

Table 7 Distribution of concerns regarding *in vitro* fertilization (IVF) and intracytoplasmic sperm injection (ICSI) treatments among graduating students of KAHS, IIUM (n= 124)

Statement Questions (Type of Concern)	Frequency of Answers		
	Yes (%)	No (%)	Not Sure (%)
Economical Concern			
1) *In vitro* fertilization (IVF) and intracytoplasmic sperm injection (ICSI) are costly.	101 (81.5)	0 (0)	23 (18.5)
Physical Concern			
2) IVF and ICSI procedures are painful but bearable.	73 (58.9)	2 (1.6)	49 (39.5)
Emotional Concern			
3) Getting an IVF or ICSI treatment will emotionally bring you down.	84 (67.7)	5 (4)	35 (28.3)
4) IVF and ICSI treatment will breach both you and your partner's privacy.	92 (74.2)	5 (4)	27 (21.8)
5) The decision of getting an IVF or ICSI treatment will distance your relationship with your partner.	58 (46.8)	16 (12.9)	50 (40.3)

6) IVF and ICSI treatment will help you and your partner to become emotionally stronger.	88 (71.0)	0 (0)	36 (29.0)
7) The support from partners and families are highly needed during the IVF and ICSI phase and lack of understanding from them will cause disappointment to you.	105 (84.7)	0 (0)	19 (15.3)
8) IVF and ICSI procedures are against nature.	5 (4)	62 (50)	57 (46)

A total of 81.5% of the respondents have concerns related to financial implications of the infertility treatments while for physical concerns, 58.9% of the respondents replied 'yes', 1.6% 'no' and 39.5% 'not sure'. Findings on emotional concerns showed that an average of 58% of respondents answered 'yes', 12% 'no' and 30% 'not sure' as a whole. Following the scoring step, *p*-value for the association of concerns of IVF and ICSI between male and female respondents was found to be 0.264 (Table 8).

Table 8 Comparison of level of concerns on IVF and ICSI treatments between male and female graduating students of KAHS, IIUM (n=124)

Gender	n	Score on Concerns (Median ± IQR)	*p*-value
Male	22	70.16	0.264
Female	102	60.85	

Association between level of knowledge and awareness of infertility and ART with level of concerns on IVF and ICSI treatments

To investigate the association, the raw data was first analysed by reviewing the histogram, mass and skewness. The normality assumptions were however not met. Therefore, Spearman's Correlation Coefficient was used in this study. Results are as shown in Table 9 and Figure 1.

Table 9 Correlation between knowledge and awareness of infertility and ART with concerns of IVF and ICSI

Variables	Spearman's Correlation Coefficient, ρ	*p*-value
Knowledge score - Concerns score	+ 0.249	0.005

* ρ (rho) value shows a weak positive correlation.

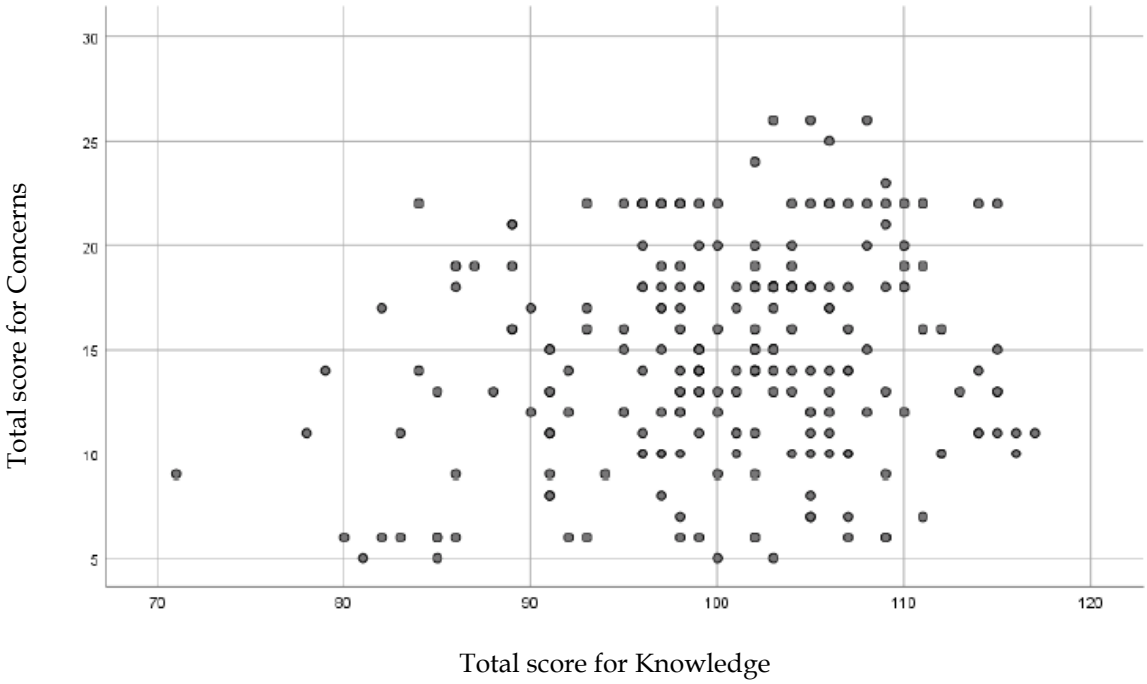


Figure 1 Correlation between knowledge of infertility and ART with concerns of IVF and ICSI

The discrepancy between the number of male (17.7%) and female (82.3%) respondents among the fourth-year students of KAHS in IIUM Kuantan can be explained by the trend that have been observed for many years in every intake for health sciences programs in the faculty. The results with regards to knowledge on infertility and ART, whereby all respondents fell into the 'good knowledge' category, are expected as these graduating students are science- and biomedical-based and should have some knowledge on the reproductive system as well as some awareness of technologies important in the treatment of infertility. Studies such as that conducted by Nouri et al. (2014), have found that students with a medical background had more understanding and awareness of infertility than students without a medical background. Sound levels of knowledge and awareness regarding ART, specifically IVF and ICSI, were also observed. This study highlights that all respondents agreed with the definition cited from the WHO except for the 1% who disagreed.

In the concerns section, it is interesting to find that most respondents in this study believed that infertility can be caused by both genders and not solely due to possible causes belonging to females. In the survey done by Afolabi, et al. (2017), the majority of respondents claimed that women are more usually blamed in society for infertility. This may be true in a lot of cultures hence it is valuable to know that respondents among students of KAHS have a perspective that failure to conceive and achieve successful pregnancy may be due to multiple factors and not specific to any gender. In addition, WHO has also emphasized that infertility is the disease of male or female reproductive system (World Health Organization, 2020).

It seemed that the aetiologies of male and female infertility were not foreign to the respondents as the students were well aware of disorders of the reproductive system either in male or female such as abnormal sperm function, injury at the scrotum or testicles as well as polycystic ovary syndrome (PCOS) and endometriosis. The majority of the respondents were also aware about the risks associated with infertility treatments such as IVF and ICSI. These findings gave an impression that students belonging to the health sciences faculty would have attended lectures and talks or may have had exposure to reproductive biology and disorders throughout their tertiary study. However, it was apparent that a high number of the respondents (64.5%) were unsure of available fertility services as well as centres which could assist in matters of infertility. This is a clear indication that perhaps fertility centres can enhance engagement efforts in order to increase the awareness on available fertility services and support in the community.

A high score with regard to concerns on IVF and ICSI (82.3%), suggested substantial concerns regarding the treatments. The *p*-value of 0.264 indicated that concerns on IVF and ICSI were not statistically significant between male and female respondents. This may be appropriate as both treatments would need the participation of both genders and economical, physical and emotional

concerns could affect anyone. One of the main issues that is closely related to services of ART is the cost implications. In the analysis of low- and middle-income countries done by Njagi et al. (2023), access to the services and the unaffordable high costs of ART have hindered the progress of infertility treatments to those who are in need. Affordability by patients can be realised with better policies and financial mechanisms which could be provided by the government. Couples who are not financially stable and unable to afford but are still planning to proceed with the fertility treatments shall undoubtedly be in debt due to the exorbitant prices of these ART services.

It is noteworthy to find that in terms of physical concerns, 58.9% of the respondents (n=73) agreed that IVF and ICSI are painful treatments but the pain is bearable. Pain is inherently a subjective experience and pain levels vary from one individual to another. As for emotional concerns, almost all of the respondents (n= 92, 74.2%) agreed that IVF and ICSI treatments will violate their privacy. Being present at a fertility centre or consulting a fertility expert may cause embarrassment to the couples as it may label them as being infertile. A previous qualitative study on women's decision-making on IVF treatment has shown that it is hard for them to reach the point of acceptance of childlessness. Being childless is something they feel forced into since facing up to the fact that they are unable to conceive is incredibly upsetting (Peddie et al., 2005).

CONCLUSION

In our study, the association between the level of knowledge of infertility and ART with the level of concerns on IVF and ICSI showed a correlation coefficient (r) of +0.249, indicating a weak positive correlation between both aspects but the association between the variables were significant (p=0.005). This finding showed that a good knowledge on infertility and ART among the students surveyed may not necessarily allay their concerns with regards to the infertility procedures involved. Being students who are about to graduate and possibly embarking on married life may be daunting in itself and this would be even disconcerting when planning to have children. The study by Fauser et al., (2019) recommended potential discussions between patients and stakeholders in support of infertility treatments and ART. Likewise, a heightened awareness programmes on the subject matter by the government and authorities in-charge in Malaysia could well benefit all ages of our community and especially among the young adults.

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ASSESSMENT OF BACKGROUND RADIATION IN SPORT AND RECREATIONAL PLACES IN KUANTAN

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ABSTRACT

Introduction: The purpose of this study is to assess the background radiation level (BRL) in seven sport and recreational places in Kuantan district whether it is within the acceptable limit stated by radiation protection regulatory bodies. There has never been research done to assess the BRL in the sport and recreational places in Kuantan by using optically stimulated luminescence (OSL) dosimeter. **Methods:** Reading of BRL was monitored using Inlight Environmental Dosimeter. Seven sport and recreational places inside Kuantan district were identified and located as venues for location of study. Data was collected at the designated locations for seven cycles where one cycle consists of seven days. Readings from OSLDs were taken at the end of each cycle and analyzed using Landauer microStar computer system. All background radiation doses for each designated area were also compared with the recommended value by radiation protection regulatory bodies such as IAEA, NCRP and AELB**. Results:** The accumulated BRL shows trend of increasing level of background radiation over the seven cycles. The highest annual dose reading was noted in Stadium Hoki Wisma Belia with a reading of 2.286 mSv. The lowest annual dose was at Futsal Playground with a reading of 1.321 mSv. **Conclusion:** The accumulated dose calculated to represent estimated annual BRL of the designated places exceeded the recommended value of background radiation for public (1 mSv per year) from radiation regulatory bodies; ICRP, AELB and IAEA. Comprehensive monitoring of the designated locations must be done to ensure the safety of the surroundings. However, there are some possible influencing factors that can affect the results such as geographical, types of building materials used and infrastructure development. This study suggests that this study to be continued for a longer study period to obtain more reliable results in order to construct a platform for environmental radiation monitoring in Malaysia.

KEYWORDS: Background radiation, public exposure, Ionizing radiation, Natural source of radiation, Effect of background radiation, Annual dose limit

INTRODUCTION

Background radiation is in invisible form and can cause harm to human health. Turner (1998) reported that too much exposure to sunlight may cause cutaneous malignant melanoma and non-melanocytic skin cancer. Moreover, a fact stated by the National Council on Radiation Protection and Measurements (NCRP) in 2009 that the largest source of human made exposure or dose is from medical testing and treatment. However, study done by United States Environmental Protection Agency (US EPA) in 2012 stated that, radon (which is naturally available radioactive materials) causes an estimated 20000 lung cancer death each year. This finding is also supported by Mishra, Sapra, and Mayya (2014), that concluded increasing mortality is closely related to the high background radiation area.

The complex relationship between cancer and background radiation supports the need for environmental surroundings monitoring to increase the awareness among the public regarding risk of ionising radiation. There are many types of radiation monitoring devices, also known as dosimeter that are capable of measuring low dose measurement with respect to background radiation. One of the recent popular dosimeter is the Optically Stimulated Luminescence dosimeter (OSLD). Medeiros and de Alencar (2013), emphasized that OSL dosimetry has become a successful technique in personal and environmental dosimetry due to high luminescence efficiency, excellent reproducibility, and fast readout signal. Environmental OSLD can detect all the alpha, beta and gamma radiation present in the surrounding.

Physical activity plays an important role in leading a healthy and balanced lifestyle. Mentioned by Deputy Minister of Tourism and Culture Malaysia Datuk Mas Ermieyati (2017), sport and recreation should be a fundamental part of the lives. Most of the sport and recreational places are designated outdoor, hence people have a high chance to be exposed to sunlight. Sunlight is the form of ultraviolet (UV) light and one of the ionising radiation sources (World Health Organization [WHO], n.d.).

A study done by US EPA (2010), stated that people who spent a lot of time under the sun has higher risk of getting skin cancer, cataracts, suppression of immune system, and premature aging of the skin. Sport and recreational places that exposed to high background radiation might increase the risk of cancer to the visitors. There was limited research done to assess the level of background radiation (BRL) in the sport and recreational places in Kuantan by using OSLD. Therefore, it is necessary to monitor the environmental surroundings in Kuantan, in order to have the safe conditions for leisure activity.

METHODS

Design of Study

This was an experimental study done with seven chosen sports and recreational places available in Kuantan, Pahang: Futsal Taman Polo, Stadium Hoki Wisma Belia, Stadium Darul Makmur, Esplanade, Taman Gelora, Teluk Cempedak, and Futsal Playground.

Optically Stimulated Luminescence Dosimeter (OSLD)

InLight Environmental Dosimeter by Landauer, Inc. was chosen as OSLD for the data collection. The material used in this dosimeter was Al_2O_3 as the layer of detector element for detecting four types of doses namely deep dose, lens dose, shallow dose and beta dose.

Table 1: D**etection capabilities of InLight Environmental Dosimeter**

Types of radiation	Range of energies detected
Photons (X and gamma rays)	Energies above 15keV nominally: 1mrem to 1000 rem
Beta particles	Energies greater than 500 keV average energy: 20 mrem to 1000 rem

Preparation and Labelling of OSLD

Before process of OSLD placement, the OSLDs were annealed using white light. This standard of procedure was done at least one day before the OSLD placement. OSLDs were placed inside plastic zippers as protective measure to prevent any damage caused by dirt or water during the placement of OSLDs. The front of plastic zippers was labelled with code numbers representing the designated places. All annealed OSLDs were placed inside a lead container to prevent exposure to external radiation that will contaminate and interfere to the reading value. The bar code of the OSLD was noted according to the designated places to make sure that the same OSLD was used at the same places throughout seven weeks of data collection.

Placement of OSLD at Designated Places

The labelled OSLDs with designated place were carefully placed at a suitable position after considering the possible external factors that might cause damage to the OSLDs. There were seven cycles of data collection throughout the experiment. One cycle consists of seven days. On the first day, the OSLDs were prepared and placed inside the lead container then brought to designated places for placement. Then the OSLDs were left for six days. The collection of OSLDs were done on the seventh day of the cycle and brought to Diagnostic Imaging Laboratory in KAHS, IIUM for reading purposes using the InLight microStar system.

Data Analysis

All the data generate in the microStar system was sync and converted to Microsoft Excel format for analysis purposes. Details extracted from the data and visualized in Microsoft Excel were actual dose per week, cumulative dose and annual dose. The background radiation doses in the designated area were also compared with the recommended value by radiation protection regulatory body such as IAEA, AAPM and AELB.

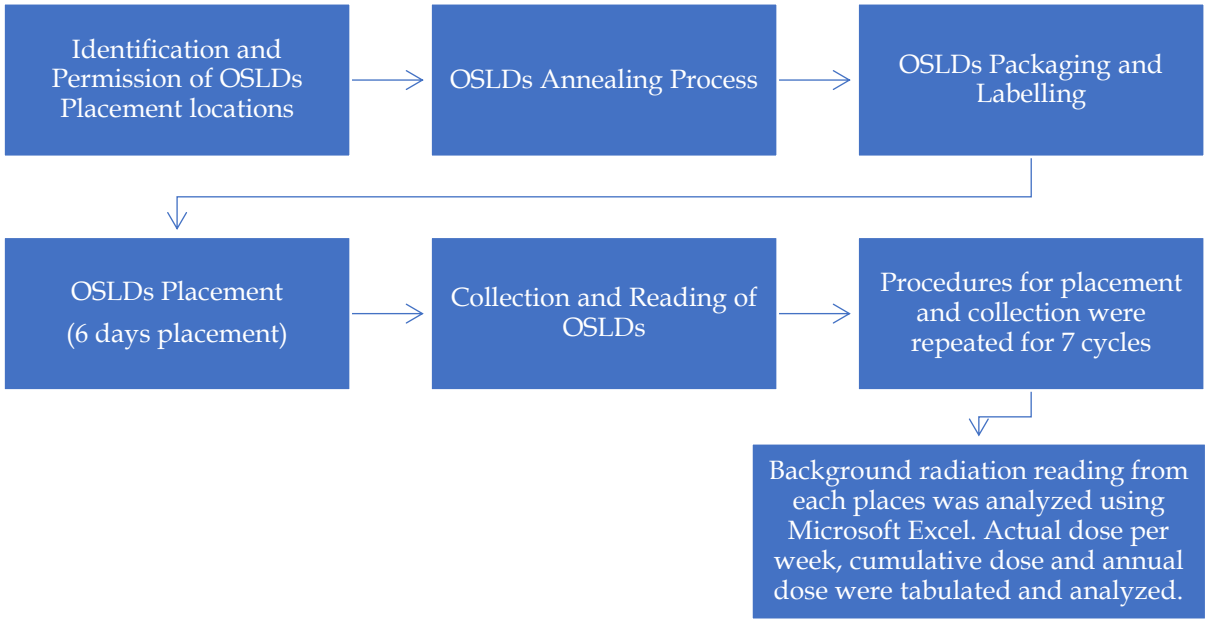


Figure 1: The Flow of OSLDs procedure.

Figure 1 shows the flow of procedure throughout the study for seven cycles. The procedures include pre-data collection, during data collection and post data collection.

RESULTS

Different windows in the OSLD give out different values according to the types of radiation detected. Deep dose refers to penetrating energy from gamma or x-rays. Shallow dose refers to low energy and less penetrating radiation such as beta and low energy x-rays. Lens dose refers to the intermediate range of radiation energy. In this study, deep and lens dose represent the cumulative dose whereas shallow and beta dose are not detected.

Accumulated Background Radiation Dose in Different Sport and Recreational Locations in Kuantan

The accumulated background radiation level (BRL) shows an increasing trend in BRL over the seven cycles as shown in Figure 2. The highest cumulative dose reading was recorded in Stadium Hoki Wisma Belia on the seventh cycle with a reading of 0.263 mSv. The lowest cumulative deep dose on the seventh cycle was at Futsal Playground with a reading of 0.152 mSv. The recorded cumulative doses for all designated places were different starting in Cycle 2 until Cycle 7 although the initial values (Cycle 1) were relatively similar. The differences in the recorded values are probably influenced by several factors such as geographical factors and infrastructure development factors.

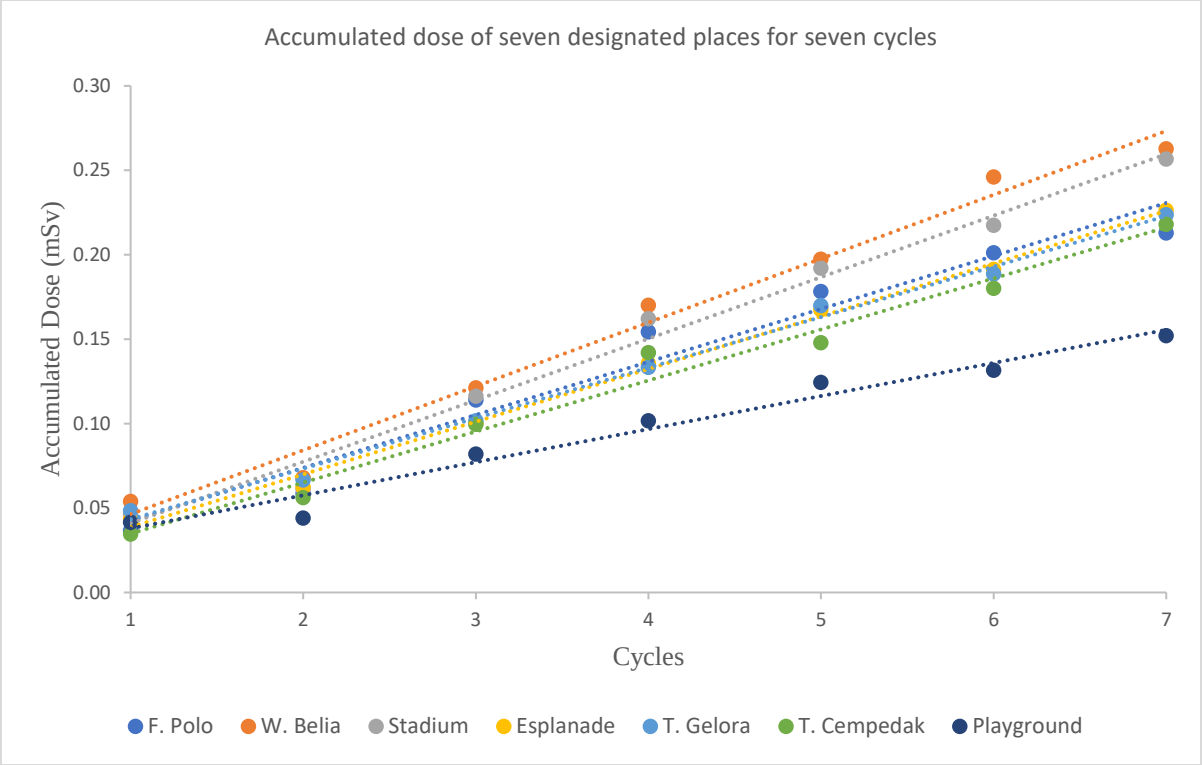


Figure 2: Accumulated dose of seven designated places for seven cycles.

Comparison of Estimated Annual Dose with Recommended Background Radiation Guideline for Public by Radiation Regulatory Bodies

Cappelan and Unhjem (2009) highlighted the recommended public and non-occupational exposure limit by International Commission on Radiological Protection (ICRP) of 1 mSv per year. The same recommended value was also highlighted by Atomic Energy Licensing Board (AELB) in "Code of Practice on Radiation Protection of Non-Medical Gamma & Electron Radiation Facilities" published in 2008.

For the comparison purposes, the background radiation level (BRL) obtained in this study was calculated and converted to the estimated annual dose value. The estimated annual dose was calculated by using simple equation based on the time of the OSLD placement; the cumulative actual dose was divided with days of placement and then multiplied with 365 days occupied in a year. The estimated annual dose and the percentage differences with the recommended value for each location were tabulated in Table 3. The percentage difference between the readings obtained and the value from radiation protection regulatory bodies was calculated using the following formula:

$$\textit{Percentage Difference} = |V_1 - V_2| / (V_1 + V_2/2) \times 100$$

$\mathbf{V_1}$= Estimated Annual Dose of a designated location
$\mathbf{V_2}$= Annual Dose recommended by radiation regulatory body

Table 3 Comparison of estimated annual dose with recommended background radiation guideline for public by radiation regulatory bodies

Location	Estimated Annual Dose (mSv/year)	Recommended annual public dose by ICRP, AELB and IAEA (mSv/year)	Percentage Difference %
Futsal Polo	1.851		59.70
Stadium Hoki	2.286		78.27
Stadium Darul Makmur	2.233		76.28
Esplanade	1.964	1.0	65.05
Taman Gelora	1.947		64.27
Teluk Cempedak	1.895		61.83
Futsal Playground	1.321		27.66

DISCUSSION

Throughout the study, readings obtained in lens and deep windows from the OSLD were the same. There were no differences of reading between all seven designated places. Supposedly, these two windows are able to differentiate two different types of radiation energy, high penetrating energy from gamma or x-rays and intermediate radiation energy. According to the Landauer specialist, this situation is due to the presence of radiation with high energy peak but low in radioactivity. Therefore, due to these conditions, the background radiation values for both windows in the OSLDs recorded the same value.

The two locations with the highest cumulative actual deep dose reading were Stadium Hoki Wisma Belia (3.8274° N, 103.2825° E) and Stadium Darul Makmur (3.8149° N, 103.3238° E) with reading of 0.263 mSv and 0.257 mSv respectively. Both places were surrounded with tall and big buildings. Nearby Stadium Hoki Wisma Belia exists a huge swimming pool centre, big restaurant building and massive convention centre. Stadium Darul Makmur was in the centre of Kuantan city with tall buildings around it. The surrounding factors (development of infrastructure) contribute to higher probability of high background radiation level detection as the building materials are one of the radiation potential sources. The type of raw material or industrial waste used for building material production determines the radioactivity of building materials (Mustonen, Pennanen, Annanmaki & Oksanen, 1997). Thus, this geographical setting may have contributed to the reading obtained from the OSLD.

The existence of several influencing factors can be related to the findings of estimated annual dose for background radiation in sports and recreational places Kuantan, Pahang that exceeded the recommended guideline for public by radiation regulatory bodies. The first factor is geographical factor. According to a study done by Ramachandran (2011), the cosmic ray dose rates increase as the altitude increases. This explanation is applicable for Esplanade, Teluk Cempedak and Taman Gelora where the annual dose from these locations is almost identical (1.964 mSv, 1.895 mSv and 1.947 mSv respectively) reflecting the almost similar elevation above sea level (2m, 7m and 8m respectively). Futsal Playground and Futsal Taman Polo were expected to have the highest annual background dose with elevation from sea level of 26m and 31m respectively. However, these two locations had the lowest annual dose (1.321 mSv and 1.851 mSv respectively) compared to the other designated locations. Therefore, the geographical factor (elevation above sea level) was not applicable for these two locations.

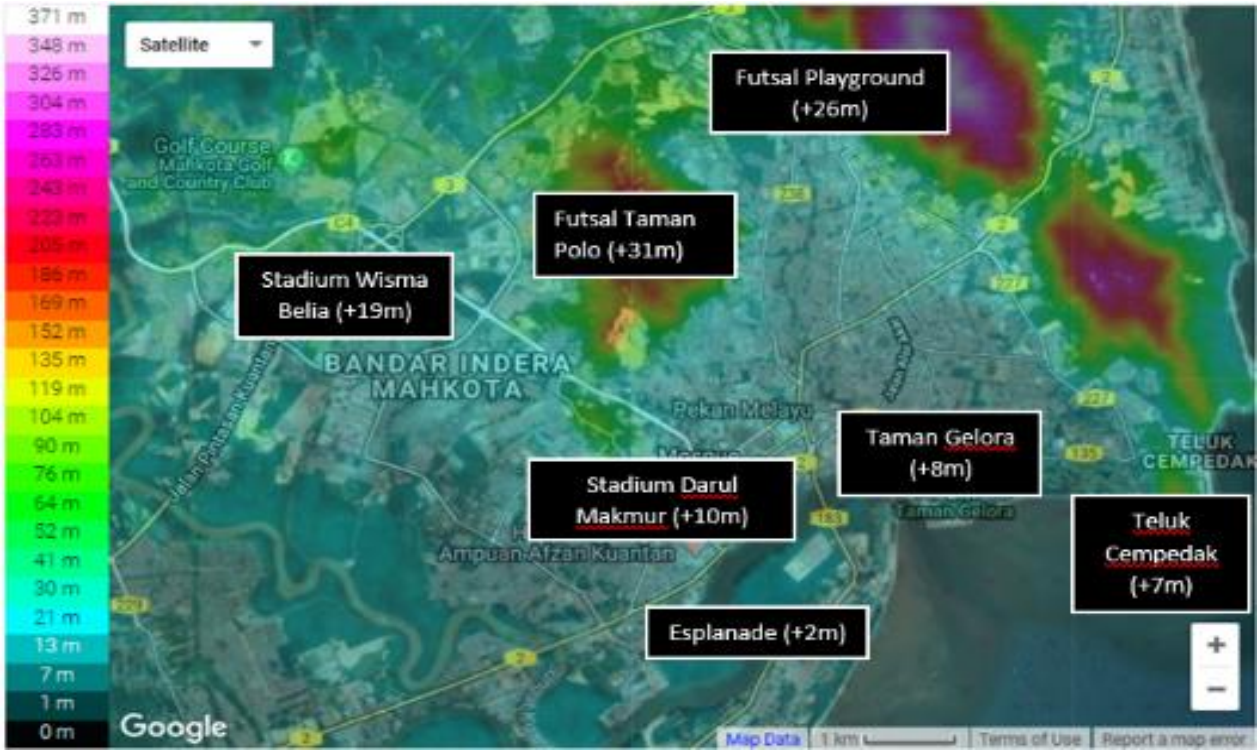


Figure 3: Topographic map of designated sport and recreational places in Kuantan, Pahang.

High estimated annual background radiation dose from Stadium Hoki Wisma Belia (2.286 mSv) and Stadium Darul Makmur (2.233 mSv) indicate that there are other influencing factors such as development of infrastructure and building materials that were affecting the reading of OSLDs at these locations. Besides natural rocks and soil, it can be identified that the difference in readings from all designated places were due to difference in content of materials presence in the building materials and the nature of the building itself. Increment of the aerial outdoor gamma dose rate by about 35% is due to the building materials instead of soils and rocks (Medeiros & Yoshimura, 2005). This statement suggested that the building materials in the location such as Stadium Hoki Wisma Belia and Stadium Darul Makmur may consist of materials that can emit radiation. In fact, these materials in the end may have contributed to the liberation of radiation gases that affect the reading of the OSLDs. The level of background gamma radiation in urban places is not only dependent on the type of building materials but also on the thickness of a layer of the building materials.

CONCLUSION

The measurement of background radiation in designated places recorded the different levels of deep dose readings and showed increasing trend throughout seven cycles representing accumulated dose. The highest annual dose reading was in Stadium Hoki Wisma Belia (2.286 mSv) and the lowest was at Futsal Playground (1.321 mSv). The estimated annual dose of the designated places exceeded the recommended value of background radiation for public (1 mSv per year) from radiation regulatory bodies; ICRP, AELB and IAEA. Some possible influencing factors are geographical, types of building materials and development of infrastructure. However, the findings in this study only recorded the background

radiation dose for a short duration and only reported the estimated annual dose. Therefore, it is suggested that this study to be continued for a longer study period to obtain more reliable results and can be used as a guideline as well as platform for environmental radiation monitoring in Malaysia.

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ASCERTAINING THE INFLUENCE OF GRID VS. NON-GRID TECHNIQUES ON RADIATION DOSE TO THE SKULL, EYES, AND THYROIDS AND IMAGE QUALITY IN ANTEROPOSTERIOR (AP) SKULL X-RAY EXAMINATIONS: A PHANTOM STUDY

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ABSTRACT

Introduction: Skull radiography plays a pivotal role in diagnosing traumatic head injuries, yet concerns persist regarding radiation exposure to organs, such as the brain, eyes, and thyroids. This study addresses the often-overlooked radiation protection measures for these organs, particularly in antero-posterior (AP) skull radiography cases. The utilization of a grid is essential for visualizing intricate cranial details, encompassing both soft tissues and bony structures. However, grid usage typically necessitates higher exposure settings compared to the non-grid technique. Thus, we investigate the effects of grid and non-grid techniques on entrance surface dose (ESD) to the brain, and radiation dose to the eyes and thyroid, and image quality. **Methods:** The Kyoto Kagaku Anthropomorphic PBU-50 head phantom was exposed with the Siemens Multix Top X-ray system. Various exposure parameters were explored, including (68 kVp, 9 mAs), (68 kVp, 12.5 mAs), (75 kVp, 9 mAs), and (75 kVp, 12.5 mAs). ESD for skull, eyes, and thyroid were measured using optically stimulated luminescence dosimeters (OSLDs) positioned at the glabella, eyes, and thyroid on the phantom. Image quality was assessed using the Image Criteria Score (ICS). **Results:** The analysis revealed that there was no significant difference in ESD between the grid and non-grid techniques when considering the larger OID ($p > 0.05$). However, a significant distinction in image quality emerged between the two techniques, especially for lower exposure factor ($p < 0.05$). Remarkably, the non-grid technique with a 4 cm air gap (OID) exhibited slightly higher ESD values in comparison to the grid technique (no air gap) when employing identical exposure parameters. **Conclusion:** Using the grid technique with no air-gap led to lower ESD values and better image quality, even at the lowest exposure settings. Additionally, this study found that the radiation dose values for the eyes and thyroid remained remarkably low for images attaining the highest ICS scores. These findings underscore the importance of optimizing radiographic techniques to achieve a balance between image quality and radiation dose for brain, eyes and thyroids in AP skull radiography.

Keywords: ESD, OSLD, OID, Grid, Skull examination, Exposure factors

INTRODUCTION

Medical imaging, including skull X-ray examinations, plays a crucial role in diagnosing diseases, localising abnormalities, and characterising pathologies (Karami et al., 2017). However, it is imperative to assess and justify the radiation dose and physical parameters applied to patients to ensure radiation protection in diagnostic radiology. Skull X-ray examinations, linked to low levels of radiation exposure, are now standard practice for patients who have had head injuries (IAEA, 2002). Skull x-ray radiography uses minimal doses of radiation, but repeated examinations on the same patient can

nevertheless cause radiation overload. This could potentially contribute to the development of cancer and, in some cases, lead to cognitive issues in adulthood (Mazonakis et al., 2004). Often, healthcare practitioners may underestimate the radiation dose absorbed by these radiosensitive organs during skull x-ray examinations. Additionally, the omission or inadequate use of shielding can result in unnecessary radiation exposure to tissues. To address these concerns, European Diagnostic Reference Levels (DRLs) set maximum values for Entrance Surface Dose (ESD) for skull X-rays, emphasising the importance of dose optimisation (Mazonakis et al., 2004). Dose optimisation aims to use the minimum necessary radiation exposure without compromising image quality (Gogos et al., 2013), aligning with the As Low As Reasonably Achievable (ALARA) principle (Donya et al., 2014).

One aspect often overlooked during skull X-ray examinations is the radiation dose to the eyes and thyroid tissues. These tissues are particularly sensitive to radiation due to their actively dividing and less-differentiated cells. Proper patient preparation, including the use of lead shielding, can help achieve dose optimization. Unfortunately, many routine examinations do not provide patients with wearable safety shielding devices like thyroid shielding or eye covers (Fetterly et al., 2017).

Dose monitoring is essential to ensure radiation exposure remains within reference limits and that patient protection is upheld (Omar et al., 2019). In skull radiography, the posteroanterior (PA) projection can reduce the absorbed dose to the eyes by up to 95% compared to the anteroposterior (AP) projection (IAEA, 2002). Some skull projections require caudal angulation of the X-ray tube to minimise thyroid dose, and beam collimation helps reduce unnecessary radiation to the thyroid gland. Research has shown that the use of shielding significantly reduces thyroid doses (Shortt et al., 2008).

Moreover, there are various techniques to reduce radiation dose in skull X-ray examinations, including decreasing the collimator field size, using more sensitive detectors, and implementing the air gap technique (Tsuji et al., 2006). While the use of anti-scatter grids can enhance image quality, it typically increases the dose by 50%, as higher X-ray intensity is required to maintain the signal-to-noise ratio (SNR) (IAEA, 2002). Increasing the object-to-image distance (OID) through the air-gap technique reduces scattered effects and contributes to improved image quality, although it may magnify the image.

In the field of radiological practice, the issue of radiation dose during skull radiography has become a subject of debate due to the use of low exposure factors. While the doses may appear low, there are concerns regarding the direct primary beam exposure to the eyes and scattered radiation affecting areas outside the collimated region, such as the thyroid gland. Protecting these sensitive organs, the thyroid and eyes, is of paramount importance during skull imaging (Omar, M et al., 2019). Chang et al. (2017) mentioned that conventional radiography, particularly in skull can result in the thyroid gland receiving significant doses of radiation. Moreover, a study by Omar, N. A. et al. (2019) highlighted the potential for x-ray exposure to impact the eyes' lenses, leading to eye problems.

This study aims to measure the radiation dose received by the skull, eyes, and thyroid during skull X-ray procedures by employing optically stimulated luminescence dosimeters (OSLD). The study employs both anti-scatter grid and non-grid techniques (air gap technique). Importantly, this research excludes shielding for the thyroid. The anti-scatter grid plays a crucial role in improving image quality by selectively rejecting scattered radiation while transmitting primary radiation. In summary, the primary goals are to gain insights into optimising radiation dose and image quality in skull radiography, with a focus on enhancing patient safety and minimising radiation exposure while maintaining diagnostic image quality.

MATERIALS AND METHODS

In this experimental study, Siemens MULTIX TOP X-ray imaging system was employed. The Kyoto Kagaku Anthropomorphic PBU-50 head phantom was exposed. To accurately simulate the positioning of a patient with a traumatic head injury, the PBU-50 head phantom was placed in a supine position on the bucky table, which was oriented for an anteroposterior (AP) projection as shown in Figure 1. This supine presentation closely resembles the posture adopted by patients in trauma conditions, especially when a skull examination is required. A 24 x 30 cm image receptor (IR) was carefully positioned lengthwise on top of the bucky table. This precise placement is vital in capturing the entire area of interest in the skull examination. The choice of exposure factors, specifically kilovoltage peak (kVp) and milliampere-seconds (mAs) settings, was influenced by prior research conducted by Khoshdel-Navi et al., (2016).



Figure 1. Shows the PBU-50 head phantom on the bucky table with grid (no air gap).

According to Khoshdel-Navi et al., (2016) the acceptable range of exposure factors for the AP skull projection is 60 to 78 for kVp and 8 to 50 for mAs. In this study, two kVp settings, namely 68 kVp and 75 kVp, were selected. Additionally, mAs adjustments were made, with 9 mAs and 12.5 mAs applied for both methods. The source-to-image receptor distance (SID) of 100 cm and a small focal spot size was selected. A summary of these parameters can be found in Table 1.

Table 1. Parameters used in this experimental study

PARAMETERS	DETAILS
Kilovoltage (kVp)	68, 75
Milliampere-second (mAs)	9, 12.5
Imaging plate size (cm)	AP projection: 24 x 30, lengthwise
Central ray	Perpendicular to the center of IR, AP projection: at the level of glabella
Source-to-image distance (cm)	100
Object-to-image distance (cm)	0, 4
Focal spot	Small focal spot
Grid (grid ratio)	Stationary grid (8:1)
AEC	Off

For non-grid technique with a 4cm air gap (OID). The head phantom was positioned directly onto the imaging plate, with a 4cm air gap achieved using a skull foam positioning pad. Sponges were placed on both sides of the head phantom to immobilise it as shown in Figure 2.



Figure 2. Shows the PBU-50 head phantom on the bucky table without grid with air gap (4cm OID)

To measure the ESD naonDot OSLDs were placed at specific locations; glabella, eyes, and thyroid on the skull as shown in Figure 3A and B. Before the exposure to the OSLD process was conducted, an initial reading of the OSLD was taken and recorded. This initial reading was documented in a lab logbook. To determine the ESD, the result of the post-irradiated dosimeter was subtracted from the initial reading. This calculation provided the radiation dose at the entrance surface of the tissue. Each exposure and dose reading were repeated three times for each kilovoltage peak (kVp) used, and an average dose reading was calculated. This repetition ensured accuracy in the measurements. The experiment involved variations in the use of grids and object-to-image distance (OID). Figure 3 (A) depicts the setup with a grid - no air gap, while Figure 3 (B) shows the setup without a grid and with a 4cm OID – air gap.



Figure 3. Positions of nanoDot OSLDs on PBU-50 head phantom for the measurement of ESD with a grid (A) and without a grid (B).

For image quality assessment a total of 8 images were obtained using the technical parameters summarised in Table 1 and subsequently evaluated by four experienced radiographers. To ensure the competency of the radiographers conducting the evaluation, a minimum requirement of at least 2 years

of experience in the radiography field was set. To maintain objectivity and prevent bias during the evaluation process, the images were intentionally labelled with 8 alphabet codes, concealing any information regarding the technique and exposure factors used to capture the images. This practice aimed to ensure that the evaluation was solely based on the image quality and not influenced by any extraneous factors. Each of the four radiographers received a set of evaluation forms (as detailed in Table 2) for their individual assessment of the images. The evaluation process employed the Image Criteria Scoring (ICS) method, focusing on image quality criteria relevant to AP skull images, including clarity, contrast, and anatomical details.

Table 2. Shows the Image Criteria Scoring (ICS) method and image quality criteria.

No	Criteria	Scale	Image Quality
1	Visually sharp reproduction of apex of petrous temporal bone	1 2	Very poor Poor
2	Visually sharp reproduction of outer and inner lamina of cranial vault	3 4	Fair Good
3	Visually sharp reproduction of inner auditory canal Overall contrast	5	Excellent
4	Overall density		
5	Overall image resolution		
6			

IBM's Statistical Package for the Social Sciences (SPSS) version 26 was used to compile and analyse the study's data. The resulting ESD and the image quality of the AP skull projections using the grid approach and the non-grid technique with an OID increase were compared using the Kruskal-Wallis test for statistical significance.

RESULTS

Entrance Surface Dose (ESD) to Skull in AP Skull Examination

Entrance surface dose (ESD) for anterior-posterior (AP) skull radiography was investigated under different exposure factors, and comparing the use of a grid technique without air gap (0 cm OID) and without a grid technique with 4 cm air gap (OID). The study aimed to assess the impact of grid usage and OID variation on ESD and to understand how variations in kVp and mAs affect ESD. The key findings are as follows:

Figure 4 presents the mean ESD values for AP skull radiography with a grid and no grid (4 cm air gap). The ESD for the skull was slightly higher when no grid was utilized, indicating that the grid technique effectively reduced ESD. This observation aligns with the intended purpose of grids in radiography, which is to minimize scattered radiation. The ESD decreased when kVp was increased with low mAs, demonstrating that higher-energy X-rays (kVp) can produce diagnostic images with reduced radiation exposure.

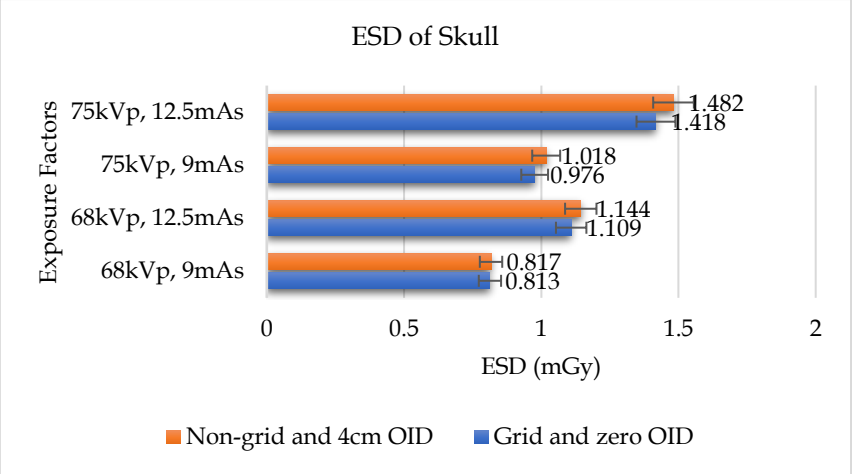


Figure 4. Mean ESD of AP skull with a grid (no air gap) and without a grid at 4 cm air gap (OID)

Conversely, when the same kVp was used with higher mAs, ESD increased, highlighting the direct relationship between mAs (exposure) and ESD. The radiographic settings of 75 kVp and 12.5 mAs caused the highest ESD to the skull. This was true for both grid and no grid techniques, with values of 1.418 mGy and 1.482 mGy, respectively. The Kruskal-Wallis test was conducted. The statistical analysis revealed that there was no statistically significant difference in the average ESD between the skull imaging conducted using the grid approach without object-image distance (OID) and the non-grid technique with a 4 cm OID. The p-value obtained from the analysis was 0.564, which is more than the predetermined significance level of 0.05.

Radiation Dose to Eyes in an AP Skull Examination

According to the findings of the study, the AP skull examination without a grid resulted in a higher eye dosage of 1.558 mGy at 75 kVp and 12.5 mAs as shown in Figure 5, whereas the grid technique with lower exposure factors (68 kVp and 9 mAs) resulted in the lowest eye dose of 0.82 mGy. The grid approach also resulted in the lowest overall eye dose.

Radiation Dose to Thyroids in an AP Skull Examination

Figure 6 shows the highest measured dosage to the thyroid gland was 0.039 mGy (75 kVp, 12 mAs, no grid and 4 cm air gap), while the lowest dose measured was 0.015 mGy (68 kVp, 9 mAs, no grid, and 4 cm air gap). The thyroid gland, situated at a greater distance from the centre beam, was exposed to comparatively lower dosages for each specific technical configuration. The investigation employed a standardised collimation size and deliberately omitted the thyroid gland from the region covered by the collimation beam in order to reduce the extent of thyroid exposure.

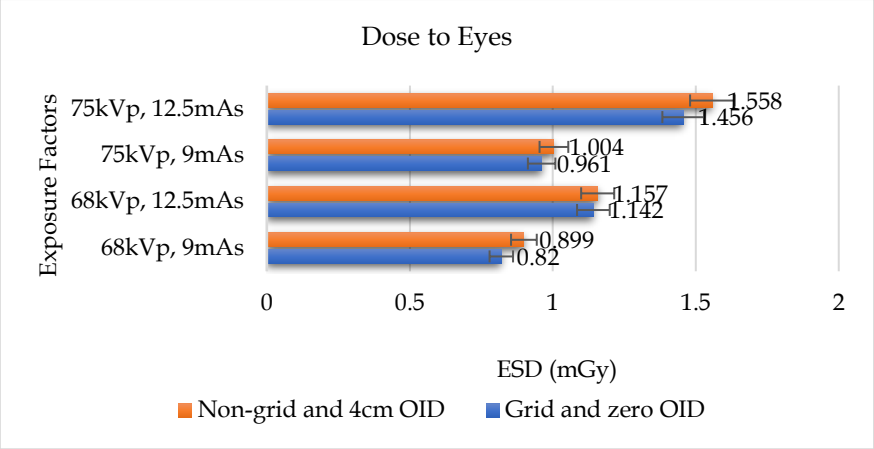


Figure 5. Mean doe to eyes with a grid (no air gap) and without a grid at 4 cm air gap (OID).

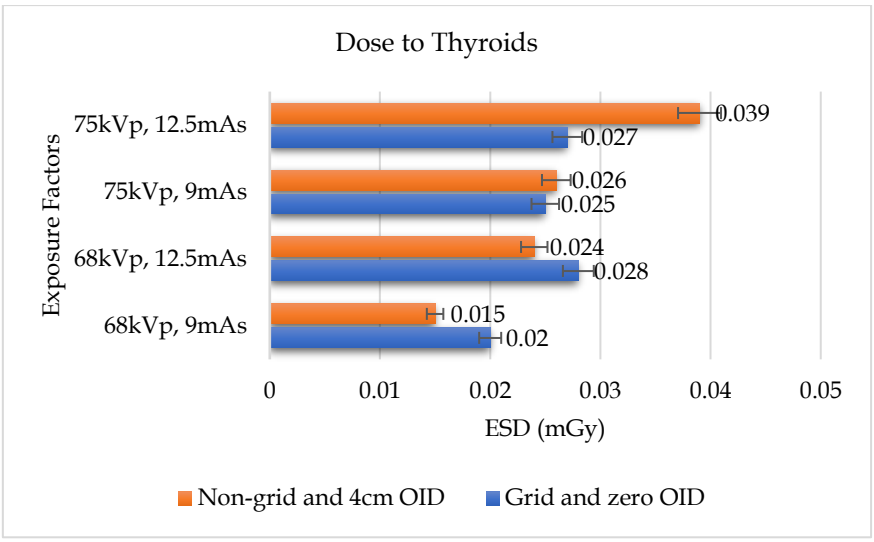
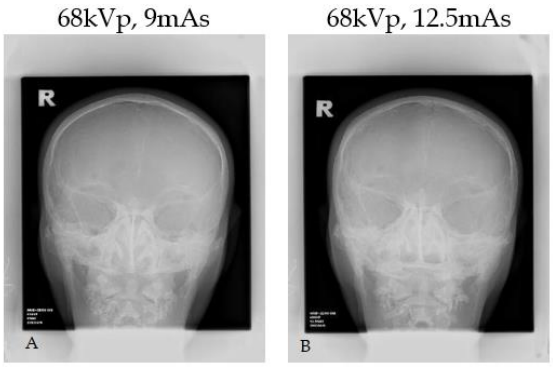


Figure 6. Mean doe to thyroids with a grid (no air gap) and without a grid at 4 cm air gap (OID).

Radiographic Images of the Anteroposterior (AP) Skull Projection

The images were obtained by varying the exposure settings with and without a grid. The acquisition of images for the AP skull projection aims to achieve optimal image quality while capturing diagnostically relevant features. The radiographs labelled as A, B, C, and D, as seen in Figure 7, pertain to the anteroposterior (AP) skull imaging approach utilising a grid and a no air gap (0 cm OID). The radiographs depicted in Figure 8 (A, B, C and D) correspond to the AP skull imaging, specifically utilising the non-grid technique with an air gap of 4 cm (OID). It is important to acknowledge that the exposure factors employed in this investigation were derived from clinical settings.

The primary aim of this part of the study was to determine the effects of AP skull radiography, specifically focusing on identifying the technique that offers the lowest exposure factor and optimal image quality. To accomplish the objective of this study, a group of four radiographers performed an evaluation of the image quality. The results were synthesised and subsequently shown in Figure 9.



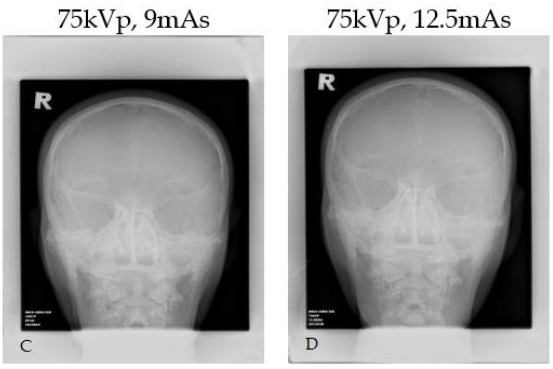
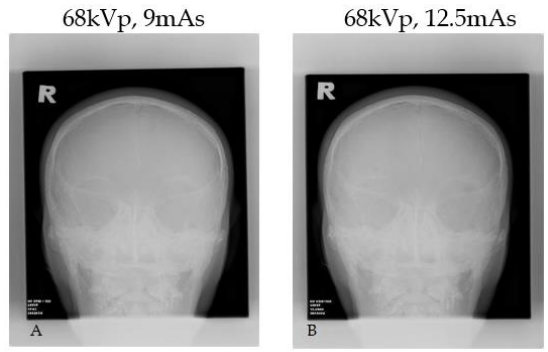


Figure 7. Radiographs of AP Skull with Grid Technique



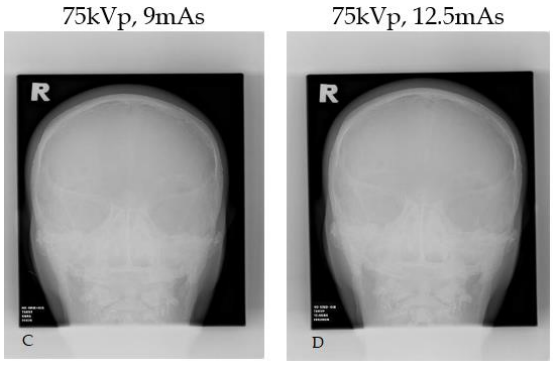


Figure 8. Radiographs of AP Skull without Grid Technique and 4cm OID

The results of the Kruskal-Wallis test revealed a statistically significant disparity in image quality when comparing the utilisation of grid and non-grid approaches in relation to the 4 cm air gap (OID) of the score derived from the ICS assessment in AP skull radiography ($p = 0.02$, $p<0.05$).

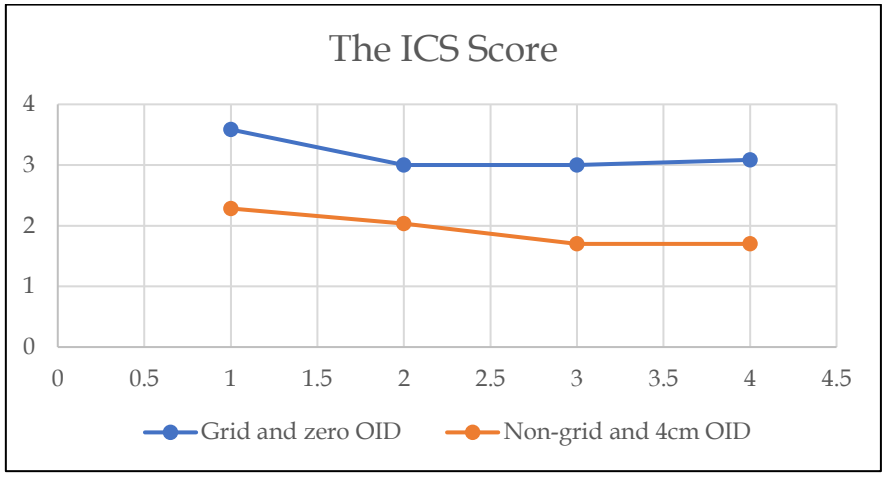


Figure 9. Average of Image Criteria Scoring (ICS) for AP skull radiography by using grid and non-grid with OID technique with different exposure factors (kVp and mAs)

DISCUSSION

In diagnostic imaging, X-ray photons interact with matter in two main ways: photoelectric absorption and the Compton Effect. These effects are mainly determined by the energy of the X-ray photons that hit the material (Carlton & Adler, 2013). Tube potential (kVp) and milliampere-seconds (mAs) are essential parameters in X-ray production. Tube potential (kVp) determines the energy of the X-ray

photons, affecting image contrast and patient dose (Martin, 2007). Milliampere-seconds (mAs), on the other hand, determines the amount of radiation produced over time, influencing radiographic image density.

The study results revealed that using high kVp with low mAs settings resulted in lower entrance skin dose (ESD) compared to lower kVp with high mAs settings. High kVp increases the energy of the photons, allowing them to penetrate deeper and exit the patient's body without significant absorption by tissues, resulting in lower ESD. Conversely, lower kVp with high mAs leads to higher ESD due to increased photoelectric absorption in body tissues.

ESD of Skull with Grid at 0cm OID and without Grid at 4cm OID

The highest recorded ESD for skull X-ray was 1.482 mGy, using exposure factors of 75 kVp and 12.5 mAs without a grid technique. However, this value is still below the Diagnostic Reference Level (DRL) of 4.8 mGy set by the Ministry of Health Malaysia (2013) for anterior-posterior (AP) skull radiography. The use of an air-gap technique without a grid reduced patient surface exposure compared to using a grid. The study's results showed only a slight difference in ESD between the grid and non-grid techniques at a 4 cm object-to-image distance (OID), with slightly higher values for the non-grid technique.

The study used medium-level exposure factors, specifically kVp in the range of 68–75 kVp, and did not employ high kVp techniques. Generally, 75 kVp settings resulted in a slightly higher ESD. Nonetheless, the doses remained within acceptable limits based on various studies, Table 3. Differences in techniques, patient characteristics, exposure settings, dosimeter types, and dosimeter placement across studies might account for slight variations in ESD measurements.

Table 3. Comparison of measured ESD to skull in AP skull examination with the other studies.

Projection	**ESD (mGy)**			
	This study	Mohamadain et al., (2015)	Suliman et al., (2006)	Compagnonet al., (2008)
AP Skull	0.81-1.48	0.66-1.25	1.41-2.26	1.32-1.64

These findings suggest that this specific combination of 75 kVp and 12.5 mAs resulted in the highest radiation exposure to the skull. When using 68 kVp with 9 mAs, the ESD to the skull for both grid and no grid techniques was the lowest at 0.813 mGy and 0.817 mGy, respectively. This combination of settings minimized radiation exposure to the skull.

These findings underscore the importance of optimizing radiographic techniques to minimize radiation doses while maintaining image quality. Using grids effectively reduces ESD, which is critical for patient safety. Furthermore, selecting appropriate combinations of kVp and mAs is essential to achieving diagnostic images while keeping radiation exposure as low as reasonably achievable (ALARA). This research work offers significant contributions by shedding light on the variability of dose in anteroposterior (AP) skull radiography, hence providing useful guidance for optimising radiation dosage in clinical environments.

Dose to the Eyes and Thyroid with and without the Grid Technique

Eyes

Radiation exposure is a critical concern in medical imaging, particularly for procedures involving the head. This section discusses the findings of our study on radiation dose in anterior-posterior (AP) skull X-rays and compares them with a related study by Saeed and Almalki conducted in 2022. The objective

of the study was to assess how variations in exposure factors, such as kilovoltage peak (kVp) and milliampere-seconds (mAs), impact the radiation dose to the eye lens.

The study revealed significant variations in eye lens dose depending on the selected kVp and mAs values. When using higher values of kVp (75) and mAs (12.5) for skull X-rays, the eye lens dose increased. Specifically, the highest eye dose measured in this study was 1.558 mGy during AP skull examinations performed without the use of a grid. Conversely, the lowest dose recorded was 0.82 mGy, achieved with a grid technique and lower exposure factors (68 kVp and 9 mAs). Despite these variations, all measured doses remained below the established threshold dose range of 0.5 to 2.0 Gray (Gy) associated with the development of eye lens opacities.

Compared to Saeed and Almalki (2022), who used DoseCal and CALDose_X software to measure radiation doses to the eyes during AP skull examinations. Their findings reported doses of 2.2 mGy and 2.5 mGy, respectively. It becomes clear from comparing these outcomes to the doses measured in our study that the doses we obtained were lower than those Saeed and Almalki reported. This suggests that the choice of equipment, technique, and exposure factors can significantly impact radiation doses to the eye lens during AP skull X-rays.

Radiation dose management is of paramount importance in medical imaging to minimize potential health risks to patients. The study discussed here demonstrates the significance of exposure factors such as kVp and mAs in influencing eye lens doses during AP skull X-rays. Despite variations, all measured doses remained below the threshold dose associated with eye lens opacities. Furthermore, a comparative analysis with a previous study indicates the potential for optimization of radiation doses to the eyes, emphasizing the importance of choosing appropriate equipment and techniques for such procedures.

Thyroids

Radiological imaging plays a critical role in modern medicine for diagnostic and therapeutic purposes. However, it is essential to consider the potential radiation exposure to sensitive organs. Among the various organs vulnerable to radiation, the thyroid gland is of particular interest due to its location in the neck and its sensitivity to ionizing radiation. Our study investigated thyroid radiation doses in AP skull examination and how various factors, including technological advancements, have contributed to minimizing thyroid exposure. Additionally, historical data is presented to provide context for the study's results.

An important part of the study looked at how radiation dose patterns, especially kVp (kilovolt peak) and mAs (milliampere-seconds), affect thyroid doses. The results revealed that higher kVp and mAs settings correlated with increased thyroid doses, with the maximum recorded dose being 0.039 mGy and the lowest being 0.015 mGy. Interestingly, the thyroid, situated farther from the central ray, received relatively lower doses for each technical setting as compared to eyes. This variation underscores the importance of optimizing imaging parameters to minimize thyroid exposure.

To minimize thyroid exposure, the study employed various strategies. It utilized a fixed collimation size and excluded the thyroid from the collimation beam area, effectively shielding it from unnecessary radiation. Additionally, factors such as the number of projections and mAs were identified as influencing thyroid doses, emphasizing the importance of precise and tailored settings during imaging procedures.

Melo et al. (2016) presented historical patient data from 1930 to 2009 in order to contextualize the significance of the study's findings. According to this historical data, the average thyroid dose for the years 2000–2009 was 0.42 mGy. This historical perspective highlights a remarkable reduction in thyroid radiation exposure over the years. The study acknowledges that several technological advancements have played a pivotal role in achieving a noteworthy decrease in thyroid radiation exposure over time. These advancements include the implementation of collimators, filters, films, and intensifying screens, which collectively contribute to enhancing radiation safety in medical imaging.

Collimators are instrumental in shaping and limiting the X-ray beam, ensuring that only the necessary area is exposed to radiation. Filters are used to selectively absorb low-energy X-rays, further reducing unnecessary radiation exposure. Films and intensifying screens work together to improve image quality while reducing the amount of radiation required to obtain diagnostic images.

In summary, the study on thyroid radiation doses underscores the importance of optimizing imaging parameters and employing technological advancements to minimize radiation exposure to the thyroid gland. The historical context presented by Melo et al. (2016) reveals a significant reduction in thyroid doses over the years, showcasing the effectiveness of these measures in enhancing patient safety during medical imaging procedures. By adhering to best practices and leveraging technological innovations, healthcare providers can continue to ensure that thyroid radiation exposure remains at safe and minimal levels, thereby safeguarding the health and well-being of patients.

Image Quality of AP Skull Radiographs with and without Grid Technique

The image quality of AP skull radiographs with and without grid technique, reveals important insights into the impact of various radiographic techniques on image quality in skull radiography. The analysis of the findings provide a deeper understanding of the implications.

The study clearly demonstrates that the use of a grid technique significantly improves the image quality in skull radiography. The images taken with the grid technique consistently received higher scores from the evaluators compared to those without the grid or using the air-gap technique. This finding aligns with previous research indicating that grids are effective in reducing scatter radiation, which can degrade image quality (Bushberg et al., 2013).

Additionally, the research indicates that the use of the air-gap technique as a potential alternative to the grid may necessitate modifications in the characteristics of such approach. The the 4 cm OID employed in this investigation may have played a role in diminishing the quality of the images obtained using the air-gap approach. This is because scattered photons were able to reach the image receptor, so impacting the overall contrast and resolution. In order to raise the efficacy of the air-gap approach, it may be imperative to modify technical parameters or increase the OID to optimise the elimination of scattered radiation.

In addition, a greater number of scattered photons may reach the detector due to Compton scattering, which becomes more prevalent at higher kVp levels. Image noise is reduced and quality is enhanced because of grids' ability to absorb scattered radiation before it reaches the detector. Consequently, the findings of this study align with the aforementioned phenomena (Bushberg et al., 2013).

Moreover, the results of this study suggest that tube voltage (kVp) plays a crucial role in controlling contrast in skull radiography. Higher kVp values result in greater penetration of X-rays through the patient's tissues, which can affect image contrast. The study's findings support the principle that subject contrast, related to the differences in X-ray absorption by various tissues, is influenced by kVp selection (Schueler, 1998). For instance, the image at 75 kVp with 12.5 mAs showed slightly lower contrast compared to the image at 68 kVp with 9 mAs. This reinforces the importance of optimizing kVp settings to achieve the desired image contrast.

Additionally, the study highlights that mAs selection primarily affects image density but also has a secondary influence on contrast. Over exposure and under exposure can lead to reductions in image contrast. In this study, both 9 mAs and 12.5 mAs were considered for skull radiography, emphasizing the importance of appropriate mAs selection to achieve optimal image quality.

Furthermore, the findings of the research work show that using medium kVp selection along with the grid technique improves the visibility of important anatomical structures in skull x-rays, like the petrous temporal bone and the inner lamina of the cranial vault. This finding has clinical significance, as it suggests that specific technique parameters can improve the diagnostic value of skull radiographs.

In summary, this study provides valuable insights into the factors affecting image quality in skull radiography. It proves that the grid technique works to cut down on scatter radiation, stresses how important it is to choose the right tube voltage and mAs for contrast control, and stresses how important it is to use the right OID in the air-gap technique. These findings have implications for radiographic practice, emphasizing the importance of optimizing technique parameters to achieve high-quality skull radiographs and improve diagnostic accuracy.

CONCLUSION

This study has provided valuable insights into the use of grid technique and non-grid technique with a 4 cm air gap technique in anterior-posterior (AP) skull examinations. While no significant differences were observed in entrance surface dose (ESD) between the grid and non-grid techniques, the application of the grid led to significantly enhanced image quality. Further, the study also showed that using the lowest exposure factors produced the highest image quality. Notably, the ESD was higher when the skull phantom was close to the X-ray source and a non-grid technique was used with a 4 cm OID. Moreover, the dose for critical organs like the eyes and thyroid gland was also remarkably elevated when using the non-grid technique. This suggests that, from a radiation safety perspective, employing the grid technique is not only beneficial for image quality but also for minimising unnecessary radiation exposure to the thyroid and eyes. Additionally, the use of the grid technique also ensures improved visualisation of critical regions such as the petrous temporal bone and inner auditory canal, as well as density and contrast throughout the image. This highlights the potential for optimising radiation doses for patients while adhering to the "As Low As Reasonably Achievable" (ALARA) principle. In summary, the findings from this study emphasise the significance of employing the grid technique for AP skull radiography to achieve superior image quality and optimise radiation exposure for patients. This not only enhances diagnostic accuracy but also ensures patient safety by minimising unnecessary radiation exposure to sensitive organs. Furthermore, these results underscore the importance of adhering to the ALARA principle and adopting the right technique for the benefit of both patients and healthcare practitioners.

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NIGHT EATING SYNDROME AND ITS ASSOCIATION WITH SLEEP QUALITY AND STRESS BETWEEN MALE AND FEMALE UNDERGRADUATE STUDENTS

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Abstract

Introduction: Late-night eating habits, poor sleep hygiene, and stress are no longer uncommon due to their increasing prevalence in today's society. They typically affect young individuals, particularly students in developing nations. Nevertheless, there are limited research on night eating syndrome (NES) among Malaysian students. Thus, this cross-sectional study aimed to assess the association of night eating syndrome, sleep quality and stress level among undergraduate students. **Method:** A convenience sampling of undergraduate students aged between 19 and 25 years at International Islamic University Malaysia (IIUM) Kuantan was recruited and the total respondents were 436 students (218 female and 218 male respondents). A combination of Night Eating Questionnaire (NEQ), Pittsburgh Sleep Quality Index (PSQI), and Perceived Stress Scale (PSS) was used to collect the data from the respondents. The data were analysed using SPSS version 29 (SPSS 29.0) using Mann-Whitney U and Pearson Correlation tests. P value was set at $p<0.05$ as statistically significant. **Results:** The percentage of students having NES was 14.7%. However, there were differences between the prevalence of NES between male and female ($p=0.03$, $z = 2.163$). Also, there was a significant negative but weak correlation between NES and sleep quality ($r = - 0.149$, $p=0.002$). For association between NES and stress, there was a significant positive but weak correlation between those two ($r = 0.260$, $p=0.001$). **Conclusions:** The prevalence of NES is significantly higher among male than female students. A high level of NES was associated with a higher value of stress and poor sleep quality. Therefore, corrective strategies need to be taken place accordingly to enhance their well-being. Further research is warranted as these circumstances could potentially impair undergraduate students' academic performance.

KEYWORDS: Night Eating Syndrome, Sleep quality, Stress level, Undergraduate students

Introduction

The intake of nutrients, food groups, or general dietary patterns has a favorable impact on health and helps prevent chronic non-communicable diseases (NCDs) like diabetes and cardiovascular disease, according to a significant and growing body of research (Cena & Calder, 2020). Other than eating healthily, the quantity and quality of food also play an important role in well-being. Furthermore, the social and cultural preferences of people and households have a big impact on people's understanding of food and their food choices.

Night Eating Syndrome (NES) is a unique disorder characterized by a delayed pattern of food intake in which nighttime eating and/or excessive food consumption happens often after the evening meal. Due to its association with obesity, correlation with other psychiatric diseases, and sleep issues, NES is a clinically significant disorder (Kucukgoncu et al., 2015). Energy intake is lowered in the first half of the day and dramatically raised in the second half, disrupting the sleeping pattern. The absence of accompanying compensatory behaviors, the time of food intake, and the fact that food ingestions are limited, similar to repeated snacks rather than actual binges distinguish the condition from bulimia nervosa and binge eating disorder.

Salman & Kabir (2022) also stated that NES is linked to a number of sleep disruptions, including worse overall sleep quality, longer sleep latency, reduced sleep efficiency, and more frequent sleep disruptions. Additionally, issues with mood and anxiety are linked to both eating and sleeping difficulties. The severity of eating disorder symptoms is also linked to lower sleep quality. Some of them create coping mechanisms that describe food to cope with overwhelming and unpleasant emotions. Kim et al. (2023) studied 34,358 people and discovered that those who experience episodes of night eating have higher average depression ratings than those who do not. There were significant variations in stress levels between participants who experienced episodes of night eating and those who did not. The extent of this rise was especially noticeable in people who reported sleeping nine hours or more every night. Those who are prone to emotional eating may be more inclined to eat to lessen emotions of bad impact.

Gan et al. (2019) stated that male participants showed to have NES more than females and this is prevalent among technical field students. Kwan et al. (2021) reported that males were the risk factors for NES, but this study was conducted during Covid-19. There was another study that had been conducted by Dzulkafli et al. (2020) at IIUM Kuantan, however this study only investigated female subjects. Thus, the purpose of this study is to assess whether male university students have higher NES score compared to their female counterparts post-COVID 19 pandemic. This study also aimed to assess correlation of NES with sleep quality and stress level among university students since disordered eating behaviors have recently been gaining much attention and become a global concern due to their consistent growth trends throughout time. This study is therefore at the forefront of examining this topic.

Materials And Methods

Study Design and Population

A cross-sectional study was conducted at IIUM Kuantan which consists of six *kulliyyahs* (faculties): Kulliyyah of Medicine (KOM), Kulliyyah of Dentistry (KOD), Kulliyyah of Allied Health Sciences (KAHS), Kulliyyah of Pharmacy (KOP), Kulliyyah of Sciences (KOS) and Kulliyyah of Nursing (KON). Determination of sample size was calculated using a two-proportion formula based on the prevalence of night eating syndrome -among male and female public university students in Malaysia (Gan et al., 2019).

A convenient sampling method was used to select the respondents. The inclusion criteria for the respondents were undergraduate students aged 19 until 25 years. An online consent form for

participants was provided at the front page of the online questionnaire to make sure the participants were aware of the information. All information was treated as strictly confidential.

The study protocol was approved by the Kulliyyah of Allied Health Sciences Postgraduate and Research Committee (Reference No: IIUM/310//14/11/2) and IIUM Research Ethics Committee.

Questionnaire

For this study, a self-administered online questionnaire in Google Form was constructed in English. The questionnaire consisted of four sections: i)Sociodemographic data (respondent's age and gender, year of study, *kulliyyah*, financial status, self-reported weight, and height of the students), ii) Night eating evaluation using Night Eating Questionnaire (NEQ), iii) Sleep quality evaluation using Pittsburgh Sleep Quality Index (PSQI), iv) Stress level evaluation that assessed using Perceived Stress Scale (PSS). Body mass index (BMI) was calculated as the weight in kilograms divided by height in meters squared. It was categorized according to the World Health Organization (2000) classification: underweight (<18.50 kg/m^2), normal (18.50-24.99 kg/m^2), overweight (25.00-29.99 kg/m^2), and obese (≥30.00 kg/m^2).

Night Eating Evaluation

The respondents were assessed by using the Night Eating Questionnaire (NEQ) (Allison et al., 2008). This questionnaire was extensively used by researchers who performed studies on late-night eating behavior or night-eating syndrome (NES). In addition, this questionnaire has been validated and it is a potential measure to investigate night eating habits among general populations (Innamorati et al., 2018). Gan et al., (2019) used NEQ in their study to determine the risk factors for NES among public university students in Malaysia.

The NEQ was developed to determine whether any of the participants had NES. The NEQ has 17 measures that are capable of capturing the behavioral and psychological syndrome of NES, including the absence of morning appetite (two items), loss of control, and degree of urges to overeat before bed and during the night (four items), initial and middle sleeplessness (three items), mood (two items), frequency of eating during the night (three items), and belief that one has to eat to sleep (one item), as well as the level of awareness of these eating episodes (one item). A 4-point Likert scale was used to score each item, with the options being "not at all (0)," "a little (1)," "somewhat (2)," "moderately (3)," and "extremely (4)." Items 1, 4, and 14 were scored in reverse. The overall score for NEQ was determined by adding the scores of Items 1 through 12 and 14, and the score fall into two categories which were Non-NE (Non-Night Eater) and NE (Night Eater). The higher the score, the higher the NES possibility. A score from 0 to 5 indicates Non-NE while 5 to 64 indicates NE.

Sleep Quality Evaluation

For sleep quality evaluation, the Pittsburgh Sleep Quality Index (PSQI) questionnaire established by Buysse et al. (1989) was used. A study conducted by Farah et al. (2019) provided evidence to support the use of the PSQI-M (Pittsburgh Sleep Quality Index Malay Version) in a general Malaysian adult population. This questionnaire was widely used by many researchers to assess sleep quality and sleep habits. One research that utilizes this form was a study about poor sleep quality among medical students at IIUM by Said et al. (2020). Thus, this questionnaire was chosen for this study which also included IIUM female students as respondents. This questionnaire consists of 10 main questions and some of them have a few sub-questions. PSQI has two ways for the participant to answer, like writing information and choosing the best answer.

The PSQI contains 19 self-rated questions and 5 questions rated by the roommate. Only self-rated questions are included in the scoring. The self-rated items are combined to form seven "component"

scores, each of which has a range of 0-3 points. In all cases, a score of "0" indicates no difficulty, while a score of "3" indicates severe difficulty. The seven component scores are then added to yield one "global" score, with a range of 0-21 points. "0" indicates no difficulty and "21" indicates severe difficulties in all areas.

Based on the participants' self-reported retrospective evaluation, the seven sleep components: sleep latency, sleep duration, habitual sleep efficiency, sleep disruptions, use of sleeping medicine, and daytime dysfunction were measured by answering the questionnaire (Buysse et al., 1989). The range of scores for each component was 0 to 3, resulting in a global PSQI score of 0 to 21. The sleeping quality of the participants was rated based on the overall score, with points ranging from no difficulty in sleeping to significant difficulty in sleeping as the points increased. The subjects were then classified based on their PSQI global scores, with a PSQI score up to 5 indicating good sleep quality and a PSQI score of > 5 indicating poor sleep quality.

Stress Level Evaluation

The Perceived Stress Scale (PSS) (Cohen, Kamarck, and Mermelstein, 1983) was utilized in this evaluation. The PSS was one of the most popular psychological tools for assessing stress perception. It is a gauge of how stressful a person perceives their life's circumstances to be. The questions were created to get a sense of how unpredictably chaotic and overburdened respondents believe their lives to be. A few direct questions about current levels of experienced stress are also included on the scale. The PSS was created to be used in community samples that have completed at least junior high school. Shariff & Azlan (2021) had also chosen this questionnaire in their research concerning stressors among Malaysian undergraduate nursing students during the COVID-19 pandemic.

The PSS consists of 10 questions and the way to answer it is by choosing a score of 0-4 for each question. The PSS score can be determined by, first, reversing the scores for questions 4,5,7, and 8. On these 4 questions, the score needs to be reversed, like 0 = 4, 1 = 3, 2 = 2, 3 = 1, 4 = 0. Then, the scores for each item are added up to get a total. Individual scores on the PSS can range from 0 - 40 with higher scores indicating higher perceived stress. Scores ranging from 0-13 would be considered low stress, 14-26 considered moderate stress, and 27-40 considered high perceived stress.

Statistical Analyses

The data obtained were statistically analyzed using IBM SPSS Statistics for Windows, version 29 (SPSS 29.0). Mann-Whitney U Test was to compare the prevalence of NES between male and female. The association between NES and sleep quality was analysed using Pearson Correlation and same goes to association between NES and stress. The significance level for the 95% confidence interval (CI) was set at $p<0.05$.

Results

Sociodemographic Information

A total of 436 respondents (218 males and 218 females) were recruited in this study. The sociodemographic details are presented in Table 1.

Table 1 Sociodemographic data of respondents (N=436)

Category	Participants (n, %)
Gender	
Male	218 (50.0)
Female	218 (50.0)
Age	
19	11 (2.5)

20	103 (23.6)
21	110 (25.2)
22	126 (28.9)
23	68 (15.6)
24	15 (3.4)
25	3 (0.7)
Kulliyyah	
KAHS	141(32.3)
KOD	20 (4.6)
KOM	48 (11.0)
KON	52 (11.9)
KOP	41 (9.4)
KOS	134 (30.7)
Year of Study	
Year 1	119 (27.3)
Year 2	109 (25.0)
Year 3	150 (34.4)
Year 4	55 (12.6)
Year 5	3 (0.7)
Scholarship Status	
PTPTN	89 (20.4)
JPA	65 (14.9)
MARA	114 (26.1)
Self-Sponsored	131 (30.0)
Others	37 (8.6)
BMI category	
Underweight	51 (11.7)
Normal	286 (65.6)
Overweight	69 (15.8)
Obese	30 (6.9)

A total of 436 students from year 1 up to year 5 consisting of all male and female students from 6 different Kulliyyahs. Of all 436 students, 32.3% were from Kulliyyah of Allied Health Sciences (KAHS), 4.6% from Kulliyyah of Dentistry (KOD), 11.0% from Kulliyyah of Medicine (KOM), 11.9% from Kulliyyah of Nursing (KON), 9.4% from Kulliyyah of Pharmacy (KOP) and 30.7% from Kulliyyah of Sciences (KOS). All respondents are between the age of 19 and 25, and for their scholarship status, 89 (20.4%) of students funded by *Perbadanan Tabung Pendidikan Tinggi Nasional* (PTPTN), 65 (14.9%) funded by *Jabatan Perkhidmatan Awam* (JPA), 114 (26.1) funded by *Majlis Amanah Rakyat* (MARA), 131 (30.0) are self-sponsored and the balance which is 37 (8.6%) sponsored by others such as *Yayasan* from their states of origin, and scholarship from some organizations like Bank Rakyat and Sime Darby. With regards to their BMI, a total of 286 (65.6%) respondents had normal BMI, 69 (15.8%) were overweight, 51 (11.7%) were underweight, 23 (5.3%) and 7 (1.6%) of respondents were in obese class I and II, respectively.

NES based on night eating questionnaire (NEQ)

Table 2 indicates late night eating behavior of the students using NEQ. The questionnaire is to determine whether the respondents have met a NES criterion. NES criteria were divided into 2 categories which are normal (Non-NE) where the respondents did not meet any NES criteria at all and

night eater (NE) where the respondents have met almost all the NES criteria. Most respondents fall under the normal category (Non-NE) with the total number of 372 respondents (85.3%) whereas the balance fall under the night eater (NE) category with 64 respondents (14.7%)

Table 2 Respondent's night eating categories (N=436)

NES Categories	Frequency	Percentage (%)
Non - NE	372	85.3
NE	64	14.7

Stress level evaluation

Table 3 indicates the level of stress of the respondents. Based on the results, the number of respondents who were having moderate perceived stress was the highest with a total of 348 respondents (79.8%) while the lowest value was 34 respondents (7.8%) who were having high perceived stress.

Table 3 Respondent's stress levels (N=436)

Stress Categories	Frequency	Percentage (%)
Low	54	12.4
Moderate	348	79.8
High	34	7.8

Sleep quality evaluation

Table 4 below indicates the categories of sleep quality of the respondents. Based on the results shown in Table 4, respondents who were having good sleep quality is only 91 (20.9%) of respondents which was less than a quarter of the total of the respondents. Meanwhile, respondents who have poor sleep quality was 345 of respondents (79.1%).

Table 4 Respondent's sleep quality (N=436)

Sleep Quality Categories	Frequency	Percentage (%)
Good	91	20.9
Poor	345	79.1

Comparison Between Male and Female in NES

The first main objective of this study was to assess the comparison of the prevalence of night eating syndrome between male and female undergraduate students at IIUM Kuantan which was investigated using Mann – Whitney U Test. Based on Table 5, the test revealed a significant difference in NES between males and females ($p = 0.031$, $z = 2.163$).

Table 5 Comparison between male and female respondents (N=436)

Mann-Whitney U	Test Statistic	Standard Error	Standardized Test Statistic	p-value
26604.000	26604.000	1313.691	2.163	0.031

The median score for males was 17.00 which is significantly higher than females' median score (16.00).

Association between NES and Sleep Quality

Regarding the relationship between NES and sleep quality among undergraduate students at IIUM Kuantan, a negative, weak correlation between NES and sleep quality ($r = -0.149$, $p = 0.002$) was found. Thus, a higher level of NES is associated with poorer sleep quality.

Association between NES and Stress

A significant positive correlation ($r = 0.260$, $p < 0.001$) was found between NES and stress level. Therefore, a higher value of NES is associated with a higher level of perceived stress.

Discussion

This study examined NES and its association with sleep quality and stress level among undergraduate students. Findings of this study indicated that male respondents have higher median score than females which reflected a higher rate of NES. Gan et al. (2019) study demonstrated that men were 3 times more likely than women to have NES. Also, based on Dzulkafli et al. (2020), the prevalence reported from the study was only 4.2% and that applied for female since their research only focused on female. Moreover, Kwan et al. (2021) conducted research during COVID-19 pandemic found that male have higher NES prevalence than female which are 51.3% and 27.3%, respectively.

Furthermore, the existence of food delivery companies like Food Panda, Grab Food and McDelivery increase the opportunities for the students to buy food because they do not need to go out to purchase. The process of online food order is as simple as browsing through mobile application, choosing the desired food, making the payment and subsequently the process completed. In addition, women often tend to choose healthier food options and are more concerned in maintaining appropriate eating practices to keep in shape, according to Alkazemi (2019). Additionally, women have healthier living habits and engage in health-promoting behaviors than males do. Even though males were aware of "healthy eating guidelines," they frequently expressed skepticism and a lack of interest in nutrition education messages while frequently viewed good eating as boring and uninteresting. The author went on to highlight that women are more aware of nutrition and the consequences of the relationship between diet and health, accepting suggested dietary modifications, and display higher degrees of dietary constraint and disinhibition than men. This can also be explained by the fact that women have larger degrees of body dissatisfaction with the desire to be skinny than men (Thompson et al., 2015). Thus, it is notable that there are disparities between male and female perspectives on eating practices.

University students typically sleep for shorter periods with lower-quality sleep. According to Yu and Wan's study in 2022, which also used PSQI as one of their research tools, 62.3% of the 377 undergraduate participants were bad sleepers. They slept for roughly 6.5 hours each day in total. 79.1% of the respondents in this present study had trouble sleeping. It should be noted that the prevalence is significantly higher than the finding reported by Yu and Wan (2022). Canuto et al. (2013) claimed that irregular sleep-wake patterns can lead to internal circadian desynchrony, poor sleep quality, and delayed timing of calorie intake. People are more likely to become bored and feel the want to eat if their sleep time is cut short.

Chung et al. (2020), who identified meal timing related to the NES associated with sleep quality, found that gastroesophageal reflux and regular digestion could be the contributors for the correlation between these, because eating close to bedtime has been linked to gastroesophageal reflux as well as disturbed sleep. In addition, the time it takes for the stomach to empty is between two and four hours. Besides, according to Kee et al. (2021), lifestyle factors that affect university students' ability to regulate their sleep include excessive late-night technology use, caffeine consumption that affects sleep arousal and physiological regulation, and cultural norms that place little value on sleep.

According to Gan et al. (2019), students with mild stress level possessed a high tendency (3.58 times) in practicing NES. Besides, students with higher levels of depression had significantly higher NES scores (Braga et al., 2017). It was also discovered that NES was correlated with increased stress, worsened depressive symptoms, trouble falling asleep, and daytime drowsiness (Gundogdu, 2022). Additionally, stressed students who were prone to emotional eating were more likely to get up in the middle of the night and eat to lessen the harmful impacts of their negative emotions. The hypothalamic-pituitary-adrenal (HPA) axis, which controls the cortisol stress response, may become disturbed in people with NES.

Cortisol, a stress hormone, was discovered to be higher in the NES group than in the control group, which may contribute to hunger among NES sufferers. According to research by AlJaber et al. (2019), stressed-out students prefer to eat more high-calorie, high-fat items including fast food, sweets, and snack-type foods. Additionally, stress-related eating factors, such as workloads or assignments, as well as the accessibility of fast-food restaurants close to their university, increase their temptation to frequently purchase unhealthy foods due to its high accessibility.

A limitation of this study is that the scope was only within a single university campus. Nevertheless, the use of validated questionnaires which are globally recognized was a major strength to ensure reliability of the study findings.

Conclusion

The prevalence of NES is significantly higher among male than female students. It has also been established that stress levels and sleep quality are related to NES. A high level of NES was associated with a higher value of stress and poor sleep quality. Hence, this issue needs to be addressed by educating students about healthy eating patterns and healthier options for snacks to prevent any further adverse effects related to their physical and mental health.

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CAFFEINE INTAKE AND ITS ASSOCIATION WITH STRESS AND SLEEP QUALITY AMONG UNDERGRADUATE STUDENTS AT INTERNATIONAL ISLAMIC UNIVERSITY MALAYSIA (IIUM) KUANTAN

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ABSTRACT

Introduction: Caffeine (1,3,7-trimethyl xanthine) has become one of the most popular and globally distributed ergogenic aids as well as the most used stimulant in the world. University students in Malaysia and globally tend to consume caffeinated beverages to stay up late and complete their daily tasks, especially during examination period and for coursework completion, which lead to stress and trouble getting enough restful sleep due to their irregular bedtime routines. Thus, this cross-sectional study is aimed to determine the frequency of caffeine intake among undergraduate students in International Islamic University Malaysia (IIUM) Kuantan and its association with stress and sleep quality. **Methods:** A convenience sampling involving 290 (n=145 male, n=145 female) undergraduate students aged 19 to 25 years were recruited from six different Kulliyyah. A combination of Caffeine Consumption Pattern, Perceived Stress Scale (PSS) and Pittsburgh Sleep Quality Index (PSQI) questionnaires were used to collect the data from the respondents. The data were assessed using SPSS (Version 26.0) using descriptive analysis and Fisher's Exact Test. **Results:** This study found no significant association between the frequency of caffeine intake among male and female students (p=0.068). There was also no significant association between the frequency of caffeine intake and stress level (p=0.548), and sleep quality (p=0.349). **Conclusions:** Although most of the students frequently consumed caffeine in a week, no association between frequency of caffeine intake, stress level and sleep quality among IIUM Kuantan students were identified. It can be concluded that the relationship between frequency of caffeine consumption, stress levels, and sleep quality is complex and varies from person to person due to multiple factors.

Keywords: Caffeine, Stress, Sleep Quality

INTRODUCTION

Caffeine is a chemical that can be found naturally in a variety of plant-based foods and beverages. Caffeine is one of the most used substances in the world. Most caffeine is consumed through food products, such as tea, coffee, energy drinks, and chocolate or cocoa-containing products (Quadra et al., 2020). The expansion of global population is the primary driver behind the rise in the overall consumption of caffeine. The amount of caffeine that is contained in each product varies widely, however when compared to other types of beverages, coffee often contains one of the highest concentrations of caffeine (Mitchell et al., 2014). Nowadays, caffeine consumption is still rising, and it is becoming an incredibly prevalent beverage, especially among young generations (Rahim et al., 2019).

In Malaysia, drinking local coffee has been a cultural tradition for a very long time, and it has now become a habit for the local populace, as in other western nations such as the United States (Ramli et al., 2019). The growth of the Asian coffee market has been acknowledged by the global coffee industry. The coffee shop industry is growing and developing, including both worldwide coffee chains and local cafés. The local aesthetic coffee shops not only sell coffee, but also sell a variety of caffeinated beverages such as tea, chocolate and matcha.

Nowadays, students in Malaysia and throughout the world tend to use caffeinated energy drinks to stay up late and complete their daily tasks, especially during exams and coursework completion (Norshafarina et al., 2018). Several studies have shown that university students deal with stressful academic situations by drinking a lot of caffeinated drinks (Kale & Reddy, 2017). The most often reported reasons for consuming caffeinated beverages were to increase energy, maintain wakefulness, improve mood, enhance productivity, and facilitate social interaction (Malinauskas et al., 2007).

As a result, many university students have trouble getting enough restful sleep due to their irregular bedtime routines. Several students experience sleep disturbances due to poor sleep quality as well as discontent with their sleeping arrangements. The closer it gets to the final week of class, the fewer hours of sleep that students receive because they are typically too busy finishing their assignments and reviewing materials before the exam week (Sakinah et al., 2018). This issue arises as a result of some students consuming caffeine to stay up at night.

Previous research highlighted that excessive caffeine use may result in poor sleep quality (Kerpershoek et al., 2018). There have been numerous studies that show excessive caffeine consumption occurs when there is perceived stress (Richards & Smith, 2015). While it is true that caffeine improves emotions, alertness, and long-term memory, it is best to adhere to the suggested amounts. However, there is limited literature regarding the association between caffeine intake, stress level and sleep quality among undergraduate students in Malaysia. Thus, this research focused to obtain further insights into this topic among IIUM Kuantan students which has never been investigated.

METHODS

Subjects

This study was conducted among male and female undergraduate students at IIUM Kuantan. IIUM Kuantan is the science-based campus that consists of six different kulliyyahs (faculties) which are Kulliyyah of Allied Health Sciences, Kulliyyah of Dentistry, Kulliyyah of Sciences, Kulliyyah of Nursing, Kulliyyah of Pharmacy and Kulliyyah of Medicine. The ethical approval was obtained from the Kulliyyah Postgraduate and Research Committee (Reference No. KAHS 12/23) and IIUM Research Ethics Committee (IREC).

Study Design

Cross-sectional design was used in this study to find the association between habitual caffeine consumption, stress level, and sleep quality. This study design can be done at one time in one place. Participants in a cross-sectional study are simply selected from a population that may be relevant to the research question.

Sampling Methods

Convenience sampling was implemented for this research considering the accessibility and approachability to the participants (Stratton, 2021). Both inclusion and exclusion criteria have been set in order to choose suitable respondents and to achieve the specific objectives of this research. Inclusion criteria were undergraduate students from all the six kulliyyahs aged between 19 to 25 years, whilst postgraduate students and age group beyond specified were excluded.

Instruments

The data were obtained through self-administered questionnaires that consists of four sections: sociodemographic data including self-reported weight and height, caffeine consumption pattern, Perceived Stress Scale (PSS) and Pittsburgh Sleep Quality Index (PSQI). Body mass index (BMI) was categorized according to World Health Organization (2000) guidelines: underweight (<18.50 kg/m^2), normal (18.50-24.99 kg/m^2), overweight (25.00-29.99 kg/m^2), obese class I (30.00-34.99 kg/m^2), obese class II (35.00-39.99 kg/m^2) and obese class III (≥40.00 kg/m^2), which are determined by calculating the weight in kilograms divided by the height in meters squared.

Caffeine Consumption Patterns

The consumption of caffeinated products was asked to the participants through a set of questions. Some questions were adapted from Md Isa et al. (2021), which listed various sources of caffeine and frequency of caffeine intake. In addition, the questions covered a variety of intentions and social practices for consuming coffee and other caffeinated beverages. The questions also addressed caffeine dependence, withdrawal symptoms, and side effects (Kharaba et al., 2022).

Perceived Stress Scale

The level of stress was examined using the Perceived Stress Scale (PSS-10), a 10-question instrument used to evaluate the perception of stress over the previous 30 days. The Perceived Stress Scale (PSS), created by Cohen, Kamarck, and Mermelstein (1983), is a recognized self-report instrument based on the psychological conception of stress.

The shorter 10-item scale (PSS-10) demonstrated marginally enhanced reliability (Cronbach alpha =.78 vs. Cronbach alpha =.75) and similar validity and is therefore recommended for epidemiological and clinical research. It has been shown to have sufficient psychometric qualities to serve as a valid stress questionnaire. The PSS used a five-point Likert scale (“never”, “almost never”, “sometimes”, “fairly often”, and “very often”) to record the responses. A score of 0 to 13 is regarded as low stress, 14 to 26 as moderate stress, and 27 to 40 as severe stress (Cohen et al., 1983).

Pittsburgh Sleep Quality Index

The Pittsburgh Sleep Quality Index (PSQI) is a 19-item self-reported questionnaire to examine the sleep quality of students and sleeping disorders over the past month. The PSQI was established by Buysse (1989) and his colleagues to measure sleep quality and help distinguish between those with bad sleep and those with good sleep. With a Cronbach's alpha for the total score of 0.83, the dependability of the scale is regarded as good. The dependability of test–retest is likewise deemed to be satisfactory. Each part is given a score between 0 (no dysfunction) to 3 (severe dysfunction). The component scores were

then added up to produce a global score ranges from 0 to 21, with a score up to 5 indicating good sleep and >5 representing poor sleep quality.

A pilot study with 30 undergraduate students was conducted for the questionnaires with reliable Cronbach's Alpha value of 0.727, 0.874 and 0.768, respectively. The questionnaires were presented in English in Google Form format for all respondents to fill in. The link to the questionnaires was distributed to the participants through online platforms such as WhatsApp, Instagram and Telegram. The participants were required to provide informed consent prior to their participation in the study.

Statistical Analysis

The data were analysed using the SPSS version 26.0 software. Descriptive analysis was used to provide an overview of the sociodemographic data of respondents. Fisher's Exact Test was used to determine the association between caffeine intake frequency, stress level, and sleep quality. Statistically significant value was set at $p<0.05$.

RESULTS

Sociodemographic Data

The sociodemographic data of the respondents are as shown in Table 1. A total of 290 subjects were recruited among students at IIUM Kuantan, Pahang. The results of the study showed that the number of male respondents (n=145) was the same as female (n=145). The age of respondents was within the range of 19 to 25 years. Most of the students have normal BMI and none from Obese Class III. Kulliyyah of Allied Health Sciences have the highest respondent rate of 33.1% compared to Kulliyyah of Science, Kulliyyah of Nursing, Kulliyyah of Pharmacy and Kulliyyah of Medicine, and Kulliyyah of Dentistry which were 31.4%, 11.4%, 10.7%, 9.7%, and 3.8% respectively. Most of the students who participated were 3rd year students (38.3%), while the least were 5th year students (1.0%). Only 28.3% did not receive any scholarships while the rest are under the scholarships of either *Jabatan Perkhidmatan Awam* (JPA), *Majlis Amanah Rakyat* (MARA), *Perbadanan Tabung Pendidikan Tinggi Nasional* (PTPTN) or others.

Table 1. Sociodemographic data of the respondents (N=290)

Sociodemographic Data	Frequency (n)	Percentage (%)
Gender		
Male	145	50
Female	145	50
Age		
19	4	1.4
20	67	23.1
21	74	25.5
22	91	31.4
23	42	14.5
24	10	3.4
25	2	0.7
BMI		
Underweight	35	12.1
Normal	190	65.5
Overweight	49	16.9
Obese Class I	13	4.5

Obese Class II	3	1.0
Obese Class III	0	0
Kulliyyah		
Kulliyyah of Allied Health Sciences	96	33.1
Kulliyyah of Science	91	31.4
Kulliyyah of Nursing	33	11.4
Kulliyyah of Pharmacy	31	10.7
Kulliyyah of Medicine	28	9.7
Kulliyyah of Dentistry	11	3.8
Year of Study		
Year 1	74	25.5
Year 2	70	24.1
Year 3	111	38.3
Year 4	32	11.0
Year 5	3	1.0
Scholarship Status		
Self-sponsored	82	28.3
MARA	73	25.2
PTPTN	67	23.1
JPA	44	15.2
Others	24	8.2

Caffeine Consumption Patterns

Table 2 indicates the patterns of caffeine consumption among undergraduate students at IIUM Kuantan. Overall, nearly half of the respondents consume caffeinated beverages 1 to 3 times per week. Thirty percent (n=87) of the respondents took caffeine once per day. The number of students who consumed caffeinated drinks 2-3 times a day and 4-6 times a week are 36 (12.4%) and 23 (7.9%) students respectively. Only 2.1% (n=6) of students consume 4 to 5 times a day, and all of them are male. None of the respondents consume caffeinated beverages more than 5 times a day. Besides, majority of the students took coffee as a source of caffeine followed by tea, chocolate, caffeinated soft drinks, matcha and only 9.3% of students consume energy drinks. Moreover, most of the students preferred to have caffeine because they like the taste of caffeine and to stay awake. Only a few students consumed caffeine to deal with stress and help the digestion process. Other than that, the respondents usually consumed caffeine at night and the least in the afternoon. Some of them were having withdrawal symptoms such as headaches and drowsiness. Only 2.1% experienced muscle pain after consuming caffeinated beverages. Meanwhile, around 41.0% experienced rapid heartbeat and difficulty falling asleep as side effects after having caffeine.

Table 2 Caffeine consumption patterns among undergraduate students (N=290)

Caffeine consumption patterns	**Male** (n=145)	**Female** (n=145)	**Total** (n=290)
	n (%)	n (%)	
How often do you consume caffeinated beverages?			
1-3 times weekly	63 (43.4)	75 (51.7)	138 (47.6)
Once daily	42 (29.0)	45 (31.0)	87 (30.0)
2-3 times daily	21 (14.5)	15 (10.3)	36 (12.4)

4-6 times weekly	13 (9.0)	10 (6.9)	23 (7.9)
4-5 times daily	6 (4.1)	0 (0)	6 (2.1)
More than 5 times daily	0 (0)	0 (0)	0 (0)
Sources of caffeine			
Coffee	113 (77.9)	114 (78.6)	227 (78.3)
Tea	99 (68.3)	104 (71.7)	203 (70.0)
Chocolate	96 (66.2)	93 (64.1)	189 (65.2)
Matcha	50 (34.5)	70 (48.3)	120 (21.4)
Caffeinated soft drinks (eg: Pepsi, Coca-cola, Mountain Dew, Sprite, 7-Up)	66 (45.5)	44 (30.3)	110 (37.9)
Energy drinks (eg: Red bull, Livita, Power Root)	21 (14.5)	6 (4.1)	27 (9.3)
Why do you prefer having caffeinated drinks?			
Like the taste	123 (84.4)	129 (89.0)	252 (86.9)
To deal with stress	52 (35.9)	51 (35.2)	103 (35.3)
To stay awake	98 (67.6)	78 (53.8)	176 (60.7)
To help with digestion	21 (14.5)	38 (26.2)	59 (20.3)
What time of the day do you usually consume caffeine?			
Morning	70 (48.3)	82 (56.6)	152 (52.4)
Afternoon	33 (22.8)	44 (30.3)	77 (26.6)
Evening	62 (42.8)	78 (53.8)	140 (48.3)
Night	119 (82.1)	97 (66.9)	216 (74.5)
Do you experience any withdrawal symptoms after having caffeine?			
Headaches	26 (17.9)	50 (34.5)	76 (26.2)
Nausea	6 (4.1)	19 (13.1)	25 (8.6)
Muscle pain	3 (2.1)	3 (2.1)	6 (2.1)
Drowsiness	24 (16.6)	36 (24.8)	60 (20.7)
Fatigue	24 (16.6)	33 (22.8)	57 (19.7)
Irritability/Poor mood	15 (10.3)	28 (19.3)	43 (14.8)
Do you experience any side effects after having caffeine?			
Tense	10 (6.9)	29 (20.0)	39 (13.4)
Shakiness	18 (12.4)	47 (32.4)	65 (22.4)
Anxious	31 (21.4)	52 (35.9)	83 (28.6)
Restless	34 (23.4)	39 (26.9)	73 (25.2)
Rapid heartbeat	49 (33.8)	70 (48.3)	119 (41.0)
Trouble concentrating	16 (11.0)	18 (12.4)	34 (11.7)
Difficulty falling asleep	61 (42.1)	58 (40.0)	119 (41.0)

The Association between Frequency of Caffeine Intake and Gender

Table 3 indicates the association between the study participants' gender and the frequency of caffeine intake. In this study, the frequencies of caffeine consumed by male and female students were approximately the same. Most males and females students consumed caffeine 4 to 6 times weekly, followed by once daily and 1 to 3 times per week. Neither males nor females consumed caffeine more than 5 times a day. As a result, the Fisher's Exact test below showed no statistically significant association between the frequency of caffeine intake and gender, $X^2(4) = 8.610$, $p = 0.068$.

Table 3 Association between frequency of caffeine intake and gender (N=290)

Variable	Gender		n	X^2-statistic (df)	P-value
Frequency of Caffeine Intake	Male n (%)	Female n (%)			
4-6 times weekly	63 (21.7)	75 (25.9)			
Once daily	42 (14.5)	45 (15.5)			
1-3 times weekly	21 (7.2)	15 (5.2)	290	8.610 (4)	0.068
2-3 times daily	13 (4.5)	10 (3.4)			
4-5 times daily	6 (2.1)	0 (0)			
> 5 times daily	0 (0)	0 (0)			

The Association between Caffeine Intake and Stress Level

Table 4 below indicates the association between the subjects' caffeine consumption pattern and the stress level. Most of the students who experienced moderate stress level only consume caffeinated beverages once per day and 1 to 3 times a week. However, the number of students who consumed caffeinated drinks as much as 4 to 6 times a week and experienced poor and high stress levels were the same (1.0%). As a result, the Fisher's Exact test showed no statistically significant association between caffeine consumption patterns and stress level among undergraduate students at IIUM Kuantan, $X^2(8) = 6.637$, $p = 0.548$.

Table 4 Association between frequency of caffeine intake and stress level (N=290)

Variable	Stress Level			n	X^2-statistic (df)	P-value
Frequency of Caffeine Intake	Poor n (%)	Moderate n (%)	High n (%)			
1-3 times weekly	30 (10.3)	90 (31.0)	18 (6.2)			
Once daily	15 (5.2)	63 (21.7)	9 (3.1)			
2-3 times daily	10 (3.4)	20 (6.9)	6 (2.1)	290	6.637 (8)	0.548
4-6 times weekly	3 (1.0)	17 (5.9)	3 (1.0)			
4-5 times daily	1 (0.3)	3 (1.0)	2 (0.7)			
> 5 times daily	0 (0)	0 (0)	0 (0)			

The Association between Caffeine Intake and Sleep Quality

Table 5 shows the association between subjects' caffeine consumption pattern and sleep quality. The result showed that most of the students who experienced poor sleep quality only consume caffeinated beverages once per day and 1 to 3 times a week. However, there were 1.4% of students who consumed caffeinated drinks 4 to 5 times a day but experienced good quality of sleep. The Fisher's Exact test below showed no statistically significant association between caffeine consumption patterns and sleep quality among undergraduate students at IIUM Kuantan, $X^2(4) = 4.437$, $p = 0.349$.

Table 5. Association between frequency of caffeine intake and sleep quality (N=290)

Variable	Sleep Quality		n	X^2-statistic (df)	P-value
Frequency of Caffeine Intake	Poor n (%)	Good n (%)			
1-3 times weekly	87 (30.0)	51 (17.6)			
Once daily	54 (18.6)	33 (11.4)			
2-3 times daily	27 (9.3)	9 (3.1)			
4-6 times weekly	15 (5.2)	8 (2.8)	290	4.437 (4)	0.349

4-5 times daily	2 (0.7)	4 (1.4)
> 5 times daily	0 (0)	0 (0)

DISCUSSIONS

The Frequency of Caffeine Intake among Male and Female Students

Caffeine is widely used among students in IIUM Kuantan. The current findings revealed that male and female students, on average, predominantly consume caffeine on a weekly basis, ranging from one to three occasions. In this study, no significant association was detected in the frequency of caffeinated beverages intake between male and female undergraduate students in IIUM Kuantan. Upon comparing the findings of the present study with those of the previous one, it is evident that a significant proportion of male and female students regularly consumed caffeine. The consumption of caffeinated beverages was a common practice for both male and female. This result is consistent with a previous study conducted by Knapik et al. (2022), where there was only minimal disparity between genders with reported slightly higher percentages ± SE intake among male (87.0 ± 0.2) than female (86.1 ± 0.6) in terms of the prevalence of caffeine consumption.

Furthermore, with regard to specific sources of caffeine, such as coffee, variations exist in consumption habits between gender. According to previous research, males indicate a higher average coffee intake in comparison to females (Demura et al., 2013). However, in this study, coffee has been identified as the primary source of caffeine consumption among both male and female students. In addition, a previous finding highlighted that males are more likely to consume higher caffeine contents from other sources such as energy drinks, which could contribute to higher overall consumption (Demura et al., 2013; Dillon et al., 2019). This is consistent with our study where male students consumed more energy drink and caffeinated soft drinks as compared to female students. Females, on the other hand, show a greater preference for green tea or other lower-caffeine options.

Caffeine Intake and its Association with Stress

University education, particularly the undergraduate phase, is a crucial stage in a student's development. It is a challenging journey for them, as evidenced by the annual increasing psychological distress rates associated with tertiary education. Therefore, students might consume caffeine to counteract the effects of stress and weariness because it is a stimulant that can briefly improve cognitive performance and boost alertness. While individuals may have habits and coping mechanisms that involve caffeine consumption during periods of stress, but there was no significant evidence from this study that demonstrated stress being directly associated with the frequency of caffeine consumption.

A study conducted by Al-Ateeq et al., (2021) found that there was a significant positive relationship between the frequency of caffeine consumption and the level of perceived stress. The researchers added that students who consumed caffeine frequently had substantially higher mean perceived stress scores than those with a low caffeine intake. This is also supported by other study that found a significant positive relationship between the frequency of caffeine consumption and stress level (Pettit & DeBarr, 2011). Nevertheless, the result from present study does not conform with the previous findings, where the undergraduate students at IIUM Kuantan consumed caffeine frequently regardless of their stress level and it might be due to the addictive taste of caffeine as well as its accessibility. It has been demonstrated that students' caffeine use is driven more by their routine, taste preferences, and daily habits than by their stress levels (Simpson, 2016).

Caffeine Intake and its Association with Sleep Quality

University students frequently report poor sleep quality due to sleep disturbances caused by insufficient sleep, early morning awakening, and trouble falling asleep. The findings of this study indicated that 2/3 undergraduate students in IIUM Kuantan suffered from a suboptimal level of overall sleep quality, with 63.8% out of 290 students having poor sleep quality according to the PSQI criteria. The results corresponded with those of another study, which revealed that students frequently

experienced poor sleep quality (Kabrita et al., 2014). Based on most of the previous research findings, the frequency of consuming caffeinated beverages is significantly associated with quality of sleep especially among students. According to Al-Sharif et al. (2018), the study found that there was a statistically significant difference in sleep quality between students who consumed higher amounts of caffeinated beverages and those who did not ($p= 0.003$); which is consistent with results from Lemma et al. (2012). In the present study, the results indicate opposite finding with no significant association between both variables.

Among the studies that support this argument is the research conducted by Lohsoonthorn et al., (2013) which demonstrated that there was no significant association between frequency of caffeine intake and sleep quality. In addition, the researchers added information on the variables such as consumption time that would contribute to poor sleep quality. Caffeine consumption in the hours before bed or in the evening might make it difficult to fall asleep and may disturb sleep patterns. However, once an appropriate amount of time has elapsed since caffeine consumption, the amount of caffeine consumed does not appear to have a significant effect on sleep quality. This suggests that as long as caffeine is consumed earlier in the day and sufficient time is allowed for it to be metabolised and eliminated from the body before sleep, the exact amount consumed becomes less of a factor in sleep quality.

Limitation and Strength

The limitation in this study included the scope of the subjects which was limited to undergraduate students at IIUM Kuantan only, where all of them were science-based students. Despite the limitation, one of the strengths in this study is that it has an equal number of male and female respondents although it is quite difficult to recruit male respondents due to the smaller population size of male compared to female students. Moreover, the questionnaires used in this study were used worldwide and have been validated.

CONCLUSION

The frequency of caffeine consumption has been found to be unaffected by either male or female based on no statistically significant finding. Besides, this present study demonstrated that the level of stress and quality of sleep are not influenced by the frequency of caffeine consumption. These may infer that the relationship between frequency of caffeine consumption, stress levels, and sleep quality is complex and varies from person to person due to multiple factors, including individual differences, caffeine sensitivity, metabolism, and overall well-being. It is important for students to be mindful of how their daily caffeine intake affects their stress levels and ability to sleep. Thus, future research is warranted to explore other potential factors that cause consumption of caffeine, high stress level and poor sleep quality experienced by students.

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THE EFFECT OF CHRONONUTRITION ON MENTAL WELL-BEING AMONG IIUM STUDENTS

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ABSTRACT

Introduction: Chrononutrition, also referred to as the circadian timing of meals, has been found to have an impact on health outcomes, particularly on metabolic health. However, limited evidence exists regarding the influence of chrononutrition on mental well-being. Given the increasing concern about the mental well-being of university students due to various factors affecting their overall health, this study aimed to explore the association between chrononutrition behavior and mental well-being among students. **Method:** An online questionnaire was administered to 336 IIUM students from the Gombak, Kuantan, and Pagoh campuses. The participants completed the Depression, Anxiety and Stress Scale-21 (DASS21) questionnaire and the Chrononutrition Profile Questionnaire (CP-Q). The CP-Q assessed six components of chrononutrition that are likely to influence health, namely breakfast skipping, largest meal, evening eating, evening latency, night eating, and eating window. This is a cross sectional study and the source of the population was selected through convenient sampling. A chi-square test of independence was conducted to study the association between chrononutrition behavior and mental well-being among IIUM students. **Results:** The findings revealed a significant correlation between specific chrononutrition behaviors, particularly evening latency, and evening eating on all states of mental well-being, namely stress, anxiety, and depression. The results suggest that engaging in poor evening latency and evening eating behaviors are associated with increased levels of stress, anxiety, and depression. There is a significant association between the eating window and skipping breakfast with stress although there are no significant associations found with anxiety or depression. No significant associations were found between night eating and stress or anxiety, whilst a significant association was identified between night eating and depression. The largest meal shows a significant association with stress and depression with no significant association found with anxiety. **Conclusion:** These findings emphasize that chrononutrition behaviors impact not only physical health but also mental health and overall well-being. It also highlights the significance of considering chrononutrition in interventions aimed at promoting better mental health outcomes.

KEYWORDS: chrononutrition, mental well-being, circadian rhythm

INTRODUCTION

University students exhibit bad eating habits and receive insufficient amounts of nutrients, according to research by Wy et al. (2011). According to Chin & Nasir (2009), Malaysian female students exhibited unhealthy eating behaviours including meal skipping and frequent snacking.

Nutrition and eating behaviours have a significant impact on mood, mental health, and sleep (Godos et al., 2021). Meal timing is no less important than the type and amount of food taken. Meal timing or known as chrononutrition is the understanding that the timing of food consumption interacts with internal circadian rhythms to impact health outcomes. Meal timing needs to be taken care of, especially among students who usually skip their meals when they are occupied with classes and work (Wehrens et al., 2017).

According to the World Health Organization (WHO, 2020), health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity. Often, individuals who experience poor physical health receive treatment to alleviate their symptoms and ailments. While it may be relatively easy to identify the cause of the illness through physical and medical assessments and address it accordingly, it is essential to recognize that health encompasses not only physical well-being but also mental well-being.

Factors that lead to mental disorders and disruption in emotional well-being may come from internal and external factors. Poor dietary habits and eating behaviour are examples of external factors. Students who undergo the transition to university life often exhibit unhealthy eating habits. While these behaviors are commonly perceived as temporary and associated with university life, they often persist into adulthood, carrying potential long-term consequences (Ganasegeran et al., 2012).

A study by Murca et al. (2020) showed that university students who exhibit unhealthy eating habits have shown a strong correlation with increased prevalence of anxiety, stress, and depression scores. Among the unhealthy eating habit, chrononutrition and its effect on mental health and emotional well-being among students need attention. Chrononutrition is an emerging field in nutritional psychiatry based on the relationship between temporal eating patterns, circadian rhythms, and health. In addition to dietary composition, the food intake window and the daily distribution of food intake are also critical factors for mental health (Gombert & Cenit, 2023).

The data on the effect of irregular meal timing on mental health remains elusive and thus needs further research and studies (Tahara et al., 2021). Therefore, this study will investigate the effect of chrononutrition on the mental well-being of the students.

MATERIALS AND METHODS

Study Design and Population

This study was conducted towards International Islamic University Malaysia (IIUM) students from three campuses; Gombak, Kuantan, and Pagoh. This study was conducted via a cross-sectional study whereby data collections were conducted from February until May 2023.

Determination of sample size was calculated using a single proportion formula adopted from the previous study by Tahara et al (2021), where 24% of the participants aged 20-69 years practiced irregular meal timing. A total of 308 participants were required for the sample size. The inclusion criteria for the respondents were undergraduate IIUM students who are free from mental health disorders.

The study protocol was approved by the Kulliyyah of Allied Health Sciences Postgraduate and Research Committee (Reference No: IIUM/310/14/11/2). A written consent for the respondents to participate in this study was attached to the online questionnaire. All information was treated as strictly confidential.

A total of 336 students participated in this study via convenient sampling. The finalized set of online questionnaires was distributed through social media applications, such as WhatsApp and Instagram. The participants were well informed of the inclusion and exclusion criteria to ensure those who participated fit in the inclusion criteria.

Questionnaire

The questionnaire comprises of 3 sections. The first section is about the demographic details of the participants such as gender, year of study, kulliyyah, and anthropometry measurement. The next section consists of questions on mental health assessment in which the DASS21 questionnaire was used. The third section is on the chrononutrition whereby chrononutrition Profile – Questionnaire (CP-Q) was used. The CP-Q assessed 6 components of chrononutrition that are likely to influence health (breakfast skipping, largest meal, evening eating, evening latency, night eating, and eating window). This questionnaire is designed to assess general chrononutrition behaviours and preferred timing of food intake (Engwall, 2018).

a) Demographic Data

The information that was collected consists of the students' gender, year of study, campus, kulliyyah, weight, height and BMI. The BMI was calculated by the students themselves using an online BMI calculator that was included in the questionnaire. The BMI is subsequently classified into categories such as underweight, normal weight, overweight, or obesity based on specific BMI ranges.

b) DASS21 Questionnaire

For the assessment of mental health, Depression, Anxiety and Stress Scale (DASS21) is used, which consists of 21 questions. The scoring consists of 4 categories for each of the questions which are:

a) Score 0: Did not apply to participants
b) Score 1: Applied to participants some degree or some of the time
c) Score 2: Applied to participants a considerable degree or a good part of the time
d) Score 3: Applied to participants very much or most of the time

The scoring was calculated and total up altogether according to each question that has been classified for each of the mental health problems multiplied by 2 in order to evaluate each level of the mental health problems. Thus, the rate of the total score for each mental health problem was assessed based on 5 stages which is normal, mild, moderate, severe and extremely severe.

c) Chrononutrition Profile – Questionnaire (CP-Q).

A summary of the scoring procedures can be found in Table 1. In essence, numerical values are computed and/or extracted for various chrononutrition behaviours, such as eating window, breakfast skipping, evening latency, evening eating, night eating, and largest meal. Since the CP-Q assesses behaviours separately for weekdays and weekends, additional calculations are necessary to generate a weighted aggregate score that accurately reflects weekly patterns (Engwall, 2018).

Table 1 Chrononutrition behaviour descriptions and scoring cutoffs for the chrononutrition profile

Chrononutrition Cutoff	**Description**	**Format**	**Scoring Cutoffs (Poor; Fair; Good)**
Eating Window	Duration between first eating event and last eating event	HH:MM	> 14:00 12:01 to 14:00 ≤12:00
Breakfast Skipping	Frequency of breakfast skipping	Days/Week	≥ 4 days/week 2-3 days/week 1 day/week or less
Evening Latency	Duration between last eating event and sleep onset	HH:MM	≤2:00 2:01 to 6:00 >6:00
Evening Eating	Last eating event of the day	HH:MM	≥23:00 20:00 to 22:59 < 20:00
Night Eating	Frequency of night eating	Days/Week	≥ 4 days/week 2-3 days/week 1 day/week or less
Largest Meal	Meal in which largest amount of food is eaten	Meal Name	Dinner/Supper Lunch Breakfast

To be more specific, separate values are computed for weekdays and weekends, which are then weighted to account for 5 weekdays and 2 weekend days. For instance, if the eating window is calculated as 10 hours on weekdays and 14 hours on weekends, the overall estimated eating window is determined as 11.14 hours. This calculation is derived by adding the product of weekday eating window (10 hours) multiplied by the number of weekdays (5 days) and the product of weekend eating window (14 hours) multiplied by the number of weekend days (2 days), and then dividing the sum by the total number of days (7 days).

The aggregate values of the Chrononutrition Profile (CP) are subsequently classified into one of three "chrononutrition behaviour cutoffs" for each specific behaviour (good, fair, and poor). The categorization of chrononutrition behaviour cutoff scores, which considers weekly frequencies (such as breakfast skipping and night eating), is determined by the percentage of days used as cutoffs in the CP scoring (Engwall, 2018).

Statistical Analyses

The Statistical Package for Social Sciences (SPSS) version 26.0 was used to analyse the data in this study. The significance level for a 95% confidence interval (CI) is set at 0.05.

For the type of analysis, the descriptive analysis is used to study the chrononutrition behavior and the mental well-being of the students. The Chi-Square Test of Independence is utilized to study and assess the association between chrononutrition behavior and mental well-being among IIUM students.

RESULTS AND DISCUSSIONS

Sociodemographic Information

A total of 336 undergraduate students from year 1 up to year 5 from all kulliyyahs of the Gombak, Kuantan, and Pagoh campuses participated in this study. Among these respondents, female students were the highest as compared to males with a percentage of 65.5% while 34.5% were contributed from male students. Students from Kulliyyah of Allied Health Sciences constitute the largest portion of 38.1% from the total sample. A total of 69% of students who participated in the study were from the Kuantan campus, 28.6% from Gombak, and only 2.4% from Pagoh campus. With regards to their BMIs, a total of 184 students (54.8%) has normal BMI, 68 students (20.2%) were overweight, 52 students (15.5%) were underweight, and 32 students (9.5%) were obese. Majority of the students have a normal BMI (Table 2)

Table 2 Demographic Data of the Students

Demographic	Category	Frequency (n)	Percentage (%)
Gender	Male	116	34.5%
	Female	220	65.5%
Year of study	Year 1	48	14.3%
	Year 2	92	27.4%
	Year 3	148	44.0%
	Year 4	44	13.1%
	Year 5	4	1.2%
Campus	Gombak	96	28.6%
	Kuantan	232	69.0%
	Pagoh	8	2.4%
Kulliyyah	Kulliyyah of Medicine (KOM)	16	4.8%
	Kulliyyah of Dentistry (KOD)	16	4.8%
	Kulliyyah of Pharmacy (KOP)	4	1.2%
	Kulliyyah of Allied Health Sciences (KAHS)	128	38.1%
	Kulliyyah of Nursing (KON)	4	1.2%
	AbdulHamid AbuSulayman Kulliyyah of Islamic Reveal Knowledge And Human Sciences (AHAS KIRKHS)	24	7.1%
	Ahmad Ibrahim Kulliyyah of Laws (AIKOL)	8	2.4%
	Kulliyyah of Architecture & Environmental Design (KAED)	20	6.0%
	Kulliyyah of Economics & Management Sciences (KENMS)	12	3.6%
	Kulliyyah of Education (KOED)	4	1.2%

	Kulliyyah of Engineering (KOE)	20	6.0%
	Kulliyyah of Information & Communication Technology (KICT)	8	2.4%
	Kulliyyah of Languages and Management (KLM)	8	2.4%
	Kulliyyah of Science (KOS)	64	19.0%
BMI Category	Underweight	52	15.5%
	Normal	184	54.8%
	Overweight	68	20.2%
	Obesity	32	9.5%

n=336

Chrononutrition Behaviour of IIUM Students

Table 3 provides data on the chrononutrition behaviour of IIUM students. It includes various categories of chrononutrition behaviour, along with their frequency and percentage distribution.

Table 3 Chrononutrition Behavior of IIUM Students

Chrononutrition Behaviour	Category	Frequency (n)	Percentage (%)
Eating Window	Good (≤12:00)	152	45.2%
	Fair (12:01–14:00)	108	32.1%
	Poor (>14:00)	76	22.6%
Breakfast Skipping	Good (1 d/wk or less)	64	19.0%
	Fair (2–3 d/wk)	64	19.0%
	Poor (≥4 d/wk)	208	61.9%
Evening Latency	Good (>6:00)	24	7.1%
	Fair (2:01–6:00)	220	65.5%
	Poor (≤2:00)	92	27.4%
Evening Eating	Good (<20:00)	48	14.3%
	Fair (20:00–22:59)	172	51.2%
	Poor (≥23:00)	116	34.5%
Night Eating	Good (1 d/wk or less)	296	88.1%
	Fair (2–3 d/wk)	32	9.5%
	Poor (≥4 d/wk)	8	2.4%
Largest Meal	Good (Breakfast)	12	3.6%
	Fair (Lunch)	224	66.7%
	Poor (Dinner/supper)	100	29.8%

For eating window behaviour, most of the students (152 students, 45.2%) have good eating behaviour. Eating window indicates the duration between the first eating event and the last eating event. Students with good eating window only have an eating duration of 12 hours or less per day, while those with a fair eating window eat for more than 12 hours up until 14 hours per day. Students with a poor eating window eat more than 14 hours most of the day.

With regards to breakfast-skipping behaviour, the students were mostly categorized under the poor behaviour which indicates the practice of skipping breakfast more than 4 times per week. A high percentage of students (61.9%) were in this category.

Evening latency refers to the time interval between the last meal of the day and the time the students go to sleep. Students with good evening latency have a gap of more than 6 hours, while those with fair evening latency have a gap between 2 hours to 6 hours. Students with poor evening latency have a gap of 2 hours or less. In this study, it is important to highlight that 220 students (65.5%) have fair evening latency behaviour.

Evening eating represents the time at which students have their last meal of the day. Students with good evening eating behaviour finish their meal before 8:00 PM, while those with a fair behaviour finish between 8:00 PM and 10:59 PM. Students with poor behaviour have their last meal at 11:00 PM or later.

Majority of the students, which consists of 88.1% (296 students) have a good behaviour at night eating. This category indicates the frequency of eating during the night. Students with a good night eating behaviour eat during the night once a week or less. Those with a fair behaviour eat 2-3 times a week, while those with poor behaviour eat four or more times a week during the night.

Lastly, the largest meal of the day for the majority of the students was during lunch. Only a few students, consisting of 3.6% eat a lot during their breakfast. In this category, having the largest meal of the day during breakfast indicates a good chrononutrition behavior. Meanwhile having lunch as the largest meal is categorized fair chrononutrition behavior. Those who eat their largest meal of the day at night were considered to have poor chrononutrition.

State of IIUM students' emotional well-being.

Table 4 indicates the emotional well-being of the students according to each category. Based on the results, students with moderate depression are the highest with a total of 152 students (45.2%) while the lowest is the students who experience extremely severe stress with a total number of only 4 students (1.2%).

Table 4 Emotional Well-Being State of the students

Emotional State	Category	Frequency (n)	Percentage (%)
Stress	Normal	148	44.0%
	Mild	56	16.7%
	Moderate	84	25.0%
	Severe	44	13.1%
	Extremely severe	4	1.2%
Anxiety	Normal	84	25.0%
	Mild	52	15.5%
	Moderate	92	27.4%
	Severe	44	13.1%
	Extremely severe	64	19.0%
Depression	Normal	112	33.3%
	Mild	36	10.7%
	Moderate	152	45.2%
	Severe	28	8.3%
	Extremely severe	8	2.4%

This study found that the prevalence of moderate to extremely severe stress, anxiety and depression among IIUM students are 39.3%, 59.5% and 55.9%, respectively. This is higher compared to a previous study towards undergraduate students in Malaysia during the COVID-19 pandemic, whereby the prevalence for depression and anxiety were 29.4% and 51.3% respectively (Moy & Ng, 2021).

Experts declared that anxiety and depression are the top causes of mental health disorders among Malaysian students (Kotera, et al., 2020). Because of academic stress, students may struggle to prioritize their well-being, neglecting important aspects such as sleep patterns, dietary quality, and physical activity. These factors eventually contributed to having mental health issues among students.

Association between Chrononutrition Behaviour and Mental well-being among IIUM students

To analyze the association between chrononutrition behavior and mental well-being among IIUM students, a chi square test of independence was performed. The analysis focused on six specific chrononutrition behaviours: eating window, breakfast skipping, evening latency, evening eating, night eating, and largest meal. Table 5 shows the results of Chi-Square tests between each chrononutrition behavior towards each aspect of mental well-being state, namely stress, anxiety and depression.

Table 5 Summary of *p*-value of Chi-Square Test between Chrononutrition Behavior and Mental Well-Being State

Chrononutrition Behaviour	Stress	Anxiety	Depression
Eating Window	<0.05	0.59	0.107
Breakfast Skipping	<0.05	0.101	0.079
Evening Latency	<0.05	<0.05	<0.05
Evening Eating	<0.05	<0.05	<0.05
Night Eating	0.18	0.423	<0.05
Largest meal	<0.05	0.19	<0.05

Based on the results of chrononutrition behavior, the majority of IIUM students (61.9%) are categorized as "poor" under the breakfast-skipping behavior. This indicates that most of IIUM students skip breakfast more than four times a week. Breakfast is the most important meal of the day because it helps the human body to start their daily metabolism (Heo et al., 2021). Across all age groups, skipping breakfast showed a positive association with the likelihood of experiencing depression, stress, and psychological distress. In adolescence, it was also linked to higher odds of anxiety (López-Gil et al., 2022).

Eating window duration refers to the duration between the first eating event and last eating event. The majority of IIUM students (45.2%) have an eating window of less than 12 hours, indicating good behavior. Conversely, a total of 22.6% of students demonstrate poor eating window behavior, with a duration exceeding 14 hours of eating per day. A good eating window should be less than 12 hours per day, and it is aligned with the principle of time restricted feeding (TRF) which is a form of intermittent fasting in which all nutrient intake occurs within less than 12 hours every day (Gombert & Cenit, 2023). TRF has shown to give positive benefits towards the cardiometabolic health such as prevent excessive body weight gain, enhance sleep quality, and mitigate the decline in cardiac performance associated with age and poor diet (Melkani & Panda, 2017).

Next, two significant aspects of chrononutrition that have potential health implications are evening latency behavior, which denotes the time gap between the last eating event and sleep onset, and evening eating, which refers to the timing of the final meal of the day. This behavior refers to the evening chronotype. Chronotype represents an individual's preference for engaging in daily activities at specific times of the day. Individuals with an evening chronotype are inclined to experience a higher prevalence of health issues, such as psychological, neurological, and gastrointestinal morbidities, as well as higher mortality rates, in comparison to those with morning chronotypes (Makarem et al., 2020). According to Zou et al. (2022), having an evening chronotype poses a risk for developing depressive disorders and substance use disorders, whereas being a morning chronotype serves as a protective factor against these conditions. This study reveals that 27.4% and 34.5% IIUM students have poor evening latency and evening eating behavior respectively.

Next is the largest meal behavior. The largest meal refers to the meal in which the largest amount of food is eaten. More than half of IIUM students (66.7%) have their largest meal during lunch. In terms of behavior, having the largest meal during breakfast is considered good, while having it during lunch is deemed fair. Conversely, having the largest meal during dinner or supper is considered poor behavior. A total of 29.8% of IIUM students eat a large amount of food during their dinner and supper while only 3.6% have their largest meal during breakfast. There is a consistent correlation between the timing of the largest meal and their preference for sleep and wake times throughout the day and their overall health (Engwall, 2018).

Night eating on the other hand indicates the behavior of waking up at night to eat. Notably, it is worth mentioning that the majority of IIUM students (88.1%) exhibited positive behavior in this aspect, as they reported either not waking up at all or waking up only once per week to eat during the night.

CONCLUSION

In conclusion, the findings suggest that chrononutrition behaviors play a role in mental well-being. The timing of meals, breakfast skipping, evening latency, evening eating, night eating, and the largest meal are all important factors that may influence stress, anxiety, and depression levels. These findings highlight the significance of considering chrononutrition in interventions aimed at promoting better mental health outcomes.

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LATE NIGHT EATING OUT BEHAVIOUR: HAS IT BECOME CULTURE IN KUANTAN, PAHANG?

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ABSTRACT

Introduction: The prevalence of eating out practice is increasing as a result of lifestyle changes. Almost half of Malaysians eat out at food premises these days. Due to the availability of food services outside of the usual mealtimes, eating out is no longer confined to mealtimes. The main objective of this study was to explore the practice of eating out late at night among adults in Kuantan, Pahang. **Method:** A cross- sectional study design was applied to determine the association between sociodemographic factors and the frequency of eating out late at night. A newly developed and validated questionnaire on practice of eating out late at night was utilized . A total of 135 adults (43 males and 92 female) aged between 19 and 59 years old who lived in rural (Beserah) and urban (Kuala Kuantan) areas of Kuantan, Pahang, were involved in this study. Data were collected through an online questionnaire that was disseminated through group chat applications and face-to-face interviews at the study areas.. The data obtained were analysed using SPSS Version 26: descriptive analysis and Fisher's Exact Test. **Results:** The results showed that more than two-thirds of the respondents ate out late at night 1 to 2 times a week. However, there was no significant association between sociodemographic data (gender, age, ethnicity, marital status, living area, educational level, working status, working hours, and monthly household income) and the frequency of eating out late at night. **Conclusion:** Public awareness is important to prevent any further increase in this behaviour, as the practice of late night eating behaviour has been linked to negative health consequences.

KEYWORDS: Eating out, Late night eating behaviour, Sociodemographic factors

INTRODUCTION

Eating out is increasing in prevalence as a result of lifestyle changes, which are influenced by a variety of social, individual, environmental, socioeconomic, biological, and psychological factors, as well as the unique cultural characteristics of each nation or location (Choi et al., 2011). The patterns of eating have changed with social transformation vis-a-vis urbanization in recent years. The culture of eating out is one of the manifestations of the changes. These environmental changes, such as the growing number of food outlets in residential areas, are connected to lifestyle changes, which include a noticeable shift in eating culture (Bodicoat et al., 2015). The growth of restaurants such as fast-food make eating out convenient and economical. Eating out commonly being practiced in most of the country worldwide, including Malaysia. Malaysian Adult Nutrition Survey (MANS) 2014 found that almost half of Malaysian adults obtain food outside home, higher among those who live in Peninsular Malaysia and in urban areas (IPH, 2014). Malaysian Food Barometer Survey was consistent with MANS 2014 with high prevalence of food away from home reported. About 64% of Malaysians had at least one meal per day outside of home, 23.4% had meals at home, and 12.5% will eat at home with outside food (Fournier et al., 2016).

Due to the availability of food services outside of the usual mealtimes, eating out is no longer confined to mealtimes. Thus, people can eat whenever and wherever they want. Teenagers, night labourers, and late sleepers have been influenced by the availability of 24-hour eateries to eat late at night. The post-pandemic transition phase of business premises' operating hours allowed the owners of the premises to implement their operating hours based on their premises' operating license. This is quite worrying as Malaysians are back to the habit of having meals late at night outside at restaurants or convenience stores. 24-hour eateries are part of the culture in Malaysia before the pandemic as they can freely enjoy their meals at the food premises in the middle of the night. Therefore, this study defined eating out late at night as eating anything between 11PM and 4AM, regardless of the number of calories ingested. The foods can be prepared by food vendors such as in food courts, *warung*, *mamak* restaurants, fast food chains, or ordered through food delivery services such as GrabFood or FoodPanda.

Late-night eating is associated with an increase in risk for cardiometabolic health complications including obesity and metabolic syndrome (Simon et al., 2022). In addition, food prepared away from home is high in calories, fat, and sodium intake. There is a positive association between the frequency of consumption of food prepared outside the home and both fat intake and body fatness. These will lead to multiple health complications if associated with the frequency of eating out especially late at night (Simon et al., 2022).

Many studies in Malaysia have explore eating out habit during various mealtime, but the comprehensive data on this subject remain scarce. Moreover, there is a gap in research focusing on late night eating out habit among Malaysian. Thus, this study aimed to explore the practice of eating out late at night among adults in Kuantan, Pahang. This study will explore frequency and sociodemographic correlates of eating meals out and take-away meals at home late at night by conducting an online survey and interview.

MATERIALS AND METHOD

Subjects

Study Design and Population

A cross-sectional study design was used in this study. A total of 135 adults (male, n=43 and female, n=92) aged between 19 to 59 years old who lived in rural (Beserah) and urban (Kuala Kuantan) areas of Kuantan, Pahang, were recruited to participate in the study. Consent of participation was obtained from the respondents prior to answer the sets of questionnaires distributed. The study protocol was approved by Kulliyyah Postgraduate and Research Committee (KPGRC) and International Islamic University Malaysia Research Ethical Committee (IREC), ID number: KAHS 2/23.

Development of Questionnaire

This questionnaire was self-developed via the understanding of literature review because currently there was no study that developed questionnaire regarding eating out late at night either local or international. The questionnaire was constructed in Malay and consist of two parts:

a) Part 1: Sociodemographic

It consists of the respondent's demographic profile including age, gender, ethnics, marital status, living area, education level, employment status, working hours and monthly household income.

b) Part 2: The Practice of Eating Out Late at Night

This was a newly developed questionnaire that focuses on respondent's practice of eating out late at night. An eight-item questions designed to assess an individual's practice of eating out late at night. Respondents must choose one best answer because it was designed as multiple-choice question for this part.

Validation of Questionnaire

Six questions were validated by six experts, but two out of six questions did not achieve the Content Validation Index (CVI) acceptable values of at least 0.83 (Lynn, 1986; Yusoff, 2019). The CVI values for questions 1 to 3 were 1.0, question 4 was 0.61, question 5 was 0.78, and question 6 was 0.86. It was shown that question 4 and 5 did not achieve the acceptable value for CVI. The content validation of this questionnaire required minor corrections before proceeding to face validation by the target populations. Eight questions were evaluated using the Face Validation Index (FVI). The results showed that all questions achieved FVI value of 1.0, and no amendments necessary were needed.

Procedure of Study

A set of questionnaires was distributed through group chat applications among adults in Kuantan, Pahang by sharing a Google Form link to the participants. This study also conducted via face-to-face interview at the study areas.

The method used to categorize the frequency of eating out late at night in this study was to analyze the responses provided by each respondent to two specific questions: *'Soalan 1: Berapa kerapkah anda makan lewat malam di luar?'* and *'Soalan 2: Berapa kerapkah anda memesan makanan menggunakan perkhidmatan penghantaran makanan pada lewat malam?'* to determine the frequency of eating out late at night according to the study's definition. The higher frequency reported in both questions was chosen to categorize respondents' frequency of eating out late at night and used to determine the association between sociodemographic data and the frequency of eating out late at night.

Meanwhile, the method used to categorize the working hours in this study was to analyze the responses provided by each respondent. It was categorize based on the definition of normal working hours and other than normal working hours. Normal working hours are the standard working hours established by an organization or industry. These hours typically range from 9AM to 5PM, Monday to Friday. Other than normal working hours include evening shifts, night shifts, rotating shifts, or any other schedule that falls outside the typical 9AM to 5PM timeframe.

Statistical analysis

SPSS Version 26 was used to assess and analyze the data that had been obtained. The descriptive analysis was performed to identify the frequency (n), percentage (%), mean and standard deviation of the sociodemographic data, and the information on practice of eating out late at night. Besides, Fisher's Exact Test was used to determine the association between sociodemographic characteristics and frequency of eating out late at night. The value of $p < 0.05$ shows a significant association.

RESULTS

Sociodemographic data

As shown in Table 1, a total of 135 adults aged 19 to 59 years from Kuantan, Pahang participated in the study. Most of the respondents in this study were female (n=92, 68.1%), aged 19-29 years old (n=77, 57%), Malay (n=130, 96.3%), single (n=75, 55.6%), living in a rural area (n=91, 67.4%), possessing tertiary education (n=85, 63%), employed (n=91, 67.4%) working within normal hours (n=61, 67%), and earning an income less than RM4850 (n=63, 46.7%).

Practice of eating out late at night

Table 2 provides an overview of the respondents' practice of eating out late at night. The data shows that most respondents eat out late at night 1-2 times per week (n=97, 71.9%). Meanwhile, the most common frequency of ordering food using delivery services late at night was never (n=75, 55.6%). The average time of eating out late at night was 23:17, indicating a wide range of dining times among the respondents. The most common types of food premises visited or ordered late at night were fast food and *mamak* restaurants, each with 37.8% (n=42) of the responses and followed by *restoran masakan panas* (n=36, 32.4%). In terms of companions, friends were the most common company for eating out late at night (n=47, 42.3%), and followed by family members (n=32, 28.8%).

Table 1: Descriptive analysis of respondents' sociodemographic data (N=135)

Sociodemographic characteristics	Frequency (n)	Percentage (%)
Gender		
Male	43	39.1
Female	92	68.1
Age		
19 – 29 years old	77	57
30 – 39 years old	23	17
40 – 49 years old	23	17
50 – 59 years old	12	8.9
Ethnicity		
Malay	130	96.3
Chinese	3	2.2
Indian	2	1.5
Marital status		
Single	75	55.6
Married	55	40.7
Divorced/Widowed	5	3.7
Living area		
Rural	91	67.4
Urban	44	32.6
Educational level		
Non-formal school	2	1.5
Primary education	0	0
Secondary education	48	35.6
Tertiary education	85	63
Working status		
Working	91	67.4
Not working	17	12.6
Students	27	20
Working hours		
Normal working hours	61	67
Other than normal working hours	30	33
Monthly household income		
<RM4850	63	46.7
RM4850 – RM10959	24	17.8
Above RM10960	19	14.1
No income	29	21.5

The frequency of eating out late at night based on the definition of this study, encompassing both eating out and ordering food using delivery services. The results align with Table 2, indicating that the most common frequency of eating out late at night was 1-2 times per week (n=92, 68.1%).

Table 2: Descriptive analysis of respondents' practice of eating out late at night (N=135)

Practice of eating out late at night	Frequency (n)	Percentage (%)	Mean ± SD
Frequency of eating out late at night			
Never	25	18.5	
1 - 2 times in a week	97	71.9	
3 - 4 times in a week	13	9.6	
More than 5 times in a week	0	0	
Frequency of ordered food using delivery services late at night			
Never	75	55.6	
1 - 2 times in a week	52	38.5	
3 - 4 times in a week	7	5.2	
More than 5 times in a week	1	0.7	
Time eating out late at night			23:17 ± 23:07
Type of food premises visited or ordered late at night			
Fast food	42	37.8	
Mamak	42	37.8	
Restoran makanan panas	36	32.4	
Convenience stores	28	25.2	
Hawker food	11	9.9	
Companion to eat out late at night			
Friends	47	42.3	
Family members	32	28.8	
Self	19	17.1	
Partner	13	11.7	
Average spending per meal eating out late at night			
Less than RM5	2	1.8	
RM5.01 – RM10	32	28.8	
RM10.01 – RM15	23	20.7	
RM15.01 – RM20	17	15.3	
RM20.01 – RM25	16	14.4	
More than RM25.01	21	18.9	

Duration time spends eating out late at night		
Less than 15 minutes	3	2.7
15 – 30 minutes	40	36
30 – 45 minutes	36	32.4
45 – 60 minutes	16	14.4
More than 1 hour	16	14.4
Duration between eating out late at night and bedtime		
Less than 30 minutes	10	9
30 – 60 minutes	37	33.3
1 – 2 hours	51	45.9
More than 3 hours	13	11.7
Frequency of eating out late at night		
Never	23	17
1 to 2 times in a week	92	68.1
3 to 4 times in a week	19	14.1
More than 5 times in a week	1	0.7

Association Between Sociodemographic Data and Frequency of Eating Out Late at Night

Table 3 displays the associations between sociodemographic data and the frequency of eating out late at night, using Fisher's Exact Test. The results indicate that gender, age, ethnicity, marital status, living area, educational level, working status, working hours, and monthly household income do not have a significant association with the frequency of late-night dining out (all p-values > 0.05).

Specifically, among female respondents, 44.4% (n=60) reported dining out late at night 1-2 times per week, while 23.7% (n=32) of male respondents reported the same frequency. The highest percentage of respondents who ate out late at night 1-2 times per week were aged 19 to 29 years old (n=53, 39.3%). The majority of respondents were Malay (n=90, 66.7%) and reported eating out late at night 1-2 times per week. Single individuals (n=53, 39.3%) and rural residents (n=64, 47.4%) were more likely to dine out late at night at the specified frequency. Tertiary-educated and working individuals also reported higher rates of late-night dining. However, no significant associations were found between any of these factors and the frequency of eating out late at night.

Table 3: Association between sociodemographic data and frequency of eating out late at night (N=135)

Variable	Frequency of eating out late at night (in a week)				X^2-statistic (df)	*p*-value
	Never n (%)	1-2 times n (%)	3-4 times n (%)	More than 5 times n (%)		
Gender						
Male	5 (3.7)	32 (23.7)	6 (4.4)	0 (0.0)	1.842 (3)	0.672
Female	18 (13.3)	60 (44.4)	13 (9.6)	1 (0.7)		
Age						
19–29 years old	9 (6.7)	53 (39.3)	15 (11.1)	0 (0.0)		
30–39 years old	6 (4.4)	16 (11.9)	1 (0.7)	1 (0.7)	11.427 (9)	0.222
40–49 years old	5 (3.7)	15 (11.1)	2 (1.5)	0 (0.0)		
50–59 years old	3 (2.2)	8 (5.9)	1 (0.7)	0 (0.0)		
Ethnicity						
Malay	22 (16.3)	90 (66.7)	17 (12.6)	1 (0.7)		
Chinese	1 (0.7)	2 (1.5)	0 (0.0)	0 (0.0)	12.449 (6)	0.081
Indian	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)		
Marital status						
Single	8 (5.9)	53 (39.3)	14 (10.4)	0 (0.0)		
Married	14 (10.4)	36 (26.7)	4 (3.0)	1 (0.7)	10.834 (6)	0.072
Divorced/ Widowed	1 (0.7)	3 (2.2)	1 (0.7)	0 (0.0)		
Living area						
Rural	15 (11.1)	64 (47.4)	12 (8.9)	0 (0.0)	2.428 (3)	0.506
Urban	8 (5.9)	28 (20.7)	7 (5.2)	1 (0.7)		

Educational level						
Non-formal school	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)		
Secondary education	7 (5.2)	34 (25.2)	7 (5.2)	0 (0.0)	4.016 (6)	0.948
Tertiary education	16 (11.9)	56 (41.5)	12 (8.9)	1 (0.7)		
Working status						
Working	16 (11.9)	58 (43.0)	6 (11.9)	1 (0.7)		
Not working	7 (5.2)	34 (25.2)	7 (5.2)	0 (0.0)	5.883 (6)	0.460
Students	5 (3.7)	19 (14.1)	3 (2.2)	0 (0.0)		
Working hours						
Normal	10 (7.4)	36 (26.7)	14 (10.4)	1 (0.7)	8.628 (6)	0.147
Other than normal	6 (4.4)	22 (16.3)	2 (1.5)	0 (0.0)		
Monthly household income						
B40	8 (5.9)	41 (30.4)	13 (9.6)	1 (0.7)		
M40	6 (4.4)	16 (11.9)	2 (1.5)	0 (0.0)	8.289 (9)	0.518
T20	13 (9.6)	1 (0.7)	0 (0.0)	5 (3.7)		
No income	4 (3.0)	22 (16.3)	3 (2.2)	0 (0.0)		

DISCUSSION

The practice of eating out late at night

This study found that most respondents (68.1%) in Kuantan, Pahang ate out late at night. The frequency of eating out was 1-2 times in a week. This is a reasonable frequency, as it is not too often, but it is also not too infrequent. It is a frequency that many individuals may find to be a good fit for their lifestyle. There is no research that has specifically looked at the common frequency of eating out late at night. Nevertheless, this frequency aligns with the mealtime habits observed in Malaysia, where individuals frequently dine out during dinner and lunch (Rakuten, 2023). This suggests that eating out is a common practice in Malaysia, and it is not surprising that many people would also eat out late at night.

This study found that the habit of eating out late at night among respondents aligns with previous studies in Malaysia and China, where a significant percentage of people (27%) engage in late-night dining between 10PM until midnight (Rakuten, 2023; Xiaoyu, 2019). The availability of food establishments operating during late hours contributes to this trend. The study also revealed that respondents frequently visit fast-food restaurants, *mamak* stalls, and *restoran masakan panas*, which is consistent with previous studies highlighting Malaysians' preference for casual dining and fast food (Rakuten 2023; Ali & Abdullah, 2012). This study found out most respondents prefer to eat out late at night with friends, followed by family members. This aligns with a previous study indicating that Malaysians generally dine out with family members (Rakuten, 2023), but prefer to gather with friends for late-night dining (Ali & Abdullah, 2012).

Association between sociodemographic data and frequency of eating out late at night

The majority of respondents in this study were young, single Malay females with tertiary education, living in rural areas, and earning below RM4850. However, the frequency of eating out late night was not associated with any specific sociodemographic characteristics. This contrasts with previous studies on eating out, suggesting that factors such as personal preferences or lifestyle choices may have a greater influence on this practice than sociodemographic factors.

This finding contrasted with previous studies conducted in Shanghai and Malaysia, which found that men tend to eat out more often than women (Zang et al., 2018; Ashari et al., 2022; Orfanos et al., 2007). Additionally, the previous studies were not conducted specifically for eating out late at night. Therefore, it is also possible that the findings of this study were simply a reflection of the current trends in eating out late at night. This suggests that there may be a cultural or social norm in Kuantan, Pahang that encourages women to eat out more often than men. Respondents aged 19-29 were the most likely to eat out late at night. There is a lack of research on the frequency of eating out late at night among young people in Malaysia. Nevertheless, Kleynhans (2003) and Rakuten (2023) found that the younger generation tends to eat out more often than older generations in general meal timing.

This study discovered a discrepancy in the association between living area and the frequency of eating out late at night. It was found that more respondents residing in rural areas reported eating out late at night 1-2 times per week compared to those in urban areas. This contradicts the findings of a previous study by Tan (2010), which suggested that urban residents are more likely to dine out. The contrasting result in this study may be attributed to the higher proportion of rural areas (70%) compared to urban areas (30%) in Kuantan, based on the data from *Majlis Bandaraya Kuantan (MBK)*. It was observed that the rural area had numerous food establishments that operated until midnight, and food delivery services were also available. Therefore, it is possible that the data from this rural area differ from other rural areas due to environmental and social differences, leading to the inconsistent result.

The data on working individuals with normal working hours (9AM to 5PM) contradicts the findings of other studies on eating out. In a study conducted by Ali and Abdullah (2012), individuals who work late-night shifts or irregular hours find it necessary to eat out late at night. This is because it is a convenient option to satisfy their hunger when there are various limited food options available during late-night hours, such as 24-hour fast-food restaurants, *mamak* restaurants, or food delivery services. However, the data on working individuals with normal working hours suggests

that they may be eating out late at night for other reasons. For example, they may be socializing with friends or family, or they may be simply enjoying the convenience of having food delivered to their door.

CONCLUSION

In conclusion, the findings of this study suggest that eating out late at night is a common practice in Kuantan, Pahang. The most frequency of eating out was 1-2 times in a week, which is a reasonable frequency. The findings of this study on frequency of eating out late at night were not associated with any of the sociodemographic factors. This may be due to the cultural or social norm in Kuantan, Pahang, where eating out late at night is a common practice regardless of age, gender, or other factors.

Although the current frequency of eating out late at night appears to be reasonable and acceptable, it is crucial to raise public awareness in order to prevent any further increase in this behaviour. Eating out late at night has been linked to negative health consequences, such as weight gain, obesity, and other chronic diseases. Therefore, it is essential to promote awareness regarding the potential health risks associated with eating late at night. Health professionals and authorities should take action by implementing public education campaigns through various channels, including social media. For example, they could collaborate with local authorities, restaurants, and community organizations to implement targeted interventions. These efforts would contribute to the development of a healthier eating lifestyle among the general public.

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PROXIMATE ANALYSIS OF SELECTED MARINE FISHES IN KUANTAN, PAHANG

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ABSTRACT

Introduction: Marine fish is a good of protein and fatty acids. The nutrient compositions of fish vary due to many factors including different species, maturity of the fish and geographical regions. Hence, this study aimed to analyse proximate composition of four marine fish that commonly consumed by Malaysian, namely Silver Pomfret, Black Pomfret, Yellowstripe Scad and Yellowtail Scad. **Methods:** The proximate composition of moisture, protein, fat, and ash were measured according to method described by Association of Official Analytical Chemists (AOAC) 1990 with slight modifications. Data was analysed using Analysis of Variance (ANOVA), with a significance level used for all tests was at 95%. **Results:** There were no differences in the percentages of fat and protein among the selected fish except for ash and moisture contents. Silver Pomfret and Yellowstripe Scad had significantly higher moisture contents than Black Pomfret, Yellowtail Scad ($p<0.05$). Yellowstripe Scad exhibited the lowest ash content among the selected fish species, with a significant difference only when compared to Silver Pomfret ($p<0.05$). **Conclusion:** While there was no significant variation in protein and fat content, this study highlights the differences in moisture and ash composition among the four fish species. Future studies could further investigate the mineral contents present in the ash.

KEYWORDS: Marine fish, proximate analysis

INTRODUCTION

Marine fish is one of the main sources of protein, essential fatty acids such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), as well as vitamins and minerals that are crucial for sustaining health and supporting body function (Nurnadia et. al 2011, Babji et. al 2015 & Priatni et.al 2018). Indeed, it is recommended to incorporate fish into our daily diet, with an emphasis on consuming a diverse range of fish species, as outlined by the Ministry of Health (MOH, 2020).

Many consumers may not be aware that marine fish exhibit variations in nutritional contents. For this reason, fish selection is often influenced solely by factors such as availability, price, freshness, flavour, and physical characteristics (Nurnadia et. al, 2011). The nutrient composition of fish varies significantly depending on species, season, location, water quality, pH, size, body part, sex, and

maturity of the fish (Sonavane, 2017, Ghassem et. al 2009, Memon et. al 2010, Thammapat et. al 2010, Palani et. al 2014 & Paul et. al 2015). For example, a study on Pomfret fish showed higher protein content during the late post-spawning season compared to the early pre-spawning season (Nair & Suseela, 2000). Other studies have reported that n-6 fatty acids were higher at lower temperatures while protein content was higher at higher temperatures (Norambuena et. al 2016 & Castillo et. al 2017). Therefore, despite numerous studies examining the nutrient composition of marine fish, available data may still be incomplete due to various factors as described above.

Marine fish can be broadly categorized into two types: pelagic fish and demersal fish. Pelagic fish are mainly located near the sea's surface or at intermediate depths and primarily feed on plankton. In contrast, demersal fish reside on the sea bottom with benthic organism serving as their food source. According to Ackman (1989), fish can be classified into four groups based on their fat content: lean fish (<2%), low fat (2-4%), medium fat (4-8%) or high fat (>8%) (Nurnadia et.al., 2011). Marine fish such as Silver Pomfret (*bawal putih*), Black Pomfret (*bawal hitam*), Yellowstripe Scad (*selar kuning*) and Yellowtail Scad (*selar*) fall into the category of low-fat fish. In this study, we investigated these four fish, which are commonly found in Malaysia, to assess their moisture, protein, fat, and ash contents.

METHODS

Sample preparation

Four species of marine fish which are commonly consumed and found in Kuantan were selected. Silver Pomfret, Black Pomfret, Yellowtail Scad and Yellowstripe Scads were obtained from wet markets in *Pasar Pagi Kuantan* and *Lembaga Kemajuan Ikan Malaysia* (LKIM). It was confirmed by the vendors that the fish were caught from Kuantan coast. The fish were put into ice box during transportation from the market to the Food Preparation Laboratory to preserve the freshness and quality. Then, they were dissected to remove their skin, scale, and bones into fillet. They were further weighed, labelled into plastic and kept in the freezer at -22°C until further analysis.

Proximate analysis

The proximate analysis was conducted in the Food Analysis Laboratory, Department Nutrition Sciences, Kulliyyah Allied Health Sciences, International Islamic University Malaysia. The proximate composition namely moisture, fat, protein, and ash were determined according to the Official Method of Analysis of AOAC International as discussed in the following sections. Each analysis was carried out in three replicates to ensure accuracy.

Moisture analysis

Moisture content was analysed by oven drying method. First, empty crucibles with lids were dried in the oven at 105°C overnight. Then, the crucibles were cooled into a desiccator for 30 minutes. For each fish, 5g of samples was used and placed into the dried crucibles. The crucibles that contained samples were weighed and immediately put into the oven at 105°C overnight. After overnight drying, the crucibles were cooled into a desiccator for 30 minutes. This process was repeated until the constant weight was obtained. The differences in weight between pre and post drying were used to calculate the percentage of moisture content.

Crude protein analysis

The protein content was analyzed using the Kjeldahl method. The principle of the method involves digestion, neutralization, distillation, and titration to calculate the nitrogen content. Briefly, 3g of the sample was added into the digestion tubes followed by catalyst salts. About 12ml of concentrated

sulphuric acid was added into the tubes and swirled gently. Then, the digestion tubes were placed into digestion unit at 420°C for 90 minutes. Once completed, the tubes were cooled and transferred into the automated protein analyzer. The protein analyzer was set with conversion factor of nitrogen 6.25. The percentage of protein was calculated automatically by the protein analyzer.

Crude fat analysis

The fat content was analyzed using Soxhlet extraction method. Briefly, the extraction cups were placed into the oven at 105°C for one hour. Then, the cups were cooled in the desiccator and weighed. About 2g of sample was added into the dried cups followed by 70ml petroleum ether. The cups were placed into the automated fat extraction machine. Once completed, the extraction cups were dried into the oven at 105°C for one hour. In the final step, the cups were cooled in the desiccator and weighed. The fat content was measured using the following formula:

$$\text{Fat (g/100g)} = \frac{\text{Weight 2 – Weight 1}}{\text{Weight of Sample}} \times 100$$

Weight 1 = the weight of pre-dried empty extraction cups.
Weight 2 = the weight of extraction cups after extraction

Ash analysis

The ash content was analyzed using the dry-ashing method. Briefly, crucibles were dried in a muffle furnace at 550°C overnight. Then, the crucibles were cooled in the desiccator for 30 minutes and weighed. About 5g of sample was put into the dried crucibles and placed again into muffle furnace at 550°C overnight until the sample turned into whitish or greyish ash. Once completed, the crucibles were cooled in the desiccator and weighed. The percentage of ash content was calculated usingthe following formula:

$$\text{Ash (\%)} = \frac{\text{W3 – W1}}{\text{W2-W1}} \times 100$$

W1 = Weight of dry crucible
W2 = Weight of dry crucible with sample (after moisture analysis)
W3 = Weight of dry crucible and dried sample

Statistical analysis

The statistical analysis was performed using SPSS (version 12.0.1) software. Theresults for the nutrient composition were analyzed using one-way analysis of variance (ANOVA). Post hoc Tukey test was used to observe significant differences between species. The data was presented as means and standard deviation. The significance level used for all the tests was at 95% ($p<0.05$).

RESULTS

Table 1 indicates proximate analysis of the four selected marine fish; Silver Pomfret, Black Pomfret, Yellowtail Scad and Yellowstripe Scad. Our results show that the moisture content of Silver Pomfret and Yellowstripe Scad was significantly higher than that of Black Pomfret and Yellowtail Scad ($p<0.05$). Interestingly, Yellowstripe Scad displayed significantly lower ash content when compared to Silver Pomfret ($p<0.05$). However, this difference was not observed when comparing it to the other two fish. As

for fat and protein contents, there were no significant differences observed among all the fish species.

DISCUSSION

There were no significant differences in the fat percentage among the fish species. Silver Pomfret and Black Pomfret displayed fat contents of less than 1% which is slightly lower than those reported in other studies at 2.91% and 2.33%, respectively (Osman et. al 2001, Nurnadia et. al 2011). The variations in fish size used in the analysis could account for these differences. It is worth noting that fat is not uniformly distributed throughout a fish. The fish body may contain more fat compared to the flesh near the tail (FAO, 1995).

Similarly, the protein percentage did not show significant differences among the fish species. However, other studies have reported higher protein contents compared to our findings (Nurnadia et. al 2011, Priatni et. al 2018). The timing of fish catch, and analysis could contribute to the variation in protein contents. According to Nair & Suseela (2000), pre-spawning season can result in lower protein content in fish. In addition, starvation due to natural or physiological factor such as spawning, or migration can lead to reductions in both fat and protein contents (Boran & Karacam, 2011).

Furthermore, factors such as storage condition may also impact protein content. Samples stored at slow freezing temperature (-20°C) as in our study, can forms larger and irregular crystal that may deteriorate the surface of connective tissue. This could potentially lead to damage to the muscle tissues (Dawson et. al. 2018). Besides, slow freezing may only kill some of the pathogens, leading to protein denaturation when proteolysis is induced by enzymatic activities during psychotropic microbial growth (Gandotra, 2012).

Interestingly, our Silver Pomfret and Yellowstripe Scad exhibited higher water content compared the other two fish. A study by Nurnadia et. al 2011 reported a similar percentage of water for Silver Pomfret as observed in our study while Palani et.al (2014) found a slightly lower moisture content in Yellowstripe Scad. Furthermore, the ash content was the highest in Silver Pomfret but lowest in Yellowstripe Scad. Our findings were comparable to values reported in other studies (Nurnadia et al. 2011, Palani et. al 2014). Teame et. al (2016) stated that the variation in ash percentage could be due to differences in mineral content within the fish habitat, the physiological state of the fish or the ability of the fish to absorb elements from its diets. This highlights the fact that fish from different environments may contain varying mineral elements.

CONCLUSION

Apart from moisture and ash contents, there were no significant differences in protein and fat contents among the fish species studied. It is worth noting that our results exhibited lower protein and fat levels than those reported in several other studies. Such variations in the values are expected, as fish of the same or different species can have diverse nutrient compositions influenced by many factors including geographical areas, sub-species, seasons, water quality, pH, age, maturity, and part of the fish analyzed.

Table 1: Proximate analysis of Silver Pomfret, Black Pomfret, Yellowtail Scad & Yellowstripe Scad

English name	Local name	Component (%)			
		Moisture	**Fat**	**Protein**	**Ash**
Silver Pomfret	*bawal putih*	79.96 ± 3.60[a]	0.93 ± 0.39[a]	2.99 ± 1.05[a]	1.88 ± 1.01[a]
Black Pomfret	*bawal hitam*	73.10 ± 1.98[b]	0.39 ± 0.14[a]	2.61 ± 0.83[a]	1.26 ± 0.28[ab]
Yellowtail Scad	*selar*	75.50 ± 0.47[b]	0.54 ± 0.52[a]	2.68 ± 0.62[a]	1.70 ± 0.65[ab]
Yellowstripe Scad	*Selar kuning*	79.37 ± 0.45[a]	0.49 ± 0.47[a]	3.20 ± 1.12[a]	0.76 ± 0.22[b]

Values are given as Mean ± SD from three replicate tests

Different superscripts (*a* vs *b*) in the same column indicate significant different ($p<0.05$)

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KNOWLEDGE, ATTITUDE AND PRACTICE ON FUNCTIONAL FOOD CONSUMPTION AMONG HEALTH SCIENCE AND NON-HEALTH SCIENCE STUDENTS

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ABSTRACT

Introduction: It is widely recognized that functional foods can address specific health needs of consumers, potentially contributing to enhancing overall public health. While numerous studies have explored consumer perception and acceptance of functional food products, research examining knowledge, attitude, and practice (KAP) remains limited, especially among university students. Hence, this study aimed to assess KAP regarding functional foods consumption among both health science and non-health science students. **Methods**: A total of 118 students participated in this study, including 77 from the health science group and 41 from the non-health science group. Respondents were provided with a self-administered questionnaire that covered demographic profiles, knowledge, attitude, and practice related to functional foods consumption. **Results**: The study showed that students at IIUM Kuantan exhibited poor knowledge, moderate attitude, and poor practice regarding functional foods consumption. Notably, health science respondents demonstrated significantly higher levels of knowledge and attitude compared to their non-health science counterparts. Interestingly, both groups showed a similar frequency of functional foods consumption per week. **Conclusion**: Overall, students at IIUM Kuantan had poor levels of knowledge, moderate attitude, and practice about functional foods intake, although health science groups had higher knowledge and attitude than non-health science groups. Additional efforts are needed to increase knowledge and awareness regarding the consumption of functional foods.

KEYWORDS: Functional foods, knowledge, attitude, practice, university students

INTRODUCTION

Functional foods, a category of nutritionally enhanced food products, have gained prominence for their potential to offer health benefits beyond basic nutrition. While there is no universal definition of functional foods, the International Life Sciences Institute describes them as "*foods that by virtue of physiologically active food components provide health benefits beyond basic nutrition'* (Bagchi, 2008). Functional foods include a diverse range of products, whether naturally occurring or processed, including fortified or enriched foods. These foods have the ability to modulate metabolic processes in the human body, subsequently improving health conditions and reducing the risk of chronic diseases (Bleich et al. 2015; Büyükkaragöz et al. 2014; El Sohaimy, 2012).

In recent times, people began to rely on functional foods to improve their health (Shariff et al. 2017). The inclusion of these foods, however, depends not only on their availability and affordability but also on the knowledge, attitudes, and practices of the consumers. Many consumers include functional foods in their diet unaware that the food belongs to this food category. For instance, a cross-sectional

study in Thessaloniki, Greece, indicated that over 70% of the consumers include functional foods in their daily diet without realizing them as such (Christidis et al. 2011). Another study reported that a high percentage of US consumers were unaware that consuming functional foods could have positive effects on their health (Urala et al. 2011). In addition, Wahba et al. (2006) stated that many of the respondents believe that certain food components contribute to better health, yet their understanding of functional foods remains limited. Nevertheless, those with a strong understanding of the health benefits offered by functional foods are more likely to include them in their regular diets (Wansink et al. 2005).

Factors such as age, gender, and education levels can have a significant influence on knowledge, attitude, and practice related to functional foods consumption. Rezai et al. (2012) found that individuals under the age of 25 years old demonstrated higher awareness on functional foods than older counterparts. Meanwhile, females tend to have greater acceptance of functional foods than male (Sääksjärvi et al. 2009; Dogan et al. 2011) as they seem to be more conscious on their health (Bogue et. al 2006). According to Dogan et al., 2011, higher education levels are linked to increased knowledge and awareness of functional foods. Consequently, university students, particularly those in health-related disciplines are presumed to possess a better understanding of functional foods compared to their non-health discipline counterparts. This study, therefore, seeks to evaluate the Knowledge, Attitude, and Practice (KAP) regarding functional food consumption among university students, with a specific focus on health and non-health disciplines.

METHODS

Subjects

This cross-sectional study utilized convenience sampling involving a total of 118 students, with 77 students from health science disciplines and 41 students from non-health science disciplines at International Islamic University Malaysia (IIUM) Kuantan. Inclusion criteria encompassed local undergraduate students, while exclusion criteria were foundation, postgraduate and foreign students. The proportion of health-science to non-health science students in the sample was determined based on the actual population of IIUM Kuantan, with 65% representing health science students and 35% non-health science students. Respondents in health science disciplines came from *Kulliyyah* of Allied Health Sciences, *Kulliyyah* of Medicine, *Kulliyyah* of Dentistry, *Kulliyyah* of Pharmacy and *Kulliyyah* of Nursing. Respondents in non-health science discipline were selected from various departments within *Kulliyyah* of Science including Marine, Biotechnology, Applied Plant, Applied Physics, Applied Chemistry and Computational and Theoretical Sciences. Furthermore, respondents in this study were limited to students in their second year and third year of study to ensure equivalent knowledge level among respondents. The gender distribution in this study was also based on the actual population at IIUM Kuantan, with approximately 75% female students and 25% male students.

Self-Administered Questionnaire

This study utilized self-administered questionnaire. Before distributing questionnaires, a pilot study was conducted with 28 respondents, and their feedback was used to revise the questionnaire. The questionnaires were structured into four sections: demographic data, knowledge, attitude, and practice related to functional foods intake. The knowledge section consisted of 15 statements, where respondents needed to indicate whether they were “true” of “false”. The attitude section comprised 10 statements and respondents were asked to express their opinion by selecting from options such as “strongly disagree”, “disagree”, “neutral”, “agree” or “strongly agree”. In the practice section, the participants were presented with 10 selected functional foods, and they needed to indicate the frequency of their consumption per week.

Scoring System

A scoring system was applied to the knowledge and attitude sections before incorporating them into SPSS. In the knowledge section, a score of one was given for a correct answer and zero for incorrect or when respondents chose 'not sure". In the attitude section, a score of one was given for "strongly disagree", two for "disagree", three for "neutral", four for "agree" and five for "strongly agree".

Statistical Analysis

SPSS version 12.01 was used to analyse all the information. The statistical significance level was set at $p<0.05$. When describing the level of knowledge, attitude and practice, percentages were used. For the comparison between groups, independent T-test was used.

RESULTS

Knowledge, attitude, and practice regarding functional foods

Table 1 shows knowledge, attitude, and practice levels among health science and non-health science respondents. The majority of the IIUM Kuantan respondents (76.3%) had a low level of knowledge regarding functional foods. Likewise, both health science and non-health science disciplines respondents demonstrated low levels of knowledge. Meanwhile, most respondents (69.5%) exhibited a moderate level of attitude toward functional foods. Similarly, both health science and non-health science disciplines respondents showed moderate levels of attitude. The majority of the respondents demonstrated a low level of practice, as reflected by the poor frequency of functional foods intake per week. Likewise, both health science and non-health science disciplines respondents showed a low level of practice, but this difference was not statistically significant.

Table 2 shows knowledge, attitude, and practice scores between health science and non-health science groups. Health science respondents achieved an average knowledge score of 7.2, significantly higher than their non-health science counterparts, with an average score of 5.6 ($p=0.001$). Similarly, health science respondents demonstrated a significantly higher attitude score compared to non-health science groups, with average scores of 3.7 and 3.4, respectively ($p=0.006$). On the contrary, non-health science respondents exhibited slightly higher practice scores for the frequency of functional foods consumption per week than health science group, but this difference was not statistically significant.

DISCUSSION

Most respondents, whether considered collectively or when analysed by groups, exhibited a low level of knowledge level about functional foods. This outcome aligns with the finding reported by Afina and Retnaningsih (2018) where over half of undergraduate students managed to correctly answer only six out of 15 questions. Notably, our results also demonstrated that health science respondents had a higher score of knowledge compared to non-health science counterparts. This is consistent with a study by Morawska et al. (2016), who reported that Dietetics students possessed higher levels of knowledge on functional foods compared to Pharmacy students. Despite both groups falling under the health science category, Dietetic students may benefit from a more specialized exposure to functional foods in line with their academic background.

Approximately two-thirds of the respondents had a moderate attitude regarding the consumption of functional foods. This result corresponds to the finding reported by Afina and Retnaningsih (2018) where 80.0% of undergraduate students exhibited a moderate level of attitude. Our finding, however, differed slightly from a study among young Malaysian consumers conducted by Rezai et al. (2012), which reported a positive attitude regarding the consumption of functional foods for the purpose of achieving good health. This moderate attitude observed despite a low level of knowledge could be attributed to the increasing awareness among IIUM Kuantan students regarding the importance of maintaining good health.

As for dietary practice, this study found that most respondents, regardless of academic disciplines, had a low frequency of functional foods intake. The reason for this limited consumption of functional foods among students may be due to low level of knowledge about these foods. This is in line with a study by Bilgiç and Yüksel (2012), in which about 114 university students argued that their lack of knowledge was the reason for not consuming the functional foods.

Table 1: Distribution of the knowledge, attitude, and practice levels.

	Level	Overall	Health Science	Non-Health Science
		%	%	%
Knowledge	High (≥80)	3.4	5.2	0
	Moderate (60-79)	20.3	28.6	4.9
	Low (≤59)	76.3	66.2	95.1
Attitude	High (4)	22.9	31.2	7.3
	Moderate (3-3.9)	69.5	63.6	80.5
	Low (<3)	7.6	5.2	12.2
Practice	High (>29)	5.9	2.6	12.2
	Moderate (15-28)	27.1	29.9	22.0
	Low (0-14)	66.9	67.5	65.9

Table 2: Knowledge, attitude and practice scores between health science and non-health science.

Score	Health Science		Non-Health Science		*p-value*
	Mean	SD	Mean	SD	
Knowledge	7.3	(2.6)	5.7	(2.1)	0.001
Attitude	3.7	(0.6)	3.4	(0.5)	0.006
Practice	11.7	(7.9)	13.4	(9.9)	0.325

CONCLUSION

Overall, students at IIUM Kuantan had poor levels of knowledge, moderate attitude, and practice about functional foods intake, although health science respondents had higher knowledge and attitude than non-health science respondents. Additional efforts are needed to increase knowledge and awareness regarding the consumption of functional foods. When students understand the role of functional foods in maintaining their health and reducing the risk of chronic diseases, they are more likely to consume them more frequently.

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NUTRITIONAL STATUS AND FEEDING BEHAVIOUR OF YOUNG CHILDREN IN THE NORTHEASTERN REGION OF MALAYSIA

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ABSTRACT

Introduction: The dietary choices of young children can significantly impact their nutritional well-being, particularly if they exhibit selective eating habits. Avoiding familiar foods and failing to consume sufficient amounts of nutritious food can harm a child's overall nutritional status. As such, this study aims to assess the feeding behaviour and nutritional status of young children in the Northeastern region of Malaysia. **Methods:** A cross-sectional study was conducted involving 60 children aged one to five years in five districts of Kelantan, Malaysia. Online questionnaires were used to collect data, including sociodemographic information and the Child Eating Behaviour Questionnaire (CEBQ). Individual Dietary Diversity Scores (IDDS) were calculated to evaluate the children's eating habits. Anthropometric measurements were also taken, including body mass index (BMI), weight-for-age (WAZ-score), height-for-age (HAZ-score), and weight-for-height (WHZ-score). The data were analysed using the Statistical Package for the Social Sciences (SPSS) version 26.0. **Results:** Findings revealed that 55% of young children were picky eaters and had low IDDS scores. Picky eaters were more likely to be underweight (11.7%), stunted (15%), and wasted (6.7%) compared to non-picky eaters. However, no significant association existed between nutritional status and feeding behaviour or IDDS scores. **Conclusion**: To address picky eating, it is crucial to provide nutrition education and raise caregiver awareness about their children's feeding habits. This approach can help improve the nutritional well-being of young children in Kelantan, Malaysia, and potentially contribute to broader efforts to combat childhood malnutrition.

KEYWORDS: Nutritional status, picky eater, feeding behaviour, children, Kelantan

INTRODUCTION

A child's growth throughout the first five years of life is significantly influenced by their dietary intake (Mkhize & Sibanda, 2020). Children who consume minimal nutrients will struggle to grow and acquire weight as they should, which eventually causes them to become persistently malnourished (Tan et al., 2022). According to the World Health Organization (2019), malnutrition is caused by insufficient or excessive dietary intake as well as an inefficient use of energy, macronutrients, and micronutrients. Undernutrition, unrecognised hunger, and obesity are the three strands of malnutrition (UNICEF, 2019). These traits can be addressed in some circumstances because undernutrition is a major contributor to stunting and wasting, while overnutrition can contribute to being overweight. Since malnutrition raises the risk of illness and death in children, this is an urgent public health concern in the majority of countries. In Malaysia, 14.8% of children under the age of 17 are obese and 15% are overweight. According to the reports, stunting affects 22% of children under the age of five, with an increasing trend from 17% in 2011 to 18% in 2015 (National Health and Morbidity Survey, 2019). Among the factors contributing to stunting is feeding behaviour created within the family's structure which most certainly has an impact on the child's experience (Pai & Contento, 2014).

It is crucial for a child's diet to have a balanced ratio of macronutrients to micronutrients and a healthy eating pattern (Braet et al., 2014). This pattern is usually influenced by the child's family members and can promote physical growth and food preferences (Ek et al., 2016). It includes various behavioural patterns that enable children to consume food that satisfies them while also getting all the necessary nutrients. However, studies have shown that about 50% of picky eater children have a family history of picky eating behaviour (Mok et al., 2022). In modern families, there may be a tendency to consume too much or too little energy, leading to obesity or undernutrition (Herle et. al., 2020). A study by Kwon et al. (2017) mentioned that about 70% of children were picky eaters, and 30% of them were eating small amounts of food, reducing their energy and micronutrient intake. These children also exhibited neophobic behaviour, characterised by a constant fear of trying new foods and the refusal of specific food groups or preparation methods. If these eating patterns persist, malnutrition may develop, which could negatively affect young children's health and well-being. However, in Malaysia, only a few studies have documented the nutritional status of young children aged below five years old (Hanapi et al., 2022). Therefore, this study aims to identify the current nutritional status and feeding behaviour of young children in Kelantan to address this gap.

METHODS

Participants

A cross-sectional study was conducted in February 2023 whereby caregivers and their children aged one to five years old were recruited using stratified random sampling. Nine kindergartens were randomly selected from five districts (i.e., Kota Bharu, Pasir Mas, Tanah Merah, Machang, Tumpat) and caregivers were randomly selected from the name list. Caregivers with children aged below 5 years old were recruited. Caregivers of children with illnesses that affect their dietary habits or were previously hospitalised over six months were excluded.

Anthropometric assessments

Children's anthropometric assessments including height and weight were measured at the kindergarten. The height was measured in centimetres (cm) using measuring tape and the weight was measured in kilogrammes (kg) using a digital weighing scale at least 2 times. The body mass index (BMI) and sex-specific Z-scores for height-for-age, weight-for-age, and weight-for-height were assessed using WHO AnthroPlus Software. Their nutritional statuses were classified according to the WHO Child Growth Standard 2006.

Dietary assessments

Caregivers were interviewed for their children's 3-day diet recall, of which two days were weekday and one weekend day. Caregivers were asked to report their children's portion size in household measurements such as teaspoons, tablespoons, cups, bowls, and other daily household measures provided during the session. Individual Dietary Diversity Score (IDDS) which includes 12 food groups was used to evaluate children's daily meals based on the dietary assessment (FAO, 2010). The total score was calculated to be between 0 and 12. Using IDDS terciles, the total scores were then classified into low (≤8.0) and high (9.0-12.0) groups.

Children Eating Behaviour Questionnaire

Feeding behaviour was assessed using the Children Eating Behaviour Questionnaire (CEBQ) consisting of 35 items which demonstrated 8 subscales of enjoyment of food, food responsiveness, emotional overeating, desire to drink, satiety responsiveness, slowness in eating, emotional under-eating, and food fussiness. On a 1–5 point scale, caregivers were required to rate their children's feeding behaviour as the following, 1=never; 2=rarely; 3=sometimes; 4=often; 5=always. The mean total score of the picky eater subscale was analysed to determine the children's feeding behaviours using Steinsbek's cut-off to determine the prevalence of picky eaters among the children. Picky eaters were those with a mean total score of≥3.0, whereas non-picky eaters were those with a mean total score of <3.0.

Statistical analysis

A descriptive analysis was performed to evaluate participant characteristics and the nutritional status of young children. An independent t-test was conducted to assess the feeding behaviour among young children. Meanwhile, the chi-square test was used to assess the relationship between feeding behaviour and children's nutritional status. The Statistical Package for the Social Sciences (SPSS) version 26.0 was used for all analyses, with a significance level set at $p < 0.05$.

Ethical Approval

This study has been granted ethical approval by the International Islamic University Malaysia Research Ethical Committee (IREC) *(KAHS 3/24)*.

RESULTS

Participants' characteristics

The sociodemographic characteristics of the caregivers are presented in Table 1. Majority of the responding Malay caregivers were female (73.3%, N=44), with those aged between 30 and 39 years old (68.3%, N=41) and had tertiary education (38.3%, N=23). In this study, the majority (83.3%, N=50) of them had more than 4 people in a house. The mean household income of the respondents was RM4935.35 (SD±3447.78), as most of them were employed (80%, N=48) and in the category of B40 (60%, N=36).

Meanwhile, a total of 60 Malay children aged 1 to 5 years old participated in this study, in which 56.7% (N=34) of them were boys and 43.3% (N=26) were girls. The mean age of the children was 3.48 years±1.36, with most of them aged 5 years old (31.7%, N=19).

Table 1: Sociodemographic characteristic of respondent, N=60

Variables	*n*	*(%)*	*Mean ± SD*
Gender of caregiver			
Male	16	(26.7)	
Female	44	(73.3)	
Age of caregiver			36 ± 6.65
21-29 years old	5	(8.4)	
30-39 years old	41	(68.3)	
40-49 years old	14	(23.3)	
50-59 years old	0	0	
≥60 years old	0	0	
Relationship status			
Father	16	(26.7)	
Mother	44	(73.3)	
Gender of children			
Boy	34	(56.7)	
Girl	26	(43.3)	
Age of children			3.48 ± 1.36
1 years old	6	(10.0)	
2 years old	10	(16.7)	
3 years old	12	(20.0)	
4 years old	13	(21.7)	
5 years old	19	(31.7)	
Level of education			
Degree/Master/PhD	23	(38.3)	
Diploma	21	(35)	
SPM	16	(26.7)	
PMR	0	0	
Occupation status			
Employed	48	(80)	
Self-employed	10	(16.7)	

Pensioner	0	0	
Not working	2	(3.3)	
Household income			4935.35 ± 3447.78
B40 (<RM4850)	36	(60)	
M40 (RM4851-RM10959)	20	(33.3)	
T20 (>RM10959)	4	(6.7)	
Household size			4.95 ± 1.56
2 people	1	(1.7)	
3 people	9	(15)	
≥ 4 people	50	(83.3)	

Nutritional status of young children

The children's nutritional status and anthropometric measurements are presented in Table 2. Their average weight was 13.05 kg (SD±3.30), average height was 93.49 cm (SD±12.04), and average BMI was 13.39 kg/m² (SD±3.01). The mean z-scores for weight-for-age, height-for-age, and weight-for-height were -0.91 (SD±1.19), -1.19 (SD±1.20), and -0.38 (SD±1.31), respectively. Based on the WHO growth chart, 16.7% (N=10) of the children were underweight, 23.3% (N=14) were stunted, 6.7% (N=4) were wasted, and 10% (N=6) were overweight.

Table 2: Anthropometric assessment and nutritional status of children of children, N=60

Variables	*n*	*%*	*Mean ± SD*
Height			93.49 ± 12.04
Weight			13.05 ± 3.30
BMI			13.39 ± 3.01
Weight-for-age (WAZ-score)			-0.91 ± 1.19
Normal	50	(83.3)	
Underweight	10	(16.7)	
Height-for-age (HAZ-score)			-1.19 ± 1.20
Normal	46	(76.7)	
Stunting	14	(23.3)	
Weight-for-height (WHZ-score)			-0.38 ± 1.31
Normal	50	(83.3)	
Wasting	4	(6.7)	
Overweight	6	(10.0)	

Diet Diversity Scores

According to Figure 1, legumes, nuts, and seeds are the least consumed food category among young children (0.17±0.38), while cereals are the most consumed food category among children (1.00±0). Findings revealed that the mean IDDS score among young children was 7.59 (1.52). The majority (73.3%, N=44) of the children fell within the low IDDS group, while 26.7% (N=16) were in the high IDDS group (Table 3).

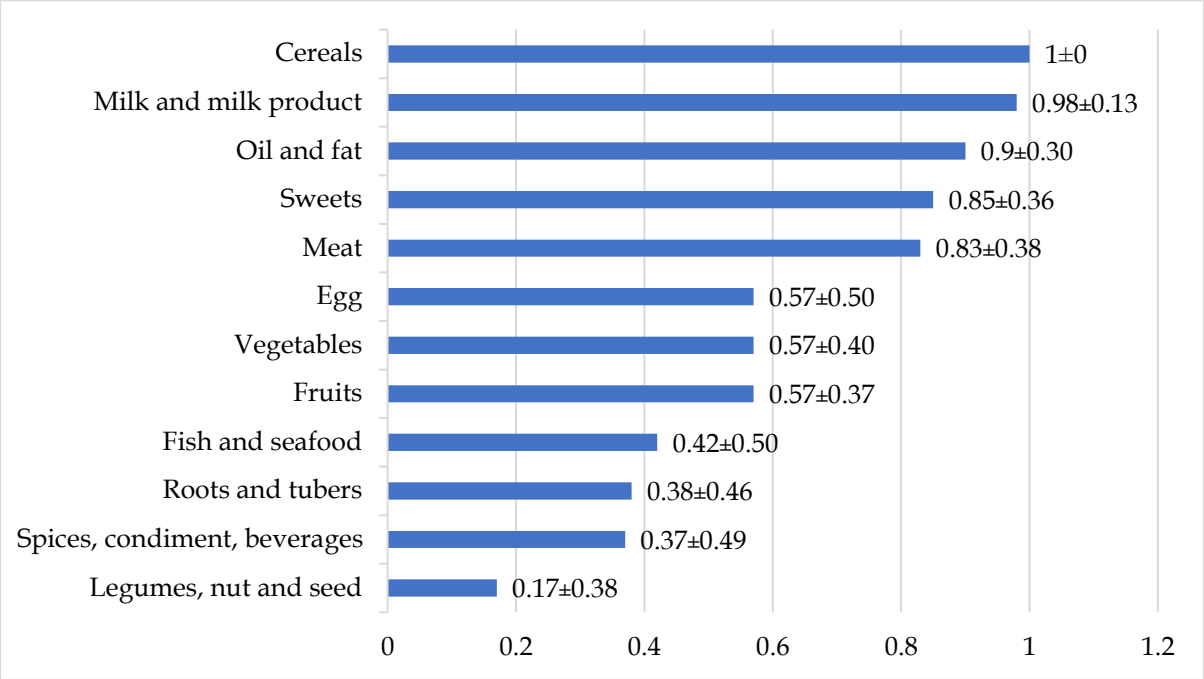


Figure 1: Mean dietary diversity of the different food groups.

Table 3: Mean dietary diversity score group.

Variables	*n (%)*	*Mean (SD)*
Low	44 (73.3)	7.59 (1.52)
High	16 (26.7)	

Children's Mealtime and Picky Eating Behaviour

As shown in Table 4, the majority (55%, N=33) of children were classified as picky eaters by using Steinsbekk's cut-off. With regards to their mealtime behaviour, the most problematic mealtime behaviour was seen in the enjoyment of food (3.5±0.75) while the least problematic behaviour was reported in emotional over-eating (1.48±0.54).

Table 4: Children's Eating Behaviour characteristics, N=60

Variables	*Mean ± SD*	Prevalence of picky eater *Steinbekk's score*	
		<3.00 (n, %)	*≥3.00 (n, %)*

Food responsiveness (FR)	2.7 ± 0.76		
Emotional over-eating (EOE)	1.48 ± 0.54		
Enjoyment of food (EF)	3.5 ± 0.75		
Desire to drink (DD)	3.08 ± 0.81		
Satiety responsiveness (SR)	3.13 ± 0.62		
Slowness in eating (SE)	2.71 ± 0.65		
Emotional under-eating (EUE)	2.42 ± 0.90		
Food fussiness (FF)	2.89 ± 0.49	27, 45%	33, 55%

Children Eating Behaviour Questionnaire (CEBQ) subscales between picky eaters and non-picky eaters.

Picky-eater children had significantly higher mean scores for food fussiness ($p<0.001$), emotional overeating ($p=0.002$), desire to drink ($p=0.009$) and satiety responsiveness ($p=0.004$) when compared to non-picky eaters (Table 5).

Table 5: Mean difference of Children Eating Behaviour Questionnaire subscales between picky eaters and non-picky eaters, N=60

Variables	*Picky eater (n=33)*	*Non-picky eater (n=27)*	*Mean difference (95% CI)*	*df*	*p-value*
	Mean ± SD	*Mean ± SD*			
Food responsiveness (FR)	2.8 ± 0.76	2.58 ± 0.76	0.22	58	0.714
Emotional over-eating (EOE)	1.62 ± 0.60	1.31 ± 0.42	0.32	58	0.002
Enjoyment of food (EF)	3.62 ± 0.78	3.36 ± 0.71	0.26	58	0.744
Desire to drink (DD)	3.13 ± 0.67	3.01 ± 0.96	0.12	58	0.009
Satiety responsiveness (SR)	3.13 ± 0.46	3.13 ± 0.78	-0.01	58	0.004
Slowness in eating (SE)	2.80 ± 0.55	2.60 ± 0.75	0.20	58	0.090
Emotional under-eating (EUE)	2.58 ± 0.86	2.22 ± 0.93	0.35	58	0.543
Food fussiness (FF)	3.22 ± 0.24	2.49 ± 0.42	0.72	58	0.001

*Using independent t-test

Association between feeding behaviour and nutritional status of young children

Table 6 showed no significant association between picky eating behaviour with weight-for-age z-score (p=0.524), height-for-age z-score (p=0.907) and weight-for-height z-score (p=0.420).

Table 6: Association of picky eating behaviour and nutritional status, N=60

Variables	*Picky eater* n (%)	*Non-picky eater* n (%)	X^2	*df*	*p-value*
Weight-for-age			0.406	1	0.524
Underweight	7 (11.7)	4 (6.7)			
Normal	26 (43.3)	23 (38.3)			
Height-for-age			0.014	1	0.907
Stunting	9 (15.0)	7 (11.7)			
Normal	24 (40.0)	20 (33.3)			
Weight-for-height			1.737	2	0.420
Normal	27 (45.0)	23 (38.3)			
Wasting	4 (6.7)	1 (1.7)			
Overweight	2 (3.3)	3 (5.0)			

*Using Chi-square test

Association between feeding behaviour and dietary diversity score of young children

Similarly, picky eating behaviour was not significantly associated with diet diversity score (p=0.639) (Table 7).

Table 7: Association of picky eating behaviour and dietary diversity score, N=60

Variables	*Picky eater* n (%)	*Non-picky eater* n (%)	X^2	*df*	*p-value*
Low	25 (41.7)	19 (31.7)	0.22	1	0.639
High	8 (13.3)	8 (13.3)			

*Using Chi-square test

DISCUSSION

The Northeastern region of Malaysia still has significant rates of underweight (17%), wasting (7%), stunting (23%), and overweight (10%) among young children, which is comparable to data from the National Health Morbidity Survey (NHMS) 2022. In the year 2020 – 2021, 15% of children were underweight, 11% were wasting, 21% were stunted, and 6% were overweight (NHMS, 2022). Meanwhile, Chile and Barbados had similar rates of overweight children at 9.3% and 12.2%, respectively, according to Corvalán et al. (2017). According to Pai and Contento (2014), parents often do not effectively monitor their children's food intake and dietary preferences, which can lead to

uncontrolled eating habits and a lack of nutritional food consumption. These eating-related problems can be linked to malnutrition.

The data shows that 73.3% of the children had inadequate dietary diversity scores, while only 26.7% had excellent scores. This means that most children did not consume the required 9 to 12 food groups for proper growth and nutrition in the previous 24 hours. The food categories that were consumed the least were legumes, nuts and seeds, roots and tubers, and fish and seafood. On the other hand, cereals were the most frequently consumed food group. A similar study conducted by Ogechi et al. (2016) among Nigerian children aged 2 to 5 years showed that 73.5% had low IDDS, while 25.2% and 1.3% had medium and high IDDS respectively. The least consumed food group was eggs, while cereals and vegetables were commonly consumed. The poor IDDS can be attributed to food insecurity, as nutritious food sources were not readily available in the area.

This study identified that 55% of young children were picky eaters. This percentage is comparable to the findings of Mok et al. (2022), who discovered that the majority of children (61.9%) are non-picky eaters while the remaining 38% and 15.9% are moderate and severe picky eaters, respectively. The research highlighted that picky eaters tend to have particular preferences for their favourite foods, which was evident from the high enjoyment scores. Picky eaters showed reluctance towards trying new foods and often felt full or thirsty even before or during meals, indicating a lack of interest in eating. Similar results were reported by Sandvik et al. (2018) and Cardona Cano et al. (2015), who identified high satiety responsiveness, slow eating, and reduced enjoyment of food among picky eaters aged between 1 to 5 years old. Maternal negative affectivity was identified as a potential risk factor for picky eating, leading to heightened child emotionality and the onset of fussy behaviour (Cardona Cano et al., 2015). According to Krijnen and colleagues (2022), maternal negative affectivity is a consistent personality trait in mothers characterized by their tendency to experience negative thoughts, feelings, and emotions. This trait has been linked to more psychosocial problems in their children and poorer quality of mother-child interactions.

This study found no correlation between picky eaters and their nutritional status in terms of weight-for-age, height-for-age, and weight-for-height. In fact, picky eaters were more likely to have a normal weight, height, and BMI for their age. This is consistent with previous studies which have shown that mild to moderate picky eaters generally have a normal weight (Antoniou et al., 2016; Li et al., 2017). However, when compared to non-picky eaters in this study, picky eaters were found to have significantly lower weight, height, and BMI. These findings have been observed in other studies, such as those conducted by Hanapi et al. (2022) and Chao (2018). This suggests that picky eater children may be at risk of being underweight, stunted, or wasted.

Picky eaters who are malnourished often have insufficient nutrients necessary for their growth throughout life. The majority of picky eater children in this study did not consume the recommended daily servings of fruits, vegetables, and seafood. Similar to studies conducted by Mok et al. (2022) and Chao (2018), picky eater children in this study consumed fewer fruits, vegetables, dairy products, and protein sources.

CONCLUSION

The study found that picky-eater children in Kelantan were more likely to become underweight, stunted, and wasted compared to non-picky eaters. However, there was no association found between the nutritional status of picky eaters and their food preferences. Picky eaters exhibited higher satiety responsiveness, slower eating and greater enjoyment of food. The low dietary diversity score was attributed to their fussiness in food preference. They consumed fewer vegetables, fruits, fish, and legumes than non-picky eaters. It is important to note that the sample size of 60 participants may not fully represent the entire population of Kelantan. Therefore, it is recommended that caregivers introduce nutrition education for children.

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THE READINESS EVALUATION ON FOOD INDUSTRIES TO IMPLEMENT MANDATORY MALAYSIA HALAL CERTIFICATION SCHEME (MHCS)

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ABSTRACT

Introduction: Food industries in Malaysia have implemented Malaysia Halal Certification Scheme (MHCS) on voluntary basis for almost 50 years. This long experience should be exploited to enhance the implementation of MHCS as mandatory and involve wider categories of food industries. **Aim:** This study aimed to evaluate the readiness level of food industries in Malaysia for the implementation of mandatory MHCS. **Methods:** About 514 food companies in Malaysia from almost all categories of food premises involved in this study. All the companies were structured randomly selected and the study data were collected using a special pilot tested questionnaire. The data were then statistically analysed using computer program SPSS 25.0 of Windows. **Results:** The study showed that Malaysia food industries are at 64.0% ready (moderately high level) to implement mandatory MHCS. The level was not influenced significantly by location (state and area of the premises) factor. The type of food premises as well as gender, age, marital status, level of education, race and religion factors showed only small or very small effect on the readiness level. Only educational level, racial and religious factors have some impacts of more than ten percent. Food company owners and food handlers who received high school education show to have highest readiness level. The same goes to Malays and Muslims respondents. On the other hand, food company owners and food handlers who only got primary school education show to have the lowest readiness level. The same goes to Indian respondents as well as Christian and Hindu respondents. **Conclusion:** The finding of this study should be considered by Malaysia government in the implementation of mandatory MHCS in the future.

KEYWORDS: Halal Certification, Food Company, Mandatory Practices, Religious Factors.

INTRODUCTION

The revelation of Islamic law veritably suitable for all mankind especially when it involves food matters. Halal food is not only meant for Muslims but also favorable for non-Muslims. Halal food indicate high quality of food, safe for consumption and suitable for all people. Unfortunately, real data show that the number of Halal certified food industries in Malaysia is still low and at certain situation create confusion. JAIP (2019) for example has reported that only 59 hotels in Pahang applied halal certificates in 2020. In fact, there were about 430 hotels in Pahang in 2020 that have food preparation services in total (Hirschmann, R., 2019). This situation shows only 3.0% of hotels in Pahang have halal certificates. JAKIM (2020) through its official website also displayed only 430 hotels in Malaysia that have halal certificates. The total number of hotels with food services in Malaysia exceeded 4800 (Hirschmann, R., 2019). This means that only 8.9% of hotels in Malaysia have halal certificates. The rest (91.1%) of hotels in Malaysia did not have halal certificates. The involvement of bumiputera Muslim food entrepreneurs in MHCS is also low. JAKIM (2019) reported that 8,805 halal certificates were issued in 2019, of which 71% were issued to non-bumiputera Muslim entrepreneurs and only 29% to bumiputera Muslim entrepreneurs. The Malaysian Insight (2019) reported that their data which receive from JAKIM shows that more than 60% of halal certificate owners in Malaysia are non-Muslim entrepreneurs. This situation confirms that the involvement of Muslim bumiputera food

entrepreneurs in MHCS is still low and disproportionate compared to non-Muslim bumiputera entrepreneurs.

There are still too many Muslim bumiputera food entrepreneurs who are less interested or do not feel the need to apply halal food certificate. A study conducted by Noor Fiteri and Masnisah (2015) on food entrepreneurs in Perlis found that many Muslim food entrepreneurs do not feel the need to apply halal certificate because without halal certificate they still can continue their business as well and have their own regular users. Jamal Abdul Nassir Shaari (2019) also reported that some Muslim entrepreneurs ignore and do not care about the importance of halal certificate. This is because without halal certificate, their company's performance is still encouraging. The customers have put their trust to food companies which founded by Muslim entrepreneurs. Muslim food entrepreneurs often think that the food they produce are definitely halal as the food are prepared by Muslims workers. However, many Muslim food entrepreneurs are not realized about the halal status of the raw materials that they used, thus the status of the food that they prepare have an element of doubtful.

Although the support from non-Muslim food entrepreneurs on MHCS appears to be higher compared to Muslim food entrepreneurs, the involvement of non-Muslim entrepreneurs is more to gain business opportunities. Marliana binti Abdullah *et al*. (2015) reported that food entrepreneurs among non-Muslims still do not understand the main objective of MHCS where many of them put the main goal of obtaining halal certificate more toward getting of marketing tool. That is why there are many integrity problems in MHCS such as the existence of fake halal certificates, inconsistent food hygiene and safety conditions after obtaining the halal certificate, the halal certificates are not renewed after the expiration, the halal certificate is suspended or revoked and so on. According to Mohd Al'Ikhsan & Siti Salwa (2015) many food entrepreneurs no longer practice proper food quality standards according to the MS1500:2009 after their food products have been certified halal by JAKIM.

The mandatory implementation of MHCS may overcome the problem of low number of halal certified food industries, can remove many doubts in determining the status of food subtleties and make Malaysia one of the countries in the world that have completely halal food. However, the scheme may burden the food industry especially entrepreneurs from the B40 group, entrepreneurs who are just about to start a business or entrepreneurs who are working on micro and small businesses. The scheme may also limit their business activities. The implementation of mandatory MHCS may also be opposed by non-Muslim food entrepreneurs.

The aim of this study was to evaluate the readiness level of food industries in Malaysia covering all types of food production and services towards the proposal of implementing mandatory MHCS.

MATERIALS AND METHODS

This study was conducted quantitatively, involving company owners and employees who were structured randomly selected at food premises throughout Malaysia. The data from the respondents were collected using specific questionnaire (should include the name of the question) and analyzed using the statistical software SPSS 25.0 (Windows). Descriptive and inferential analyses were carried out on all the data in accordance with establish parameters and were presented in the form of frequency, average value and central inclination (mean, standard deviation, median and mode). The comparison of two parameters was done using chi-squared test while comparison of three or more parameters was performed using ANOVA test. The difference in the comparison data was calculated at a confidence level of 95%, which is at a probability value of $p<0.05$.

RESULTS AND DISCUSSIONS

Respondents and Demographic Factors

A total of 514 respondents were involved in this study where they were structured randomly selected according to state, location and type of food premises. Table 1 to Table 3 shows the number and percentage of the respondents according to state, location and type of food premises respectively.

Table 1 Number and Percentage of Respondents by State

State	Number of Respondents	%
Perlis	34	6.6
Kedah	37	7.2
Penang	39	7.6
Perak	41	8.0
Selangor	48	9.3
Wilayah Persekutuan Kuala Lumpur	33	6.4
Melaka	36	7.0
Negeri Sembilan	33	6.4
Johor	33	6.4
Pahang	47	9.1
Terengganu	36	7.0
Kelantan	32	6.2
Sabah	33	6.4
Sarawak	32	6.2
Total	514	100.0

Table 2 Number and Percentage of Respondents by Location of Food Premises

Location	Number of Respondents	%
City / Municipal Area	257	50.0
Sub-Urban Area	111	21.6
Traditional Village Area	115	22.4
Settlement Land (Felda Area)	31	6.0
Total	514	100.0

Table 3 Number and Percentage of Respondents by Type of Food Premises

Country	Number of Respondents	%
Hotel	56	10.9
Restaurant	102	19.8
Food Stall	109	21.2
Street Food Hawkers	71	13.8
Food Factory	106	20.6
School Canteen/Hostel Kitchen /Factory Canteen	34	6.6
Mass Catering	36	7.0
Total	514	100.0

From Table 1 to Table 3, it was found that the number of respondents is sufficient to represent the population of food company entrepreneurs and food handlers in Malaysia for this study. The distribution of the respondents was tested as normal distribution using Kolmogorov-Smirnova and Shapiro-Wilk tests.

A total of 290 (56.4%) respondents were male and 234 (45.5%) were female. Table 4 shows the age-related information of the respondents in this study.

Table 4 Age-Related Information of The Respondents

	Age (Years)
Minimum	18
Maximum	66
Range	48
Mean±SD	32.1±11.4
Median	28
Mode	23

From Table 4, it was found that the age range of the respondents was very wide, ranging from 18-66 years old with an age range difference of 48 years. The average age of the respondents is 32.1 years old with the median and mode age being 28 and 23 years old respectively. From the age information data, it was understood that the majority respondents are mature enough to provide feedback in this study.

Table 5 shows the distribution of respondents according to race, religion and category of Muslim and non-Muslim.

Table 5 Distribution of Respondents By Races and Religions

		Number of Respondents	%
Races	Malay	338	65.8
	Chinese	118	23.0
	Indian	58	11.3
Religions	Islam	338	65.8
	Buddhist	46	8.9
	Christian	70	13.6
	Hindu	60	11.7
Category of Muslim/Non-Muslim	Muslim	529	60.5
	Non-Muslim	346	39.5

From Table 5, the number of Malay respondents was 338 (65.8%) compared to Chinese (118 or 23%) and Indians (58 or 11.3%). According to religion, the number of Islamic respondents was 338 (65.8%) compared to Buddhist (46 or 8.9%), Christian (70 or 13.6%) and Hindu (60 or 11.7%). The breakdown of respondents according to the category of Muslim and non-Muslim was 60.5% and 39.5% respectively.

Table 6 shows the distribution of respondents according to marital status and level of education.

Table 6 Distribution of Respondents by Marital Status and Level of Education

		Number of Respondents	%
Marital Status	Single	170	33.1
	Married	312	60.7
	Divorce / Single Mother or Father	32	6.2
Level of Education	Primary School	65	12.6
	Secondary School	102	19.8
	Diploma	204	39.7
	Degree	143	27.8

The distribution of respondents according to all measured parameters in this study was normally distributed as tested using Kolmogorov-Smirnova test and Shapiro-Wilk test as shows in Table 7.

Table 7 Distribution of Respondents as Tested by Kolmogorov-Smirnova test and Shapiro-Wilk tests

Normal Distribution Test	Kolmogorov-Smirnova Test			Shapiro-Wilk Test		
	Statistics	df	P Value	Statistics	df	P Value
State	0.11	514	0.00	0.95	514	.00
Location	0.31	514	0.00	0.78	514	.00
Types of Food Premises	0.16	514	0.00	0.93	514	.00
Gender	0.37	514	0.00	0.63	514	.00
Race	0.40	514	0.00	0.66	514	.00
Religion	0.40	514	0.00	0.66	514	.00
Age	0.15	514	0.00	0.87	514	.00
Marital Status	0.35	514	0.00	0.73	514	.00
Education Level	0.25	514	0.00	0.86	514	.00

Note: P value <0.05 indicates the normal distribution of the respondents.

Readiness Level of Food Industries to Implement Mandatory MHCS

Table 8 shows the number (%) of respondents according to readiness level to implement mandatory MHCS.

Table 8 Number (%) of Respondents according to Readiness Level of Implementation of Mandatory MHCS

	Number of Respondents	%
Strongly disagree	9	1.8
Disagree	132	25.7
Uncertain	44	8.6
Agree	221	43.0
Strongly Agree	108	21.0
Total	514	100.0

From Table 8, 221 (43.0%) respondents agree to implement mandatory MHCS and 108 (21.0%) respondents strongly agree to implement mandatory MHCS. Cumulatively, about 329 (64.0%) respondents feel ready to implement mandatory MHCS. On the other hand, only 132 (25.7%) of respondents disagreed with implementing mandatory MHCS and 9 (1.8%) respondents strongly

disagree to implement mandatory MHCS. Cumulatively, about 185 (36.0%) respondents feel not ready to implement mandatory MHCS. From the above findings, it can be said that the level of readiness of food industries in Malaysia towards the implementation of mandatory MHCS is moderately high (64.0%).

Table 9 shows the results of the statistical analysis of the study data according to the measured variable factors: state, location and type of food premises as well as the gender, age, marital status, level of education, race and religion of the respondents.

Table 9 Results of Statistical Analysis of Study Data According to the Measured Variables Factors

Variable Factors	P Value	Eta Square Value
State	0.17[b]	0.04*
Location	0.70[b]	0.00*
Types of Food Premises	0.00[a]	0.08*
Gender	0.00[a]	0.02*
Age	0.00[a]	0.18*
Marital Status	0.00[a]	0.04*
Education Level	0.00[a]	0.30*
Race	0.00[a]	0.46**
Religion	0.00[a]	0.48**

Note: [a] means significant difference at P<0.05, [b] means no significant difference at P≥0.05, * means the effect of the variable is very small, **means the effect of the variable is small.

From Table 9, it is found that state and location factors do not provide any significant difference in the respondent's agreement to implement mandatory MHCS where their P value are more than 0.05. On the other hand, type of food premises as well as gender, age, marital status, level of education, race and religion provide significant difference in the respondent's agreement to implement mandatory MHCS where their P value are less than 0.05. However, most of the factors either give very small or small impact on the level of the agreement. The eta squared values indicate these effects. Only age, education level, race and religion factors have an impact of more than ten percent.

Table 10 shows the relationship between age factor with and the level of respondents' agreement to implement mandatory MHCS.

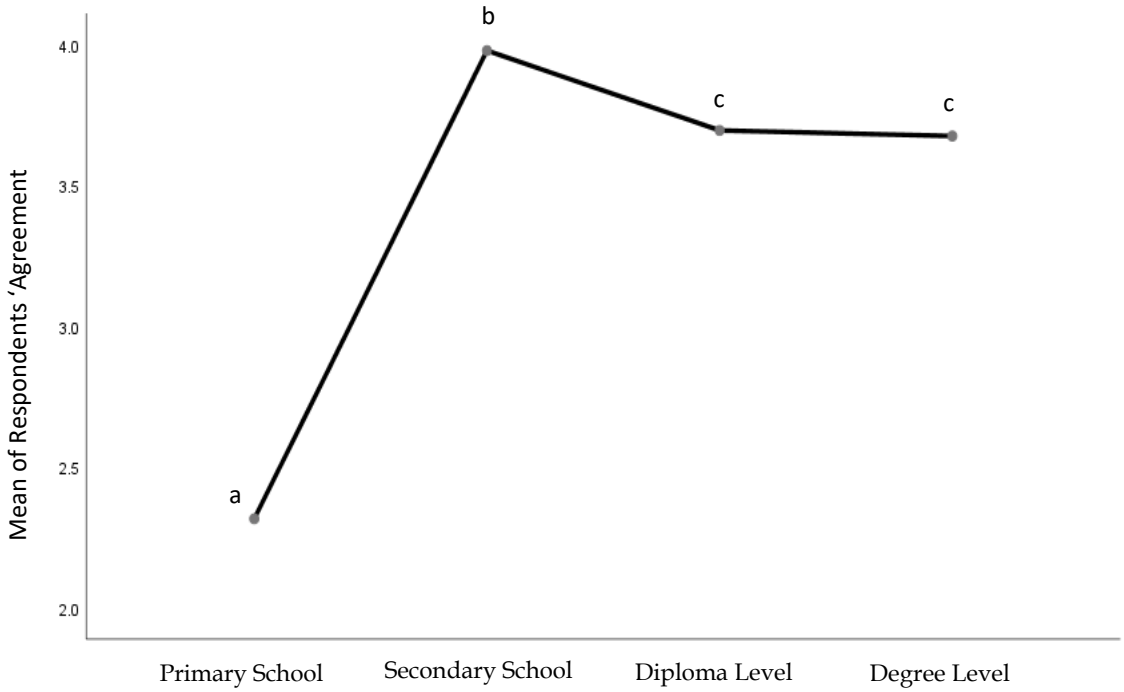
Table 10 The Relationship Between Age and Respondents' Agreement to Implement Mandatory MHCS

Relationship	P Value.	Correlation Coefficient
Age and Level of Agreement	0.78	0.01

Note: The value of P>0.05 indicates that there is no significant relationship.

From Table 10, it was found that there is no significant relationship (P>0.05) between age factor and the level of respondents' agreement to implement mandatory MHCS even though the age factor has a significant different in the respondents' agreement as shown in Table 9.

Figure 1 shows the distribution of the mean values of respondent's agreement level to implement mandatory MHCS according to the level of education.

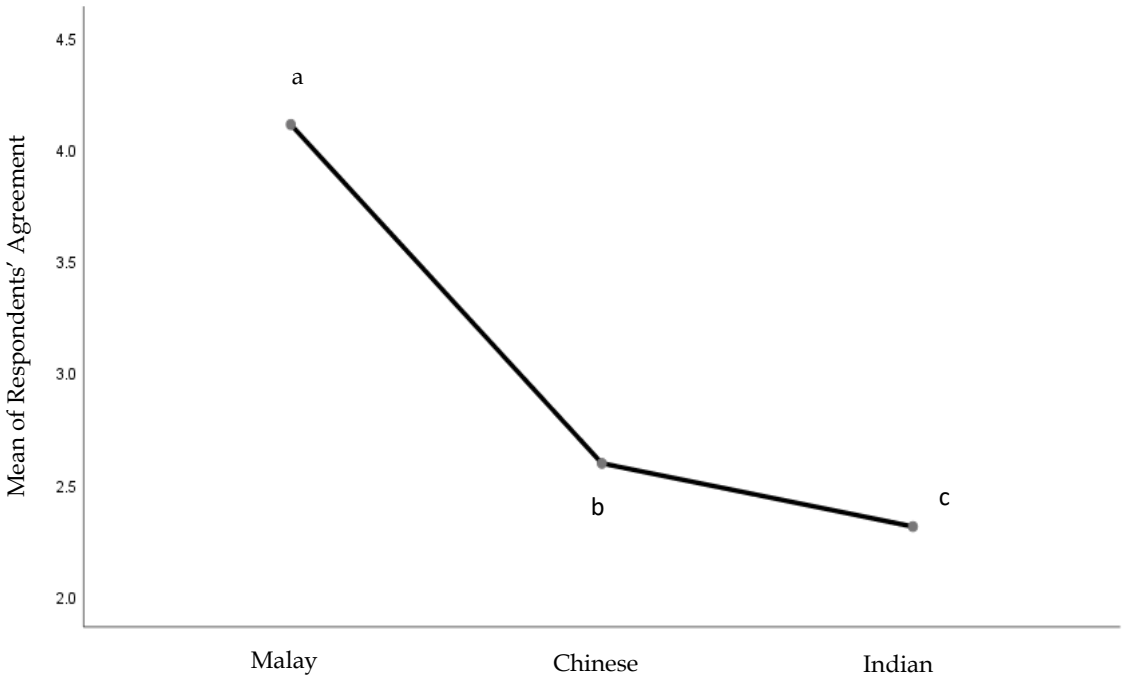


Note: The same letter indicates no significant difference value (<0.05) while different letters indicate a significant difference value (P>0.05)

Figure 1 Distribution of Mean Value of Respondents' Agreement to Implement Mandatory MHCS According to Education Level Factors

From Figure 1, respondents who only got primary school education have the lowest level of agreement with a mean value of 2.32 and the mean value varied significantly with all other respondents. Respondents who got secondary school education, diploma and degree have higher agreement than those who just got primary school education. Even though there are significant differences in the level of agreement between respondents who got secondary school education compared to those who got diploma and degree, the mean values between them are not too different.

Figure 2 shows the distribution of the mean values of the respondent's agreement to implement mandatory MHCS according to races factor.

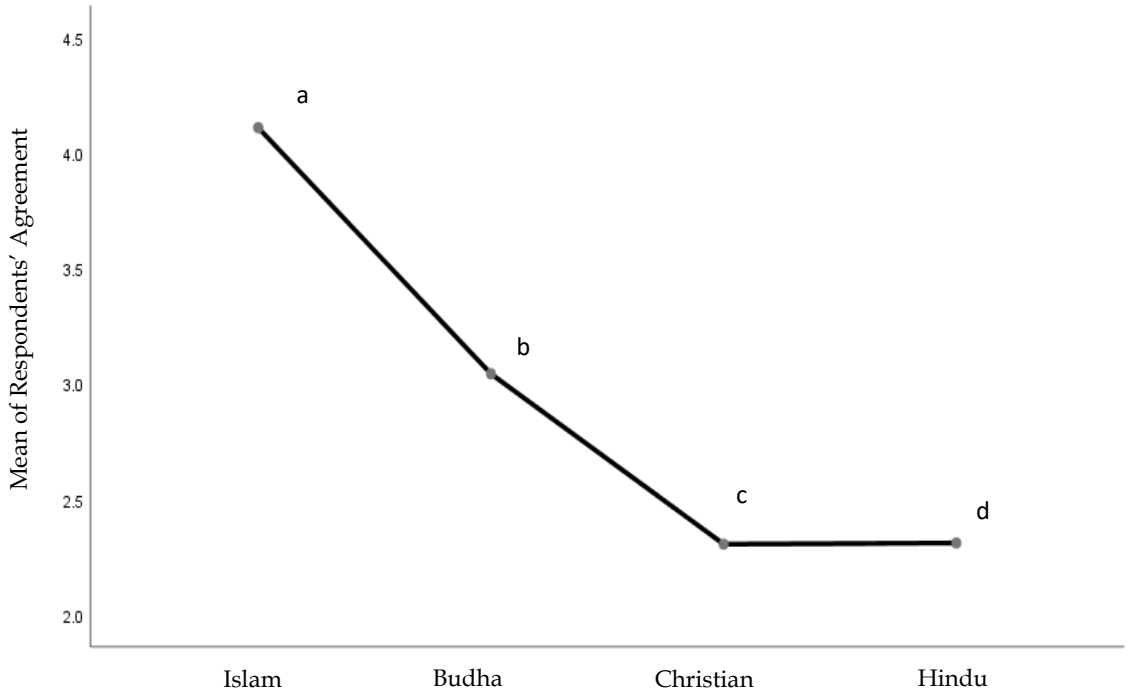


Note: The same letter indicates no significant difference value (<0.05) while different letters indicate a significant difference value (P>0.05)

Figure 2 Distribution of Mean Values of Respondents' Agreement to Implement Mandatory MHCS According to Races Factors

From Figure 2, Malay respondents show the highest level of agreement to implement mandatory MHCS with a mean value of 4.11, which is significantly different. The value is significantly different compared to the mean values of Chinese and Indian respondents. Chinese respondents have the second high level of agreement (mean value of 2.59) and Indian respondents show to have the lowest level of agreement with the mean value of 2.31.

Figure 3 shows the distribution of the mean values of the respondent's agreement to implement mandatory MHCS according to religious factors.



Note: The same letter indicates no significant difference value (<0.05) while different letters indicate a significant difference value (P>0.05)

Figure 3 Distribution of Mean Values of Respondents' Agreement to Implement Mandatory MHCS According to Religious Factors

From Figure 3 it was found that Muslim respondents show to have the highest level of agreement with the mean value of 4.11 and the value varied significantly with the mean values of other religious respondents. Buddhist respondents show to have lower level of agreement (mean value of 3.04) compare to Muslim respondents and the level is significantly different compare to the level of other religious respondents. Hindu and Christian respondents show similar level of agreement (both mean values of 2.31 respectively) and the two mean values did not significantly differ.

CONCLUSION

The study showed that Malaysian food industries are at 64.0% ready (moderately high level) to implement mandatory MHCS after nearly 50 years of implementing voluntary MHCS. The level of readiness is not influenced significantly by the location (state and area of the premises) factor. The type of food premises as well as gender, age, marital status, level of education, race and religion factors show to have only small or very small effects on the readiness level. Only educational level, racial and religious factors have some impacts of more than ten percent. Food company owners and handlers who received high school education show the highest readiness level. The same goes for Malays and Muslim respondents. On the other hand, food company owners and food handlers who only got primary school education show to have the lowest readiness level. The same goes to Indian respondents as well as Christian and Hindu respondents.

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CONSUMERS' KNOWLEDGE AND READINESS TO ACCEPT THE IMPLEMENTATION OF MANDATORY MALAYSIA HALAL CERTIFICATION SCHEME (MHCS)

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ABSTRACT

Abstract: Food Industries in Malaysia have implemented the Malaysian Halal Certification Scheme (MHCS) on voluntary basis for more than 49 years. This long experience should be exploited to boost the implementation of mandatory MHCS involving all categories of food premises. **Aim:** This study aimed to analyze the level of knowledge and readiness of consumers in Malaysia to accept the implementation of mandatory MHCS by food industries. **Methods:** The study was quantitatively conducted involving consumers who were structured and randomly selected from five different zones in Malaysia. All the study data were collected using a specific pre-tested questionnaire and analyzed using the statistical computer program SPSS 25.0 (Windows). **Results:** The results of the study show that the level of knowledge and readiness of consumers in Malaysia toward the implementation of mandatory MHCS is at a satisfactory level or at a medium-high level. The knowledge and readiness status of Malay Muslim consumers is higher than non-Malay and non-Muslim consumers. **Conclusion:** The consumers' knowledge level could be used to indicate country readiness in implementing mandatory MHCS.

KEYWORDS: Level of Knowledge, Readiness Status, Consumers, Halal Certificate

INTRODUCTION

The Malaysian Halal Certification Scheme (MHCS) for food industries officially began in 1974. To date, the implementation was up to 49 years and was conducted on voluntary basis as stated in the Trade Description Act 2011 (Trade Description Act, 2011) under the Trade Description (Certification and Halal Marking) and (Halal Description) Order 2011. In the act, all commercial food manufacturers or providers are not required to obtain halal certificate of their food products or their food services from JAKIM or MAIN/JAIN, but they are strongly encouraged to apply and obtain the certificate.

Malaysia's experience in voluntarily implementing the MHCS is seen as a strength to elevate the implementation by proposing mandatory implementation of MHCS involving all types of food industries; food production/manufacturing, food preparation/services, food import/export at any stages; micro, small, medium or big scale. It should also involve all categories of food entrepreneurs of various races and religions throughout the country.

Some questions may arise from this motion: (1) have the consumers or the general public in Malaysia really understood halal food? (2) Can the consumers or the general public in Malaysia as a whole accept the mandatory implementation of the MHCS by food industries? and (3) Are the non-Muslim communities in Malaysia ready to accept the mandatory implementation of MHCS? There were several studies done before by other researchers to evaluate the level of understanding of consumers about halal food as written by Othman et al. (2020), Nor Aini Haji Idris & Mohd Ali Mohd Noor (2013), Siti Fatimah Hamidon (2016) and Zaimah, R.1 (2014). But all of the research before focused on a specific group of respondents and using a small number of respondents.

This study aimed to evaluate the level of understanding and readiness of consumers in Malaysia involving all races and religions in accepting the implementation of mandatory MHCS by all food industries in Malaysia.

MATERIALS AND METHODS

The study was conducted quantitatively involving consumers who were randomly selected from five different zones in Malaysia covering all major races and religions. The data were collected using specific pre-tested questionnaires and all the data were analyzed using the statistical computer software program SPSS 25.0 (Windows). Descriptive and inferential analyses were carried out on all the data in accordance with established parameters and were presented in the form of frequency, average value and central tendency values (mean, standard deviation, median and mode). The comparison of two parameters was done using the chi-squared test while the comparison of three or more parameters was performed using the ANOVA test. The difference in data values are calculated at a confidence level of 95% or at a probability value of $p<0.05$.

RESULTS AND DISCUSSIONS

Respondents and Demographic Factors

In this study, about 875 respondents participated in answering the questionnaire. Table 1 shows the distribution of respondents according to states and zones in Malaysia where the number of respondents is sufficient to represent the consumer population in Malaysia and the distribution is normally distributed according to the states and zones.

Table 1 Distribution of Respondents by State and Zones in Malaysia

Country	Number of Respondents	%	Malaysia Zone	Number of Respondents	%
Perlis	32	3.7	North	165	18.9
Kedah	43	4.9			
Penang	41	4.7			
Perak	49	5.6			
Selangor	149	17.0	Middle	203	23.2
Kuala Lumpur	54	6.2			
Melaka	34	3.9	South	141	16.1
Negeri Sembilan	36	4.1			
Johor	71	8.1			
Pahang	158	18.1	East	262	29.9
Terengganu	56	6.4			
Kelantan	48	5.5			
Sabah	59	6.7	Sabah & Sarawak	104	11.9
Sarawak	45	5.1			
Total	875	100.0	Total	875	100.0

In this study, about 59% of the respondents were female and 41% were male. The age distribution of the respondents was found to be very wide between 17-81 years which illustrates very large age coverage. The average age of the respondents is 35.8 years while the median and mode age of the respondents are 33 and 22 years respectively. Table 2 shows the distribution of respondents according to race, religion and Muslim and non-Muslim categories.

Table 2 Distribution of Respondents by Race and Religion

		Number of Respondents	%
Race	Malay	525	60.0
	Chinese	246	28.1
	Indian	88	10.1
	Sabah Ethnic	9	1.0
	Sarawak Ethnic	7	0.8
Religion	Islam	529	60.5
	Buddhist	74	8.5
	Christian	177	20.2
	Hindu	86	9.8
	No Religion	9	1.0
Category of Muslim/Non-Muslim	Muslim	529	60.5
	Non-Muslim	346	39.5

The distribution of respondents in this study according to demographic factors; gender, race and religion were normally distributed as tested using the Kolmogorov-Smirnova test and the Shapiro-Wilk test.

Respondents Comprehension Scores

The results show that the mean comprehension score obtained by the respondents in this study was about 75.4%, which is a moderately high level. The lowest score is 38%, while the highest score is 100%. A moderately high score level was also showed by the median value (80%) and mode value (88%). The results of the study also show that only the respondents' comprehension scores according to gender are not significantly different (at $p>0.05$) while the respondents' comprehension scores according to other factors were all significantly different (at $p<0.05$). The study also showed that zone, gender, marital status and membership in the consumer association factors have a small impact on the differences of the comprehension scores. State, education levels and employment or study factors havee a modest impact on the difference respondents' comprehension scores while race, religion and Muslim/non-Muslim factors significantly impact the difference respondents' comprehension scores. The study also found that there is a significant and positive straight relationship (positive linear correlation) between the age and level of understanding. It means that the higher the age of the respondents the higher level of understanding in matters related to the halal or non-halal food. The correlation coefficient between age and understanding is not too big, which is only at 27%. Figure 1 below shows the distribution of comprehension scores among respondents according to race factor.

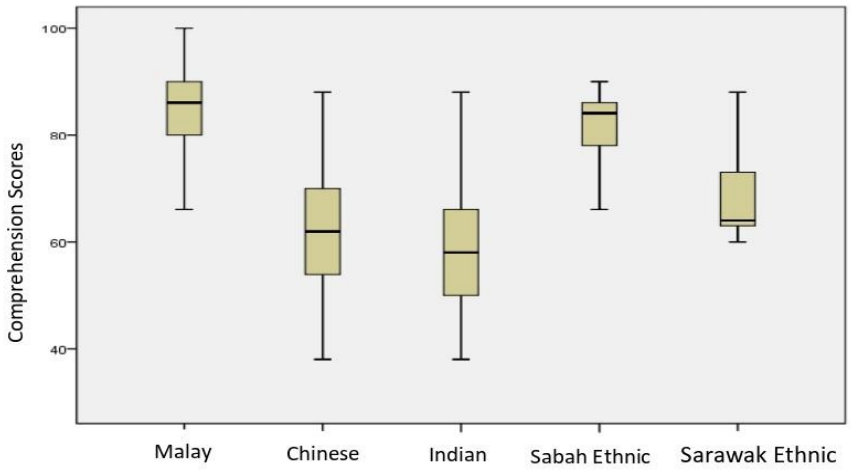


Figure 1 Distribution of Respondents' Comprehension Scores by Race

From Figure 1, it was found that the Malays had a smaller range of score differences among them (between 66-100% marks or a difference in score distance of 44%) compared to the Chinese (difference of 50%) and Indians (also a difference of 50%). Sabah and Sarawak Ethnic should be ignored in this study. Although both respondents have a small score difference of 38% and 28% respectively, they were influenced by too small numbers of respondents of nine and seven respectively. These results mean that the difference in understanding among the Malays is smaller compared to other races. Figure 1 also shows that the median score for Malay respondents is higher at 86% compared to the median score for Chinese (62%) and Indians (58%). This situation showed that most (more than 50%) of the Malay respondents scored higher than the Chinese and Indian respondents. This also means that the level of understanding of the majority of the Malay respondents is higher compared to the level of understanding of other races.

Comprehension scores among respondents according to religious factors were found to be similar to racial factors, where Muslim respondents had a smaller range of difference in scores among them (between 66-100% or 34% difference in score distance) compared to Christian respondents (difference of 42%), Buddhist (difference of 50%) and Hindu (the difference is also 50%). The range of differences in scores of non-religious respondents was small (difference of 50%) but a small number of respondents influenced it. This results also mean that the difference in understanding among Muslim respondents is also smaller compared to other religious respondents. The median score for Muslim respondents was also found to be higher (86% score) compared to the median score for Christian respondents (62%), Buddhist (62% score) and Hindu (58% score). This situation showed that most (over 50%) of Muslim respondents scored higher than other religious respondents. This also means that the level of understanding of most Muslim respondents is higher than that of other religious respondents.

Respondent Answer Analysis

Table 3 shows a list of inaccurate respondents' answers by highest percentage.

Table 3 List of Inaccurate Answers by Highest Percentage

Question No.	Question	Inaccurate Answer (%)	Level of Understanding
1.iii	The order to eat halal food is for Muslims only.	71.5	Basic understanding
10.iv	Enzymes extracted from the blood of animals that are halal and slaughtered according to Syariah laws are halal for use in food manufacturing.	56.5	Technical understanding / high level
1.i	Halal food is a food that does not contain pork only (Pork Free).	48.7	Basic understanding
5.ii	Alcohol obtained not from liquor is halal to be used.	42.4	Technical understanding / high level
10.ii	Proteins extracted from chicken feathers and the chicken is slaughtered according to Islamic law are prohibited from being used.	40.3	Technical understanding / high level
9.iv	The use of unclean equipment does not affect the status of halal food.	40.1	Basic understanding
1.v	Syubhah food is a food that can be ascertained of its halal or haram status	39.7	Basic understanding
9.v	Canned soft drinks can be stored in the same refrigerator that stores alcohol.	39.3	Technical understanding / high level
7.iii	Foods that contain probiotics from not clearly halal sources are halal to be eaten.	37.9	Technical understanding / high level
8.iv	Alcohol is categorized as Najs Mughallazah.	36.8	Technical understanding / high level

From Table 3, it shows that the inaccuracy answers by the respondents, not only involving technical understanding or question of high understanding level but also involving the basic understanding questions. Table 4 shows the percentage of respondents according to Muslim and Non-Muslim categories who answered the question inaccurately.

Table 4 Percentage of Respondents by Muslim and Non-Muslims Categories Who Answer the Questions Inaccurately

Question No.	Muslim	Non-Muslim			Inaccurate Answer (%)
	Islam (%)	Christian (%)	Buddhist (%)	Hindu (%)	
1.iii	68.6*	83.8*	76.3*	73.3*	71.5
10.iv	49.5*	64.9*	65.0*	73.3*	56.5
1.i	26.7	82.4*	76.8*	96.5*	48.7
5.ii	37.6	68.9*	40.7*	47.7*	42.4
10.ii	25.3	67.6*	61.0*	67.4*	40.3
9.iv	35.9	51.4*	46.9*	44.2*	40.1
1.v	21.7	71.6*	65.0*	69.8*	39.7
9.v	42.9*	36.5	33.9	32.6	39.3
7.iii	15.7	73.0*	71.2*	77.9*	37.9
8.iv	29.9	52.7*	45.8*	46.5*	36.8

Note: * indicates inaccurate answers above 40%.

From Table 4, most Muslim respondents do not understand exactly (answer inaccurately more than 40%) the basic question as in question number 1.iii (the order to eat halal food is for Muslims only), while for high-level technical understanding questions, most Muslim respondents do not understand exactly the question number 10.iv (enzyme extracted from the blood of animals that are halal and slaughtered according to Islamic law is halal to be used in manufacturing food), 9.v (canned soft drinks can be stored in the same refrigerator that stores alcohol) and 5.ii (Alcohol obtained not from liquor is halal to be used). Non-Muslim respondents including Christians, Buddhists and Hindus did not understand exactly almost the entire questions in the above questions except for question 9.v. The non-Muslim community may already be familiar with the question of the segregation of liquor with halal drinks.

Table 5 shows the percentage of respondents by race who answered questions inaccurately.

Table 5 Percentage of Respondents by Race Who Answer Questions Inaccurately

Question No.	Malay (%)	China (%)	India (%)	Inaccurate Answer (%)
1.iii	68.8*	76.4*	72.7*	71.5
10.iv	49.5*	65.0*	73.9*	56.5
1.i	26.7	76.8*	95.5*	48.7
5.ii	37.9	48.4*	47.7*	42.4
10.ii	25.5	61.0*	65.9*	40.3
9.iv	36.0	47.6*	44.3*	40.1
1.v	21.7	65.9*	69.3*	39.7
9.v	42.7*	35.4	33.0	39.3
7.iii	15.8	69.5*	76.1*	37.9
8.iv	29.9	48.4*	45.5*	36.8

Note: * indicates inaccurate answers above 40%.

From Table 5, it was found that Malay, Chinese and Indian respondents followed the same trend as Muslim and Non-Muslim respondents (Table 2) where most Malay respondents did not understand exactly the basic question in question 1.iii (the order to eat halal food is for Muslims only), while for high-level technical understanding questions, most Malay respondents do not understand exactly the question 10.iv (enzyme extracted from the blood of a halal animal and slaughtered according to Islamic law is halal for use in the manufacture of food), 9.v (canned soft drinks can be stored in the

same refrigerator that stores alcohol) and 5.ii (Alcohol obtained not from liquor is halal to be used). Most Chinese and Indian respondents did not understand exactly almost the entire question in the above questions except for question 9.v.

CONCLUSION

This study involves many respondents and is more than sufficient to represent the consumer group in Malaysia. The consumers' level of understanding about halal food is satisfactory at a moderately high level. The understanding level shows the consumers' readiness to accept the implementation of mandatory MHCS. There is no significant difference in the level of understanding and readiness among consumers according to most of the demographic factors except the race and religion factors which are most likely to influence the difference in the level of understanding and readiness. The level of understanding and readiness of the Malay consumers is higher compared to the level of understanding and readiness of the consumers of other races.

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DETERMINING A CONVENIENT MOBILE PEDOMETER APP AND ITS PERFORMANCE IN ASSESSING PHYSICAL ACTIVITY STATUS AMONG UNIVERSITY STUDENTS

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ABSTRACT

Introduction: Many young people nowadays have sedentary lifestyle which might contribute to obesity prevalence. With the technology advancement, pedometer mobile applications (apps) are now available to promote physical activity and track steps. Nevertheless, not many studies have systematically evaluated the convenience and reliability of these apps in objectively measuring physical activity. Thus, this study aimed to identify the most convenient pedometer app to be used in tracking the number of steps and validate it against a subjective assessment (self-reported) method using the International Physical Activity Questionnaire-Short Form (IPAQ-SF) in identifying physical activity status among university students. **Methods:** Undergraduate students at the International Islamic University Malaysia aged 18 to 27 years were recruited using convenient sampling. A preliminary study was conducted among 10 study participants to select between Accupedo® and Map My Walk® pedometer apps for tracking steps count. They were required to use both pedometer apps and rate their experience. Subsequently, the selected pedometer app (Accupedo® Pedometer) and the IPAQ were used to assess physical activity status of study participants (N=86) over three days (two weekdays and one weekend day). Data obtained by the pedometer app were categorized as low active, moderate active and active while IPAQ-SF data were categorized into low, moderate, and high status. The relative agreement between these data were analysed using Kappa statistics, cross-classification, and Pearson correlation. **Results:** It was found that 74% (based on IPAQ) and 91% (based on pedometer app) of the study participants were categorized as low active. The Kappa value was k=0.126 (p=0.016) indicating a slight but significant agreement between these two methods. Cross-classification demonstrated that 40% (n=34) of the study participants were correctly classified into the same tertiles whereas 16% (n=14) were grossly misclassified. In addition, the average steps count/day (by pedometer app) was significantly correlated (r=0.235, p=0.03) with total MET-minutes/week as recorded by the IPAQ-SF. **Conclusion:** The pedometer app was comparable to the IPAQ-SF in assessing physical activity status. This shows that a cost-free and convenient mobile app is applicable to be used for daily physical activity assessment among young people.

KEYWORDS: Pedometer app, IPAQ-SF, Physical activity, Mobile app

INTRODUCTION

The prevalence of overweight and obesity is rising around the world, and it has become a global issue. The modernisation of transportation is believed to reduce the physical activity level and lead to a sedentary lifestyle (Mohamad Nor et al., 2016). A study by Lee et al., (2014) found that daily physical activity and screen time were associated with measures of obesity during childhood. On the other hand, with the advancement in technology, people had the ability to monitor their own physical activity using a motion sensor device known as pedometer (Tudor-Locke et al., 2004). Pedometer is a self-reported method in measuring physical activity and at the same time as tools to motivate people to be active by monitoring the steps daily (Tudor-Locke, 2001). It is easy-to-use and offers cost-effective objective measure of physical activity (Strycker, Duncan, Chaumeton, Duncan, & Toobert, 2007). These devices are popular because they are simple, low cost, and able to catch up short durations of physical activity that commonly lacked in self-report measures. Pedometers provide cheap, objective, precise and reliable measurement of ambulatory activity by tracking number of steps taken per day. Other than pedometer, the use of accelerometer had been acknowledged in several research studies. Accelerometers are well-known devices considering the accuracy, ability to get a lot of data, and considerable ease of use especially in large studies (Westerterp, 2009). Nevertheless, they are costly and demand for technical expertise, individual programming, and particular hardware and software (Dishman, 1994). In addition, certain accelerometers are not able to distinguish walking intensity or body positions such as lying, sitting, and standing (Dollman et al., 2013).

Several studies have examined the relationship between pedometer use and body composition. One study found a positive association between pedometer-assessed ambulatory activity and body composition variables such as body mass index (BMI) and fat percentage (Tudor-Locke et al., 2001). In addition, correlation with biological predictors and outcome such as age and BMI can be made with pedometer data (Cleland, 2011). A study by Bassett et al., (1996) and Welk et al., (2000) had shown that pedometers give a precise and valid measure of walking activities in free-living circumstance. Furthermore, by using pedometers, it is associated with significant increase in physical activity and BMI values and blood pressure (Bravata et al., 2007). Somehow, pedometers can contribute to under- or over- calculating of steps. A pedometer which is less accurate would result in negative responses to the device, so it is not encouraged to be used (Melanson et al., 2004).

Previously, a pedometer is known as a device to count the steps. Nowadays, the increased number of pedometer applications (apps) and the rapid evolution of technology allow the smartphone to be used as steps counter (Presset et al., 2018). Additionally, the pedometer app can easily be downloaded from the online store. This allows the mobile phone to be used as a pedometer and measurement of physical activity to be done by a device already being used by many people (Akerberg, Lindén, & Folke, 2012). In Malaysia, the total number of smartphone users was estimated to reach 19.9 million (Statista, 2017).

There are several pedometer applications available in the Google Play Store (Google) and Apple App Store (Apple Inc). Despite this, not many have been systematically evaluated in terms of convenience and reliability as a tool that provides objective measurements of physical activity. Therefore, this study aimed to identify the most convenient pedometer application to be used in tracking the number of steps per day and validate it against the self-administered International Physical Activity Questionnaire-Short Form (IPAQ-SF). The research was conducted among university students as no similar study has been conducted among this population before. Furthermore, data on physical activity assessment using objective methods (such as pedometer and accelerometer) are still limited in Malaysia (Hazizi et al., 2012).

MATERIALS AND METHODS

Study Design and Population

A cross-sectional study was conducted among undergraduate students at International Islamic University Malaysia (IIUM) from December 2017 to February 2018. The sample size calculation was performed using the single proportion formula, considering a prevalence of 33.5% among inactive adults in Malaysia as reported in the National Health and Morbidity Survey (NHMS) 2015 study which yielded 86 respondents. Study participants were recruited using convenience sampling. The inclusion criteria included undergraduate students who were residing on the IIUM campus and available during the study period. On the other hand, students with physical disability or medical conditions that prevented them from engaging in physical activity were not eligible to participate in the study.

Phase I: Selection of the Most Convenient Pedometer Applications

An internet search for pedometer applications was conducted to select the apps to be used. Two apps (Map My Walk® and Accupedo® pedometers) were shortlisted since they fulfil these requirements: i) Compatibility in both Android® and Iphone® operating systems; ii) Free of charge; iii) Ability to reports number of steps, total distance, time, and calorie burnt.

Accupedo® is a precise pedometer app that monitors daily walking on the home screen of the phone (http://www.accupedo.com/). Intelligent 3D motion recognition algorithms are embedded to track only walking patterns. Non-walking activities will be filtered and ejected out. Accupedo® counts steps regardless of where the phone is located like pocket, waist belt, or bag. On the other hand, Map My Walk® functions by phone global positioning system (GPS) to track daily walking routines (http://www.wellocracy.com). The app tracks and displays distance, pace, speed, elevation, calories burned, and routes travelled on interactive map. These two apps were used in the preliminary study.

A preliminary study was conducted to determine the more convenient pedometer app between the two finalized apps. Ten participants who volunteered were included in the study. They were given an opportunity to install and use the pedometer applications (Map My Walk® and Accupedo®). To evaluate each of the apps, the study participants were instructed to answer a questionnaire that was adopted from the System Usability Scale (SUS) (https://www.usability.gov), a reliable tool originally created by John Brooke in 1986 for evaluating hardware, software, mobile devices, websites, and applications. The survey consisted of five statements with four different scales (1=Strongly disagree; 2=Disagree; 3= Agree; 4= Strongly agree) with a minimum score of five and a maximum of 20. The study participants were asked to rate their experience of using each of the pedometer apps.

Phase 2: Assessment of PA status using the selected pedometer app & IPAQ-SF

The participants (different than those in the preliminary study) were instructed to install the selected pedometer app in their mobile phone. They were requested to set and turn their pedometer app on for two weekdays and one weekend day. To ensure the accuracy in handling the pedometer app, the participants were given explanation on how to use it and then were asked to demonstrate their understanding. The phone was brought along with them from the time they started their activity in the morning until they retired for the day. Participants were asked to put aside their phones when bathing or swimming. The participants were reminded to do their physical activity as usual without any change. They were required to screenshot and sent the record of steps per day, distance, duration, and number of calories burnt from the pedometer app to the researcher each night before going to bed. In addition, the study participants were requested to complete online IPAQ-SF for each day by clicking a link sent via WhatsApp. It consists of four questions regarding time spent for vigorous activity, moderate activity, time spent for walking and time spent for sitting. The questionnaire was adapted from the original IPAQ-SF (7 days) that was obtained from the website (http://www.ipaq.ki.se). These procedures were done over the course of three days (two weekdays and one weekend day).

Data Analyses

The physical activity status using pedometer application was categorized according to Basset (2004) into sedentary, low active, somewhat active, and active categories. In this study, the level of physical activity was modified from four to three categories (low active; ≤7,499 steps/day, moderately active; 7,500-9999 steps/day and active; ≥10,000 steps/day) to suit the three physical activity levels according to the IPAQ-SF.

On the other hand, raw data from IPAQ-SF questionnaire were analysed based on "Guideline for Data Processing and Analysis and Recommendations for Data Cleaning and Processing" available in www.ipaq.ki.se. The IPAQ-SF uses the MET unit which stands for the metabolic equivalent of task. One MET is the amount of energy used while sitting quietly. Physical activities may be rated using METs to indicate their intensity. For example, reading may use about 1.3 METs while running may use 8-9 METs. Based on IPAQ Group (2002), the participants were categorized as having high physical activity if they accumulated at least one hour per day or more of moderate-intensity activity over and above the basal PA, or half an hour of vigorous-intensity activity over and above basal levels daily. Classification of moderate category is when the level of activity equivalent to "half an hour of at least moderate-intensity physical activity on most days". Low category was for those who do not meet the criteria for either in moderate or high category.

Statistical Analyses

The SPSS software, Version 21.0. was utilized to analyse the data. The alpha level is set at 0.05 and 95% of CI. Descriptive statistics were used to describe variables such as sex, gender, Kulliyyah, smartphone brand, physical activity status, as well as the preference of the participants between two shortlisted pedometer applications. It was presented and computed as mean ± SD. Histogram and Kolmogorov-Smirnov test were used to check for normality distribution. As the data for the number of steps from pedometer app and the total MET-minutes for three days were not normally distributed, the data were normalized by using log10. Relative agreement such as interrater reliability analysis using the Kappa statistics was utilized to determine the agreement between pedometer app and IPAQ-SF. Cross-classification was also done by classifying participants into tertiles (high, moderate, and low physical activity categories) based on the physical activity levels as assessed by pedometer app and IPAQ-SF. Lastly, Pearson's correlation was used to determine the potential association between the two variables, the average number of steps from pedometer app and total MET-minutes/week according to IPAQ-SF.

Ethical Approval & Participants' Consent

Ethical approval for this study was obtained from the IIUM Research Ethics Committee. Written informed consent was obtained from each study participant prior to data collection. All the data collected were strictly treated as confidential.

RESULTS AND DISCUSSIONS

Phase 1: Selection of Pedometer Application

In Phase 1 of the study, a total of 15 participants were initially recruited to evaluate their experience with the shortlisted pedometer applications. However, only 10 participants (three males and seven females) were able to complete the evaluation. Among the participants, eight used smartphones with the Android operating system, while two used smartphones with the iPhone® operating system.

Result shows that 90% (n=9) of the participants rated the Accupedo® pedometer as easier to use compared to only 40% (n=4) for the Map My Walk® pedometer. Regarding the cost criteria, all participants agreed that both pedometer applications were free of charge. Interestingly, 90% (n=9) of the participants preferred using the Accupedo® pedometer as it did not require the GPS, while only 30% enjoyed using the Map My Walk® pedometer that relied on GPS. This finding aligns with a study by Middelweerd et al. (2015), where GPS usage was associated with battery power depletion and participants often forgot to start the GPS tracking. However, 30% of the participants in our study still agreed that using GPS features was acceptable. Like the current study, some participants found GPS tracking to be more convenient due to real-time data display and automatic assessment of distance and speed. Overall, more than three-quarters (80%) of the participants preferred using the Accupedo® pedometer, considering it to be more convenient compared to the Map My Walk® pedometer application (40%).

Table 1 Comparison of scores between the Accupedo® and Map My Walk® pedometer applications (N=10)

	Score Comparison (Mean ± SD)	
Criteria	**Accupedo®**	**Map My Walk®**
Ease of use	3.6 ± 0.7	2.4 ± 0.8
Free of charge	3.6 ± 0.5	3.3 ± 0.5
GPS	3.4 ± 0.7	1.9 ± 1.1
Preference	3.3 ± 0.8	1.5 ± 0.7
Total score	**13.9 ± 2.0**	**9.1 ± 2.0**

Table 1 shows the comparison of total score rated by the participants for both pedometer apps. The Accupedo® pedometer consistently received higher scores across all criteria compared to Map My Walk® pedometer. This finding is consistent with a study conducted among 30 Dutch university students, where participants favoured an app design that was uncomplicated and well-organized (Middelweerd et al., 2015). The participants expressed a preference for a structured layout with only a few essential features that allowed for easy activity log and provided a clear overview of the results.

Similar results were reported by Rabin & Bock (2011) in their study involving fourteen adults aged 23-60 years who used three physical activity apps. These participants emphasized the importance of an app being user-friendly, applicable to various types of activities, capable of automatically tracking activity, and enabling goal setting.

In a different study conducted among 250 Chinese individuals with chronic disease, it was found that 47.2% of them reported difficulty in using physical activity apps as one main barrier in technology application. Moreover, the participants also expressed concerns about being charged extra fees for using the apps (Sun et al., 2017). Another study conducted in the Western country found that high data usage and hidden costs led to nearly half of the app users giving up on using them (Krebs & Duncan, 2015).

Therefore, based on the survey score, the Accupedo® was the most preferred pedometer app due to ease of use features, free of charge, not requiring GPS, and convenience. Thus, the Accupedo® pedometer app was then used in the next phase of this study.

Phase 2: Performance of the selected pedometer application

In Phase 2 of the study, a total of 86 students from various faculties participated, with the majority being female (85%). Analysis of the pedometer app readings revealed that most study participants (90.6%, n=78) were categorized as low active, as they achieved ≤7,499 steps per day (Table 2). Only 2.3% (n=2) of them were categorized as active, with step counts exceeding 10,000 per day. Additionally, based on the IPAQ-SF score, three-quarters of the study participants (74.4%, n=64) were classified as having low physical activity status, followed by moderate (18.6%, n=16) and high (9.3%, n=8) physical activity status.

Table 2 Physical activity status according to pedometer app (Accupedo®) and IPAQ-SF (N=86)

Physical Activity Status	Pedometer app (%)	IPAQ-SF (%)
Low Active /Low	90.6	74.4
Moderately Active/ Moderate	7.1	18.6
Active/ High	2.3	9.3

The IPAQ-SF was able to capture a higher percentage of active and moderately active study participants compared to the pedometer app. It could be explained that self-reported IPAQ-SF tended to overestimate physical activity level compared to the objective pedometer data. This finding was consistent with previous studies that have reported discrepancies between subjective and objective measures of physical activity (Ahmad et al., 2018; Sitthipornvorakul et al., 2014). Over-reporting in self-reported questionnaires like the IPAQ-SF is a recognized issue, and it may explain why some participants reported being active based on the IPAQ-SF but not the pedometer (Ahmad et al., 2018).

Next, the higher percentage of participants categorized as having low physical activity status according to the pedometer (91%) compared to the IPAQ-SF (74%) suggests that confounding factors, such as forgetting to wear the pedometer, battery depletion, or the pedometer being less sensitive to movements, may have contributed to under-counting (Ahmad et al., 2018). These findings are consistent with previous studies that have highlighted challenges related to pedometer usage, including wearing the pedometer, resetting it, and battery usage (Casey et al. 2014). Overall, self-reported measures such as the IPAQ-SF and objective data like pedometers can complement each other and provide a more comprehensive understanding of physical activity levels.

In the study, the relative agreement between objective data from pedometer applications and subjective data from the IPAQ was analysed using the Kappa statistics, cross-classification, and statistical correlation. The Kappa statistics was calculated to determine the consistency among the data collected from the pedometer application and IPAQ-SF, resulting in a Kappa value of k=0.126 (p=0.016), indicating a slight but significant agreement between the two methods. The cross-classification analysis was conducted to assess the ability of the IPAQ-SF and pedometer application to correctly classify individuals into high, moderate, and low physical activity categories. The results showed that approximately 40% (n=34) of the participants were correctly classified, while 16.3% (n=14) were grossly misclassified. Notably, there is a lack of previous comparison studies utilizing cross-classification between the IPAQ-SF and pedometer app. These findings suggest that although only a small number of study participants was relatively grossly misclassified, discrepancies between self-reported physical

activity levels and pedometer app readings did occur, potentially due to over-reporting in self-reported questionnaires like the IPAQ. Factors such as participants forgetting to set the pedometer app, battery depletion, or the app's sensitivity to movements may contribute to under-counting. A previous study by Casey et al (2014) reported challenges related to downloading and installing the app, carrying the phone, resetting the app in the mornings, and high battery usage. These findings highlight the importance of considering both subjective and objective measures of physical activity to obtain a comprehensive understanding of individuals' activity levels.

The correlation between the average number of steps and IPAQ-SF was shown in the form of a scatter plot (Figure 1). The average number of steps per day recorded by the pedometer application was found to be significantly correlated with the total MET-minutes/week according to the IPAQ (r=0.235, p=0.03). This correlation falls within the range reported in a systematic review study comparing direct versus self-report measures for assessing physical activity in adults, which ranged from -0.71 to 0.96 (Prince et al., 2008). Consistent with previous studies by Welk et al. (2000) and Bassett et al. (2004), significant and positive associations were found between questionnaire-based physical activity and step counts. In a similar study, it was shown that self-reported method can either overrate or underrate the measured parameter in comparison to objective method (Prince et al., 2008).

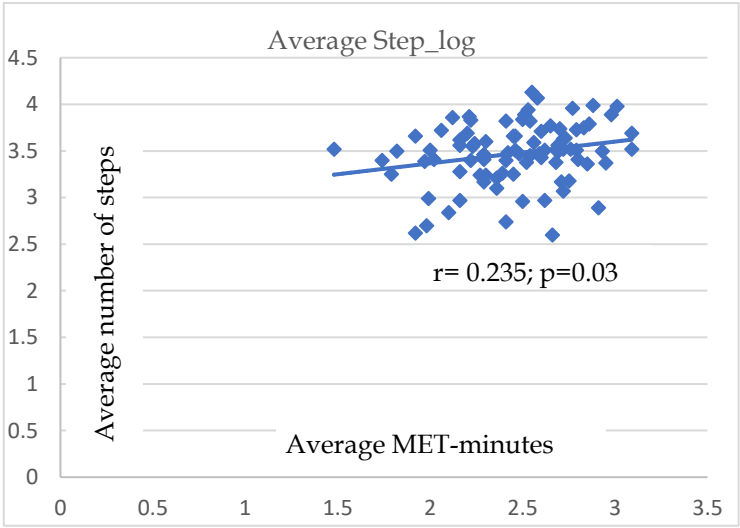


Figure 1 The average number of steps against average MET-minutes for 3 days (N=86)

To the best of our knowledge, this is the first assessment of physical activity status using a smartphone pedometer app and a comparison study between the pedometer app and IPAQ-SF specifically among university students in Malaysia. Moreover, the researchers made significant efforts to minimize errors by providing daily reminders to participants to turn on their pedometer app, submit screenshots of their data, and complete the IPAQ-SF questionnaire over the three-day study duration.

However, this study is not without its limitations. Some recruited participants did not complete the study procedures due to perceiving them as burdensome. Additionally, there were some others who were reluctant to participate due to the requirement of internet connection (mobile data) for testing the pedometer apps. A few potential participants were also unable to participate because the pedometer apps were not compatible with their mobile phone, insufficient mobile data, or storage capacity.

CONCLUSION

In conclusion, the findings of this study indicate that the Accupedo® pedometer app was the preferred choice among the participants in this study. Its ease of use, cost-effectiveness, and independence from GPS were key factors contributing to its preference. The chosen pedometer app demonstrated comparability to self-reported IPAQ-SF in determining physical activity status. While it is acknowledged that the step counts recorded by the pedometer app may be influenced by confounding factors, it remains a valuable tool for promoting daily physical activity. Further research is warranted to explore the long-term effectiveness and usability of pedometer apps in promoting sustained physical activity.

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THE ASSOCIATION BETWEEN INCOME STATUS AND DIET DIVERSITY AMONG IIUM KUANTAN STUDENTS

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ABSTRACT

Introduction: Unhealthy eating patterns are one of the contributing factors that may cause malnutrition or nutrition-related disease in an individual. However, the ability to start a healthy, nutritious, and low energy-dense food is influenced by the individual's income, especially the budget allocated to food expenditures besides other commitments. Therefore, this study aimed to determine the relationship between income level and diet diversity among students in IIUM Kuantan. **Methods:** A total of 107 respondents were chosen through proportionate stratified sampling from each Kulliyyah available in IIUM Kuantan: Kulliyyah of Allied Health Sciences (KAHS), Kulliyyah of Medicine (KOM), Kulliyyah of Pharmacy (KOP), Kulliyyah of Dentistry (KOD), Kulliyyah of Sciences (KOS) and Kulliyyah of Nursing (KON). Participants were interviewed using a structured questionnaire to obtain information on their socio-demographic characteristics, nutrient intake, and dietary diversity. A questionnaire with three sections included: section 1: socio-demographic data, section 2: the 24-hour diet recall questions, and section 3: the dietary diversity questionnaires (DDQ) were used for data collection. The data obtained were assessed with descriptive analysis, a One-Way Analysis of Variance (ANOVA) test, and a One-Sample T-Test. **Results:** There was no significant association ($p>0.05$) between income status and diet diversity among IIUM Kuantan students. The total calorie intake for female and male students did not meet the energy requirement according to Recommended Nutrient Intakes (RNI) 2017, with $p<0.001$ for both genders. **Conclusions:** It can be concluded that students' income status is not associated with their diet diversity. The female and male university students in the IIUM Kuantan campus consumed less energy than recommended by guidelines. Therefore, high or low-income students can have a limited or very diverse diet. Future studies should examine the elements that affect the variety of their diets.

KEYWORDS: Income status, Diet diversity, food intake, DDQ

INTRODUCTION

While having an adequate grasp of nutrition knowledge, most university students continue unhealthy eating habits such as skipping breakfast, frequent snacking, high consumption of fried and fatty foods, and eating less fiber daily (Yun et al., 2018). Besides, young adults are susceptible to problems in their nutritional status, especially when they adjust to university life and take on more responsibility for their daily food intake and activities (Hicks, 2018; Sogari et al., 2018 & Yun et al., 2018). Based on the study conducted among students at University Brunei Darussalam by Yun et al. (2018), the body mass index (BMI) category according to WHO, 13.2% of university students were underweight, while 28.8% were overweight/obese.

Each macronutrient, including carbohydrates, protein, and fat, has a different calorie count, influencing an individual total energy intake. As a result, consuming a variety of macro- and micronutrients could help achieve an adequate energy requirement to maintain well-being. However, not all university students lead a healthy lifestyle to maintain a normal BMI. Moreover, essential nutrients can be obtained from various foods because different foods have different nutrient content (FAO, 2016). Dietary diversity is the number of different food groups or foods consumed in a given period (FAO,2011). Diverse diet scores have been positively correlated with sufficient nutrients or energy intake for all populations, including adults (Fao, 2010). Low diet diversity can affect health due to a lack of essential nutrient intake or an excess of one single nutrient intake. Based on a study conducted by Onyeji et al. (2021), undergraduate students with obesity have low dietary diversity; thus, it shows an association between nutritional status and dietary diversity. A diversified diet contains all the essential nutrients the body requires and reflects the diet quality for individuals' health (Goh et al., 2020; Sogari et al., 2018 & Stewart & Maisonville, 2018).

Moreover, the Department of Statistics Malaysia (2022) stated that Malaysia's inflation rate in August 2022 increased to 4.7% year-on-year from 4.4% year-on-year in July 2022. The increase is attributed to food and non-alcoholic beverages, which increased by 7.2%. Most of the time, the healthy and nutritious foods available are costly compared to unhealthy and high-energy-dense foods because food purchases are influenced by perceived cost in several ways by students (Daniel, 2020). Therefore, students choose cheaper foods to save money rather than look at their nutritional value (Sogari et al., 2018). According to Yun et al. (2018), 58.7% of students chose food that costs less over healthy or nutritious food. Regardless of ignorance about the nutritional benefits of various food groups, maintaining a balanced and varied healthy diet for university students may be difficult due to a lack of money (Omage & Omuemu, 2018 & Onyeji & Sanusi, 2022).

Additionally, the socio-demographic background of each student is varied. The financial situation can be one of the risk factors affecting the diversity of dietary intake by the students. There is a contradictory finding on the relationship between income and nutritional intake. Hicks (2018) found an insignificant relationship between income and nutrition intake due to the university's unique environment and circumstances. Despite that, several other authors stated otherwise by mentioning that income is likely related to nutrient consumption based on a few studies conducted as low-income people consumed low nutrients and foods (Daniel, 2020; French et al., 2019; Mohd Abu Bakar et al., 2019; Rajikan et al., 2019 & Shabnam et al., 2021). Moreover, poor nutrition quality was also consistently linked to lower household income (French et al., 2019 & Shabnam et al., 2021).

Hence, this study will determine if there are any differences in dietary diversity scores for IIUM Kuantan students from different incomes or allowances obtained per semester that may affect their nutritional status.

MATERIALS AND METHODS

Study Design and Population

A cross-sectional study design was used among the students from all six sciences-based kulliyyah in the IIUM Kuantan campus, involving 107 male and female participants from year one to year five.

The proportionate stratified sampling method with convenient selection was used for this study. The subjects were selected according to their gender and kulliyyah to meet the proportion of each kulliyyahs and gender. Yet only those who registered at IIUM Kuantan campus, aged between 18 – 29 years old, live on campus, and were free from chronic diseases or medical problems were eligible to be the participants.

The student's distribution was 24.9% from Kulliyyah of Sciences (KOS), 24.3% from Kulliyyah of Medicines (KOM), 18.5% from Kulliyyah of Allied Health Sciences (KAHS), 12.1% from Kulliyyah of Nursing (KON), 12.1% from Kulliyyah of Pharmacy (KOP) and 8.1% from Kulliyyah of Dentistry (KOD). The proportion for genders for female and male students was 61.2% and 38.8%, respectively.

Ethical approval had been obtained from Kulliyyah Postgraduate and Research Committee (Reference No: IIUM/310/14/11/2/KAHS6/23). The participant completed the informed consent form attached with a set of questions. All information was strictly confidential.

Questionnaire

For this study, participants were interviewed in-person by the researcher with a set of questionnaires consisting of three parts: i) Socio-demographics data (participants' age and gender, level of study, Kulliyyah and income status, and anthropometry measurements such as body mass index), ii) Three days of 24-hour diet recall form – consists of two days of weekdays and a weekend day of detailed information on dietary intake and iii) Diet Diversity Questionnaire (DDQ) – consists of nine food groups to categorize students into low (≤ 3 food groups), medium (4 – 5 food groups) and highly diverse diet (≥ 6 food groups), were used to collect the relevant information from the selected participants.

Statistical Analyses

The data obtained were statistically analyzed using Statistical Package for the Social Sciences version 26.0 (SPSS 26.0). The significance level for 95% confidence interval (CI) was set at 0.05 for the variables. A descriptive analysis was used to identify the percentage, mean, median and standard deviation of the socio-demographic data, the income status among the participants, the dietary diversity scores (DDS), and anthropometric measurements. The association between income status and students' diet diversity was analyzed using the One–way ANOVA test. One Sample T-Test analysis was used to compare the mean of total energy intake among female and male students with Recommended Nutrient Intakes (RNI, 2017).

RESULTS

Socio-Demographics Data

Table 1 shows the socio-demographic characteristics data collected from 107 male and female students from year one to year five from each Kulliyyah available at the IIUM Kuantan campus. Of 107 students, 39.3% (42) were from Kulliyyah of Allied Health Sciences (KAHS), 9.3% (10) from Kulliyyah of Dentistry (KOD), 6.5% (7) from Kulliyyah of Medicine (KOM), 14% (15) from Kulliyyah of Nursing (KON), 14% (15) from Kulliyyah of Pharmacy (KOP) and 16.8% (18) from Kulliyyah of Sciences (KOS). Female responses were higher than male respondents, at 60.7% (65) and 39.3% (42), respectively. All students who participated in this study were aged 19 to 25 and single.

Table 1 Socio-demographic Characteristics of the Participants (N=107)

Variables	Frequency (n)	Percentage (%)
Gender		
Female	65	60.7
Male	42	39.3
Age		
19	4	3.7
20	16	15.0
21	16	15.0
22	60	56.1
23	9	8.4
24	1	0.9
25	1	0.9
Kulliyyah		
KAHS	42	39.3
KOD	10	9.3
KOM	7	6.5
KON	15	14.0
KOP	15	14.0
KOS	18	16.8
Year of Study		
1	23	21.5
2	18	16.8
3	58	54.2
4	7	6.5
5	1	0.9

Table 2 shows the average body mass index (BMI) among the students, was 22.6 kg/m^2, which falls in the normal range of BMI.

Table 2 Body Mass Index (BMI) Among IIUM Kuantan Students (N=107)

Variable	Minimum	Maximum	Mean
Body weight (kg)	38.0	100.0	59.2
Height (cm)	148.0	180.0	161.2
Body mass index (BMI) (kg/m^2)	15.7	33.1	22.6

Income Status Among IIUM Kuantan Students

Table 3 indicates the income status of the participants. There were 38.3% (41) participants from the B40 category, 42.1% (45) from the M40 category, and 19.6% (21) from the T20 category. The participants received financial support from parental allowance, sponsorship, study loans, and/or working while studying. Not to mention, 49.5% (53) of most students depended solely on sponsorships and study loans.

Additionally, students received allowances per semester from less than RM 3,000 to more than RM 5,001. Nevertheless, the least participants received allowances of more than RM 5,001, while most received allowances of RM 3,001 to RM 5,000 per semester, with 14.0% (15) and 61.7% (66), respectively. Besides, each participant spent variably from less than RM 150 to RM 750 for food every month.

Table 3 Descriptive Analysis of Income Status of IIUM Kuantan Students (N=107)

Variables	Frequency (n)	Percentage (%)
Parent's estimated household income		
B40	41	38.3
M40	45	42.1
T20	21	19.6
Types of allowance received		
Parental allowance	21	19.6
Parental allowance, sponsorship & study loans	28	26.2
Parental allowance, study loans & working while studying	3	2.8
Sponsorship & study loans	53	49.5
Study loans & working while studying	2	1.9
Total allowance obtained per semester		
< RM 3,000	26	24.3
RM 3,001 – RM 5,000	66	61.7
> RM 5,001	15	14.0
Spending solely on food per month		
< RM 150	9	8.4

RM 151 – RM 300	44	41.1
RM 301 – RM 450	35	32.7
RM 451 – RM 600	17	15.9
RM 601 – RM 750	2	1.9

Dietary Diversity Scores (DDS) Among IIUM Kuantan Students

Table 4 displays the diet diversity scores of the students. It shows many participants fall in the medium category for diet diversity, with a total of 54 students (50.5%), followed by the high category for diet diversity, with a total of 32 students (29.9%), and the fewest participants fall in the low category for diet diversity, with a total of 21 students (19.6%).

Table 4 Dietary diversity scores of IIUM Kuantan students (N=107)

Diet Diversity (scores)	Frequency (n)	Percentage (%)
Low (0 – 3)	21	19.6
Medium (4 – 5)	54	50.5
High (6 – 9)	32	29.9

Association Between Income Status and Diet Diversity Among IIUM Kuantan Students

Table 5 indicates the between-groups analysis was conducted to explore the impact of total incomes obtained per semester by IIUM Kuantan students on their diet diversity, as measured by the nine food groups in the Dietary Diversity Questionnaire (DDQ). Participants were divided into three groups according to their total incomes obtained per semester (Group 1: RM 3,000 or less; Group 2: RM 3,001 – RM 5,000; Group 3: RM5,001 and more). The result found no statistically significant difference between the income level and diet diversity with a p-value of 0.680 which is more than 0.05.

Table 5 Dietary Diversity Scores and the Students' Total Incomes Obtained Per Semester (N=107)

Dietary Diversity Scores (DDS)	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	1.515	2	0.757	0.386	0.680*
Within Groups	199.914	104	1.960		

*Not Significant; value at $p > 0.05$

Total Energy Intakes Among Female and Male Students in IIUM Kuantan Compared to RNI

The test value used in conducting One Sample T-Test for female and male students was 1840 kcal per day and 2240 kcal per day, respectively, according to the total energy requirement for adults aged 19 to 29 years old from Recommended Nutrient Intakes (RNI) 2017. Table 6 shows a significant difference between the total energy intake among female students in the IIUM Kuantan campus and RNI. ($M = 1604.3960$, $SD = 360.9698$) and 1840, $t(64) = -5.262$, $p < 0.001$, $\alpha = 0.05$. In tandem with that, total energy intakes among male students in the IIUM Kuantan campus also showed a significant difference compared with RNI. ($M = 1964.0397$, $SD = 470.2679$) and 2240, $t(41) = -3.803$, $p < 0.001$, $\alpha = 0.05$. Hence, the mean total energy intakes for female and male students in the IIUM Kuantan campus were lower than the total energy requirement in RNI.

Table 6 Total Energy Intakes Among Female & Male Students in IIUM Kuantan According to RNI (2017) (N=107)

Variable		**Total Energy Intake (kcal)**					
Gender	**n**	**Test Value**	**Mean (M)**	**Std. Deviation (SD)**	**Mean difference (95% CI)**	**t-statistics (df)**	**p-value**
Female	65	1840.00	1604.3960	360.9698	-235.6040 (-325.0479, -146.1601)	-5.262 (64)	< 0.001
Male	42	2240.00	1964.0397	470.2679	-275.9603 (-422.5061, -129.4145)	-3.803 (41)	< 0.001

*Significance value, $p < 0.05$.

DISCUSSION

The total income or allowances students receive every semester varies depending on the sources of allowances received. Most students rely on sponsorships and study loans only, to receive the allowances for every semester from financial institutions that offer to assist university students financially in tertiary education. The matters considered were the cost of living among students in university, including the economic challenges faced nowadays including the expenses for basics such as food and drinks, hostel, and transport to faculty (Nizad et al., 2018). According to a few previous studies regarding incomes and nutrition, the incomes or allowances obtained are associated with the diet of individuals (French et al., 2019; Rajikan et al., 2019 & Shabnam et al., 2021).

People's psychology also shapes their perceptions about diet intake or food choices instead of income status. According to the research done among university students, they found that the students did not abide by the advice on healthy dietary practices such as consuming a diverse and balanced diet, limiting fried foods, unhealthy snacking and more. However, they are conscious of the adverse consequences of excess energy intake, sugar, salt and oily foods (Sogari et al., 2018 & Yun et al., 2018). The probable factors

such as the significant life-changing adjustments in university as compared to high school, university students establish the food habits they will maintain over four to five years in college and beyond (Hicks, 2018 & Sogari et al., 2018). Their diet diversity may have developed since their early entrance into university by their preferences; they consumed highly diverse foods or limited their diet to minimal food groups. According to a study by Goh et al., (2020), the food group choices among individuals were influenced by cultural, religious, and philosophical variations. Thus, food choices are very dependent on individual preferences and habits; this can be seen from the results where the participants have a wide range of food diversity from low, medium and high diverse food groups.

This study also implies that students with higher income per semester may have a low-diverse diet, whereas students with lower income per semester may have a high diverse diet. The probable key drivers that affect students' choices of various food groups instead of their allowances include the individual and social levels, university environment and student lifestyle. At the intrapersonal level, the key components include the university students' attitude, behavior, self-belief and skills. Even though some students have similar sources of allowances they received, for instance, the same types of financial support for study loans or sponsorships, every one of the students has different food preferences. Sogari et al. (2018) also continued that a student highlighted the importance of the pleasure of eating by consuming the same foods frequently, almost every day, while claiming that healthy foods are unpleasant and do not taste as good as unhealthy foods with lots of seasoning, deep fried, sweet drinks and so forth. University students tend to spend money on foods that give them pleasure, although they eat similar foods frequently.

Besides eating the same foods frequently, university students found it challenging to eat various foods because it was troublesome to prepare foods (Sogari et al., 2018). Moreover, in early adulthood, interpersonal relationships are influenced by the feeling of social pressure (Sogari et al., 2018). Psychologically, when going out or eating out, many university students consume similar foods as their peers or family members. In general, diet intake can be significantly influenced by the surroundings in which individuals live and their lifestyle (Sogari et al., 2018). In IIUM Kuantan campus, students who lived on the campus, as the included criteria in this study, will have limited access to food variability because the students depend on on-campus dining halls that may provide similar meals daily. This circumstance prevents them from having a very diverse diet as they become choosy when entering college. The students also claimed that they eat vegetables and fruits the most at home compared to at university (Sogari et al., 2018). This is because they found most vegetables and fruits are expensive (Daniel, 2020).

In the Recommended Nutrient Intakes (RNI) 2017, the total energy requirements were taken under the guideline for adults aged more than 18 years old with a physical activity level (PAL) of 1.6, which is moderate active PAL that commonly used or selected for the comparison purposes and the general population. Hence, for males, the total energy requirement is 2240.00 kcal per day, while for females, the total energy requirement is 1840 kcal per day.

Nevertheless, based on the results, the total energy intake of the participant was lower than the recommendation regardless of their gender. The primary factors of the variability in energy requirements of adult populations, including between females and males with various lifestyles, are physical activity level and body weight. Energy needs are influenced by other variables that impact basal metabolic rate (BMR) and physical activity level (PAL), which are the two main contributors to the energy expenditure of individuals. As in RNI (2017), the other variables that impact BMR are body size, health conditions, environments, climate, temperature, altitude, food compositions, hormone balances, medicines, stimulants, and many more. The finding was similar to a previous study conducted in Pakistan, where they found

lower energy intake among male students, however, the female students met the requirement (Khattak, et al, 2002)

CONCLUSIONS

This study revealed no association between income status and diet diversity of the students in the IIUM Kuantan campus. The diversity of the diet among university students might not be driven by the students' incomes or allowances per semester but by other factors, including personal preferences, university environment, and student lifestyle. Hence, high or low-income students can have a low or highly-diverse diet depending on their preferences. Thus, authorities should initiate effective strategies that educate students about healthier diets and better food choices to prevent non-communicable diseases among young adults.

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DIETARY SUPPLEMENT INTAKE AND PERCEPTION ASSESSMENT AMONG ADOLESCENT ATHLETES

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ABSTRACT

Introduction: Studies have shown that athletes often have inadequate micronutrient intakes, and the use of dietary supplements can help address these deficiencies. However, most of the dietary supplement studies were focusing on adult and elite athletes. Thus, this study aimed to identify the prevalence and perception of dietary supplement intake among adolescent athletes in Kuantan, Pahang. **Method:** The study was conducted using a cross-sectional design among 106 athletics and team sports athletes (72.6% male; 14.6 $\pm$ 1.4 years old) The respondents were asked to complete a Dietary Supplement Prevalence and Perception Assessment Questionnaire (DSPAQ) which consisted of items on their demographic information, dietary supplement intake and perception. The prevalence dietary supplement intake between athletics and team sports was statistically analysed and the significance was ascertained using Chi-square test. **Result:** The overall prevalence of dietary supplements intake among athletes was 9.4 % with protein supplements being the predominant supplement (71%). The main reasons for the consumption of dietary supplements were to improve muscle strength, performance and maintain health. However, the prevalence was not associated to the type of sports. The adolescent athletes had a perception that they need more supplement information and believe supplement can enhances their performance. In addition, the main reason for not taking dietary supplements was related to the cost. **Conclusion**: In conclusion, adolescent athletes in this study are prone to not taking dietary supplements with the perception of needing more information about the supplement.

KEYWORDS: Dietary Supplement, Adolescent Athletes, Perception, Prevalence

INTRODUCTION

Athletes are always looking for strategies to enhance their performance, which can be achieved by optimising their diets. It is commonly known that the majority of athletes use dietary supplements to boost their performance and make their diets more nutrient-dense (Roy et al., 2021). The usage of supplements is relatively widespread in several countries. Statistics show that between 20 - 34% of young children and adolescents in the United States, Europe and Asia use dietary supplements, with multivitamins being the most common type (Sien et al., 2014). Besides, few studies found that the top five reasons for using dietary supplements were to maintain good health, increase energy, recover from exercise, build or retain muscle mass, and improve immunity. Nevertheless, these reasons varied by gender and competitive event in Kobayashi et al. (2017); Lun et al. (2012); Yazid et al., (2021). Additionally, studies have shown that athletes often have inadequate micronutrient intakes, and the use of dietary supplements can help address these deficiencies (Wardenaar et al., 2017).

In Malaysia, the use of dietary supplements is common practice but there is limited research available on this topic especially among young athletes (Balaravi et al., 2017 and Nor Azizam et al., 2022). Most of the dietary supplement studies are focusing on adult and elite athletes (Sien et al., 2014). Furthermore, considering the involvement of adolescent athletes in major sports events such as Sukan Malaysia (SUKMA), it is important to understand the patterns of dietary supplement intake among them. This study will facilitate the development education program that aims to prevent unnecessary supplement use. Moreover, it is also important to avoid unintentional doping due to the lack of knowledge about dietary supplements usage and will create awareness regarding dietary supplements consumption (Balaravi et al., 2017). Thus, the current study aims to identify the prevalence and perception of dietary supplement intake among adolescent athletes with involved in different types of sports in Kuantan, Pahang.

MATERIALS AND METHOD

Study Design and Population

A cross-sectional study design was conducted among adolescent's athletes from Kuantan, Pahang. Athletes age between 13 - 18 years old that participated in all levels of competition were included in this study. Meanwhile, athletes with injuries or diseases were excluded. To recruit the participants, purposive sampling was used. Informed consent was obtained from their sport dietitian and coaches before athletes participated in this study.

Questionnaire

This study used Dietary Supplement Prevalence and Perception Assessment Questionnaire (DSPAQ) to identify the prevalence and perception of dietary supplement intake among adolescent athletes in Kuantan, Pahang. DSPAQ was adapted from Lockie et al., (2015) ; Mohamad Shalan et al., (2018) and undergoes back-to-back translation into Malay language, content validation and face validation. The content validation involved by four dietetics lecturers, one sport nutrition lecturer, one sport & exercise sciences lecturer and one sports nutritionist from National Sport Institute (ISN). The content validity index (CVI) for this questionnaire was 0.976 which indicated that the items were relevant to the domain, clear, and comprehensible to the target participants. Additionally, the face validation index (FVI) was 0.994 which indicated high scale of clarity for all items in the questionnaire. All the processes can be viewed in Figure 1.

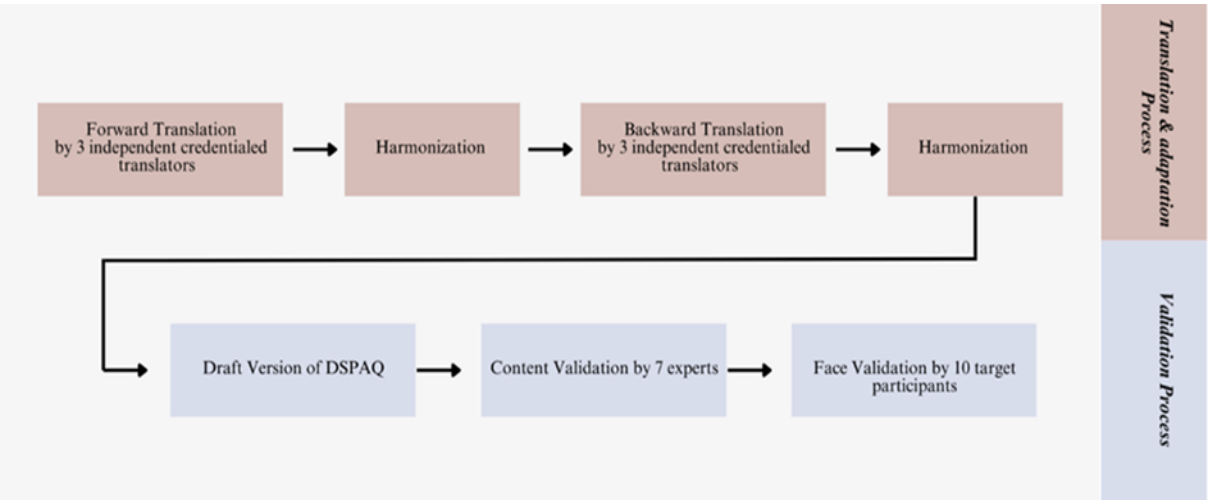


Figure 1 The flow of translation, adaptation, and validation process for the Dietary Supplement Prevalence and Perception Assessment Questionnaire (DSAPQ)

The DSPAQ comprises of 18 questions, divided into 4 main parts. The first part collected demographic and personal information on the study respondents: age, gender, ethnicity and sports that in which they are competing. The second part obtained information on their anthropometry: weight(kg), height(m) and body fat percentage. The third part identify their dietary supplements intake which include type of supplement intake. Lastly the fourth part investigate the athlete's perception on dietary supplements. The respondents required to answer each of the items by ticking one best answer.

Procedure

The data collection was immediately started after obtaining permission from International Islamic University Malaysia Research Ethical Committee (IREC), Ministry of Education (MOE) under Educational Research Application System (ERAS 2.0), '*Bahagian Sukan Kokurikulum dan Kesenian (BSKK)*' and the Headmaster of Sekolah Sukan Malaysia Pahang. The school dietitian and coaches were contacted and introduced to the study in order to recruit athletes. Then school dietitian provides the researcher with athlete's appointment schedule. The questionnaires were distributed to respondents according to the schedule. The data collection was conducted face to face, thus any discrepancies or inquiries were solved during the session. All answer booklets were check by the researcher to make sure all questions were answered.

Statistical Analysis

The statistical analysis was carried out using the SPSS Statistics version 26. The descriptive analysis was performed to identify the percentage, mean and standard deviation of the socio-demographic data. Besides that, chi-square test was used to compare the frequency of dietary supplements intakes and perception.

RESULT

Respondents Demographic and Anthropometry Information

The Table 1 shows demographic data collected from 106 respondents aged between 13 - 18 years old with majority of male athletes (72.6%). Sixty-six respondents were categorised in team sports, while the remaining 40 were in athletics. The team sports comprise of rugby and basketball athletes. Meanwhile athletics comprise of running, jumping, walking, throwing, and hurdling athletes. As for ethnicity, most of the respondents were Malay (82.1%) followed by Chinese (13.2%) and Indian (0.9%) players. The remaining 2.8% of athletes were from various ethnic origins such as Kadazan, Iban, Bugis and Siamese. Next for anthropometric measurement, most respondents (66%) had normal BMI followed by 25.5% were underweight, 4.7%were overweight and only 3.8% were Obese Class I. Furthermore, in terms of fat percentage, the majority of respondents exhibited a healthy fat percentage with 87% among males and 48.3% among females.

Table 1 Demographics and athletes details (*n=106*)

	n	%	Mean Score (SD)
Age			14.6 (1.4)
Gender			
Male	77	72.6	
Female	29	27.4	
Height (cm)			1.7 (0.8)
Weight (kg)			57.5 (12.9)
BMI Status (kg/m²)			
All			17.1 (3.4)
Underweight	27	25.5	
Normal	70	66.0	
Overweight	5	4.7	
Obese Class I	4	3.8	
Fat Percentage [a]			
All			18.728 (14.97)
Male			16.0 (15.3)
Under fat	3	3.9	
Healthy	67	87.0	
Overfat	4	5.2	
Obese	3	3.9	
Female			25.92 (11.4)
Under fat	9	31.0	
Healthy	14	48.3	
Overfat	1	3.4	
Obese	5	17.2	
Education Level			
Secondary School	106	100	
Race			
Malay	87	82.1	
Chinese	14	13.2	
Indian	1	0.9	
Others	4	3.8	
Sports Category			
Team	**40**	**37.7**	
Basketball	15	14.2	
Rugby	25	23.6	
Athletics	**66**	**62.3**	

Sprinter	27	25.5
Jumper	12	11.3
Walker	14	13.2
Thrower	5	4.7
Hurdle	8	7.5
Current Training		
Preparation	99	93.4
Competition	7	6.6

[a] Tanita (2020)

Dietary Supplement Prevalence among adolescents athletes

The result found that only 10 out of the 106 respondents in the study reported taking dietary supplements. Among the respondents who reported taking dietary supplements, 9 individuals (8.5%) were athletes involved in athletic sports, while only 1 individual (0.9%) was involved in team sports. A chi-square test was conducted to identify the association between types of sports and dietary supplement intake. The test indicated that no statistically significant association (p=0.118) was found between types of sport and dietary supplement intake.

Type Of Dietary Supplement

From the 10 respondents who reported taking the dietary supplement, only 7 provided information about the specific type of supplements they were taking. Out of 7 respondents, 4 (57%) of them consumed whey protein,2 respondents (29%) consumed lean gain protein and 1 respondent (14%) consumed vitamin C.

Reasons For Taking Supplement

As presented in Figure 2, adolescent athletes provide various reasons for taking supplements. The primary reasons were to improve muscle strength, followed by maintaining health, improve energy and improve performance, reduce fatigue, boost immunity and incorporating it into a dietary routine.

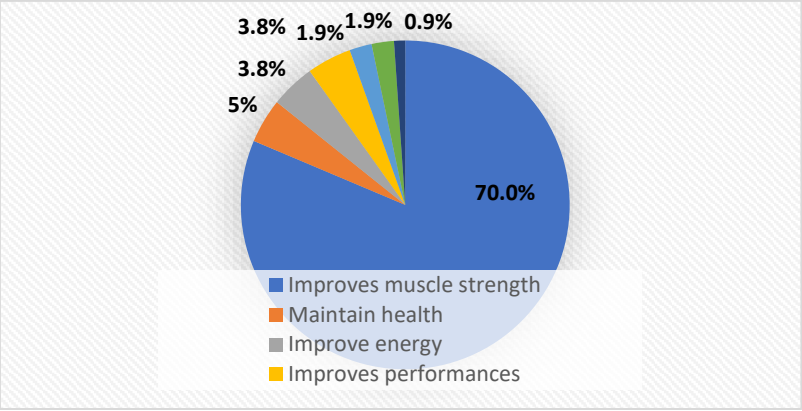


Figure 2 Reasons for taking dietary supplements by adolescent athletes (n=10)

Reasons For Not Taking Dietary Supplements

From Figure 3, it show about who did not consume dietary supplements, which the cost of supplements was the main factors influencing their decision, followed by being afraid of side effects from the supplement, and lack of information about the supplement. Other reasons were reported included the preference for relying on natural food sources for energy boosters and consumption of a balanced diet, perceived unsuitability with their body, and some of them being too lazy to consume the supplements.

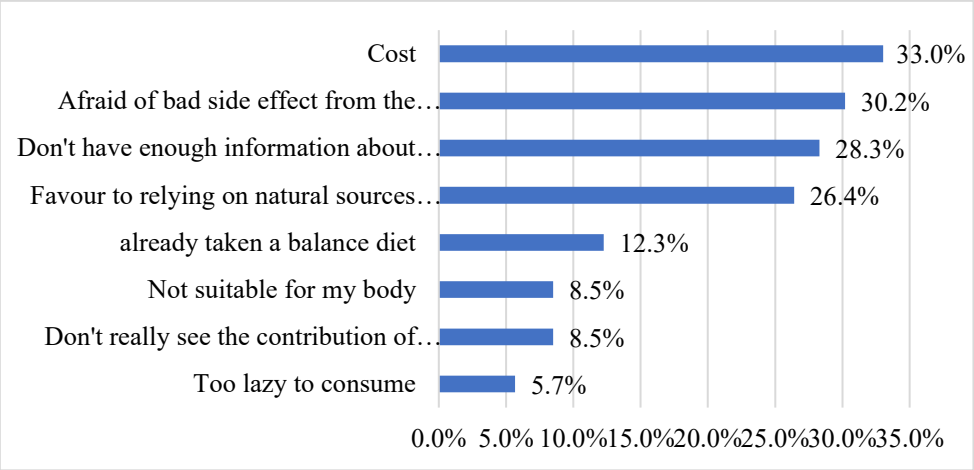
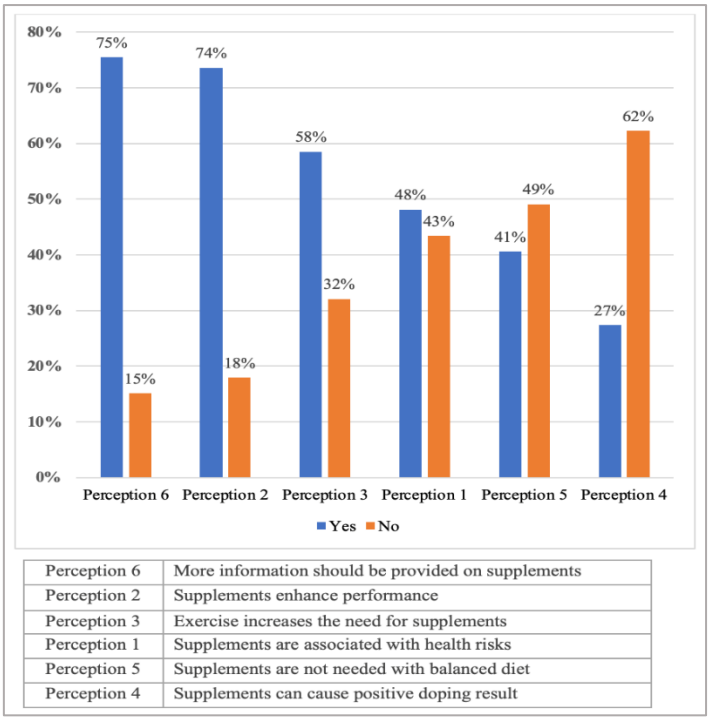


Figure 3 Reasons for not taking dietary supplements by adolescent athletes (*n*=96)

Perception Towards Dietary Supplement

Based on Figure 4, most of the respondents agreed that more information should be provided on the supplements. Next, athletes also had high agreement with statement that suggesting supplements can enhance their performance while a substantial respondent also agreed with the idea that exercising increases the need for supplements. Next, almost half of respondents agreed with the statement suggesting that supplements are associated with health risks. Nevertheless, there were almost half of respondents did not agree on the statement that supplements are not needed with a balanced diet. Lastly, just over half of respondents disagree on the idea that supplements can cause positive doping result.



Perception 6	More information should be provided on supplements
Perception 2	Supplements enhance performance
Perception 3	Exercise increases the need for supplements
Perception 1	Supplements are associated with health risks
Perception 5	Supplements are not needed with balanced diet
Perception 4	Supplements can cause positive doping result

Figure 4: Bar graph of perception toward dietary supplements among adolescent athletes *(n=106)*

DISCUSSIONS

Current study dealt with the prevalence and perception of dietary supplement intakes among adolescents athletes that were in the in two categories (individual athletics and team sports) who are competing at national level.

Prevalence of dietary supplement intake

The observed prevalence of dietary supplement intake was lower in the current study compared to studies finding conducted elsewhere (Alfawaz et al., 2017; Garthe & Maughan, 2018; Jovanov et al., 2019 and Sien et al., 2014). Study conducted on a large number of young athletes in the community showed that supplements are used to enhance their athletic performance (Tawfik et al., 2016). Moreover, study by Jovanov et al., (2019), observed that 82.2% of their individuals and team sports young athletes took supplements. Higher prevalence of dietary supplement intake can also be observed in various countries such as 87.5% among Australian athletes (Dascombe et al., 2010), 77.0% among Singaporean athletes (Slater et al., 2003), 71.2% among USA adolescents (Hoffman et al., 2008), 62.0% among the British athletes (62.0%) and 45.0% among Iranian athletes (Darvishi et al., 2013). The difference of prevalence between studies might be explained by the sample size, age categories and level of competition among athletes.

Current study found that the most frequently cited reason for supplement used among adolescent's athletes was associated with improvement on muscle strength. Nevertheless, according to Wiens et al. (2014), older athletes were more likely to use supplements associated with increased muscle strength, such as creatine and protein, compared to younger athletes. Motivation for supplement use included increasing muscle strength and power. Other studies found that common reason for supplement intake among the young athletes was the improvement of athletic performance (Mohamed & Abdelaziz, 2022), staying healthy, increasing energy, supporting the immune system and aiding in recovery (Parnell et

al., 2015). Therefore, it is important for athletes to be aware of the potential benefits and risks associated with supplement use and to make informed decisions based on their individual needs and goals.

Next, current study also reveal that the most frequent reported reason for not using any dietary supplement include the cost of supplements and lack of information on evidence of benefits and potential risk. The study by Baltazar-Martins et al., (2019) found that young athletes who do not use dietary supplements did not consider supplements necessary (72% of non-users). This suggests that these athletes may believe that they can meet their nutritional needs through their regular diet and do not see the need for additional supplementation. Another factor that may effect on their decision not to use supplementation was the presence of sports dietitians who control the athletes' dietary supplement intakes. According to Sports Dietitian Australia (SDA), nutrient demands should be met through basic foods rather than supplements, as they believe that dietary supplements are often overemphasized in terms of their ability to enhance performance. However, in current study it is still unclear whether access to sports dietitian is associated with supplement intake. Therefore in overall, athletes should undergo complete nutrition assessment by sports dietitian and make informed decision about supplement use (Maughan et al., 2018).

Perception of Dietary Supplement Intake

In the current study, the majority of athletes believe that more information should be provided regarding dietary supplementation. Nowadays the number of supplements in the market (online or physical) are huge and the highly accessible which can cause confusion for athletes to choosing the right supplement. Moreover, according to Geyer et al., (2008), a considerable percentage of nutritional supplements on the market are contaminated with compounds prohibited by anti-doping organisations. The investigation discovered a variety of illegal drugs in nutritional supplements regularly used by athletes, including anabolic agents, stimulants, and masking agents. Similarly, Martnez-Sanz et al., (2017) discovered that nearly 15% of dietary supplements tested were positive for illegal drugs, indicating the possible hazards connected with their usage. To solve this issue, athletes must exercise prudence and acquire reliable information from credible sources. Additionally, providing athletes with reliable resources/information for evaluating the safety, purity, and efficacy of dietary supplements can help them make informed decisions and avoid potentially harmful products (Buell et al., 2013).

Next, the current study found that almost all of the respondents agreed with the perception that supplements can enhance performance and exercise increases supplement needs. Similar observations were recorded in other studies conducted by Lun et al., (2012) and Maughan et al., (2018). Creatine, caffeine, proteins and branched-chain amino acids (BCAAs) are examples of ergogenic aid and it can help in enhancing athletes' performance and health. Furthermore, half of the respondents (58%) agreed that exercise can increase the supplement needs and this was reported earlier by Rodriguez et al., (2009) where exercising can result in increased energy expenditure, muscle protein breakdown, oxidative stress, and nutritional loss. These variables might increase the need for particular nutrients, which can be difficult to supply just through diet, especially in case of intensive or extended exercise. For example, studies have demonstrated that carbohydrate-electrolytes sports beverages may aid endurance athletes during prolonged exercise by replenishing glycogen stores and maintaining hydration (Coombes & Hamilton, 2000). Furthermore, resistance training athletes have shown improved muscle protein synthesis and recovery when supplementing with protein, such as whey protein (Cermak et al., 2012). It is crucial to highlight, that dietary supplements should not be viewed as a replacement for a well-balanced and nutrient-rich diet. Nevertheless, the consumption of any supplementation should be

guided by qualified health professionals such as sports dietitian and medical practitioners (Desbrow et al., 2014).

Other than that, concerns have been raised about supplement consumption is that it affect their health. Previous study reveals prevalence rate of anabolic-androgenic steroids (AAS) misuse among Iranian athletes of 36.2%, where the misuse was higher among elite, male, and younger athletes (Selk-Ghaffari et al., 2012). The main use of AAS is for performance enhancement but the long-term usage had led to variety of health hazards including cardiovascular difficulties, hormonal imbalances, liver damage, and psychological abnormalities (Bahrke & Yesalis, 2004). Therefore, athletes should receive comprehensive education about the risks and consequences of using illegal supplements. This includes understanding the potential health risks, the importance to follow the anti-doping regulations, and the potential impact on their athletic careers.

Current study found that more than half of the respondents believe that dietary supplements do not contribute to positive doping result. However, studies identified the misuse of dietary supplements among young athletes and the potential risk of doping is of a significant concern (Eichner & Tygart, 2015 and Bloodworth et al., 2010). Studies have shown that some athletes have tested positive for doping due to the intake of dietary supplements with poor labelling or product contamination (Eichner & Tygart 2015). Therefore, enhancing athlete awareness of the risks associated with dietary supplements are important strategies to prevent doping. Again, it is crucial to ensure that athletes have access to accurate information, reputable sources, and resources to make informed decisions about supplement use and avoid unintentional doping.

CONCLUSION

This study found low prevalence of dietary supplement intake among adolescent athletes. The adolescent athletes were prone to not taking dietary supplements with the perception of needing more information on evidence of benefits and potential risk about the supplement. Thus, the result of this study can be used to develop targeted education programs and provide accurate information about the potential benefits and risks of supplementation.

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ASSOCIATION BETWEEN CHRONONUTRITION PROFILE AND DIET QUALITY AMONG IIUM KUANTAN STUDENTS

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ABSTRACT

Introduction: Chrononutrition is explained as a relationship between our body's circadian rhythm, that is 24 hours cycle changes that occur in the body in terms of physical, mental and behavioral changes. Certain physiological effects play an important part in regulating 24-hour cycle body clocks, affecting a person's eating behavior. The patterns of chrononutrition that were assessed in this study is important aspects that indicate the diet quality of IIUM Kuantan students since students are vulnerable to practice unhealthy lifestyles and poor dietary choices. Therefore, this study is aimed to determine whether there are association between chrononutrition profile and diet quality among IIUM Kuantan students. **Methods:** A cross-sectional study was conducted in order to determining the association between chrononutrition profiles and diet quality. A total of 129 undergraduate students participated in this study. Two questionnaires, which are Malaysia-translated version Chrononutrition Profile Questionnaire (CPQ-M) and Malaysia Healthy Eating Index (M-HEI) were distributed to the targeted participants and the data was collected to be analyzed for the results of the study. **Results:** The data obtained were statistically analyzed by using Statistical Package for Social Sciences (SPSS 26.0). The result showed no statistical significant for association between chrononutrition profile and diet quality (p>0.05). This contradicts with our prediction, where poor or good chrononutrition profile may influence the diet quality of the students. **Conclusion:** Thus, there was no association between chrononutrition profiles and diet quality among IIUM Kuantan students who live in the campus.

KEYWORDS: Chrononutrition, Diet Quality, Circadian Rhythms, Eating behaviors

INTRODUCTION

'Chrono-nutrition' is the study that show the interaction between biological rhythms and nutrition. It is related with distribution of energy, meal frequency and regularity, duration of the eating period, as well as the relative importance of chrononutrition to the metabolic health and chronic diseases risk (Flanagan et al., 2020). Oda (2015) said in the study that chrononutrition is a well-regulated eating habits that have a negative effect on regulatory feedback for transcription via the binding of Clock Bmal 1 to E-box, which forms the basis of biological clocks. Clock Bmal 1 and E-box are genes which control the regulation of circadian rhythms. Besides, Engwall (2018) also stated in the research study where the chrononutrition is known as the food intake that occurs throughout the 24-hour day or the circadian timing of food intake.

Meals are said to be an important part that have been discussed in relation to chrononutrition since it is expected from a few of the previous study that it may have correlation with the diet quality of an individual. A study has reported that meals are known as the strongest synchronizer which functions to synchronize the brain clock. "Chrono-nutrition" is the study that shows the interaction between biological rhythms and nutrition. It is related to the distribution of energy, meal frequency and regularity, duration of the eating period, as well as the relative importance of chrononutrition for metabolic health and the risk of chronic diseases (Flanagan et al., 2020). In the study, Oda (2015) stated that chrononutrition involves well-regulated eating habits that negatively affect regulatory feedback for transcription via the binding of Clock Bmal1 to the E-box, forming the basis of biological clocks. Additionally, Engwall (2018) noted in their research that chrononutrition refers to food intake throughout the 24-hour day or the circadian timing of food intake. Meals are considered crucial in relation to chrononutrition since several previous studies suggest a potential correlation with an individual's diet quality. One study reported that meals are the strongest synchronizer, functioning to align the brain's internal clock.

Well-regulated eating behavior is closely associated with circadian rhythm functioning and also impacts an individual's diet quality. This statement indirectly influences an individual's body mass index and determines their nutritional and health status. Some studies indicate that poor chrononutrition can be attributed to unbalanced diets, frequent skipping of breakfast, increased snacking frequency, and insufficient time between the last meal and sleep onset. This underscores the importance of daily health management, including controlling behaviors like meal timing and sleep scheduling, to establish a healthy lifestyle. The primary focus of this study is to elucidate the association between the chrononutrition profile—how the circadian rhythm affects diet quality—among undergraduate university students. Most university students are noted to exhibit poor eating patterns and dietary intake due to academic demands, leading to unhealthy food choices stemming from inadequate chrononutrition behaviors.

A recent study highlighted certain behavioral patterns that may impact an individual's chrononutrition profile, such as the eating window (time-restricted feeding), evening latency (time between eating and bedtime), breakfast skipping, night eating, timing of evening eating, and timing of the largest meal (Engwall, 2018). Chrononutrition involves the interplay between nutrition and the circadian rhythm, providing valuable insights into managing food intake throughout the day (Norsham et al., 2023). According to Rosnani & Nor Azwani (2020), poor food intake can diminish diet quality. Insufficient nutritional intake may arise from unhealthy dietary practices and eating behaviors, particularly among university students. Consequently, the chrononutrition profile can influence diet quality in terms of meal timing and eating practices.

MATERIALS AND METHODS

A cross-sectional study was conducted among 156 students from all Kulliyyahs of IIUM Kuantan. The sample size was determined using a single proportion formula based on a study by Yong Qi Kwan et al. (2021), which found that 38.6% of the participants were engaged with night eating syndrome (NES).

A convenient sampling method was employed to collect data from the targeted respondents. The inclusion criteria encompassed undergraduate male and female students from all Kulliyyahs on this campus. Postgraduate students were excluded from this study as it primarily aimed to assess the understanding level of undergraduate students. Additionally, international students were not included due to their minority representation and students diagnosed with sleep disorders were also excluded.

The study protocol was approved by the IIUM Research Ethics Committee (IIUM/504/14/11/2 IREC 2023-KAHS/DNS). A consent form was attached to each questionnaire distributed to respondents, providing them with the necessary information to answer the questions. All provided information was treated as strictly confidential.

Questionnaires

Two types of questionnaires have been selected for use: the Malaysia-translated version of the Chrononutrition Profile Questionnaire (CPQ-M) and the Malaysia Healthy Eating Index (M-HEI). The questionnaire items were originally crafted in English to ensure comprehension among the students. The CPQ-M was adopted from Chong et al. (2022) and consist of short-answer and multiple-choice questions, along with scoring methods from Engwall (2018). The questionnaire is divided into six sections, with questions depend on the individual's meal timing, including morning, lunch, nighttime, late nighttime, and early and late eating behaviors.

The M-HEI questionnaire, adapted from the study by Karami & Mohd Shukri (2022), explores deeper into participants' dietary intake by requiring them to provide the number of daily servings consumed for nine food groups. These groups align with the Malaysia Dietary Guidelines (MDG) 2020 and encompass vegetables, fruits, rice, other cereals, whole grain cereal-based products and tubers, fish, poultry/eggs/meat, legumes, milk and milk products, and fats/oil and sugar. To aid participants in responding to the questionnaire, examples of foods corresponding to each of the nine food groups were provided as references.

Statistical Analyses

The statistical analysis was done using Statistical Package for the Social Sciences Version 26 (SPSS 26.0). Each of the chrononutrition profile and diet quality data were analyzed using descriptive analysis and Fisher's exact test was used to determine the association between chrononutrition and diet quality among IIUM Kuantan students. The study was set with a 95% confidence interval (CI) at p values <0.05 was considered statistically significant.

RESULTS

Sociodemographic Characteristics

A total of 129 respondents from both male (12.4%, n=16) and female (87.6%, n=113) undergraduate students of IIUM Kuantan participated in this study. The sociodemographic characteristics are presented in Table 1.

Table 1 Sociodemographic characteristics of respondents (N=129)

Sociodemographic Characteristics	Subjects		Mean ± SD
	n	%	
Age			21.56 ± 1.463
Gender			
Male	16	12.4	
Female	113	87.6	
Kulliyyah			
Kulliyyah of Allied Health Sciences	79	61.2	
Kulliyyah of Sciences	22	17.1	
Kulliyyah of Pharmacy	14	10.9	
Kulliyyah of Medicine	7	5.4	
Kulliyyah of Nursing	4	3.1	
Kulliyyah of Dentistry	3	2.3	
Year of Study			
Year 1	30	23.3	
Year 2	22	17.1	
Year 3	70	54.3	
Year 4	7	5.4	
Scholarship			
JPA	17	13.2	
MARA	32	24.8	
PTPTN	28	21.7	
Self-Sponsored	46	35.7	
Others	6	4.7	
Medical History			
Yes	28	21.7	
No	101	78.3	
Smoking Status			
Actively smoking	1	0.8	
Not smoking	128	99.2	
Alcohol Intake			
Yes	0	0	
No	129	100	
Exercise Patterns (or is it Physical Activity Level?)			
Active	34	26.4	
Sedentary	95	73.6	

The majority of respondents who participated in this study were around 21 to 22 years old, corresponding to second- and third-year undergraduate students. The distribution was consistent across all six Kulliyyahs,

with the highest response rate coming from the Kulliyyah of Allied Health Sciences (61.2%, n=79). Over a quarter of the total respondents were self-sponsored (35.7%, n=46). Additionally, there were students who received scholarships and financial assistance during their studies. Furthermore, majority of students reported having no medical history (78.3%, n=101), and nearly all students stated that they were non-smokers (99.2%, n=128). All participants refrained from alcohol intake, and the majority of students reported having a sedentary daily lifestyle (73.6%, n=95).

Chrononutrition Profile

Five aspects were assessed to determine the chrononutrition profile: eating windows on weekdays and weekends, evening latency, breakfast skipping, evening eating, and night eating. Among these, eating windows on weekdays and weekends, as well as night eating, received mostly good scores from the students. The remaining aspects of the chrononutrition profile displayed a high number of students scoring fair to poor."

Table 2 Chrononutrition profiles of respondents (N=129)

Chrononutrition Profile		Mean ± SD	Score	n (%)
Eating Windows	Weekdays	0.70 ± 0.777	Good	64 (49.6)
			Fair	40 (31.0)
			Poor	25 (19.4)
	Weekends	0.36 ± 0.624	Good	92 (71.3)
			Fair	27 (20.9)
			Poor	10 (7.8)
Evening Latency	Weekdays	1.34 ± 0.508	Good	2 (1.6)
			Fair	81 (62.8)
			Poor	46 (35.7)
	Weekends	1.23 ± 0.508	Good	5 (3.9)
			Fair	89 (69.0)
			Poor	35 (27.1)
Breakfast Skipping		1.18 ± 0.814	Good	33 (25.6)
			Fair	40 (31.0)
			Poor	56 (43.4)
Night Eating		0.07 ± 0.285	Good	121 (93.8)
			Fair	7 (5.4)
			Poor	1 (0.8)
Evening Eating		1.12 ± 0.559	Good	13 (10.1)
			Fair	87 (67.4)
			Poor	29 (22.5)

Diet Quality

The assessment of diet quality reveals that a majority of undergraduate students having poor diet quality(n=111), while only a small number of them indicated practicing a moderate diet quality (n=18). None of the students reported of having a good quality diet during their time living on campus.

Table 3 Diet quality of the respondents (N=129)

Diet Quality Category	n (%)
Poor diet quality	111 (86.0)
Moderate diet quality	18 (14.0)
Good diet quality	0 (0.0)

Association between Chrononutrition Profile and Diet Quality

Table 4 shows the association between chrononutrition profile and diet quality among IIUM Kuantan students. The result shows that there are no statistically significant association between diet quality and five chrononutrition profiles—eating windows, evening latency, breakfast skipping, night eating, and evening eating.

Table 4 Association between chrononutrition profile and diet quality (N=129)

Association between diet quality and:		*p*-value
Eating Windows	Weekdays	0.643
	Weekends	0.353
Evening Latency	Weekdays	1.000
	Weekends	0.806
Breakfast Skipping		0.340
Night Eating		0.082
Evening Eating		0.608

DISCUSSION

Food intake that occurs throughout the 24 hours per day for a week indicates the chrononutrition profile of a person. The result of the descriptive analysis showed that more than half of the students that participated in this study had less than 12 hours gap between their first and last eating events for both weekdays and weekends. Time-restricted feeding (TRF), defined as consuming food within a designated time frame, has been associated with health benefits. Students often have early morning schedules due to classes and late sleep onset due to commitments and assignment workload (Sing Chen Yeo et al., 2023 and Jansen et al., 2020). This study also reported that most of the students had a period of 2 to 6 hours between their last eating event and their sleep onset since it shows a fair result that indicates the undergraduate students had hours of break before starting to sleep. Prior studies suggest that allowing the body 2 to 3 hours before sleep for digestion may be beneficial (Kinsey & Ormsbee, 2015).

In this study, 43.4% of students reported of skipping breakfast more than four days a week. Breakfast skipping is common among students due to their busy lifestyles. According to Jayaveloo, Mat Daud, and Abd Rahman (2021), students need to rush in the morning and have different classes to attend, contributing to have a breakfast on their own rather than with friends. Moreover, evening eating that has been observed among students indicates that a high number of them had their last meal between 8.00 p.m. to 10.59 p.m. (67.4%) and more than a quarter of students also reported that they were still eating after 11.00 p.m. Engwall (2018) stated in the research study that those with a later sleep midpoint tend to have unhealthier diets and and consume more calories in the evening. Other than that, night eating among students was observed during this study where it can be concluded that students who had already fallen asleep were less likely to wake up to eat.

The present study revealed that the majority of students had poor diet quality (86%), with no students achieving a good diet quality score. This finding highlight that, despite being science students, their dietary intake and knowledge about diet quality are still poor (Rosnani Ayob & Nor Azwani, 2020). Abraham et al. (2018) clearly expressed that young adults commonly establish their eating patterns during their years in college and the behavior continues until they become adults. The university environment and student life are also another element that contributes in shaping their food choices for their daily meal routines (Sogari et al., 2018).

The chrononutrition profile closely relates to the timing of meals in determining a person's diet quality. The issue of late chronotype or evening chronotype has arisen among students because of their hectic schedules and workloads. Most of the students are practicing late chronotype behaviors. Late chronotype behaviors are associated with poorer dietary adherence (Fatin Hanani Mazri et al., 2019). However, in this

study, the association between diet quality and five chrononutrition profiles—eating windows, evening latency, breakfast skipping, night eating, and evening eating were not statistically significant. In line with the findings, Steger et al. (2022) discovered that the eating windows had no impact on the diet quality while Marie-Pierre St-Onge et al. (2016) confirmed that diet quality closer to bedtime influences sleep architecture, which is in contrast with the present findings.

Moreover, the most common behavior practice by the students is skipping breakfast at least once a week on campus. According to Min et al. (2011), individuals who regularly consume breakfast tend to have a more diverse dietary intake across various food groups when compared to those who frequently skip breakfast. This study also shows that there is no association between night eating among students and their diet quality. This finding contradicts the research conducted by Hernandez et al. (2016), which demonstrated that eating at night is associated with higher food consumption, encompassing both regular meals and snacks, during these late hours. Lastly, evening eating was also found to have no association with diet quality among students since the result shows no statistically significant. These findings also differ from a previous study by Sebastian et al. (2022), where the impact of late evening eating on the total Healthy Eating Index (HEI) score demonstrated statistical significance for nearly all common late evening eating patterns.

CONCLUSION

In conclusion, the dietary habits of IIUM Kuantan students, referred to as chrononutrition profiles, were found to have no significant association with their diet quality. Despite possessing good knowledge about nutrition, they tend to adopt an unhealthy lifestyle with poor dietary choices during their early adulthood phase. The majority of students exhibited poor diet quality, with only a few demonstrating a fair diet quality. This indicates that the importance of maintaining good dietary quality is not being practiced among IIUM undergraduate students. Based on the results of this study, it can be concluded that the hypothesis is not supported, as there is no significant association between chrononutrition profiles and diet quality. Consequently, it is crucial to promote and emphasize healthy dietary compliance and practices among these students to improve the future health of this population

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AN INVESTIGATION OF COMPUTER VISION SYNDROME IN OPTOMETRY STUDENTS DURING THE COVID-19 OUTBREAK

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ABSTRACT

Introduction: COVID-19 has forced the conventional face-to-face teaching method to online learning. Consequently, students spend more time in front of video display terminals (VDT) which is one of the risk factors for Computer Vision Syndrome (CVS). To date, limited studies have investigated the prevalence of CVS and its associated risk factors during COVID-19. **Aim:** This study aimed to investigate the prevalence of CVS, its associated risk factors and the correlation between CVS presence with the year of study and CVS presence with gender among 85 undergraduate optometry students in Kulliyyah of Allied Health Sciences (KAHS), International Islamic University Malaysia (IIUM). **Methodology:** This cross-sectional study recruited 85 undergraduate optometry students from KAHS, IIUM, who responded to a self-administered online questionnaire. A descriptive analysis was performed to calculate the prevalence of CVS. The Chi-square test and Fisher's Exact Test were conducted to measure the association between CVS and the variables of VDT usage. The phi-correlation coefficient (φ) was conducted to find the association between CVS presence with gender and CVS presence with the year of study. **Results:** The prevalence of CVS was 68.2% among optometry students. There was no statistically significant association ($p>0.05$) between CVS and VDT usage variables. Gender and year of study showed a strong correlation with CVS presence ($\varphi>0.15$). **Conclusion:** The presence of CVS in the study populations warrants further investigation so that measures can be implemented to alleviate this condition, and the learning process could proceed without dire consequences.

KEYWORDS: Computer Vision Syndrome (CVD), COVID-19, visual display terminals (VDT)

INTRODUCTION

The recent COVID-19 has caused unprecedented changes to the whole world. In the education sector, conventional face-to-face teaching is converted to online learning. As such, students spend more time in front of video display terminals (VDT) such as laptops, computers, and smartphones (Noreen, Ali, Aftab, & Umar, 2021). Studies have shown that prolonged use of VDT is one of the risk factors for Computer Vision Syndrome (CVS) (Abudawood, Ashi, & Almarzouki, 2020; Dessie, Adane, Nega, Wami, & Chercos, 2018; Logaraj, Madhupriya, & Hegde, 2014; Noreen, Ali, Aftab, & Umar, 2020; Reddy et al., 2013). CVS is defined as the combination of eye and vision problems associated with the usage of VDT (Rosenfield, 2011).

The optometry students in Kulliyyah of Allied Health Sciences, International Islamic University Malaysia are expected to attend more online classes during the pandemic compared to students from other courses due to their higher credit hours (IIUM, n.d.). Further, it has been proven that in general, students also spend a lot of their time in front of the screen for other academic-related matters such as conducting their research work and finding resources for their study (Altalhi et al., 2020; Noreen et al., 2021). This causes the students to be accustomed to staring at screens for long hours during the period of studying at home, possibly leading them to develop CVS symptoms.

Previous studies found a high prevalence of CVS among university students before the pandemic (Abudawood et al., 2020; Altalhi, Khayyat, Khojah, Alsalmi, & Almarzouki, 2020; Cantó-Sancho, Sánchez-Brau, Ivorra-Soler, & Seguí-Crespo, 2021; Logaraj et al., 2014; Reddy et al., 2013). However, only a few studies have investigated the prevalence of CVS among university students during the COVID-19 pandemic (Noreen et al., 2020; Setyowati et al., 2021). This study aims to investigate the prevalence of CVS and its associated risk factors among optometry students in KAHS during the COVID-19 pandemic. This study also aims to determine the association between CVS with the year of study and CVS with gender in optometry students in KAHS.

Due to the rampant use of electronic devices during online learning, it is hypothesized that the prevalence of CVS among undergraduate optometry students in KAHS will be high during the COVID-19 pandemic. The second hypothesis is that seating position, viewing distance, level of the top of the screen, presence of glare on the screen and duration of use are the associated risk factors for causing CVS. The third hypothesis is that gender and year of study have a strong association with CVS. In

essence, this study will provide data on the prevalence of CVS, its associated risk factors and the association with gender and year of study.

MATERIALS AND METHOD

Study design and population

A retrospective, cross-sectional study was conducted among 85 undergraduate optometry students of KAHS, IIUM. The single population proportion formula was used to calculate the required sample (Daniel, 1999). The following assumptions were taken to calculate the sample size: precision of 5%, the prevalence of CVS at 95% (Abudawood et al., 2020) and confidence interval of 95%. From the calculation, a total sample size of 80 subjects was obtained (after considering the 10% non-response rate). We recruited 85 undergraduate optometry students for this study. All undergraduate optometry students from KAHS who were enrolled during semester 1 2020/2021 were included in this study. There were no exclusion criteria included in this study. This study complied with the tenets of the Declaration of Helsinki, and ethical approval was obtained from IIUM Research Ethics Committee (KAHS 132/21).

Data collection

Optometry student that participated in this study were recruited using convenience sampling and asked to complete an online questionnaire via JotForm, distributed via WhatsApp and email. They were given a summary of the study's aim, objectives, and instructions for completing the questionnaire before data collection commenced. Informed consent was obtained before subject proceeded with this study. The questionnaire comprised of three sections: (i) socio-demographic data, (ii) VDT usages and (iii) symptoms of CVS. The data pertaining to best corrected visual acuity for distance and near was based on the subject's last eye examination. The CVS symptoms and presence were assessed via the CVS-Q (Seguí et al., 2015), while the CVS risk factor was assessed using the questionnaire regarding VDT usage from Peter (2020).

The CVS-Q assesses the frequency and intensity of 16 symptoms associated with CVS, which are burning, itching, foreign body sensation, tearing, excessive blinking, eye redness, eye pain, heavy eyelids, dryness, blurry vision, diplopia, focusing problem, photophobia, seeing coloured halos, worsening sight and headache (Seguí et al., 2015). Subjects were required to report the frequency of the symptoms, whether they occurred "often or always", "occasionally", or "never". If the respondents report "occasionally" or "often", they need to proceed to answer whether the intensity of the symptoms is "moderate" or "intense". The total score was calculated by multiplying the intensity by the total sum of frequency. The respondents were categorized as having a CVS presence when the total score was equal to or exceeded 6 points (Seguí et al., 2015). Subject that participated in this study were asked about the presence of CVS symptoms during the period of studying at home since the closure of universities.

Questions on the usage of VDT were derived from Peter (2020) to investigate the associated risk factors of CVS. The questions consist of seating positions, viewing distance, level of the top of the computer screen and presence of glare while using the VDT. Duration of VDT use was also asked, such as the number of days per week and hours per day they work on the VDT devices. The questionnaire was pre-tested in the pilot study and it was found to be feasible and appropriate to be used (Peter, 2020).

Data analysis

Data analysis was conducted using IBM Statistical Package for Social Science (SPSS) version 23.0 (IBM Corp., Armonk, NY, USA). The normality distribution of the data was analysed using the histogram, skewness and kurtosis value. The assumption of normality for CVS-Q scores was not satisfied, as assessed by visual inspection of the histogram. In addition, the CVS-Q scores had a skewness of 1.179 (SE = 0.261) and a kurtosis of 2.426 (SE = 0.517). According to Leguina (2015) skewness values >+1 or <-1 and kurtosis values >+1 or <-1 are considered non-normal. Based on these criteria, our CVS-Q data were confirmed to be non-normally distributed. Descriptive analysis was conducted for the categorical variables. The frequency and percentages were calculated and presented in Table 1. The prevalence of CVS presence was also calculated. To find the associated risk factors of CVS, Chi-square and Fisher's

exact test were used as univariate analysis and logistic regression was planned to be used as multivariate analysis (Cantó-Sancho et al., 2021). A p-value < 0.05 was taken as significant. Correlation analysis using phi-coefficient (φ) was conducted to test the correlation between CVS presence with gender and CVS presence with the year of study (Akoglu, 2018).

RESULTS

A total of 85 subjects (optometry students) participated in this study. The distribution of the subjects according to socio-demographic data were shown in Table 1. Eighty percent of the subjects were females and twenty percent were males. The highest number of subjects in descending order are from Year 4, Year 3, Year 2, Year 1 and Year 5. A total of eight subjects had the presence of chronic disease, which is allergy (n = 6) and asthma (n = 2). Only 2.4% presented with chronic ocular disease, with one subject having open-angle glaucoma in one eye and coat's disease in another eye (n = 1) and one subject having macular edema in one eye (n = 1). In addition, 10% of subjects reported using contact lenses. Among the 85 subjects, 77.6% had the best corrected visual acuity for distance (BCVA) of 6/6 or better, 9.4% had distance BCVA worse than 6/6, and 12.9% were unsure of their distance BCVA. For BCVA at near, 81.2% had N5 or better, 2.4% worse than N5, and 16.5% were unsure.

For the VDT usage, a total of 50 subjects positioned their face at the same level of the VDT screens, while 25 subjects did not position their face at the same level of VDT. Among the subjects, 25.9% reported the distance with VDT screen greater than 50 cm (> ¾ of arm's length), whereas 74.1% reported less than or equal to 50 cm (~ < ¾ of arm's length). For the level of screen of VDT, 45.9% had the screen below their eye level, 44.7% at the eyes level and 9.4% above the eyes level. Only 11.8% of the subjects used VDT less than 7 days per week whereas 88.2% used VDT every day. Among 85 subjects, 62.4% spent an estimated time from 4 to 8 hours using VDT, while 37.6% spent more than 8 hours daily.

Table 1 Distribution of the subjects (n=85) according to socio-demographic data

Variables	N	%
Gender		
Male	17	20.0
Female	68	80.0
Year of Study		
Year 1	16	18.8
Year 2	18	21.2
Year 3	20	23.5
Year 4	24	28.2
Year 5	7	8.2
Presence of Chronic Disease		
No	77	90.6
Yes	8	9.4
Presence of Chronic Eye Disease		
No	83	97.6
Yes	2	2.4
Use of Contact Lens		
No	75	88.2
Yes	10	11.8
Best Corrected Visual Acuity (Distance)		
6/6 or better	66	77.6
Worse than 6/6	8	9.4
I am not sure	11	12.9
Best Corrected Visual Acuity (Near)		
N5 or better	69	81.2
Worse than N5	2	2.4
I am not sure	14	16.5
Position of VDT screens		
	50	58.8

My face is just at the level of the computer screen / other VDT devices	25	41.2
My face is not at the level of the computer screen / other VDT devices		
Distance with VDT		
Greater than 50 cm (> ¾ of arm's length)	22	25.9
Less than or equal to 50 cm (~ < ¾ of arm's length)	63	74.1
Level of VDT screens		
Below the level of eyes	39	45.9
At the level of eyes	38	44.7
Above the level of eyes	8	9.4
Presence of Glare during VDT use		
No	67	78.8
Yes	18	21.2
Days using VDT (days/week)		
<7	10	11.8
7	75	88.2
Hours using VDT (hours/day)		
4-8	53	62.4
>8	32	37.6

The total prevalence of CVS was 68.2%, with a median score of 7.0 *(IQR* = 4 - 10.5) scores on the CVS-Q (Table 2). For the associated risk factors of CVS, univariate analysis using Chi-square and Fisher's Exact Test did not show any statistically significant result (p>0.05) for the VDT usage variables (Table 2). As for multivariate analysis, we were unable to perform logistic regression to find the associated risk factors of CVS because our data does not satisfy the assumptions required for the test. In particular, data from this study showed no linear relationship between the parameters, presence of outliers and small sample size (Laerd Statistics, 2013).

Table 2 Prevalence of CVS and p-value obtained through univariate analysis (Chi-square and Fisher's Exact Test)

Variables	**N**	**%**	**p-value**
Total	58	68.2	
Gender			
Male	9	52.9	0.221
Female	49	72.1	
Year of Study			
Year 1	10	62.5	0.165
Year 2	9	50.0	
Year 3	17	85.0	
Year 4	18	75.0	
Year 5	4	57.1	
Presence of Chronic Disease			
No	50	64.9	0.051*
Yes	8	100	
Presence of Chronic Eye Disease			
No	57	68.7	0.537*
Yes	1	50.0	
Use of Contact Lens			
No	52	69.3	0.719*
Yes	6	60.0	
Best Corrected Visual Acuity Distance			
6/6 or better	45	68.2	
Worse than 6/6	7	87.5	0.313
I am not sure	6	54.5	
Best Corrected Visual Acuity Near			

N5 or better	47	68.1	
Worse than N5	2	100	0.597
I am not sure	9	64.3	
Position of VDT screens			
My face is just at the level of the computer screen / other VDT devices	33	66.0	0.770
My face is not at the level of the computer screen / other VDT devices	25	71.4	
Distance with VDT			
Greater than 50 cm (> ¾ of arm length	19	86.4	0.064
Less than or equal to 50 cm (~ < ¾ of arm length)	39	61.9	
Level of VDT screens			
Below the level of eyes	30	76.9	
At the level of eyes	23	60.5	0.283
Above the level of eyes	5	62.5	
Presence of Glare during VDT use			
No	42	62.7	0.067
Yes	16	88.9	
Days using VDT (days/week)			
<7	6	60.0	0.719*
7	52	69.3	
Hours using VDT (hours/day)			
4-8	35	71.4	0.616
>8	23	63.9	

VDT: video display terminal
**Fisher's Exact Test*

Based on Figure 1, the most frequent symptoms of CVS from the 16 symptoms according to CVS-Q were itching eyes (65.9%), eye redness (65.9%), eye dryness (64.7%) and headache (62.4%). The least symptoms reported by the subjects were double vision (15.3%) and coloured halos around objects (11.8%).

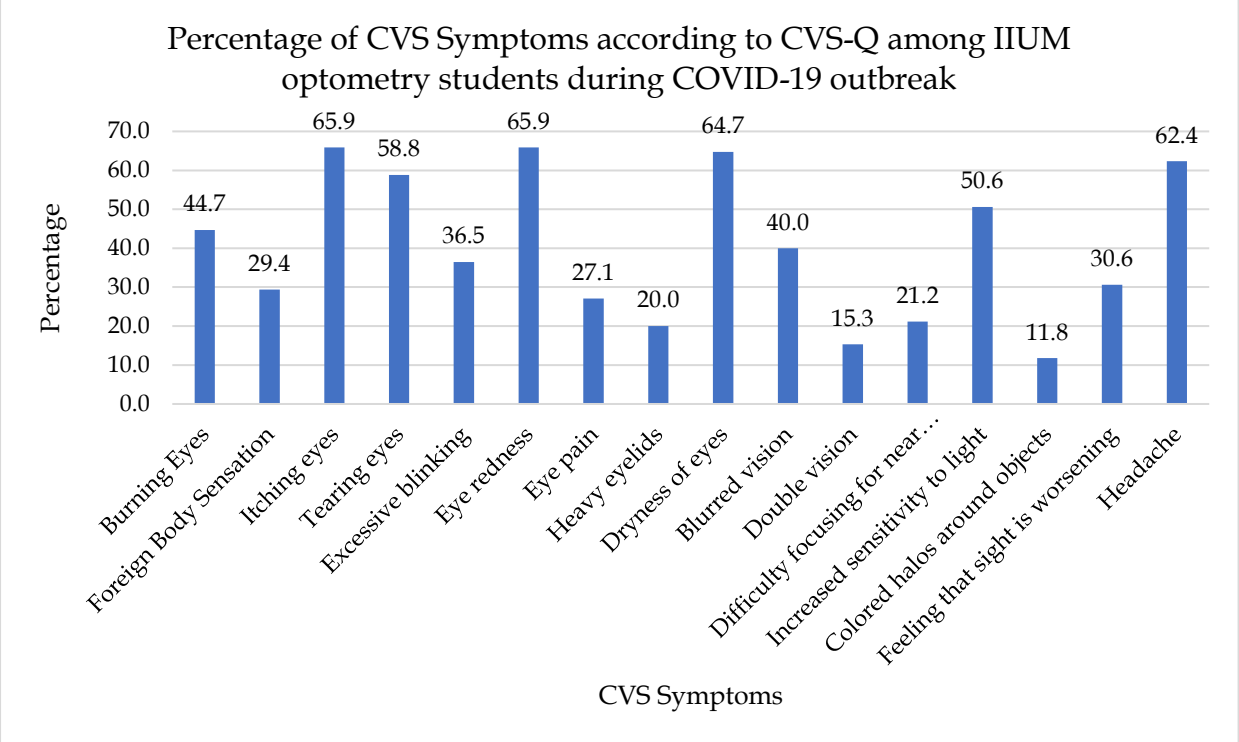


Figure 1 Percentage of CVS symptoms according to CVS-Q among IIUM optometry students during the COVID-19 outbreak

According to Akoglu (2018), the phi coefficient is a measurement of the strength of an association between two categorical variables in a 2×2 contingency table. The value of phi coefficient >0.15 is interpreted as having a strong association. Thus, we conducted a correlation factor analysis using phi-coefficient to assess the strength of associations for two variables; (a) CVS Presence and Gender and (b) CVS Presence and Year of Study. Tables 3 and 4 showed the phi coefficient result according to gender and year of study, respectively. Based on this, it was concluded that gender and year of study were strongly associated with the CVS presence (φ>0.15).

Table 3 Phi coefficient (CVS Presence and Gender)

Gender	CVS Presence (n)		Phi coefficient (φ)
	No	Yes	
Male	8	9	0.164
Female	19	49	

Table 4 Phi-coefficient (CVS Presence and Year of Study)

Year of Study	CVS Presence (n)		Phi coefficient (φ)
	No	Yes	
Year 1	6	10	0.165
Year 2	9	9	
Year 3	3	17	
Year 4	6	18	
Year 5	3	4	

DISCUSSION

The prevalence of CVS obtained from this study was approximate to values obtained in other CVS studies conducted among the university population. A study conducted among Spanish university students, which also utilized the CVS-Q to assess the CVS symptoms, found a prevalence of 76.6% (Cantó-Sancho et al., 2021). The higher prevalence compared to our study may be due to the larger sample size, which is 244 individuals compared to only 85 subjects in our study. There were limited studies available on the prevalence of CVS and its associated factors during the COVID-19 pandemic. A study conducted by Setyowati et al. (2021) found a CVS prevalence of 79.4% among the academic community in Indonesia. The authors did not utilize CVS-Q symptoms, and the presence of at least one of the CVS symptoms was considered of having CVS. Hence, this may lead to a higher prevalence of CVS among their students compared to our study. Meanwhile, Mohan et al. (2020) found a CVS prevalence of 50.23% among children using online e-learning during the COVID19 pandemic. Compared to school children, university students spent prolonged time using VDT for various academic purposes (Noreen et al., 2021). This might explain why the CVS prevalence among school children is lower compared to university students.

Eye itchiness is one of the most frequent CVS-related symptoms reported in other studies (Altalhi et al., 2020; Cantó-Sancho et al., 2021). Altalhi et al. (2020) reported a prevalence of eye itchiness of 63%, while Cantó-Sancho et al. (2021) found a prevalence of 73% among the study population. Similarly, we found a high prevalence of eye itchiness symptoms, 65.9% among KAHS undergraduate optometry students. Headache is another CVS symptom most often experienced among university students (Altalhi et al.,

2020; Noreen et al., 2020; Setyowati et al., 2021). Altalhi et al. (2020) estimated a headache prevalence of 68% among 334 students in Saudi Arabia. We found an approximate prevalence of headaches with Altalhi et al. (2020), which is 62.4 %. In other research, it was discovered that undergraduate medical students in Pakistan and Indonesia experienced a headache prevalence of 16.5% and 40.21%, respectively. (Noreen et al., 2020; Setyowati et al., 2021).

The results from the Chi-square test and Fisher's Exact Test showed that all the investigated factors related to VDT usage were not statistically significantly associated with CVS (Table 2). There was no clear explanation for this and further studies were needed to ascertain the causes. In contrast, Cantó-Sancho et al. (2021) found that longer durations of VDT use were strongly associated with CVS. Specifically, usage of VDT exceeding 4 hours per day imposes a three times risk of developing CVS than using VDT for less than 2 hours. Reddy et al. (2013) also reported that using the computer for more than 2 hours per day would cause a significantly higher number of CVS symptoms ($p < 0.001$).

Phi-coefficient analysis conducted for gender and year of study showed that the presence of CVS was strongly associated with these two variables. Toomingas et al. (2014) found that females are twice as likely to experience CVS symptoms as males. However, Cantó-Sancho et al. (2021) remarked that the association between gender and CVS was unclear. Further studies need to be conducted to determine the association between gender and CVS.

The strength of the current study was that we utilized CVS-Q developed by Seguí et al. (2015) to assess the CVS symptoms and presence. The CVS-Q is a self-administered questionnaire that has been tested and validated by experts (Sánchez-Brau et al., 2020; Seguí et al., 2015). The questionnaire's sensitivity and specificity score derived from Rasch Analysis was more than 70%, and it also obtained good test-retest repeatability (Sánchez-Brau et al., 2020; Seguí et al., 2015). Thus, it is a valid and reliable data tool to assess the CVS symptoms and their severity among subjects. Only a few previous CVS studies used CVS-Q (Cantó-Sancho et al., 2021; Mohan et al., 2020).

The current study had some limitations. The sample was relatively smaller compared to other CVS studies (Abudawood et al., 2020; Noreen et al., 2021; Setyowati et al., 2021) and only included optometry students from KAHS, IIUM. Another limitation of this study was that we did not include questions on CVS preventive strategies such as taking breaks and practice of visual hygiene. In addition, subjects might be subjected to recall bias, similar to any questionnaire-based studies.

CONCLUSION

This study found that the CVS prevalence during the COVID-19 outbreak was 68.2% among the 85 undergraduate optometry students. The most common symptoms reported were eye itchiness, dryness, redness and headache. In this current study, results from Chi-square and Fisher's Exact test showed that the risk factors of VDT usage are not statistically significantly associated with CVS. Hence, we could not identify the associated risk factors of CVS among the subjects. The phi-coefficient test conducted for gender and year of study revealed that both variables were strongly associated with CVS presence. However, due to limited evidence on the associations between gender and CVS presence in the literature, it is recommended to be further explored in future studies. Other recommendations include a larger sample size and involving students from different courses. For future studies, we also recommend incorporating questions on preventive strategies such as frequency of breaks and practice of visual hygiene in the questionnaire. Awareness regarding CVS should be raised, particularly among university students as the symptoms experienced during prolonged use of VDT could be lessened by taking preventive measures.

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ASSOCIATION BETWEEN VISUAL PERFORMANCE AND ABERRATION USING QUALITY OF LIFE IMPACT OF REFRACTIVE CORRECTION (QIRC) QUESTIONNAIRE IN MODERATE AND HIGH MYOPIC PATIENT

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ABSTRACT

Introduction: This study aimed to evaluate the association between visual performance and aberration using quality of life impact of refractive correction (QIRC) questionnaire in moderate and high myopic groups.

Methods: 120 eyes of 60 participants were recruited and both right and left eyes of the myopic subjects were measured separately. For satisfaction in visual performance, Quality of Life Impact of Refractive Correction (QIRC) questionnaire were given to all participants. For aberration measurement, WASCA wavefront analyser were done in dimmed illuminated room. Aberration was recorded as root mean square (RMS). WASCA built-in wavefront analysis computed three best measurements of RMS for third and fourth orders of aberration. The average of three measurements were taken for analysis. All data were expressed in mean and standard deviation. Statistical analyses were performed using Predictive analytics software. $P < 0.05$ was set as the level of significance. Independent T-test were done to compare all parameters between moderate and high myopia, including QIRC scores.

Results: This study found the mean QIRC scores were approximately similar between moderate and high myopia (Both $P > 0.05$). However, high order aberration (HOA) comprise of third and fourth order aberration were found significantly higher in high myopia group compared to moderate myopia group (Both $P < 0.05$).

Conclusion: This study found that QIRC questionnaire could not be able to differentiate subjective visual performance between moderate and high myopia.

KEYWORDS: aberration, refractive error, myopia, QIRC, quality of life

INTRODUCTION

Myopia is a common refractive error where distant vision are affected than near. Several studies reported the prevalence of myopia is increasing especially in the East Asian population (Morgan et al., 2012; Rudnicka et al., 2016). Recent study revealed rapid myopic transition in the East and South Asians population are evident due to rapid economic transition with near vision activities along with less outdoor activities are the contributor causes of myopia (Rudnicka et al., 2016). In general, myopia can be distinguished into axial myopia and refractive myopia as axial myopia occurs due to the increase of eye axial length while having a normal refractive power. Contrarily, refractive myopia occurs due to the increase of refractive power while having a normal axial length of the eye (Czepita, 2014). Study by Hashemi et al. (2017) showed that the prevalence of myopia was greatly higher in those with age of 21 to 30 years and over-70 years compared to the 16 to 20 years age groups and increasing especially in higher education. Association between myopia and quality of life (QoL) has been widely reported (Pesudovs et al., 2006; Lamoureux et al., 2008; Karimian et al., 2010; Kandel et al., 2017) with increasing of myopia does leads to greater challenging QoL.

Aberration can be define as imperfections of the visual system due to light being unable to focus effectively onto the retina, which also commonly known as wavefront aberration. Thus, image clarity relies on the accuracy of the eye's optical system and irregularities of the corneal curvature influenced the quality of retinal images. Aberration commonly been measured quantitatively using ray tracing technique such as ATLAS and WASCA and noted as Root mean square (RMS). A 2D topographic image is displayed to represent the wavefront distribution of the corneal surface. Previous study had reported positive correlation between refractive error and aberrations in myopic population (Karimian et al., 2010). However, to the best of our literature research, limited evidences available that discussed association of visual performance and aberrations using the QIRC questionnaire. Thus, this study aimed to evaluate visual performance and aberrations among moderate to and myopic eyes based on Quality of Life Impact of Refractive Correction (QIRC) questionnaire.

MATERIALS AND METHODS

120 eyes of 60 participants were recruited in this prospective cross-sectional study. Both right and left myopic eyes were measured separately. The inclusion criteria of the research are healthy participants with age ranging from 19 to 25 years old for both male and female having spherical refractive error between -3.00D to -5.00D (moderate myopia) or more than -5.00D (high myopia) with maximum cylindrical error of -1.25DC, and maximum pupil size of 6.5 mm. The exclusion criteria are those with abnormal tear film (Che Arif et al., 2020; Che Arif et al., 2021; Mohd Radzi et al., 2022) and corneal opacity (Hilmi et al., 2020; Che Azemin et al., 2016; Hilmi et al., 2019) or irregularity related conditions such as pterygium (Mohd Radzi et al., 2017; Mohd Radzi et al., 2018; Mohd Radzi et al., 2019; Mohd Radzi et al., 2019; Mohd Radzi et al., 2019; Mohd Radzi et al.,

2019; Che Rosli et al., 2020; Mohd Radzi et al., 2020), history of ocular trauma and systemic diseases. Participants who worn soft contact lens within two weeks of the measurements, or four weeks for rigid gas-permeable contact lens were excluded (Cook et al.. 2019; Moshirfar et al., 2019; Xu et al., 2022).

Prior to commencement of study, ethical approval was obtained from IIUM Research Ethics Committee [IIUM/504/14/11/2/IREC 2019-KAHS (U)] and it is comform with the Tenets Declaration of Helsinki. All participation are based on voluntary basis, and consent from each participants was obtained prior to any procedures. All data collection was conducted at IIUM Optometry Clinic, Kuliyyah of Allied Health Sciences, International Islamic University Malaysia (IIUM) Eye Specialist Clinic (IESC), Kuliyyah of Medicine, Kuantan, Pahang, Malaysia. Firstly, each of participant was given the Quality of Life Impact of Refractive Correction (QIRC) questionnaire to be completed. Then, standard optometric examination which includes slit-lamp examination, fundus and visual field was done.

For aberration measurement, WASCA HOAs and wavefront analysis were done using WASCA in a dimmed illuminated room. The aberrometer would sample the pupil through an array of lenslets in which the number of spots depend on the pupil diameter. Built-in wavefront analysis then compute three best measurements which include root mean square (RMS) for third and fourth orders of aberration. The average of three measurements were taken for analysis. All data were expressed in mean and standard deviation. Normality testing was based on ratio of skewness kurtosis with ± 2.50 are considered as normally distributed (Mohd Radzi et al., 2017). Statistical analyses were performed using IBM SPSS (Predictive analytics software) Version 24 (IBM Corp, Armonk, NY, USA). $P < 0.05$ was set as the level of significance.

RESULTS

The mean age of participants was 25.2 ± 64.8 years (N = 120 eyes). Normality testing revealed that all data were normally distributed ($p > 0.05$) with approximately balance number of participants for each group; moderate myopia (N = 61) and high myopia (N = 59). Based on descriptive analysis, both third and fourth order aberration were found significant in high myopia group compared to moderate group (Both P-value < 0.05), as summarised in Table 1.

Table 1: Demographic data on refractive error and root mean square (RMS) values of aberration for third and fourth order for both groups.

Parameter	Moderate	High	P-value
Degree of myopia (D)	-3.86 ± 0.56	-6.23 ± 1.03	
Aberration (Mean ± SD μm)			

Third-order	0.13 ± 0.10	0.28 ± 0.12	P < 0.001
Fourth-order	0.09 ± 0.05	0.14 ± 0.07	P < 0.05

Based on independent T-test analysis, this current study found that there were no significant difference between the mean QIRC scores in both moderate and high myopia group (Both P-value > 0.05). However, it is worth to note that the mean QIRC score for high myopia were relatively lower than moderate myopia group as summarised in Table 2 below.

Table 2: Mean QIRC scores for both moderate and high myopic groups.

QIRC Questionnaire	Moderate myopia	High myopia	P-value
	Mean ± SD	Mean ± SD	
Question 1 How much difficulty do you have driving in glare conditions?	58.30 ± 5.84	51.24 ± 13.82	0.124
Question 2 During the past month, how often have you experienced your eyes feeling tired or strained?	56.53 ± 11.22	63.57 ± 4.89	0.113
Question 3 How much trouble is not being able to use off-the-shelf (non prescription) sunglasses?	30.96 ± 8.92	37.40 ± 14.79	0.132
Question 4 How much trouble is having to think about your spectacles or contact lenses or your eyes after refractive surgery before doing things; e.g. travelling, sport, going swimming?	45.92 ± 14.30	38.20 ± 12.93	0.122

Question 5 How much trouble is not being able to see when you wake up; e.g. to go to the bathroom, look after a baby, see alarm clock?	49.67 ± 11.50	34.60 ± 13.03	0.094
Question 6 How much trouble is not being able to see when you are on the beach or swimming in the sea or pool, because you do these activities without spectacles or contact lenses?	39.90 ± 11.22	36.12 ± 6.51	0.112
Question 7 How much trouble are your spectacles or contact lenses when you wear them when using a gym / doing keep-fit classes / circuit training etc?	48.30 ± 8.14	39.72 ± 13.82	0.093
Question 8 How concerned are you about the initial and ongoing cost to buy your refractive surgery/ current spectacles and/or contact lenses/?	44.95 ± 13.98	41.44 ± 11.68	0.344
Question 9 How concerned are you about the cost of unscheduled maintenance of your refractive surgery/ spectacles/ contact lenses; e.g. breakage, loss, new eye problems?	37.45 ± 13.13	35.52 ± 8.00	0.233
Question 10 How concerned are you about having to increasingly rely on your spectacles or contact lenses since you started to wear them?	37.37 ± 6.25	34.56 ± 9.42	0.213
Question 11 How concerned are you about your vision being not as good as it could be?	34.24 ± 14.84	38.88 ± 10.43	0.144

Question 12 How concerned are you about medical complications from your choice of optical correction (refractive surgery, spectacles and/or contact lenses)?	32.80 ± 9.99	33.74 ± 10.92	0.432
Question 13 How concerned are you about eye protection from ultraviolet (UV) radiation?	42.74 ± 8.07	47.74 ± 12.88	0.221
Question 14 During the past month, how much of the time have you felt that you have looked your best?	34.35 ± 11.16	33.23 ± 11.10	0.412
Question 15 During the past month, how much of the time have you felt that you think others see you the way you would like them to (e.g. intelligent, sophisticated, successful, cool, etc)?	37.25 ± 11.63	34.97 ± 10.29	0.153
Question 16 During the past month, how much of the time have you felt complimented / flattered?	40.90 ± 10.85	37.28 ± 12.41	0.145
Question 17 During the past month, how much of the time have you felt confident?	28.54 ± 6.99	31.91 ± 13.72	0.197
Question 18 During the past month, how much of the time have you felt happy?	30.01 ± 11.43	32.10 ± 15.72	0.313
Question 19 During the past month, how much of the time have you felt able to do the things you want to do?	24.83 ± 15.08	19.37 ± 11.10	0.184
Question 20 During the past month, how much of the time have you felt eager to try new things?	33.00 ± 13.46	28.93 ± 11.10	0.134

DISCUSSION

This study aimed to evaluate relationship between higher-order aberrations (HOA) and QIRC scores as function for subjective visual performance. This study revealed HOA was found higher in high myopia compared to moderate myopia. This findings in coherent with several previous reports (Li et al., 2017; Neroev et al., 2021). There are conflicting evidences in describing HOA in comparison with types of refractive error. Some reports found higher HOA predominantly found in hyperope compared to myopes (Llorente et al., 2004; Martinez et al., 2009) myopes were higher than hyperopes (Kirwan et al., 2006; He et al., 2002) and no difference between all types of visual impairment (Carkeet et al., 2002).

Increased effect of aberration with increased of myopia could be due to changes in the internal optics of the eye such as anterior chamber depth and lens thickness. Another challenging factor in bridging the gap between HOAs and refractive error is age. A study had reported that HOA in particular spherical aberrations decreased with age [30]. Thus, this study findings could be justified as participants recruited are relatively young compared to other studies that includes cataract or elder groups as their target participants (Jing et al., 2016; Zhang et al., 2018). Another critical factor is pupil size. Pupil size plays an important role in the estimation of HOAs, and this current study was performed using a 6 mm pupil scan diameter, which is widely used to evaluate optical aberrations. Previous work (Wang et al., 2003) had commented that coma-like aberrations less affected with pupil dilation while spherical-like aberration showed significant increase in 5 - 6 mm pupil size, compared to 4 - 5 mm pupil size. Thus, variation in pupil size could misled the HOA findings.

QIRC questionnaire were meant to describe quality of life (QOL) of people with refractive correction by spectacles, contact lenses, and refractive surgery in the pre-presbyopic age group. This current study findings revealed that high myopic patients visual performance satisfaction were lower than the moderate myopic groups, however not statistically and clinically significant as reported by other study (Ang et al., 2015; Chiam and Mehta, 2019). Lower QIRC mean scores in high myopic group indicates lower satisfaction in visual performance compared to moderate myopic group. Moreover, this study found no significant association between QIRC scores and aberration, as reported by previous study (Han et al., 2020). Quality of life metrics in QIRC aimed to evaluate wellbeing of an individuals. It is worth to note that it is possible that some ocular conditions that may not cause reduced visual acuity, but create discomfort such as ocular allergy. Thus, QIRC scores should not be taken without prudent consideration.

The strength of this study includes measurement of ocular aberration which also considering the posterior cornea. This is to ensure the measurement HOA is not overestimate (Jiang et al., 2018). It is also important to highlight some limitations in this study. Three most important limitations were that aberrations were assessed using a 6

mm pupil scan diameter in relatively young participants and the number of patients recruited are generally limited. Secondly, bbnormal tear film condition could also affect measurement of aberration due to uneven ocular surface (Che Arif et al., 2020; Che Arif et al., 2021; Mohd Radzi et al., 2022), thus may affected the results. However, all participates were scrutinised to ensure abnormal tear film problems were excluded.

CONCLUSION

Aberration and QIRC scores are more prominent in high myopia compared to moderate group, however, prudent consideration need to be taken for QIRC questionnaire analysis.

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CONTENT ANALYSIS OF OCULAR PATHOLOGY INTERVENTIONS WRITTEN IN THE MALAY MEDICAL MANUSCRIPT OF PAHANG

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ABSTRACT

Introduction: A Malay medical manuscript (MMM) is a precious artefact inherited by Malay ancestors to be preserved and used as a reference in medical interventions. In recent years, MMMs have gained attention from researchers for identifying potential materials for modern clinical use. **Aims:** The aims of this study were to review the MMM of Pahang and to analyse its contents that are related to ocular pathology interventions. **Methods:** The MMM of Pahang was reviewed to identify the contents described in ocular pathology interventions. Subsequently, the contents were analysed using the Scientific Analysis of Kitab Tib Index (SAKTI), consisting of sub-indices of the Manuscript Selection (SAKTI-iMS) and the Pharmaceutical Prospectivity (SAKTI-iPharmaprospect). In comparing materials of the formulations used for ocular pathology interventions with published scientific evidence, we adapted the SAKTI subindex of the Comparison with Published Scientific Evidence (SAKTI-iComPSE). **Results:** The total score of the SAKTI-iMS for the MMM of Pahang was four over six. Four entries described ocular pathology interventions, including three physical approaches (for blurred vision, dry eye, and eye pain) and one non-physical approach (for conjunctivitis). For physical interventions, 12 materials were used in the formulations, five of which were found to be supported by published scientific evidence. Blurred vision and eye pain interventions scored more than nine, whereas dry eye intervention scored six for the SAKTI-iPharmaprospect. **Conclusions:** The findings revealed valuable insights into ocular pathology interventions, with several materials that have been scientifically proven for the treatment of targeted ocular pathologies. The integration of traditional knowledge and scientific validation underscores the potential of MMM in informing modern ocular healthcare. These results emphasise the importance of preserving cultural medical heritage for advancing evidence-based medical interventions.

KEYWORDS: blurred vision, dry eye, eye pain, Malay medical manuscript, ocular pathology

INTRODUCTION

Malay manuscripts are categorised as ancient material that is over 50 years old and written by Malay intellectuals. The written manuscript may be recorded on bark, paper, animal skin, bamboo, or other natural materials (Shafri, 2022). It is a valuable artefact inherited from Malay ancestors and documents Malay literature, traditions, philosophies, narratives, laws, and medicine (Ibrahim & Shah, 2020a).

Malay manuscripts discussing medical interventions, known as a Malay medical manuscript (MMM), usually use natural resources such as herbs, spices, and fauna as the main ingredients of medicines to treat diseases (Piah, 2015). The medicinal interventions usually included two forms that were empirical and spiritual (prayers, spells, incantations, and taboos) to treat various diseases (Ibrahim & Shah, 2020b). These included colds, headaches, malaria, chest pains, skin diseases, stomach pains and pathologies related to the ocular (Zayn al-Fatani, 2018). Therefore, the objectives of this study were twofold: i) to review the MMM of Pahang and analyse its quality, and ii) to analyse the medical content described in the MMM of Pahang in relation to ocular pathology interventions.

MATERIALS AND METHODS

The Malay Medical Manuscript of Pahang

The MMM of Pahang is the only *Kitab Tibb Melayu* found in Pahang. It is preserved under the manuscript collection of the Pahang Museum. Based on the acquisition records of the Pahang Museum, this MMM of Pahang (LMNP.0116.83H) was a gift from Mohd Piah Hamzah on 11 June 1983. The manuscript was estimated to be over 70 years old (Pahang Museum Acquisition Record: Kitab, 1983).

Review and Content Analysis

The MMM of Pahang was analysed using the Scientific Analysis of Kitab Tib Index (SAKTI) (Shafri, 2021). The SAKTI comprised four sub-indices: i) Manuscript selection (SAKTI-iMS), ii) Comparison with Published Scientific Evidence (SAKTI-iComPSE), iii) Pharmaceutical Prospectivity (SAKTI-iPharmaprospect), and iv) Consensus among Texts (SAKTI-iConText) (Shafri, 2021).

The SAKTI-iMS was used to systematically review the MMM of Pahang and objectively assess the quality of the manuscript. The evaluation was based on the following criteria: i) author profile, ii) completeness of the text, iii) readability of the text, and iv) percentage of medical content described in the manuscript. For

the author profile, which is clearly written in the MMM of Pahang, a score of ‘1’ was assigned, and for the author's utterly unknown background, a score of ’0' was assigned. For the criterion of completeness of the text, a score of ‘1’ was given if the content of the text was more than 80% complete, and a score of ‘0’ was given for incomplete texts. For the criterion of readability of the text, a score of ‘1’ was given if more than 80% of the texts of the MMM of Pahang were readable, and a score of '0' was given if less than 80% were not readable. For the criterion of percentage of medical content described in the manuscript, a score of '3', '2', '1', or '0' was assigned if more than 80%, 50 to 80%, 5 to 49%, or less than 5% of the MMM of Pahang contained medical content, respectively. The total score of the four criteria was above four, three to four, or below three, indicating that the MMM of Pahang was of high-, medium-, or low-quality, respectively. Manuscripts of medium- to high-quality should be considered for further research (Shafri, 2021).

The SAKTI-iComPSE method was adapted to compare plants, faunas and minerals used as materials for formulation in the MMM of Pahang with scientific reports on their exact or related uses. In this study, journal articles, books, and related documents were searched using the Google Scholar database. The functions of each material were described in a specific ocular pathology intervention rather than rating the level of evidence found as outlined in the original SAKTI-iComPSE (Shafri, 2021). It would be more useful for future researchers to evaluate whether the materials described in the MMM of Pahang have the potential to be investigated further or is less likely.

The SAKTI-iPharmaprospect was used to assess the potential of the formulations described in the MMM of Pahang in the context of ocular pathology interventions for development as pharmaceutical products. The evaluation was based on the following criteria: i) origin of material, ii) complexity of formulation, iii) simplicity of preparation, and iv) simplicity of administration route. For the criterion of material origin, a formulation consisting of local materials scored ‘3', foreign materials scored ‘2', and a combination of local and foreign materials scored '1'. For the criterion of formulation complexity, if a formulation contained a single substance or mixed substances, a score of ‘2' or '1’ was given, respectively. For the criterion of preparation simplicity, a score of ‘4’, ‘3’, ‘2’, or ‘1’ was given if the formulation could be prepared and used immediately, required one step of preparation within one day, required two or more steps of preparation within one day, or required more than one day for preparation, respectively. For the criterion of administration route simplicity, if the route of administration was topical, by nasal/eye drop, or oral, a score of ‘3’, ‘2’, or ‘1’ was assigned, respectively. If the total score of the four criteria was ten and above, seven to nine, or less than seven, the formulation was considerably high-, intermediate-, or low-prospect of being developed as a pharmaceutical product, respectively (Shafri, 2021).

The SAKTI-iConText is a method for evaluating consensus comparison of formulations written between MMMs. However, it was not used in this study due to the limited availability of MMMs in Pahang.

RESULTS AND DISCUSSION

Review of the MMM of Pahang

Review of the MMM of Pahang found that it contained 59 written pages in *Jawi.* No author profile or colophon was found in the manuscript. More than 80% of the texts were complete and readable. It comprised 144 entries, of which 80 (55.6%) described medical contents. Using the SAKTI-iMS, the criteria of author profile, completeness of the text, readability of the text, and percentage of medical content described in the manuscript were scored as '0', '1', '1', and '2', respectively. Overall, the SAKTI-iMS score for the MMM of Pahang was four out of six (Table 1). The findings indicated that the MMM of Pahang is a medium-quality manuscript with an acceptable score for further analysis (Shafri, 2021). Moreover, to the best of our knowledge, the MMM of Pahang is the only manuscript in the Pahang authority collection ("Pahang Museum Acquisition Record: Kitab," 1983). Thus, this manuscript fulfils the need and urgency to study the medical content written in it.

Table 1 Manuscript quality analysis for the MMM of Pahang using the SAKTI-iMS

	Criteria of the SAKTI-iMS				Total Score
SAKTI-iMS	**Author Profile**	**Text Completeness**	**Text Readability**	**Medical Content %**	
Score	0	1	1	2	4

% = percentage

Four of the 80 entries related to ocular pathology interventions, including dry eye, eye pain, conjunctivitis, and blurred vision. Of these four interventions, three were physical and another was non-physical, namely prayers (Table 2).

Table 2 Intervention approaches of the ocular pathology described in the MMM of Pahang

Ocular Pathology	Intervention Approach
Blurred vision *(*Penglihatan kabur)*	Physical
Conjunctivitis *(*Lil-ramad)*	Non-physical
Dry eye *(*Mata kering)*	Physical
Eye pain (**Sakit mata*)	Physical

**Original words written in the MMM of Pahang*

Content Analysis of the MMM of Pahang

Comparison with Published Scientific Evidence

As mentioned in the subsection "Review of the MMM of Pahang", the physical approach described in the MMM of Pahang was used in three ocular pathology interventions. A total of 12 materials were used to treat the three ocular pathologies: only one for blurred vision, nine for dry eyes, and two for eye pain. Tiger bile was written as material for blurred vision intervention. Nevertheless, there are no published journal articles, books, or other relevant documents that provide scientific evidence for the medicinal properties of tiger bile (Table 3).

For four of the nine materials, there was scientific evidence for the intervention of dry eyes: black myrobalan, cape jasmine, female breast milk, and key lime juice. The other five materials did not have scientific evidence nor were they identified (Table 3). Dry eye is a multifactorial disease of the tears and ocular surface that causes visual discomfort, visual disturbance, and tear film instability, which can lead to ocular surface damage. Moreover, it increases tear film osmolarity and causes ocular surface inflammation (Craig et al., 2017). Black myrobalan and key lime juice were found to have properties that act as anti-inflammatory agents (Ai et al., 2019; Fuentes & Granda, 1988; Piccinelli et al., 2008), while cape jasmine can help reconstruct ocular surface damage (Li et al., 2015) and protein properties in female breast milk provide protection and improve tear film stability to alleviate dry eye disease (Mudgil et al., 2022).

Only for opium poppy is there scientific evidence that it is helpful for eye pain (Table 3). It has been reported that opium poppy can be used to relieve pain not only in the eye but also in other parts of the body, such as the gall bladder, head, and teeth (Hamarneh, 1972).

Table 3 Comparison of the materials described for ocular pathology interventions in the MMM of Pahang with published scientific evidence

Material	Scientific Evidence
For Blurred Vision Intervention	
Tiger bile *(*Hempedu harimau)*	No scientific report has been found.
For Dry Eye Intervention	
Black myrobalan (**Halīlaj;* [ǂ]*Terminalia chebula*)	Act as an anti-inflammatory agent (Ai et al., 2019).
Cape jasmine *(*Air bunga kaca piring;* [ǂ]*Gardenia jasminoides)*	Assist in reconstructing ocular surface damage (Li et al., 2015).
Female breast milk *(*Air susu orang perempuan)*	Contains the proteins that provide better protection to the tear film and enhance its stability (Mudgil et al., 2022).
Key lime juice *(*Air limau nipis;* [ǂ]*Citrus aurantifolia)*	Act as an anti-inflammatory agent (Fuentes & Granda, 1988; Piccinelli et al., 2008).
Lesser celandine/ pilewort *(*Ma mayrān;* [ǂ]*Ficaria verna)*	No scientific report has been found.
Pearl (**Mutiara;* [ǂ]*Pinctada)*	No scientific report has been found.
Rock sugar/ rock candy (**Gula batu*)	No scientific report has been found.
**Shib Yamani*	The material cannot be identified.
**Ithmid Iṣfahāniy*	The material cannot be identified.
For Eye Pain Intervention	
Zinc *(*Timah sari;* [ǂ]*Zinc)*	No scientific report is found.
Opium poppy/ bread seed poppy *(*Afyūn;* [ǂ]*Papaver somniferum)*	Able to relieve eye pain (Hamarneh, 1972).

**Original words written in the MMM of Pahang;* [ǂ]*Scientific name*

Pharmaceutical Prospect

Using the SAKTI iPharmaprospect, the interventions for blurred vision and eye pain scored greater than nine out of 12 (Table 4). This indicated that these two interventions have high bio-prospect of being developed as a pharmaceutical product. To develop a pharmaceutical product that has commercial value and is viable, the formulation must contain locally sourced materials, have high efficacy even if it is singly formulated, have low complexity of the administration route, and be able to be consumed immediately or applied topically (Shafri, 2021).

The formulation for blurred vision intervention met all the above criteria. Tiger bile is a local source that can be applied immediately and topically as eyeliner. However, the efficacy of the described formulation is questionable, as no modern scientific report has been found for this material to reduce blurred vision; therefore, a future study is warranted.

For eye pain intervention, the materials of the formulation are a mixture of zinc and opium poppy, which are also available locally and can be applied topically to the eye. Nevertheless, the preparation requires more than one step within a day.

For dry eye intervention, the SAKTI-iPharmaprospect score was six over 12. The formulation is mixed between local and foreign sources of nine materials, two of which cannot be identified; the preparation involves more than two steps and is applied as eye drops (Table 4). In terms of pharmaceutical prospects, this formulation is difficult to manufacture and may have low potential to become a commercial and viable pharmaceutical product (Jaganath & Ng, 2020; Shafri, 2021).

Table 4 Pharmaceutical prospect of formulation for ocular pathology interventions the MMM of Pahang using the SAKTI-iPharmaprospect

Ocular Pathology Intervention	Score of the SAKTI-iPharmaprospect Criteria				Total Score
	Origin of Material	Complexity of Formulation	Simplicity of Preparation	Simplicity of Administration Route	
Blurred Vision	3	2	4	3	12
Dry Eye	1	1	2	2	6
Eye Pain	3	1	3	3	10

No comparison was made between the materials or formulations written in the MMM of Pahang and other MMMs, which is a limitation of this study. Thus, this study did not address any consensus that might exist with other MMMs. Despite this inconclusiveness, to the best of the authors' knowledge, the MMM of Pahang is the only MMM collection in Pahang ("Pahang Museum Acquisition Record: Kitab," 1983).

CONCLUSION

The MMM of Pahang is a medium-quality manuscript. It contains 80 entries describing medical content, including four ocular pathological interventions. Nearly 50% of the materials have been scientifically proven to treat the targeted ocular pathologies. The materials or formulations described in this manuscript for the interventions of blurred vision and eye pain have good bio-prospects of being developed as a commercially viable pharmaceutical product. Therefore, further research is warranted to evaluate the efficacy of the materials and formulations that may provide alternative ocular intervention from the MMM of Pahang in the future.

DECLARATION OF INTEREST

The authors declare that there is no conflict of interest.

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DASS SCORES AMONG STUDENTS OF ALLIED HEALTH SCIENCES AT IIUM

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ABSTRACT

Introduction: Depression, anxiety, and stress disorders are prevalent among university students, with healthcare students being more susceptible. The challenges specific to their field contribute significantly to the overall burden of mental health issues. As these students progress through clinical training, their predisposition to mental health issues increases, making it critical to address their well-being proactively. **Aim:** The purpose of this study was to explore the mental health conditions of allied health sciences students, and to compare the differences in Depression Anxiety Stress Scale (DASS)-21 scores between gender, year of study, and different departments among Kulliyyah of Allied Health Sciences (KAHS) students. **Methodology:** This was a cross-sectional questionnaire-based study conducted at the International Islamic University Malaysia (IIUM) Kuantan Campus. The completed DASS-21 questionnaire has been completed for a total of 534 allied health sciences students from six different departments at KAHS. **Results:** The prevalence of depression, anxiety and stress among allied health sciences students using DASS-21 was found to be 47%, 65.5%, and 33.3%, respectively. There were no significant differences in DASS-21 scores between gender and year of study. A statistically significant difference in DASS-21 scores between departments was found for symptoms of depression and anxiety. **Conclusion:** The student's mental health issues are concerning, with a significant level of severe anxiety reflecting psychological disorders among university students. Hence, the university should be aware of this and provide necessary aid for the student's mental well-being.

KEYWORDS: mental health, DASS-21, allied health sciences students

INTRODUCTION

For the past five years, especially after the pandemic, the prevalence of mental disorders has risen dramatically. According to the World Health Organization (WHO) (2022), nearly one billion people globally, or one out of every eight people suffer from various mental disorders. Anxiety and depressive disorders have been identified as the most prevalent mental health conditions in 2019, and the outbreak of the COVID-19 pandemic in 2020 further exacerbated the prevalence of these disorders. While mental health issues have been a major concern across various demographics, the alarming rates among university students have drawn particular attention in recent years. During their transition to higher education, university students were exposed to a variety of stressors and challenges, which could have a negative impact on their mental health.

The prevalence of mental health conditions among university students has been extensively researched, with a particular focus on depression, anxiety, and stress. It is found that the rates of depressive disorders, as well as anxiety and stress disorders are higher among Malaysian university students (Kotera et al., 2020; Kumaran et al., 2022; Nahas et al., 2019; Wong et al., 2023). Numerous studies have been conducted to investigate the risk factors, typical symptoms, and severity of these conditions in university students. A study revealed a notable increase in the prevalence of depression, anxiety, and stress as students' progress through their clinical training (Almhdawi et al., 2018). Moreover, another study demonstrated that health sciences students exhibited more severe symptoms of depression, anxiety, and stress compared to non-health science students (Thing et el., 2022).

These findings suggest that undergraduate university students, especially those pursuing healthcare degrees, are particularly susceptible to mental health issues. The clinical training phase exposes students to high workloads and clinical requirements to be fulfilled such as continuous assessment, long teaching hours, and the expectation of professionalism, which have been identified as significant stressors for students in this field (Turnbull et al., 2021). The study highlights the distinct challenges that clinical students face, which contribute to the overall burden of mental health issues.

Mental health issues can adversely affect various aspects of a student's life, including academic performance (Zada et al., 2021), overall quality of life, physical well-being, and relationships with friends and family members (Consequences of Student Mental Health Issues – Suicide Prevention Resource Center, 2015). Such concerns may have lasting impacts on students' futures. Having good mental health is crucial for students, especially those pursuing allied health sciences, as it enables them to effectively handle the intense demands of their clinical coursework.

Therefore, the purpose of this research is to explore the mental health conditions of allied health sciences students from the IIUM Kuantan Campus. This study also aims to compare the differences in DASS-21 scores between gender, year of study, and different departments among KAHS students. Hopefully, this study could raise the awareness and measures to tackle the issues at earliest stage as possible to prevent unpleasant event.

MATERIALS AND METHOD

Study design and population

This was a cross-sectional questionnaire-based study conducted among allied health sciences students at IIUM Kuantan Campus using the DASS-21 questionnaire. The target population are undergraduate students from KAHS for the 2022/2023 academic session from year one to year four of six departments (Department of Audiology and Speech-Language Pathology (DASLP), Department of Biomedical Science (DBMS), Department of Nutrition Sciences (DNS), Department of Diagnostic Imaging and Radiology (DDIR), Department of Optometry and Visual Sciences (DOVS), and Department of Physical and Rehabilitation Sciences (DPRS).

Data collection

The recruitment of participants began in November 2022 and ended in April 2023. Students were given self-administered sociodemographic and DASS-21 questionnaires to fill out with no time limit. Prior to administering the questionnaire, the study protocols and objectives were explained. Completed questionnaires indicate participants' consent to participate. This was completed during the first five weeks of the semester as it was the most convenient time without any exams.

Questionnaire

A two-section questionnaire was used: i) Information on the sociodemographic data (gender, age, year of study, department), and ii) DASS-21 questionnaire. DASS-21 was utilised since the

instrument is a well-established screening tool for depression, anxiety, and stress symptoms. It was widely used due to its reliability, accessibility, and ease of administration (Fauzi et al., 2021). DASS-21 was also reported to have high internal consistency and yield meaningful discriminations; hence this scale is suitable for the purpose of research (Beaufort et al., 2017).

DASS-21 is the short form of the DASS-42 that consists of 21 items, 7 items per subscale: depression, anxiety, and stress. This instrument can measure all the psychometric characteristics required for depression, anxiety, and stress. Depression subscale assesses depressed mood, low self-esteem, and a pessimistic perspective on the future, anxiety subscale includes psychological arousal and the fear response, while stress subscale corresponds to constant stimulation and tension. Each item will be rated by participants on a scale of 0 (did not apply to me at all) to 3 (applied to me very much). Sum scores are calculated by adding the scores from each subscale item and multiplying them by a factor of two. The results are then classified into five levels of severity based on specific score values, as shown in Table 1. Mild to extremely severe outcomes are classified as abnormal, implying depression, anxiety, and stress.

Table 1. Severity scores of depressions, anxiety and stress.

	Depression	Anxiety	Stress
Normal	0 - 9	0 - 7	0 - 14
Mild	10 - 13	8 - 9	15 - 18
Moderate	14 - 20	10 - 14	19 - 25
Severe	21 - 27	15 - 19	26 - 33
Extremely severe	28+	20+	34+

Data analysis

The Statistical Package for the Social Sciences (SPSS) version 20 software was used for the entire statistical analysis of the study. Descriptive statistics on median, interquartile range (IQR), frequency, and percentage were provided to present the demographic characteristics, as well as the depression, anxiety, and stress scores. For differences testing, the nonparametric test was used since the data is not normally distributed. Mann-Whitney U test was used to compare DASS-21 scores with gender, and Kruskal-Wallis H was used to compare DASS-21 scores with the year of study and departments.

RESULTS

Demographic Characteristics of the Participants

A total of 534 out of the 626 invited participants had completed the questionnaire, representing an 85.3% response rate. Participants ranged from the first to the fourth study year, with females accounting for most respondents (83.3%). Table 2 shows more details on the demographic characteristics of the studied participants.

Table 2. Demographic characteristics of the studied participants (n = 534).

Characteristics	Category	Frequency	%
Gender	Male	89	16.7
	Female	445	83.3
Year of Study	Year 1	177	33.1
	Year 2	133	24.9
	Year 3	126	23.6
	Year 4	98	18.4

Department / Course of Study	DASLP	86	16.1
	DBMS	149	27.9
	DDIR	63	11.8
	DNS	105	19.7
	DOVS	79	14.8
	DPRS	52	9.7

Overall severity of depression, anxiety, and stress

Anxiety (65.5%) was the most common type of mental disorder among participants, followed by depression (47%), and stress (33.3%). Frequencies and percentages of the intensity of DASS scores among the participants are shown in Table 3. More than half of the respondents (56.4%) reported moderate to extremely severe anxiety, and the remaining 233 (43.6%) participants were under the 'normal-mild' category. About three-fourths of the respondents (71.9%) were under the 'normal-mild' category of depression. The remaining 150 (28.1%) respondents fell under the 'moderate-extremely severe' category. For stress, majority of the respondents (81.1%) belonged to the 'normal-mild' category while the rest fell under 'moderate-extremely severe' (18.9%) categories.

Table 3. Frequencies and percentages of DASS-21 severity scales.

	Depression 8 (4 - 14)		Anxiety 10 (6 - 16)		Stress 12 (6 - 18)	
Severity	Frequency	%	Frequency	%	Frequency	%
Normal	283	53.0	184	34.5	356	66.7
Mild	101	18.9	49	9.2	77	14.4
Moderate	105	19.7	140	26.2	73	13.7
Severe	24	4.5	84	15.7	20	3.7
Extremely severe	21	3.9	77	14.4	8	1.5

Associations between depression with different demographic characteristics

Mann-Whitney U test showed that the p-values were >0.05 (U = 17499, p = 0.082), indicating no significant difference in depression scores between male and female participants (Table 4). A Kruskal-Wallis H test revealed no statistically significant difference between the year of study, $X^2(3)$ = 2.951, p = 0.399, with a mean rank of 261.19 for Year 1, 254.01 for Year 2, 281.87 for Year 3, and 278.73 for Year 4. When comparing the depression score between departments, the Kruskal-Wallis H test revealed there was a statistically significant difference, $X^2(5)$ = 13.123, p = 0.022, with a mean rank of 238.00 for DASLP, 257.99 for DBMS, 275.27 for DDIR, 252.77 for DNS, 309.58 for DOVS, and 299.95 for DPRS. Further analysis was done to determine the significant pairs between the departments. Dunn-Bonferroni post hoc test revealed that there was statistically significant difference between DOVS and DASLP (p = 0.042).

Table 4. Distribution of median score with IQR for depression score.

Characteristics	Median (IQR)	p-value
Gender		0.082
Male	10.0 (5.0 – 16.0)	
Female	8.0 (4.0 – 14.0)	

Year of Study			
	Year 1	8.0 (4.0 -12.0)	
	Year 2	6.0 (4.0 – 16.0)	0.339
	Year 3	10.0 (4.0 - 14.5)	
	Year 4	10.0 (4.0 – 14.0)	
Department			0.022
	DASLP	7.0 (4.0 – 12.0)	
	DBMS	8.0 (4.0 – 14.0)	
	DDIR	8.0 (4.0 – 16.0)	
	DNS	8.0 (4.0 – 12.0)	
	DOVS	12.0 (6.0 – 16.0)	
	DPRS	10.0 (4.5 – 16.0)	

Associations between anxiety with different demographic characteristics

Table 5 presented the distribution of the median score with IQR for anxiety score. Mann-Whitney U test showed that the p-values were >0.05 (U = 19764, p = 0.977), indicating no significant difference in anxiety scores between male and female participants. There was no statistically significant difference in anxiety score between the year of study when compared using the Kruskal-Wallis H test, $X^2(3) = 1.743$, p = 0.627, with a mean rank of 274.10 for Year 1, 259.62 for Year 2, 276.31 for Year 3, and 254.94 for Year 4. On the other hand, the Kruskal-Wallis H test revealed there was a statistically significant difference in anxiety scores between departments, $X^2(5) = 18.452$, p = 0.002, with a mean rank of 216.55 for DASLP, 287.61 for DBMS, 300.89 for DDIR, 252.57 for DNS, 290.38 for DOVS, and 249.08 for DPRS. Further analysis was done to determine the significant pairs between the departments. Dunn-Bonferroni post hoc test revealed that there was statistically significant difference between DASLP and DDIR (p = 0.014).

Table 5. Distribution of median score with IQR for anxiety score.

Characteristics		Median (IQR)	p-value
Gender			0.997
	Male	10.0 (6.0 – 16.0)	
	Female	10.0 (5.0 – 16.0)	
Year of Study			0.627
	Year 1	10.0 (6.0 – 16.0)	
	Year 2	10.0 (4.0 -16.0)	
	Year 3	10.0 (5.5 – 16.0)	
	Year 4	10.0 (4.0 – 16.0)	
Department			0.002
	DASLP	8.0 (4.0 – 14.0)	
	DBMS	12.0 (6.0 – 18.0)	
	DDIR	10.0 (6.0 – 18.0)	
	DNS	10.0 (4.0 – 16.0)	
	DOVS	10.0 (8.0 – 18.0)	
	DPRS	10.0 (4.0 – 16.0)	

Associations between stress with different demographic characteristics

Mann-Whitney U test showed that the p-values were >0.05 (U = 19351, p = 0.733), indicating that there was no significant difference in stress scores between male and female participants. When comparing the stress score between the year of study, the Kruskal-Wallis H test showed no significant difference, $X^2(3) = 2.094$, p = 0.553, with a mean rank of 266.35 for Year 1, 259.11 for Year 2, 283.96 for

Year 3, and 259.81 for Year 4. The same test also revealed that there was no significant difference in stress scores between departments ($X^2(5) = 9.568$, $p = 0.088$), as shown in Table 6.

Table 6. Distribution of median score with IQR for stress score.

Characteristics	Median (IQR)	p-value
Gender		0.733
Male	12.0 (6.0 – 17.0)	
Female	12.0 (6.0 – 18.0)	
Year of Study		0.553
Year 1	12.0 (6.0 – 17.0)	
Year 2	10.0 (6.0 – 16.0)	
Year 3	12.0 (6.0 – 18.0)	
Year 4	12.0 (6.0 – 16.0)	
Department		0.088
DASLP	10.0 (6.0 – 14.0)	
DBMS	12.0 (8.0 – 18.0)	
DDIR	12.0 (6.0 – 18.0)	
DNS	12.0 (6.0 – 17.0)	
DOVS	14.0 (10.0 – 18.0)	
DPRS	12.0 (6.0 – 18.0)	

DISCUSSION

Undergraduate education is a critical and complex developmental stage in which many undergraduate students struggle with mental health issues that affect both their health and academic performance (Wyatt & Oswalt, 2013; Fauzi et al., 2021; Liew et al.,2021). This study focused on the prevalence of depression, anxiety, and stress, as well as the severity of the symptoms among undergraduate allied health sciences students in KAHS, IIUM. Among the three subscales, stress was the least severe, and depression exhibited a similar pattern to the stress category. However, the anxiety subscale raised more concern, as more than half of the respondents (56.4%) were classified as 'psychologically distressed'. In detail, this study found the prevalence of depression, anxiety and stress among allied health sciences students using DASS-21 as 47%, 65.5%, and 33.3%, respectively, which is consistent with previous studies (Nahas et al., 2019; Meim et al., 2021; Thing et al., 2022). As definition, anxiety is defined as an unpleasant feeling of fear or discomfort particularly due to something unknown or triggered by strange event or uncertainty (Allen et al., 1995; Lopes et al., 2020). In general, the possibility of having anxiety among young adults do exist especially during the transition into higher education with different environments of teaching and learning as well as social routine in campus life. According to the World health Organization (WHO), anxiety is also considered one of the symptoms of depression, and when it reaches an extreme level, it may contribute to feelings of suicidality.

No significant difference in DASS score between male and female students was found (Rahman et al., 2019; Muhammad et al., 2019; Wong et al., 2023), though male students show slightly higher median score of depression (Rahman et al., 2019). However, Hamaideh et al., (2021) reported that Jordanian female university students had higher scores in depression, stress, and anxiety than male students. Previous studies stated that females were more likely to experience mental health problems due to different coping and adaptation strategies that did not help them control their psychological disturbances, attributed to hormonal changes and increased sensitivity to interpersonal relationships (Hamaideh et al., 2021; Rahman et al., 2019). However, individuals' coping responses to the changes in the life cycle stages are reliant on their capacity to adapt, and this may not be solely attributed to gender.

Further analysis has been conducted comparing DASS scores between pre-clinical and clinical year students. Though the is no specific definition on the term used, this study classify as year 1 and year 2 as pre-clinical years and year 3 and year 4 as clinical years. DASS score does not shows any significant effect between year of study in this study. However, anxiety consistently shows higher median value. Depending on factors that affects the scores, Muhammad et al., (2019) mentioned that even though there is no significant effect on level of study, but pre-clinical students are more likely to have some stress on inter- and intrapersonal related which might relate to anxiety. Chan et al., (1994) reported that anxiety might be due to the transition of level of study from theory to practical. Meanwhile, Rahman et al., (2019) reported that the symptoms of depression are more likely in final-year students (clinical year) since they concern about their future career pathway after graduating from university. Plexico et al., (2017) found that anxiety levels decreased as students advanced through the year of study (pre-clinical to clinical year) due to higher confidence in their clinical skills.

Next, the result of this study revealed that there is a significant of depression and anxiety level between the department within KAHS. Optometry students significantly shows higher depression score as compared to Audiology students, and Radiography students significantly shows higher anxiety score as compared to Audiology students. Remarkably, Audiology students consistently exhibit lower DASS scores. Vorster et al. (2022) concluded that almost half of their participants i.e., optometry students were identified with depressive symptoms, and this finding was similar to that study conducted by Turnbull et al. (2021). Based on the evidence currently available, it seems fair to suggest that optometry students reported a high amount of depression. On the other hand, Radiography students shows significant more anxiety feeling as compared to Audiology students. There are several factors that might contribute to an emotional challenge more likely in transition from theory to practical, first clinical placement, clinical placement rotation which identify as stressful situation among diagnostic radiographer students elsewhere (Emma, 2015; Girn, Punch & Jimenez, 2022; Jeyandrabalan et al.,2022). It was predicted that perhaps due to the differences of academic related matters such as clinical hours involving in clinical training and clinical placement or perhaps higher academic workload stipulated in curriculum, mode of assessments and professional examination across the department would contribute to the results. Besides, preparedness of the students facing any academic related challenge also might contribute to better wellbeing.

CONCLUSION

This study revealed that, in general, KAHS students had a moderate level of depression, anxiety and stress (based on DASS-21 questionnaires). A substantial number of students showed abnormal DASS scores, particularly anxiety. This study found a significant level of depression in Optometry students and a significant level of anxiety in Radiography students. Although the current study did not investigate why this pattern occurs, previous studies had indicated that these could be due to the difference in the academic related matters. While the DASS-21 is not intended for diagnostic purposes, the presence of moderate to severe symptoms of depression, anxiety or stress signals the necessity for proactive strategies and support from the department or kulliyyah. This assistance is vital to address these issues effectively, promoting the student's mental well-being and in turn enhancing their academic performance.

ETHICAL APPROVAL

There is no conflict of interest in this study, and we did not receive any specific grant or funding. The study adhered to the tenets of the Helsinki Declaration involving human subjects and received ethical approval from the IIUM Research Ethics Committee (IREC), with ethical approval number IREC 2022 KAHS/DOVS/9.

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DRY EYE AND SLEEP QUALITY AMONG UNDERGRADUATE KAHS STUDENTS, IIUM KUANTAN

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ABSTRACT

Introduction: Dry eye disease (DED) is one of the most common ocular diseases that could be caused by either a decrease in tear production and/or an increase in the tear evaporation rate. DED can cause eye irritation, grittiness, blurred vision, and light sensitivity, negatively affecting individuals' quality of life. Poor sleep quality has become a common public health issue worldwide. It is reported decreased sleep quality are highly prevalent among individuals with DED and poor sleep quality can worsen DED symptoms. **Aim:** The purposes of this study was to observe the prevalence of DED and poor sleep quality in a sample of university students, to investigate the relationship between sleep quality and DED and to investigate if gender leads to differences in DED and sleep quality. **Methodology:** This cross-sectional study involved undergraduate students from Kulliyyah of Allied Health Science (KAHS), International Islamic University Malaysia (IIUM), Kuantan. Validated questionnaires, consisting of the Ocular Surface Disease Index (OSDI), were used to diagnose DED, and Pittsburgh Sleep Quality Index (PSQI) questionnaire was utilised to assess sleeping quality. Data collection and analysis were performed using the SPSS Statistics software (IBM, Armonk, NY). **Results:** A total of 148 undergraduate KAHS students of IIUM Kuantan participated in the study. Approximately 63.5% of the participants had DED, and 60.1% had poor sleep quality. The relationship between DED and poor sleep quality indicated a significant positive correlation. This study also revealed that females are more prone to DED and poor sleep quality compared to males. **Conclusion:** This study showed that participants with DED had a greater risk of poor sleep quality compared to non-DED and vice versa. Individuals with DED should be educated about the methods to improve their sleep patterns. Intervention and awareness to achieve good sleep quality also should be advocated to alleviate the occurrence of DED.

KEYWORDS: DED, sleep quality, OSDI, PSQI

INTRODUCTION

Dry eye disease (DED) is a multifactorial ocular surface and tear film disease that affects millions of people worldwide, with prevalence rates varying from 5% to 50% in different populations (Helayel et al., 2023; McCann et al., 2022; Papas, 2021; Rouen & White, 2018; Schjerven, Paaske, Snieder, Hammond, & Vehof, 2021). DED is a common ocular surface condition that causes eye irritation, grittiness, and vision problems (Hakim & Farooq, 2022; Mushriff, Agarwal, & Choyal, 2019; Zemanová, 2021). In addition to the symptoms above, individuals with DED also suffer ocular pain, blurred vision, light sensitivity and ocular burning, and they also experience a lower quality of life, with limited involvement in both work and social events, as well as difficulties with daily tasks like reading, watching television and driving (Guo & Akpek, 2020; Sayegh et al., 2021; Schjerven et al., 2021). The DED could be caused by either a decrease in tear production and/or an increase in tear evaporation rate, which causes ocular surface inflammation and, ultimately, leads to the destabilisation of the cornea–tear interface (Yu et al., 2019).

Sleeping is essential for well-being and general health (Wen et al., 2019). Sleep deficiency has become a common public health issue worldwide and was found to be due to shortened sleep periods, erratic sleep timing, poor sleep quality and sleep/circadian disturbance (Albqoor & Shaheen, 2021; Eleftheriou, Rokou, Arvaniti, Nena, & Steiropoulos, 2021; S. Li et al., 2018). Sleep deprivation has been linked to significant impairments in cognitive ability and attentiveness (Lee, Koh, Hyon, Wee, & Kim, 2014). Poor quality and short sleep duration have been shown to reduce the quality of life (Schjerven et al., 2021). In addition, previous studies had established that sleep deprivation impairs autonomic and endocrine functions, resulting in extensive changes in many parts of the body system and that sleep disorder is associated with an increased risk of diabetes, hypertension, and depression (Yu et al., 2019).

Alarmingly, recent studies had highlighted a possible association between sleep dysfunction and DED (Magno et al., 2021; Wen et al., 2019; Zhu et al., 2022). Further, the correlation between DED and sleep quality has recently received more attention due to the higher prevalence of DED and poor sleep quality in the general population (Yu et al., 2019). As such, this study investigated the occurrence of DED and poor sleep quality and signify if there was any relationship between the variables in a sample of university students. University students were chosen as the study population for DED because there were limited number of studies conducted on this population (Supiyaphun, Jongkhajornpong, Rattanasiri, & Lekhanont, 2021). Several studies also reported that females have a higher prevalence of DED and have poorer sleep quality than males (Ayaki et al., 2018). Therefore, this study will attempt to investigate this phenomenon to see if such trends exist.

MATERIALS AND METHODS

Study design and sample size

This study is a questionnaire-based, cross-sectional study design which consist of Kulliyyah of Allied Health Sciences (KAHS), International Islamic University Malaysia (IIUM) undergraduate students. Approximately 148 students (74 males and 74 females) from KAHS, were recruited using the convenience sampling technique. The sample size was considered adequate based on the Central Limit Theorem and its implications for sample size determination (Gravetter & Wallnau, 2013; Hays, 1988; Kirk, 1996; Maxwell & Delaney, 2004). An online questionnaire via Google Form was distributed among the students through Whatsapp, email and QR-code.

Data collection

This study complies with the Declaration of Helsinki (World Medical Association, 2013) and ethical approval was obtained from IIUM Research Ethics Committee (IREC). Informed consent was obtained from all participants prior to data collection. The inclusion criteria for this study were (i) undergraduate students of Kulliyyah Allied Health Sciences and (ii) aged between 19-25 years old. Participants with systemic diseases, history of refractive surgery and disorders of lid margin, nasolacrimal duct or cornea were excluded.

The Ocular Surface Disease Index (OSDI) questionnaire was used to diagnose DED (Yu et al., 2019), and the Pittsburgh Sleep Quality Index (PSQI) questionnaire was used to assess the sleeping quality (Schjerven et al., 2021).

a. The Ocular Surface Disease Index (OSDI) Questionnaire

The OSDI questionnaire is a validated questionnaire that is widely used to assess the self-reported severity of dry eye (Yu et al., 2019). The OSDI consists of 12 questions covering three subscales: ocular discomfort (OSDI-symptoms), which includes symptoms such as gritty or painful eyes; functioning (OSDI-function), which measures limitations in performance of typical activities such as reading and working on a computer; and environmental triggers (OSDI-triggers), which measures the impact of environmental triggers, such as wind or drafts, on dry eye symptoms (Cho et al., 2015). All three subscale scores were computed as an overall averaged scores (Cho et al., 2015). Based on the average OSDI scores, participants were classified into different severities of DED: normal, non-DED (scores 0–12), mild (scores 13–22), moderate (scores 23–32), and severe (scores 33–100) (Yu et al., 2019). OSDI scores of 0-12 is normal or non-DED and scores >12 is considered as having DED with different severity (Yu et al., 2019).

b. The Pittsburgh Sleep Quality Index (PSQI) Questionnaire

The PSQI is the most frequently used validated questionnaire for assessing sleep quality in clinical and research settings (Schjerven et al., 2021). It is an effective and valuable tool for measuring subjective sleep quality and sleep disturbances such as insomnia (Kawashima et al., 2016). This self-reported questionnaire assesses the average sleep quality of an individual over the last month (Schjerven et al., 2021). It consists of 19 questions in seven domains: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction (Kawashima et al., 2016; Schjerven et al., 2021; Yu et al., 2019). The scores for each component ranges from 0 to 3, and the sum of the scores of these seven components provided a global PSQI scores that ranged from 0 to 21 (Kawashima et al., 2016). Poor sleep quality is defined as PSQI scores >5 (Schjerven et al., 2021).

Data analysis

The data analysis had been conducted using Statistical Package for the Social Sciences (SPSS) version 22.0 (IBM Corp., Armonk, NY, USA). Based on the histogram and Kolmogrov-Smirnov, all the parameters were not normally distributed ($p<0.05$) (Mishra et al., 2019). The Kolmogrov-Smirnov was chosen to assess the normality because the sample size in this study is larger ($n \geq 50$) (Mishra et al., 2019). Since all the data was non normally distributed, non-parametric tests were used to analysed the data. The prevalence of DED and sleep quality was analysed using descriptive analysis (Schjerven et al., 2021). The association between DED and sleep quality was analysed using correlation coefficient (Almutairi et al., 2022). The difference in DED and sleep quality between males and females was evaluated using the non- parametric test, Mann-Whitney U test (Karadimitriou, Marshall Reviewer, &

Knox Sheffield, 2022). A p-value of < 0.05 is considered statistically significant (Prajapati, Dunne, & Armstrong, 2010).

RESULTS

Demographic data

A total of 148 of undergraduate KAHS students of IIUM Kuantan participated in the study. Of the 148 participants, males constituted 50% (n=74) and females constituted 50% (n=74). Approximately 35.8% (n=53) of the participants were spectacle wearers and 9.5% (n=50) used contact lenses. None of the participants had history of refractive surgery, eye disorder or systemic disorder. Therefore, all participants met the inclusion criteria and were included in the analysis. Table 1 describes the demographic data of the study participants.

Table 1 Demographic data of study participants

Demographic data		Number of participants (n)	Percentage (%)
Gender	Male	74	50
	Female	74	50
	Total	148	100
Year of study	1	27	18.2
	2	28	18.9
	3	33	22.3
	4	60	40.5
	Total	148	100
Corrective measures	Spectacles	53	35.8
	Contact lenses	14	9.5
	Refractive surgery	0	0
	Not applicable	81	54.7
	Total	148	100
Previous eye disorder	Yes	0	0
	No	148	100
	Total	148	100
Previous systemic disorder	Yes	0	0
	No	148	100
	Total	148	100

Prevalence of DED and Poor Sleep Quality

The prevalence of DED and sleep quality were analysed using descriptive analysis. Overall, 63.5% (n=94) from 148 of the participants had a scores of OSDI more than 12 indicating the presence of DED. Among the 94 participants who had DED, 43.6% (n=41) were males and 56.4% (n=53) were females. For sleep quality, 60.1% (n=89) of the participants had a scores of PSQI of more than 5, indicating poor sleep quality. Among the 89 participants with poor sleep quality, 40.4% (n=36) were males, and 59.6% (n=53) were females. Table 2 shows the prevalence of DED and poor sleep quality in this study.

Table 2 Prevalence and Frequency of DED and poor sleep quality

Category	Frequency (n)	Prevalence (%)
DED (OSDI scores >12)*		
Total of population	94	63.5%
Male	41	43.6%
Female	53	56.4%

Poor Sleep Quality (PSQI scores >5)^		
Total of population	89	60.1%
Male	36	40.4%
Female	53	59.6%

* *A presence of DED is considered when the OSDI scores is >12.*

^ *A presence of Poor Sleep Quality is considered when the PSQI scores is >5.*

Association between DED and sleep quality

A Spearman's correlation coefficient was performed to assess the relationship between DED using OSDI scores and sleep quality using PSQI scores (Prajapati et al., 2010). Preliminary analysis showed the relationship to be monotonic, as assessed by visual inspection of a scatterplot in Figure 1. There was a statistically significant but weak positive correlation between OSDI scores and PSQI scores (r^2= 0.264, p= 0.001).

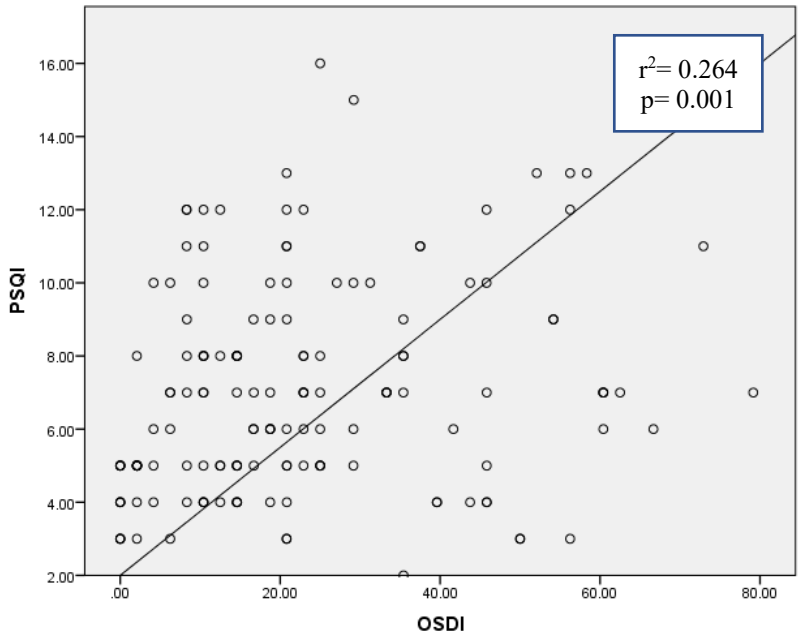


Figure 1 Correlation between OSDI scores and PSQI scores

Difference of DED and sleep quality between males and females

As suggested by Karadimitriou et al. (2022), Mann-Whitney U test was run to determine if there were differences in DED (presence or absence of DED based on OSDI scores) and poor sleep quality between males and females. Distributions of the OSDI scores for males and females were not similar, as assessed by visual inspection in Table 4. OSDI scores for females (mean rank = 85.18) were statistically significantly higher than for males (mean rank = 63.82), U = 1947.5, z = -3.034, p= 0.002 using an exact sampling distribution for U (Dinneen & Blakesley, 1973).

As for sleep quality, distributions of the poor sleep quality through PSQI scores for males and females were not similar, as assessed by visual inspection in Table 4. PSQI scores for females (mean rank = 84.11) were statistically significantly higher than for males (mean rank = 64.89), U = 2027, z = -2.748, p= 0.006 using an exact sampling distribution for U (Dinneen & Blakesley, 1973).

Table 4 The difference in DED and poor sleep quality across gender

	Gender	Mean Rank	U	z- score	p-value
OSDI scores	Female	85.18	1947.5	-3.034	0.002
	Male	63.82			
PSQI scores	Female	84.11	2027.0	-2.748	0.006

	Male	64.89

DISCUSSION

In this study, 63.5% of the participants had DED, and 60.1% had poor sleep quality (Table 2). A previous study by Sundar (2020) reported that 64.1% of engineering students studying at Saveetha Engineering College had DED, and 64.9% had poor sleep quality. Thus, our results were similar with regard to the prevalence of DED and poor sleep quality obtained from their study.

This cross-sectional study revealed a statistically significant but weak positive correlation between poor sleep quality and DED. Previous studies have shown that the association between poor sleep quality and DED is likely complex and bidirectional (Schjerven et al., 2021). Recent studies on sleep and DED have indicated that patients with DED have poorer sleep quality and that patients with sleep disorders are more likely to have DED (Schjerven et al., 2021).

Several studies speculated that DED could lead to poorer sleep quality (Ayaki et al., 2018; A. Li et al., 2022; Yu et al., 2019). Schjerven et al. (2021) reported that patients with DED had significantly poorer sleep quality across all the demographic data and this association persisted even after treatment for other related diseases. According to Schjerven et al. (2021), DED patients from Northern Europe were one and a half times more likely to be poor sleepers, and therefore, DED was found to be strongly correlated with reduced sleep quality. Patients with DED experience deteriorated quality of life, resulting in depression, anxiety, and sleep disorders, and it also has been shown that DED treatment can improve sleep quality (Yu et al., 2019). It is speculated that a psychological component, particularly depression due to DED, might be a major contributor to sleep disorder (Ayaki et al., 2016). Insomnia or sleeplessness could be triggered by dry eye symptoms and ocular pain due to nocturnal eye discomfort and its associated psychological distress that may interfere with sleep initiation (Galor, Seiden, Park, & Feuer, 2018).

This study indicated that the association is two-dimensional, indicating that poor sleep quality can also lead to DED. Several studies claimed that poor sleep quality could lead to DED (Kawashima et al., 2016; Lee et al., 2014; Wen et al., 2019; Yu et al., 2019). Poor sleep quality has been identified as one of the risk factors for DED (Kawashima et al., 2016). The lacrimal glands, which produce tears, are innervated by parasympathetic and sympathetic nerves (Mushriff et al., 2019). It is biologically reasonable that poorer sleep quality can result to dry eye because sleep disorders tend to be related to autonomic dysfunction, which affects the parasympathetic fibres in the lacrimal glands and decreases tear secretion (S. Li et al., 2018; Yu et al., 2019). Sleep deprivation induces a reduction in tear secretion, increases the tear osmolarity and shortens the tear film break-up time, which later can result in ocular surface diseases, primarily DED (Mushriff et al., 2019).

Furthermore, the current study had revealed that females are more prone to DED and poor sleep quality compared to males. There were statistically significant differences in OSDI and PSQI scores between males and females (Table 4). A study by Ayaki et al. (2018), reported that DED and sleep disorders were more prevalent in females than males, which agrees with this study. Females have been recognised as one of the risk factors for DED (Wen et al., 2019). Sex hormones play a major role in regulating ocular surface and adnexal tissues, contributing to the difference in DED prevalence between females and males (Versura, 2019). The results from Ayaki et al. (2016), indicate that sleep quality also deteriorated in women with DED. Individuals with DED have been shown to be depressed, and depression was a common psychological issue in women and is closely related to sleep disorders (Ayaki et al., 2016).

There are several strengths that can be highlighted in this study. As validated questionnaires were used to measure both DED and sleep quality, the data provided were reliable and solid on both outcome variables (Schjerven et al., 2021). Besides, this study also took into account all factors that might influence the DED and poor sleep quality in which several conditions such as history of refractive surgery, systemic diseases and eye disorder were excluded (Mushriff et al., 2019). Hence, these strengths lead to more reliable data and conclusions.

Nevertheless, the current study has several limitations. Since validated questionnaires were used to diagnose DED and poor sleep quality, the results possibly may have been influenced by some personal biases, whereby participants may not have answered all the questions honestly (Almutairi et al., 2022).

In addition, there was also a possibility that they did not fully understand the questions or some terms. Therefore, future research should be conducted by implementing objective tools to evaluate DED and poor sleep quality instead of just relying on questionnaires. In addition, the inclusion criteria of this study also resulted in a small study sample. A larger, prospective studies focusing on sleep quality and DED parameters are needed in order to establish a greater understanding of the impact of sleep quality on DED and vice versa (Schjerven et al., 2021).

CONCLUSION

In conclusion, this study found that DED had a significant positive correlation with poor sleep quality. Therefore, individuals with DED will have a greater risk of poor sleep quality compared to healthy individuals. Females also tend to develop DED and poor sleep quality compared to males. Individuals with DED should be educated on the techniques to improve their sleep patterns. Intervention and awareness to achieve good sleep quality should be advocated to alleviate the occurrence of DED. Since there were 63.5% of KAHS students had DED and 60.1% had poor sleep quality, awareness regarding DED and sleep quality should be further educated among the students to ensure their wellbeing. However, further studies are required to determine the directionality of this correlation and the efficacy of sleep hygiene interventions in alleviating DED and whether intensive DED alleviation methods could successfully improve sleep quality.

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IMMEDIATE EFFECTS OF ARTIFICIAL TEARS VISCOSITY AND PH ON OCULAR SIGNS AND SYMPTOMS

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ABSTRACT

Purpose: To evaluate the short-term effects of artificial tears (ATs) with different viscosity and pH; Systane® Hydration preservative (SH) and non-preservative (SHUD), Optive® preservative (O) and non-preservative (OUD) on patients' signs and symptoms in normal and dry eye (DE) groups.
Methods: 120 participants (55: DE group, 65: normal group) involved in this prospective, double-masked randomized study. Rheometer and digital pH-meter were used to evaluate the viscosity and pH of all ATs. Ocular discomfort between pre and post-instillation (after 60 minutes interval) was evaluated using Ora Calibra™ Ocular Discomfort and 4-Symptom Questionnaire (OOD4SQ). Drop comfort immediately assessed after ATs instillation using Ora Calibra™ Drop Comfort Scale (ODCS). Tear break-up time (TBUT) and tear meniscus height (TMH) were measured at baseline, 5, 15 and 60 minutes after instillations. Tear ferning pattern (TFP) were observed and compared at baseline and 60 minutes after instillation.
Results: Viscosity of all ATs were; SHUD: 32.73cP, SH: 26.7cP, OUD: 14.42cP and O: 13.88cP with pH of 7.74 (SHUD), 7.85 (SH), 7.19 (OUD) and 7.24 (O). Highest DCS was found in SH for both DE (2.00±1.042) and normal group (1.84±0.963). Significant reduction ($p<0.05$) in all parameters of ocular symptoms (OOD4SQ) were found after instillation of OUD in both groups. TBUT and TMH for both groups increased significantly ($p<0.05$) from baseline at all time-interval (except TBUT for O in normal group at 5 minutes post-instillation). TFP improved significantly after 60 minutes instillation of all ATs in both groups.
Conclusion: All ATs improved TBUT, TMH and TFP in both groups, regardless their viscosity and pH. OUD showed better ocular symptoms improvement and less subjective sensation compared to other tested ATs.

Keywords: artificial tears, ocular symptoms, pH, viscosity

INTRODUCTION

Artificial tears is one of the favorable treatment modalities among eye care practitioners to treat ocular surface problems such as dry eye (Asiedu et al., 2016) due to their availability in the market with affordable price, easy to use with simple steps and proven to improve and rejuvenate the ocular surface affected from dry eye (Torkildsen et al., 2017). Furthermore, artificial tears is available over-the-counter, in which the patient can easily buy the products, even without the prescription from medical personnel. Despite being the preferable treatment among eye care practitioner in managing dry eye, it is quite difficult for the eye care practitioner to prescribe the most effective artificial tears that can improve both signs and symptoms of dry eye as there are variety of brands and formulations available in the market.

Different artificial tears are formulated with different chemical components such as lubricants, polymers, solutes, electrolytes and with or without preservatives (Torkildsen et al., 2017; Che Arif et al., 2020; Che Arif et al., 2021). All these components have their own functions that contribute to the efficacy of artificial tears, and at the same time will affect the physical properties, which is also an important factor that may affect the bioavailability of artificial tears (Aragona et al., 2019; Araújo et al., 2016). Hyaluronic acid (HA) and carboxymethylcellulose (CMC) are the common lubricants used in artificial tears formulation due to their great ability in alleviating both subjective and objective signs and symptoms of dry eye (Song et al., 2017; Cagini et al., 2017; Salzillo et al., 2016; Che Arif et al., 2023).

However, it is still unclear on what factors actually lead to the improvement in term of signs and symptoms of ocular discomfort; chemical component, physical components, or both factors. While chemical components usually being listed on the leaflet, information on physical properties of artificial tears rarely being disclosed by the manufactures even though this information may be beneficial in guiding the eye care practitioners and patients in choosing the suitable artificial tears based on ocular conditions. Viscosity and pH are among physical properties of artificial tears which worth to be investigated thoroughly as viscosity anecdotally known to be associated with tear retention time, while pH was believed to affect the ocular sensation after instillation in the case of large discrepancy in pH unit between artificial tears and natural tear pH (Salzillo et al., 2016; Baranowski et al., 2014; Che Arif et al., 2023). As these factors seem to affect the performance of artificial tears in improving the signs and symptoms of dry eye, hence this study would like to observe if artificial tears with different viscosity and pH will performed differently in improving signs and symptoms of dry eye.

MATERIALS AND METHODS

This prospective, double-masked randomized study conducted at International Islamic University Malaysia Eye Specialist Clinic (IESC). A total of 55 mild to moderate dry eye

participants, along with 65 normal participants were recruited in this study. Written informed consents were obtained from all participants prior to study procedures. The study procedures were reviewed and approved by the International Islamic University Malaysia (IIUM) Research Ethics Committee (IREC 2019-125).

Inclusion criteria for this study were; participants who were having good ocular and general health, aged between 20 to 40 years old, have no known sensitivity or intolerance to any of the products used in this study, and non-contact lens wearer. Meanwhile those having these criteria; history of previous ocular trauma (Garcia-Lázaro et al., 2011), evidence of active ocular infection in either eye (Lambiase et al., 2017), significant underlying of ocular pathology affecting cornea and ocular surface such as recurrent pterygium (Hilmi et al., 2019; Hilmi et al., 2017), corneal opacity or irregularity (Hilmi et al., 2020; Che Azemin et al., 2016; Hilmi et al., 2019) and under treatment of drug affecting tearing (Torkildsen et al., 2017) were excluded from this study. For female participants who were in menstrual cycle, the data collection process was not conducted during that period as tear production and stability were affected due to hormonal changes in menstrual cycle (Gibson et al., 2017; Versura et al., 2007).

Measurement of artificial tears' viscosity and pH

Four artificial tears were used in this study; Systane® Hydration preservative (SH), Systane® Hydration non-preservative (SHUD), Optive® preservative (O) and Optive® non-preservative (OUD). Physical properties of artificial tears; viscosity and pH were measured using rheometer and compact pH meter, respectively. Thermo Scientific Rheometer (Model HAAKE RheoWin Version 3.61.0004, Thermo Fisher Scientific Inc, Massachusetts, US) was utilized to measure the viscosity of artificial tears while automated compact pH-meter (LAQUAtwin pH-meter pH33, Horiba Advanced Techno Co., Ltd., Shiga, Japan) was used for pH measurement.

Sample of artificial tear (1ml) was applied on the lower measuring plate of rheometer and upper plate was lowered until the gap between upper and lower plate was 1.000mm. The temperature of each sample was standardised to 25°C and measurement started as the upper plate started to rotate due to the torque applied (Che Arif et al., 2020). For this study, viscosity of each artificial tear was measured from shear rate of $10s^{-1}$ to $100s^{-1}$ using a 35mm plate sensor (ThermoFisher Scientific, 2017).

For pH measurement, a small amount of artificial tears (0.2ml) was dropped on the flat sensor of pH meter until it covered the entire surface. After pressing the measurement button, the instrument would automatically measure the pH of artificial tear. The average pH from three measurements for each sample was taken for analysis and prior to next measurements; the sensor of pH meter was cleaned using distilled water to avoid sample cross-contamination.

Evaluation of signs and symptoms before and after the instillation of artificial tears

All participants were required to answer the Ocular Surface Disease Index (OSDI) questionnaire (Allergan Inc, Irvine, CA, USA) and the score obtained from this questionnaire was used as the main reference to divide the participants into two groups, which were normal group; OSDI score < 13, and dry eye group ; OSDI score ≥ 13 (Doguizi et al., 2019; Wolffsohn et al., 2017; Che Arif et al., 2021). The other parameters involved in classifying the participants under dry eye group were; TBUT < 5 seconds (Li et al., 2018) and Schirmer test I ≤ 10 mm/5 minutes (Shah et al., 2017). Those participants who were having TBUT ≥ 5 seconds and Schirmer test I > 10 mm/5 minutes were classified under normal group and if there was any parameter that did not tally with the listed criteria, the main reference, OSDI score was used to determine the group.

Prior to baseline measurement, participants were asked to answer Ora Calibra™ Ocular Discomfort and 4-Symptom Questionnaire (OOD4SQ) (Ora Inc, Andover, MA, USA). This questionnaires comprise of five points; overall discomfort, burning, dryness, grittiness and stinging, with 0 to 5 scales in which 0 indicates no discomfort and 5 is the worst discomfort. Participants were asked to rate the severity on how their eyes felt at these two specific time; pre and 60 minutes post-artificial tears instillation.

Next, tear breakup time (TBUT), tear meniscus height (TMH) and tear ferning pattern (TFP) were assessed at baseline. The temperature and humidity of the examination room were kept constant at 20°C-24°C (Dutta et al., 2019) and 40%-50% (Markoulli et al., 2018), respectively. TBUT was recorded with a video camera mounted on digital high-definition slit-lamp biomicroscopy (Model SL 990, SLB Mega Digital Vision HR, Costruzione Strumenti Oftalmici, Italy). TBUT determination was later conducted by playing back the video recordings and TBUT was measured using stopwatch. Three measurements were taken and the mean value was recorded for analysis.

TMH measurement was conducted using Zeiss Visante ™ Optical Coherence Tomography (OCT) (Zeiss Meditec, Inc, Dublin, USA) in a dim-illuminated room. From the image obtained, TMH was defined as tear film height between the edge of the lower eyelid and the cornea (Rosmadi et al., 2019). 'All scans' protocol with 'Raw Image Mode High Resolution Corneal Scan' was selected in order to capture the image of tear film by focusing on lower eyelid at '6 o'clock' and the corneal refraction as reference (Rosmadi et al., 2019). The images captured from OCT were saved in Tagged Image File Format (TIFF), and being transferred to image analysis software, Image J Software (National Institutes of Health, USA) to quantify the TMH values by converting the known pixels of the image to unit of millimeter (mm); 1 pixel = 1.126 mm.

For TFP assessment, a sample of unstimulated tears was collected from temporal, lower tear meniscus of participant's eye using the glass microcapillary tube and allowed

to dry by evaporation for 5-10 minutes (Sharanjeet-Kaur et al., 2016). Microscopic appearance of the dried tear was observed under the light microscope (Ken-α-Vision Manufacturing, Inc., Missouri, USA) by using 10X magnification (Alanazi et al., 2019) and TFP observed were classified into four groups according to Rolando's tear ferning classification (Rolando et al., 2984). For the statistical analysis, the grading of TFP were based on the numerical-converted TFP grading with type I = 1.0, type II = 2.0, type III = 3.0 and type IV = 4.0 (Versus et al., 2007; Sharanjeet-Kaur et al., 2016).

After baseline measurements of TBUT, TMH and TFP, a drop of different artificial tears was instilled into the right eye, followed by the left eye for the other brand of artificial tears using a pipette with a constant volume of 60µl (Markoulli et al., 2018). Right after artificial tears instillation, participants graded the drop comfort using Ora Calibra™ Drop Comfort Scale (ODCS) (Ora Inc, Andover, MA, USA) based on 0-10 scale, in which 0 indicating very comfortable and 10 is very uncomfortable. After the instillation, TBUT and TMH were re-measured at 5, 15 and 60 minutes, while TFP was observed at 60 minutes post-artificial tears instillation.

Lastly, after 60 minutes artificial tears administration, participants were again required to answer the OOD4SQ in order to observe for any significant improvement in ocular symptoms after the artificial tears instillation. As there were four artificial tears used in this study, each participant were required to attend two visits, with at least 24 hours wash-out period between the visits (Markoulli et al., 2018; Rosmadi et al., 2019). Research randomizer software (https://www.randomizer.org/) was used to randomise the eyes and artificial tears to be used at each visit.

IBM SPSS Statistics for Windows, version 20 (IBM Corp., Armonk, N.Y., USA) was used to execute the statistical calculations, with p-value of 0.05 was set as the level of significance. Normality assumption for all the data was assessed using skewness and kurtosis of the distribution (Kim, 2013). Differences between pre and time-interval after the instillation (5, 15 and 60 minutes for TBUT and TMH, 60 minutes for TFP) of all artificial tears and differences of ocular symptoms (OOD4SQ) between baseline and after 60 minutes artificial tears administration were compared using Paired Sample T-test, while Repeated Measures One-way analysis of variance (RM-ANOVA) was employed to compare the TBUT and TMH between instillations of all the tested solutions at each time-interval. Descriptive analysis was employed to obtain the mean of drop comfort score of ODCS for each artificial tear.

RESULTS

Physical properties of artificial tears

Based on the findings, SHUD was found to have the highest viscosity (32.73 cP), followed by SH (26.7 cP) and OUD (14.42 cP), while O had the lowest viscosity (13.88 cP). pH measurements showed that pH of all artificial tears were alkaline; SHUD: 7.74, SH: 7.85,

OUD: 7.19 and O: 7.24. The viscosity and pH for all artificial tears were summarised in Table 1.

Table 1 Physical properties of artificial tears

Artificial tear brand	Manufacturer	Lubricants	Preservative	Viscosity (cP)	pH
Systane® Hydration	Alcon Laboratories Inc, Fort Worth, TX, USA	Sodium hyaluronate, Hydroxypropyl guar	Polyquaternium®-1 0.0011%	26.70	7.85
Systane® Hydration UD	Alcon Laboratories Inc, Fort Worth, TX, USA	Sodium hyaluronate, Hydroxypropyl guar	None	32.73	7.74
Optive®	Allergan Inc., Irvine, California, USA	Carboxymethylcellulose sodium 0.5%, Glycerin 0.9%	Purite	13.88	7.24
Optive® UD	Allergan Inc., Irvine, California, USA	Carboxymethylcellulose sodium 0.5%, Glycerin 0.9%	None	14.42	7.19

Signs and symptoms after artificial tears instillation

TBUT increased significantly in both groups for all artificial tears, except O in normal groups at 5 minutes of instillation (p= 0.135). For dry eye group, TBUT of all artificial tears kept increased up to 60 minutes of observation period, with highest values of TBUT was noted at this period. Meanwhile for normal group, highest increment of TBUT was observed at 15 minutes post-instillation. RM ANOVA analysis showed that mean TBUT differed significantly across the measurements after the instillation of all artificial tears, as shown in Table 2.

Table 2 Comparisons ofTBUT at different times between all artificial tears in dry eye and normal groups

Artificial tears	Groups	PRE Mean ± SD (sec)	5 min Mean ± SD (sec)	15 min Mean ± SD (sec)	60 min Mean ± SD (sec)	p value (RM ANOVA)
SH	Dry eye	4.14 ± 1.15	4.81 ± 0.82	4.69 ± 1.12	5.14 ± 1.20	**<0.001**
p value*		-	**<0.001**	**<0.001**	**<0.001**	
	Normal	6.00 ± 0.94	6.20 ± 0.77	6.27 ± 0.76	6.16 ± 0.83	**0.016**
		-	**0.037**	**0.002**	**0.033**	
SHUD	Dry eye	4.06 ± 1.07	4.78 ± 0.80	4.89 ± 0.95	5.28 ± 1.30	**<0.001**
p value*		-	**<0.001**	**<0.001**	**<0.001**	
	Normal	5.95 ± 0.96	6.16 ± 0.71	6.23 ± 0.83	6.11 ± 0.90	**0.014**
		-	**0.027**	**0.001**	**0.033**	
O	Dry eye	4.00 ± 1.12	4.69 ± 0.92	4.89 ± 1.12	5.08 ± 1.44	**<0.001**
p value*		-	**<0.001**	**<0.001**	**<0.001**	
	Normal	6.02 ± 0.88	6.16 ± 0.78	6.27 ± 0.79	6.18 ± 0.84	**0.032**
		-	0.135	**<0.001**	**0.033**	
OUD	Dry eye	4.17 ± 0.94	4.78 ± 0.80	4.86 ± 1.05	5.31 ± 1.24	**<0.001**
p value*		-	**<0.001**	**<0.001**	**<0.001**	
	Normal	5.86 ± 1.11	6.09 ± 0.86	6.23 ± 0.89	6.23 ± 0.83	**<0.001**
		-	**0.031**	**<0.001**	**<0.001**	

* p-value analysed using Paired sample T-test

Paired sample T-test in both dry eye and normal groups revealed that TMH values were significantly higher after the instillation of all artificial tears compared to baseline at every time points as demonstrates in Table 3. Higher TMH post-instillation indicated that all artificial tears were effective in increasing tear volume in both groups of participants. RM ANOVA findings indicated significant differences in TMH values after the instillation of SH, SHUD, O, as well as OUD at all-time intervals.

Table 3 Comparisons of TMH at different times between all artificial tears in dry eye and normal groups

Artificial tears	Groups	PRE Mean ± SD (mm)	5 min Mean ± SD (mm)	15 min Mean ± SD (mm)	60 min Mean ± SD (mm)	P-value (RM ANOVA)
SH	Dry eye	0.176 ± 0.040	0.200 ± 0.058	0.201 ± 0.042	0.198 ± 0.037	**<0.001**
P-value*		-	**0.002**	**<0.001**	**<0.001**	
	Normal	0.224 ± 0.037	0.238 ± 0.055	0.237 ± 0.043	0.234 ± 0.035	**<0.001**
		-	**0.001**	**<0.001**	**<0.001**	
SHUD	Dry eye	0.191 ± 0.056	0.213 ± 0.068	0.211 ± 0.054	0.216 ± 0.057	**<0.001**
P-value*		-	**<0.001**	**<0.001**	**0.001**	
	Normal	0.221 ± 0.034	0.242 ± 0.050	0.241 ± 0.048	0.235 ± 0.036	**<0.001**
		-	**<0.001**	**<0.001**	**<0.001**	
O	Dry eye	0.181 ± 0.042	0.201 ± 0.051	0.200 ± 0.043	0.201 ± 0.046	**<0.001**
P-value*		-	**<0.001**	**<0.001**	**<0.001**	
	Normal	0.223 ± 0.036	0.238 ± 0.053	0.240 ± 0.049	0.233 ± 0.038	**<0.001**
		-	**<0.001**	**<0.001**	**<0.001**	
OUD	Dry eye	0.185 ± 0.038	0.208 ± 0.051	0.216 ± 0.051	0.213 ± 0.048	**<0.001**
P-value*		-	**<0.001**	**<0.001**	**<0.001**	
	Normal	0.226 ± 0.038	0.248 ± 0.059	0.238 ± 0.045	0.238 ± 0.044	**<0.001**
		-	**<0.001**	**<0.001**	**0.002**	

* p-value analysed using Paired sample T-test

As for TFP, significant improvement was observed 60 minutes post-artificial tears instillation in both dry eye and normal groups in Table 4. However, dry eye group portrayed greater improvement compared to normal group. Lower baseline in normal

group might be the reason for the discrepancy between normal and dry eye group, with much improvement was noted in dry eye group as compared to normal group.

Table 4 Comparisons of TFP between baseline and after 60 minutes instillation of all artificial tears in dry eye and normal group

Artificial tears	Groups	Time of measurement	TFP (Type) Mean ± SD	P-value*
SH	Dry eye	Baseline	2.39 ± 1.050	**<0.001**
		Post-instillation	1.58 ± 0.692	
	Normal	Baseline	1.45 ± 0.548	**0.024**
		Post-instillation	1.34 ± 0.479	
SHUD	Dry eye	Baseline	2.36 ± 1.046	**<0.001**
		Post-instillation	1.44 ± 0.504	
	Normal	Baseline	1.43 ± 0.545	**0.044**
		Post-instillation	1.34 ± 0.479	
O	Dry eye	Baseline	2.33 ± 1.014	**<0.001**
		Post-instillation	1.47 ± 0.560	
	Normal	Baseline	1.45 ± 0.548	**0.024**
		Post-instillation	1.34 ± 0.479	
OUD	Dry eye	Baseline	2.36 ± 1.046	**<0.001**
		Post-instillation	1.47 ± 0.560	
	Normal	Baseline	1.43 ± 0.545	**0.024**
		Post-instillation	1.30 ± 0.509	

* p-value analysed using Paired sample T-test

In term of symptoms, participants in normal group rated all the artificial tears drops as comfortable, with low drop comfort score given for all artificial tears in both groups. However, for each artificial tear, higher drop comfort score was recorded in dry eye group compared to normal group, except for OUD. The highest mean score was observed after the instillation of SH, in both normal and dry eye groups. Table 5

summarizes the mean drop comfort score right after the instillation of all artificial tears in both groups.

Table 5 Drop comfort score determine using Ora Calibra™ Drop Comfort Scale (0-10 scale; 0 = most comfortable, 10 = most uncomfortable) in dry eye and normal groups

Artificial tears	Groups	Drop comfort score (mean±SD)	P-value*
SH	Dry eye	2.00±1.042	**<0.001**
	Normal	1.84±0.963	
SHUD	Dry eye	1.83±1.207	**<0.001**
	Normal	1.55±0.761	
O	Dry eye	1.83±0.775	**<0.001**
	Normal	1.68±0.674	
OUD	Dry eye	1.67±1.121	0.286
	Normal	1.68±0.909	

* p-value analysed using Independent T-test

The pre- and post-instillation analysis of ocular symptoms revealed significant improvement in all artificial tears except O (normal group) and SHUD (dry eye group) for overall discomfort. Symptom of dryness significantly decreased after the instillation of all artificial tears in both groups. Burning and grittiness showed improvement after 60 minutes instillation of SH and OUD in both groups. As for stinging, only OUD displayed significant improvement when comparing the score from baseline and 60 minutes post-instillation in both groups. Table 6 shows the comparison of ocular symptoms score at baseline and 60 minutes post-instillation for all artificial tears in both groups.

Artificial tears	Groups	Time of measurement	Overall discomfort†	Burning†	Dryness†	Grittiness†	Stinging†
SH	Dry eye	Baseline	1.14±0.990	0.22±0.422	0.92±0.770	0.22±0.540	0.22±0.591
		60 min	0.42±0.500	0.06±0.232	0.36±0.487	0.00±0.000	0.14±0.351

		p-value*	**<0.001**	**0.012**	**<0.001**	**0.019**	0.324
	Normal	Baseline	0.91±0.741	0.16±0.370	0.70±0.701	0.20±0.553	0.20±0.408
		60 min	0.68±0.639	0.02±0.151	0.48±0.549	0.00±0.00	0.16±0.526
		p-value*	**0.049**	**0.013**	**0.003**	**0.018**	0.533
	Dry eye	Baseline	0.81±0.920	0.42±0.692	0.78±0.866	0.39±0.645	0.39±0.494
		60 min	0.61±0.728	0.17±0.378	0.50±0.655	0.19±0.577	0.22±0.540
		p-value*	0.228	0.083	**0.039**	0.051	0.110
SHUD							
	Normal	Baseline	0.68±0.800	0.27±0.451	0.70±0.734	0.27±0.624	0.27±0.451
		60 min	0.48±0.664	0.16±0.370	0.45±0.548	0.09±0.291	0.14±0.347
		p-value*	**0.037**	**0.024**	**0.003**	**0.031**	0.083
	Dry eye	Baseline	0.86±0.798	0.14±0.351	0.89±0.747	0.08±0.280	0.17±0.561
		60 min	0.36±0.487	0.06±0.232	0.39±0.494	0.00±0.000	0.14±0.351
		p-value*	**<0.001**	0.083	**<0.001**	0.083	0.661
O							
	Normal	Baseline	0.64±0.750	0.11±0.321	0.75±0.781	0.14±0.462	0.14±0.510
		60 min	0.48±0.590	0.02±0.151	0.25±0.488	0.07±0.334	0.11±0.321
		p-value*	0.070	**0.044**	**<0.001**	0.083	0.660
	Dry eye	Baseline	1.25±0.967	0.89±0.887	1.03±0.810	0.83±0.845	0.61±0.688
		60 min	0.58±0.649	0.58±0.500	0.28±0.615	0.28±0.615	0.19±0.401
		p-value*	**<0.001**	**0.006**	**<0.001**	**<0.001**	**<0.001**
OUD							
	Normal	Baseline	0.50±0.699	0.34±0.479	0.48±0.664	39.0±0.618	0.41±0.583
		60 min	0.25±0.438	0.16±0.370	0.14±0.409	0.16±0.428	0.20±0.408
		p-value*	**0.015**	**0.003**	**<0.001**	**0.011**	**0.018**

Table 6 OOD4SQ (0-5 scale; 0 = no discomfort, 5 = worst) in dry eye and normal groups

* p-value analysed using Paired sample T-test
† Data displayed in mean ± standard deviation
OOD4SQ: Ora Calibra™ Ocular Discomfort and 4-Symptom Questionnaire

DISCUSSION

Physical properties of artificial tears

Previous studies had suggested that the final viscosity of artificial tears should be < 30 cP in order to avoid discomfort, blurred vision, as well as irritation (Aragona et al., 2019; Pires et al., 2013; Che Arif et al., 2023). This is because, higher viscosity artificial tears may affect the ocular bioavailability due to faster drainage of artificial tears caused by reflex tears and blinking (Pires et al., 2013; Che Arif et al., 2023). However, the shear rate were not specified in these studies. Therefore, the exact viscosity could be different depending on the shear rate applied by the rheometer. In this study, all artificial tears had a viscosity < 30 cP (at highest shear rate measured), except for Systane Hydration UD (32.73 cP).

As for pH, previous literatures reported that the pH of normal tears ranged from 6.5 to 8.06 (Iyamu and Enobakhare, 2019; Yamada et al, 1996; Norn, 1988; Abelson et al., 1981; Carney and Hill, 1976), while study comparing pH between control groups and dry eye patients showed that the mean pH of dry eye patients was slightly higher (7.46 ± 0.24) as compared to normal group (7.45 ± 0.23) (Khurana et al., 1991). Meanwhile, pH of artificial tears was suggested to be in the range of 6.6 to 7.8 pH unit in order to avoid any discomfort after instillation (Carney and Hill, 1976; Garcia-Valldecabres et al., 2004; Che Arif et al., 2023). The range of pH for all artificial tears in this study was in between 7.19 to 7.85, with 3 artificial tears having pH within ocular comfort range, while SH having pH beyond the recommended ocular comfort rate (7.85).

Ocular signs after artificial tears instillation

In term of signs after the instillation of artificial tears, for both dry eye and normal groups; significant improvements of TBUT (except for O in normal group; p=0.135) were noted at every measurement taken for all artificial tears, even with different pH and viscosity. This results suggested that both hyaluronic acid (HA)-based artificial tears (SH and SHUD) and carboxymethycellulose (CMC)-based artificial tears (O and OUD) were effective in managing tear film instability. These findings were in good agreement with previous studies, which reported that these two formulations were beneficial in improving ocular surface integrity (Song et al., 2017; López-De La Rosa et al., 2017; Wallerstein et al., 2018; Md Rejab et al., 2018).

TMH measured in this study increased significantly in both groups at every time interval after the instillation of all artificial tears, regardless of their viscosity and pH. We found a different trend of TMH between normal and dry eye group. TMH in normal group for all artificial tears reaching maximum values at 5 minutes, before starting to drop at 15 and 60 minutes post instillation, except for O, which showed maximum TMH values at 15 minutes post-instillation before started to decrease at 60 minutes. This is not

the case happened in dry eye group, where maximum values of TMH vary for each artificial tears; 5 minutes for O, 15 minutes for SH and OUD, and 60 minutes for SHUD.

Above all, in dry eye group, SHUD which was the most viscous artificial tear among all seemed to perform well compared to other artificial tears as it maintained the maximum value of TMH for up to 1 hour. This result suggested that highly viscous solution tends to remain longer in the ocular surface (Rosmadi et al., 2019; Akiyama-Fukuda et al., 2016). However, this finding was not consistent with the results for normal group as all artificial tears showing much similar performance in improving TMH. Thus, we hypothesized that viscosity alone may not fully explained the extension of retention time, but the ingredients used in the formulation of artificial tears might influence their clinical performance in improving tear volume of ocular surface (Karaca et al., 2019).

Electrolytes such as potassium chloride, sodium chloride and magnesium chloride hexahydrate added in the formulation of artificial tears lead to the improvement in TFP as electrolytes were able to maintain or lower the osmolarity of ocular surface (Masmali, 2019). This reflects the findings from this study in which the type of TFP in all artificial tears, regardless of their viscosity and pH, significantly improved after 60 minutes instillation. The electrolytes used in the formulation of SH, SHUD, O and OUD, together with the improvement in tear volume (Garcıa-Resua et al., 2014) following artificial tears instillation were believed to improve the tear quality of the participants in this study.

Ocular symptoms after artificial tears instillation

Following instillation, all artificial tears were well tolerated (Torkildsen et al., 2017; Torkildsen et al., 2018; Ousler et al., 2015), with low drop comfort score; ranged from 1.55 to 2.00 observed in both groups. SH resulted in the least comfort for both dry eye (2.00±1.042) and normal (1.84±0.963) groups. This could be due to its high viscosity and pH which lie outside ocular comfort range. Meanwhile, SHUD (1.55±0.761) and OUD (1.67±1.121) had the lowest drop comfort score in normal and dry eye groups, respectively.

All artificial tears tested in both groups decreased the symptoms after 60 minutes. However, only certain symptoms significantly improved post-artificial tears instillation. It could be seen that OUD performed better in both normal and dry eye groups in all parameters observed. Even with the same active and inactive ingredients in OUD and O, OUD was more effective in improving ocular symptoms compared to O. This could be related to the preservative (Purite®) added in O that might affect the findings. This is supported by previous study conducted by Nasser et al., (2018) which demonstrated significant improvement in ocular symptoms (OSDI score) after switching from preserved to non-preservative artificial tears, proving the clinical benefits of preservative-free artificial tears in relieving dry eye symptoms.

Even though there were two preservative-free artificial tears (OUD and SHUD) used in this study, OUD demonstrated effective symptomatic relief compared to SHUD. This could be due to ingredients used in OUD were more tolerable and contribute to the sustainability of comfort even after 60 minutes instillation. Carboxymethylcellulose (CMC) as one of the lubricants used in OUD formulation was reported to hydrate and lubricate the ocular surface, resulting in alleviation of patient-reported symptoms of dry eye (Labetoulle et al., 2017).

CONCLUSION

TBUT, TMH and TFP in both normal and dry eye groups significantly improved after 60 minutes instillation of all artificial tears, regardless of their viscosity and pH. Besides, all artificial tears were well tolerable with low drop comfort score recorded in both groups. Ocular symptoms before instillation of artificial tears improved after all artificial tears instillation, but only OUD significantly improved all the ocular symptoms observed.

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IS THERE AN ASSOCIATION BETWEEN MYOPIA AND DRY EYE SYMPTOMS AMONG THE UNIVERSITY STUDENTS IN KUANTAN, MALAYSIA?

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ABSTRACT

Introduction: Refractive errors may contribute to dry eye disease especially in myopia with the possible alterations in the corneal curvature, thickness and endothelial density as the eyeball elongates. However, the association between refractive errors and dry eye symptoms has not been fully investigated and the prevalence of myopia has yet to be identified among the university students in Kuantan, Malaysia. **Methods:** Eighty-three first year Kulliyah of Allied Health Sciences (KAHS) students of either myopes or emmetropes responded to two questionnaires namely the refractive error questionnaire to determine the refractive status, apart from undergoing a physical subjective refraction, and Ocular Surface Disease Index (OSDI) to determine their dry eye status via email, QR code and online messaging platform. The OSDI scores were compared between myope and emmetropes using Independent T-test and Spearman's rank-order correlation analysis. **Results:** The prevalence of myopia among the first-year students was about 68%. In addition, 60.24% of year 1 KAHS students reported having dry eye symptoms but there was no significant association between refractive error and dry eye symptoms ($p>0.05$). However, OSDI scores were significantly higher in myopes compared to emmetropes ($p<0.05$). **Conclusion:** The estimated high prevalence of myopia among university students may be due to prolonged near work and usage of gadgets. OSDI score in myopia is higher compared to emmetrope which may be due to the changes that occur in the anterior surface of cornea.

KEYWORDS: Dry eye, myopia.

INTRODUCTION

According to Flitcroft et al., (2018), myopia is defined as "A *refractive error in which rays of light entering the eye parallel to the optic axis are brought to a focus in front of the retina when ocular accommodation is relaxed, which usually results from the eyeball being too long from front to back but can be caused by an overly curved cornea and/or a lens with increased optical power*". Based on this definition, the probability of anterior corneal changes is high in myopia since the eyeball elongation in myopia progression may also lead to a flatter corneal curvature, decreased corneal thickness, as well as decreased endothelial density (Chang et al.,2001). Evidently, changes in corneal parameters have been shown to result in dry eye (DE) (Satitpitakul et al., 2021, Fahmy and Aldarwesh, 2018). Corneal thickness for instance, together with

lacrimal gland, are affected by the parasympathetic nervous system which might determine the association between DE and myopia (Hazra et al., 2022). Furthermore, TBUT was also associated with corneal thickness, which is related to the axial length (Hazra et al., 2022). Ilhan et al., (2014) suggested that the pathologic myopia group has an average tear break-up time (TBUT) value of 7.2 seconds, with 66.6% of patients having a TBUT of less than 10 seconds and based on the OSDI scores, 60% of patients with high myopia experienced significant symptoms of DE, indicating that they experienced ocular surface irritation. In addition, in a recent study where the myopia-associated conjunctiva microbiota was explored, it was suggested that Proteobacteria, Actinobacteria and Acinetobacter may play roles in the high myopia associated ocular surface irritation (Xiao et., al 2023). The association between DE and myopia were also revealed regardless of age and gender (Wang et al., 2022, Ayaki et al., 2023).

The OSDI is one of the most widely used ocular symptom questionnaires in dry eye studies where it was designed to assess symptoms of ocular irritation and their impact on vision-related function and to grade the severity of dry eye (Guillemin et al 2012, Ozcura et al 2007). The OSDI was also able to show treatment benefits in dry eye (Chang et al 2009, Russo et al 2007, Stevenson et al 2000,Yüksel et al 2010) and the questionnaire has good reliability and validity.

Refractive Error Questionnaire from Gameiro Filho et al., (2013) was utilised to identify the prevalence of refractive errors in medical students at the State University of Londrina (UEL) as well as the most commonly used methods of visual correction. This respective questionnaire is suitable and applicable to university students and has been utilised in several related studies (Alhibshi et al., 2021, Ferial et al., 2020, Alqudah et al., 2023, Nkashama et al., 2023, Batool et al., 2022)

The association between refractive errors and DE symptoms has not been fully investigated in Malaysia, particularly among the university students in Kuantan, Pahang. Therefore, this study aimed to investigate the association between refractive error and DE symptoms and to compare DE scores between myopia and emmetropia students. In addition, the prevalence of refractive error and DE in Year 1 KAHS students is also identified.

MATERIALS AND METHODS

Study design

This cross-sectional study enrolled the year 1 KAHS students of the 2022/2033 session. All 83 participants were requested to complete the Refractive Error Questionnaire from Gameiro Filho et al. (2013) (Appendix 1) and the Ocular Surface Disease Index (OSDI) Questionnaire from Outcomes Research Group at Allergan Inc (Irvine, Calif). The questionnaires were distributed via email, QR code and online messaging platform (WhatsApp). Apart from filling up the refractive error questionnaire, the participantS were also present for physical subjective refraction at the optometry clinic of KAHS to identify their actual dioptric values of myopia if any.

Statistical analysis

The OSDI scores of myopia and emmetropia students were compared using independent T-test and Spearman's rank-order correlation analysis was applied to determine the association between refractive errors and dry eye symptoms. The informed consent form was given to the subjects prior to answering the refractive error and OSDI questionnaires. The ethical approval for this study was acquired from IIUM Research Ethics Committee. All data collected was analysed using the Statistical Package for Social Science Software (SPSS) (version 29 for Windows, SPSS, Inc., Chicago, IL, USA).

RESULTS AND DISCUSSIONS

Prevalence of refractive error and dry eye in year 1 KAHS students

Eighty-three students participated in this study. The prevalence of myopia in year 1 KAHS students was 68% and another 31% were discovered to be emmetrope. Myopic subjects were divided into low myope (-0.50DS to -2.75DS), moderate (-3.00DS to -4.75DS), and high myope (-5.00DS or higher) groups based on their relative prevalence of 49%, 28%, and 23% respectively.

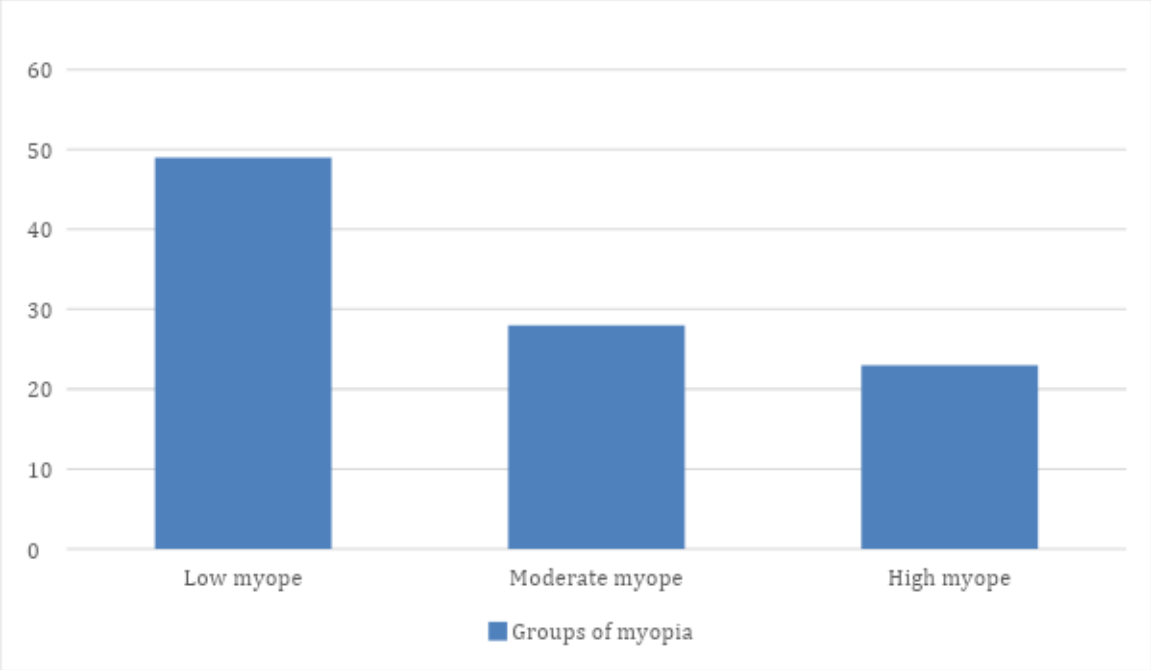


Figure 1: Groups of myopia

In addition, 60% of year 1 KAHS students reported having dry eye symptoms, which were further divided into mild (13 to 22 score), moderate (23 to 32 score), and severe (more than 32 score) dry eye, with the prevalence of 38%, 36%, and 26%, respectively.

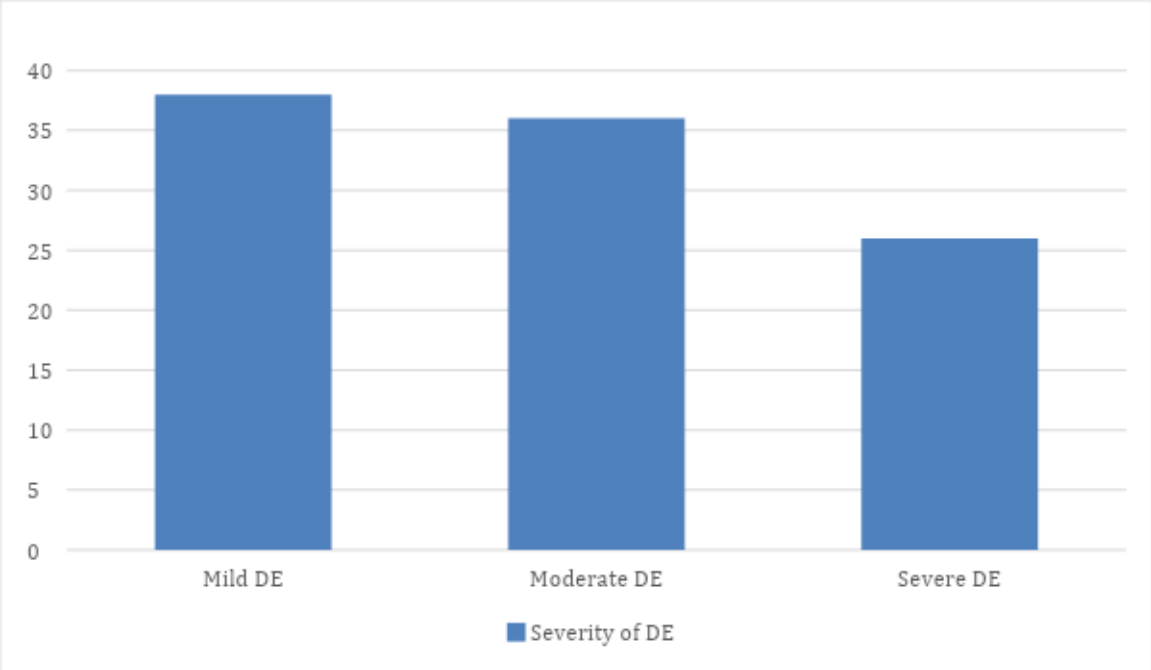


Figure 2: Severity of dry eye symptoms

Association between refractive error and dry eye symptoms

The association between spherical equivalent and OSDI score for each eye was investigated using Spearman's rank-order correlation. There was no significant association between them for either eye, RE ($p=0.120$) and LE ($p=0.057$).

Comparison of OSDI score between emmetropic and myopic students.

OSDI scores were significantly higher ($p<0.05$) in myopia with the mean score of 19.95 compared to emmetropia students with the mean score of 10.82 as shown in table 1.

Variable	Emmetropic (n = 26)		Myopic (n = 26)		p-value
	Mean	SD	Mean	SD	
OSDI score	10.82	9.392	19.95	16.554	0.019

Table 1: Comparing OSDI score between emmetropic and myopic.

DISCUSSION

Prevalence of refractive error and dry eye in year 1 KAHS students

Refractive error is caused by an optical imperfection in the eye that prevents the eye from correctly focusing light onto the retina, resulting in blurred vision (Abdul Khalid., 2016). Based on the current study, there is a high prevalence of myopia among KAHS year 1 university students as 69% of the subjects were discovered to be myopia with low myopia recorded the highest prevalence (49%) followed by 28% of moderate myopia and 23% of high myopia. According to Kumar et.al. (2018), insufficient light, extended reading hours, watching television, and long-term smartphone usage were all determined to be statistically significant risk factors for refractive error. Thus, the extensive near work and prolonged usage of gadgets such as smartphones and laptops might have contributed to the high prevalence of refractive errors among the participants in the current study.

Surprisingly, there is also a high prevalence of dry eye (60%) among year 1 KAHS students, which were further divided into mild (38%), moderate (36%), and severe dry eye (26%) respectively. According to the retrospective study conducted by Aljarousha et al. (2018), the total prevalence of dry eye disease (DED) at Jalan Hospital Eye Care, International Islamic University Malaysia (IIUM), Kuantan, Malaysia was 48.8%, which was also higher than the global prevalence estimates of 7% to 34%.

Association between refractive error and DE symptoms

Ilhan et al. (2014) suggested that the pathological myopia group has an average TBUT value of 7.2 seconds, with 66.6% of patients having a TBUT of less than 10 seconds and based on the OSDI scores, 60% of patients with high myopia experienced significant symptoms of dry eye, indicating that they had ocular surface irritation. Furthermore, according to Hirayama et al, (2022), those with high myopia reported significantly more dryness compared with the subjects with no myopia. The possible physiological change to the choroidal thickness takes place when someone performs prolonged near work who in return has a greater increased risk of evaporative DE, which directly affects the TBUT (Hazra et., 2022). However, in the current study, there is no significant association between refractive error and dry eye symptoms among the year 1 KAHS students. This could be due to only 23% of them were high myopic while the majority of them were in the range of low to medium class of myopia severity. In addition, dry eye may also occur with the absence of symptoms (Nichols et al., 2004) even with the presence of ocular surface parameter changes, which however, have not been investigated in the current study.

Comparing OSDI score between emmetropic and myopic students.

The significant difference in terms of OSDI scores between emmetropic and myopic in year 1 KAHS suggests that myope has a higher dry eye score compared to emmetrope. A comparison study between a group of 50 young female subjects (20.3 ± 1.1 years) with refractive error of (-0.25 to -6.00D) and a control group of emmetropias also identified a significant higher OSDI score and hence suggested that refractive error has a risk factor for dry eye (Mana A. et al., 2021). Furthermore, the median scores from the OSDI measurements were higher in myopic and hyperopic eyes than those recorded for emmetropes (Fagehi et al., 2022).

According to Chang et al., (2001), there are changes that occur in the anterior surface of the cornea as the eyeball elongates in myopia progression which include flatter corneal curvature, decreased corneal thickness, as well as decreased endothelial density. Clinically, as the eyeball elongates in myopia, alterations in the anterior corneal surface may lead to an increased risk of dry eye (Fahmy and

Aldarwesh., 2018). Furthermore, the extension of the axial length was identified to be significantly associated with corneal thickness and tear breakup time since the parasympathetic nervous system may be the determining factor for the relationship between dry eye disease and myopia as it affects the lacrimal glands and corneal thickness (Hazra et al. 2022). This further supports that myope may be having higher dry eye score compared to emmetrope in relation to changes that occur in the anterior surface of cornea.

Limitation

This study did not exclude contact lens wearers as participants which may have affected the OSDI scores obtained since this is an exploratory study. However, based on the feedback from the Refractive Error Questionnaire, only 7% of them were contact lens wearers. Related clinical measurements were not included in the analysis which may help to identify the associations between DE symptoms and signs among these newly enrolled university students.

CONCLUSION

There is a high prevalence of myopia among university students which may be due to prolonged near work and excessive use of gadgets. The OSDI score in myopia is also higher compared to emmetrope which might be due to the changes in the anterior surface of cornea. Therefore, further research which includes the detail investigation involving ocular surface biometry and tear functions measurements is recommended to allow us to investigate the changes that occur in the anterior surface of the cornea in myopia among the new university students.

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Appendix 1

MYOPIA AND BINOCULAR VISION FUNCTIONS AMONG ALLIED HEALTH SCIENCES STUDENTS AT IIUM

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ABSTRACT

Myopia is believed to have some effects on lag of accommodation, heterophoria and AC/A ratio. Previous studies reported that the lag of accommodation of myopic is higher compared to an emmetropic eye. It is also reported that the incident of exophoria in myopic eyes is more common compared to emmetropic eyes. Additionally, myopic individuals are anticipated to exhibit higher accommodative convergence compared to emmetropic individuals. This study aimed to investigate these effects on undergraduate students of Kulliyyah of Allied Health Sciences, particularly assessing how different the degrees of myopia impact these visual functions. The lag of accommodation, heterophoria and AC/A ratio of 82 participants were measured with full correction. The lag of accommodation was measured utilizing an autorefractor, Grand-Seiko WR-5100K while the heterophoria measurement was obtained by using the Howell Card and the AC/A ratio was measured by using the gradient method. The results revealed a significant difference in lag of accommodation between myopic and emmetropic students, but no significant differences in heterophoria and AC/A ratio between the two groups. When comparing various degrees of myopia, only the lag of accommodation showed a significant difference, while AC/A ratio and heterophoria remained unaffected. In summary, myopia primarily affects the lag of accommodation, with no significant impact on AC/A ratio and heterophoria in KAHS students' population. Thus, it is predicted that the possibility of myopia progression on these subjects are very low.

KEYWORDS: Myopia, lag of accommodation, heterophoria, AC/A ratio

INTRODUCTION

Myopia has emerged as a pressing public health issue in recent years, with its prevalence steadily rising annually (Wang et al., 2021; Singh et al., 2022; Zhang et al., 2022). This increasing trend reflects a global health concern driven, in part, by lifestyle shifts characterized by reduced outdoor activities and greater engagement in near work, as reported in various research findings (Brien et al., 2016). This surge in myopia not only increases the demand for corrective glasses but also raises concerns about eye-related problems and myopia progress. Moreover, myopia's impact extends beyond eye health, potentially influencing an individual's overall quality of life and psychological well-being (Nathan et al., 2019).

From an optometric perspective, myopia would affect various the binocular functions, such as lag of accommodation (LA), AC/A ratio and heterophoria. The LA represents the gap between the intended focus and the actual focusing response, with myopic individuals often showing higher LA than emmetropic individuals (Chen et al., 2020). Heterophoria, denoting the misalignment of the eyes when fusion is absent, can also be affected by myopia. Myopic individuals may exhibit an increased tendency toward exophoria at both near and distant vision (Jin et al., 2007). Myopia is likely to influence the AC/A ratio, which measures the connection between accommodation and convergence. This can lead to increased accommodative convergence in individuals with myopia (Gwiazda et al., 2005). Greater LA can lead to high AC/A ratio which an early sign of becoming myopic, however the rate of progression of myopia does not depending on these changes (Mutti, D.O, Mitchell, G.L., Jones-Jordan, L.A et al., 2017). Many researchers studied the effects of myopia on these visual functions in other countries with different populations (Jane, et al., 2004; Logan, et al., 2021).

This study focuses on understanding how myopia influences LA, heterophoria, and the AC/A ratio in undergraduate students at the Kulliyyah of Allied Health Sciences, IIUM. It also aims to see if different levels of myopia have varying effects on these functions.

MATERIALS AND METHODS

The study was cross-sectional, involving first year students of the Kulliyyah of Allied Health Sciences (KAHS), session 2022/2023. It utilized convenience sampling, and a total of 82 year 1 students participated (42% from the target population). The participants comprised of 20% and 80% male and female students respectively, with an average age of 20±1 years old. Data collection took place at the IIUM Optometry Clinic between October 28, 2022, and March 18, 2023.

Inclusion criteria for the study were as follows: participants needed to possess normal visual functions, normal binocular vision, have no history of ocular and systemic diseases, and had not undergone ocular surgery. The participants also had to have the best-corrected distance visual acuity of 6/6 or better and were either emmetropic or myopic, with spherical equivalent refraction (SER) ranging from -0.50DS to <-9.00DS.

The participants received an explanation about the study, and consent was obtained. Data collection included assessing participants' visual acuity using the Snellen Chart at 6 meters and determining refractive power using the Oculus PARK 1 auto-refractor and subjective refraction. Subsequently, participants were categorized into emmetropia and myopia, with the myopia group further divided into mild (≤-0.50D to – 2.75D), moderate (≤-3.00D to -4.75D), and high myopia (≤-5.00D) based on their refractive error (Tang et al., 2019; Flitcroft et al., 2019).

Following this, data regarding LA, heterophoria, and AC/A ratio were collected from the participants while they were wearing their full correction. To measure the LA, the Grand-Seiko WR-5100K was used with a crossed target. The LA was determined by calculating the difference between the average of three readings of distance and near refractive errors (Ortiz-Peregrina et al., 2021). Heterophoria measurements were carried out using the Howell Card and a phoropter, both at a distance and near. Participants were asked to report the number indicated by the arrow on the lower chart of the Howell Card with a 6-prism diopter base down was placed in front of the right eye (Anstice

et al., 2020). The AC/A ratio, which signifies the relationship between accommodation and convergence, was measured using the gradient method and a phoropter. This technique is commonly used in the clinical setting. Near phoria was measured both with and without an additional lens. If the subject exhibited esophoria, a +1.00 DS lens was employed as the additional lens, while if the participant displayed exophoria, a -1.00 DS lens was used. The AC/A ratio was then calculated using the formula described by Singh et al. (2017).

RESULTS

All the data obtained were analyzed using Statistical Package for Social Science Software (SPSS) (version 23 for Windows, SPSS, Inc., Chicago, IL, USA). The Shapiro-Wilk test is used to test the normality of all the data before running the test. As the data of LA and AC/A ratio in comparing between emmetropic and myopic students were normally distributed, independent *t*-test were used to analyze the data. However, the data for heterophoria at both distance and near were analyzed using the Mann-Whitney U test as those data were not normally distributed. When comparing the parameters between different degrees of myopia, only the data on the LA was normally distributed. Thus, a one-way ANOVA test was used. For analyzing the data of heterophoria and AC/A ratio, the Kruskal-Wallis H test was used.

Effect of myopia on LA

The independent *t*-test of the LA between the emmetropic and myopic students showed a $p<0.05$ (Table 1) which indicated that there was a significant difference between the LA of the emmetropic and myopic students (t (162) =2.74, p=0.007). The mean difference of the LA of the emmetropic students was higher than that of myopic students with a different of 0.18 (95% CI, 0.31 to 0.51).

Table 1 Comparison of lag of accommodation between emmetropic and myopic students

Variable	Emmetropic		Myopic		Mean differences (95% CI)	t-statistics (df)	*p*-value
	Mean	SD	Mean	SD			
Lag of accommodation (D)	+1.85	0.38	+1.67	0.41	0.18 (0.51, 0.31)	2.74 (162)	0.007

One-way ANOVA test of the LA between different degrees of myopia showed $p<0.05$ (Table 2). This indicated that there was a significant difference in the LA between the groups [F (3,160) =3.99, p=0.009]. A post hoc Dunnet test revealed that the LA of the high myopia was statistically significantly lower than that of the LA of the emmetropia (control group) (p=0.004, 95% CI= (-0.55, -0.08). There was no statistically significant difference in the LA between the other groups.

Table 2 Comparison of lag of accommodation between different degrees of myopic students (Control group = emmetropia)

Variable	n	Lag of accommodation (D)		F-statistic (df)	*p*-value
		Mean	SD		
Emmetropia	27	+1.85	0.37	3.99	0.009
Mild myopia	28	+1.67	0.40	(3)	
Moderate myopia	16	+1.75	0.34		
High myopia	11	+1.53	0.47		

Effect of myopia on heterophoria

Heterophoria for both distance and near between emmetropic and myopic students using the Mann-Whitney U test showed $p>0.05$ (Table 3) which indicated that there was no significant difference between both heterophoria at distance and near for the emmetropic and myopic students. The value was expressed in mean rank (Chen et al.,2003; Jung et al., 2016; Hong et al.,2020). However, the result is shown that both distance and near heterophoria of the emmetropic students was less exophoric than that of myopic students.

Table 3 Comparison of heterophoria between emmetropic and myopic students

Variable	Emmetropic	Myopic	z-value	*p*-value
	Mean rank	Mean rank		
Heterophoria at D (ΔD)	79.38	70.62	-1.24	0.214
Heterophoria at N (ΔD)	76.25	72.15	-0.55	0.577

In comparing the heterophoria at distance between the different degrees of myopia, the Kruskal-Wallis H test showed $p>0.05$, and at near showed $p>0.05$. These two results indicated that there were no significant differences in both distance and near heterophoria between the groups. Figures 1 and 2 illustrate the comparison of heterophoria at both distance and near between the different degrees of myopia, respectively.

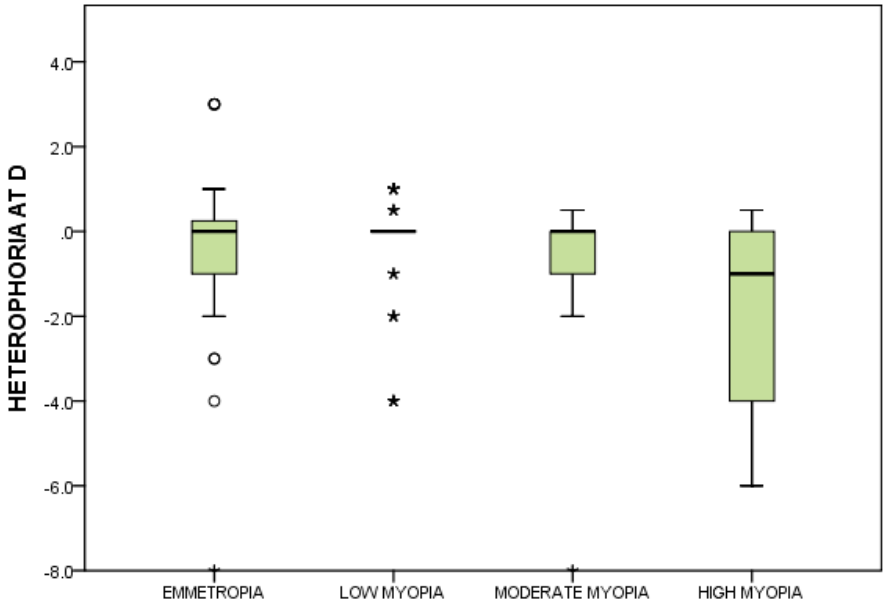


Figure 1 Boxplot of heterophoria at distance between different degrees of myopic students (Control group = emmetropia)

Note: minus sign on the y-axis indicates exophoria, while plus sign indicates esophoria.

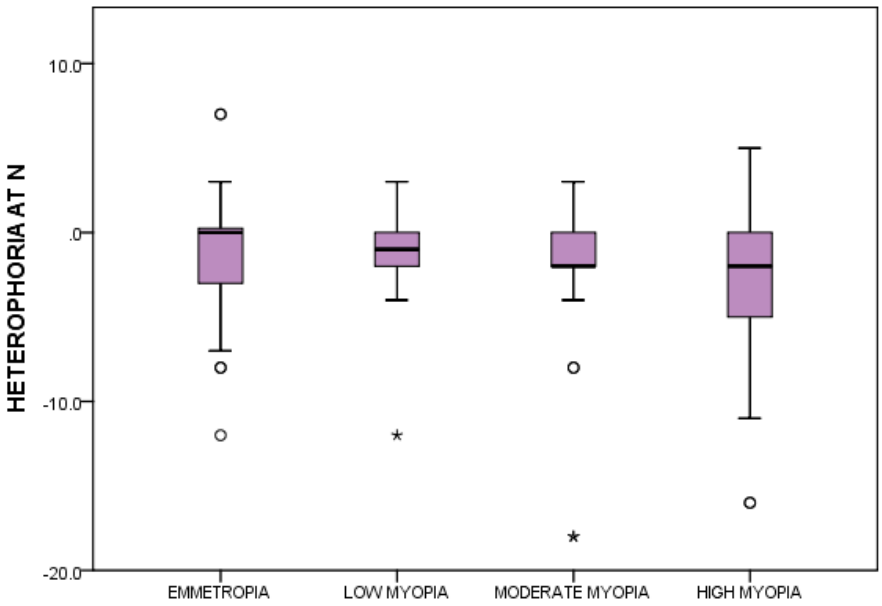


Figure 2 Boxplot of heterophoria at near between different degrees of myopic students (Control group = emmetropia)

Note: minus sign on the y-axis indicates exophoria, while plus sign indicates esophoria.

Though there is statistically insignificant result, myopic participants showed greater amount of exophoria for both distances as compared to emmetropic and lower degree of myopia.

Effect of myopia on AC/A ratio

The independent t-test of the AC/A ratio between the emmetropic and myopic students showed $p>0.05$ [t (144) =1.69, p=0.09] (Table 4). This indicated that there was no significant difference between the AC/A ratio of the emmetropes and myopes. The mean difference of the AC/A ratio between the groups showed that the emmetropes AC/A ratio was higher than that of the myopes.

Table 4 Comparison of AC/A ratio between emmetropic and myopic students

Variable	Emmetropic		Myopic		Mean differences (95% CI)	t-statistics (df)	*p*-value
	Mean	SD	Mean	SD			
AC/A ratio (D)	2.43	1.41	2.00	1.48	0.43 (-0.07, 0.94)	1.69 (144)	0.092

The Kruskal-Wallis H test of the AC/A ratio between different degrees of myopia showed a $p>0.05$. This indicated that there was no significant difference in the AC/A ratio between the groups. Figure 3 illustrate the comparison of the AC/A ratio between the different degree of myopia.

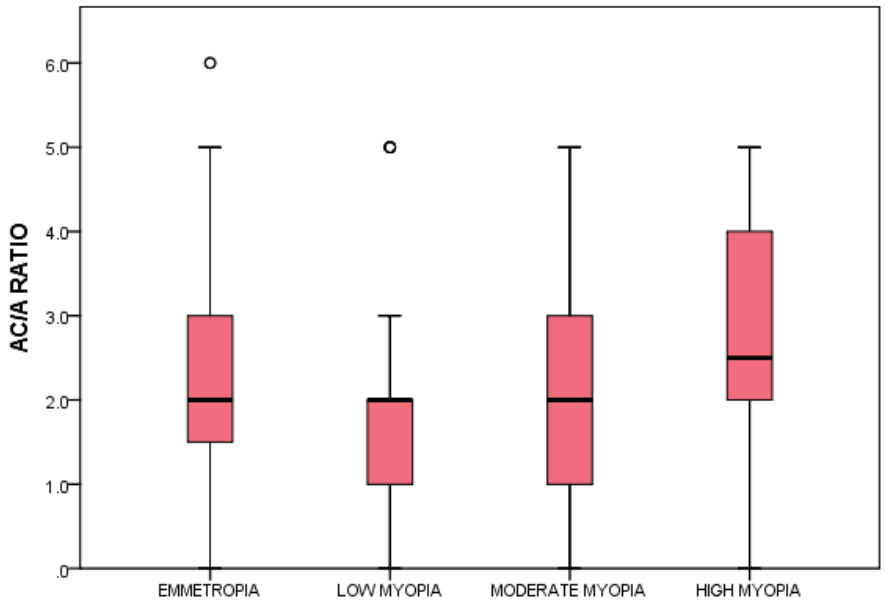


Figure 3 Boxplot of AC/A ratio between different degrees of myopic students (Control group = emmetropia)

DISCUSSION

Effect of myopia on lag of accommodation

In the investigation of the effect of myopia on the LA on KAHS year one students, it was shown that the LA of an emmetropes was higher than myopes. This study's results aligned with the findings of Tarrant et al. (2010), which had a total of 30 participants (age 23.5±2.9 years) in comparing the LA between the emmetropes and myopes utilizing Zernike and Seidel defocus wave aberrations, in which it also suggested that the accommodative LA for emmetropes was higher than that of the myopes. This similarity suggests some consistency in the results, despite differences in sample size and measurement techniques between the studies.

In contrast, findings from Nakatsuka et al. (2005) and Kaphle et al. (2022), in which these two studies found that myopes showed a larger LA than the emmetropes. The study by Nakatsuka et al. (2005) had a total of 79 Japanese children (age 9±3 years) who participated, and the LA was measured using the Grand Seiko WV-500 auto-refractometer. The result differ from current study could be due to near viewing distance of children was closer as they may accommodate inaccurately (Gwiazda, et al. 1993) as compared to adults which may lead to higher LA (Haro, C., Poulain, I. & Drobe, B. 2000). Kaphle and colleagues (2022) had a total of 76 young adults' participants (age 22.5±4.5 years) and the LA was measured using the Hartmann–Shack Complete Ophthalmic Analysis System aberrometer, utilizing pupil plane (Zernike refraction) and retinal image plane metrics. The different age groups in the study by Nakatsuka et al. (2005) and methods used in the study by Kaphle et al. (2022) may contributed to the contradicting results.

Higher LA in myopic was always related to the myopia progress which due to hyperopic defocus induced by LA, however previous finding showed that myopia progression was not related to higher LA (Chen, Y., Drobe, B., Zhang, C. et al; 2020). Though this is still unclear, at least for the group of current study, the prediction can be made that there is a low possibility of myopia progression to occur.

In addition, there was an analysis of whether the effect of myopia on the LA differs with different degrees of myopia

in the current study, but the results showed that only high myopia would give significant lower LA as compared to emmetropes.

Effect of myopia on heterophoria

The analysis of the effect of myopia on heterophoria in this study had shown that there was no significant difference in both distance and near heterophoria between the emmetropic and myopic participants. Moreover, the effect of different degrees of myopia on heterophoria also cannot be proven. The result of this study comparing the heterophoria between emmetropes and myopes was consistent with the study by Chen & Aziz (2003). The study recruited 36 students (age 21.5±2.5 years), and the heterophoria was measured using the Howell Card. The results showed that there was no significant difference in the heterophoria measured at distance and near between the emmetropes and myopes.

In contrast, the study by Hasebe et al. (2005) reported that myopes tend to be more exophoric at distance and more esophoric at near viewing distance. The study was conducted with a total of 95 Japanese children (age 9±3 years) and the measurement of heterophoria was done using a prism cover test. Myopic eye tends to exhibit esophoria at near as the have high AC/A ratio.

Similarly, a study by Leone et al. (2010) revealed that there was an association between myopia and exophoria at both distance and near among 12 years old children. The study had recruited 1740 students of age 6 years and 2353 students of age 12 years, and the heterophoria was measured using the prism cover test. The study reported a significant association between the refractive error and both heterophoria at distance and near in the age group of 12 years old, but not in the age group of 6 years old because the proportion of myopia in that age group was not sufficient to prove the association. The findings from those two studies were assumed to be different from current study due to the varying age groups and methods used to measure the heterophoria.

Effect of myopia on AC/A ratio

Regarding myopia and the AC/A ratio, it was found that there was no significant difference between the AC/A ratio of the emmetropic and myopic participants. A similar finding was reported in a study by Chen et al. (2003). The study was participated by 30 children in Hong Kong (age 10±2 years) and the AC/A ratio obtained was distance-induced and lens-induced AC/A ratio, calculated by the formula. The study had showed similar result with this study as it was reported that there was no statistically significant difference in the AC/A ratio between the myopes and emmetropes even though the study design and method were different from this study.

Furthermore, the investigation of the effect of different degrees of myopia on the AC/A ratio in this study also resulted in a non-significant difference in the AC/A ratio between the myopia groups. However, there was an apparent trend with myopia and AC/A ratio in which, the AC/A ratio tends to increase with the extent of myopia. This result was consistent with a study by Tsai et al. (2012).

In contrast, the study by Mutti et al. (2000) reported that the AC/A ratio was associated with the refractive error in which the myopes had a higher AC/A ratio than that of emmetropes. But they found that there is no significant difference in the AC/A ratio with different degrees of myopia. That study was conducted with 847 children (age 10.5±4.5 years), and the AC/A ratio was calculated using a specific formula. It was assumed that due to the difference in the population studied and the method used in those study, the results shown were also different.

CONCLUSION

The outcomes revealed that myopic individuals exhibit a significantly lower LA in comparison to those who are emmetropic. There were non-significant results on heterophoria and AC/A ratio, however, myopic individuals consistently exhibit greater exophoria values and lesser AC/A ratio as compared to emmetropic. The findings in this

study may be different from the others due to the difference in the population studied and the methods used in the research. However, based on previous studies mentioned above, it can be predicted that the participants in this group may have a reduced likelihood of myopia progression, though these association were still unclear. In the future, longitudinal study involving the same participants (in year 2 and year 4) could be conducted to ascertain whether this prediction is true.

ETHICAL APPROVAL

There is no conflict of interest in this study, and we did not receive any specific grant or funding. The study adhered to the tenets of the Helsinki Declaration involving human subjects and received ethical approval from the IIUM Research Ethics Committee (IREC), with ethical approval number IREC 2022 KAHS/DOVS/13.

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PEEK ACUITY AS AN ALTERNATIVE METHOD FOR VISUAL ACUITY MEASUREMENT FOR VISION SCREENING IN CHILDREN

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ABSTRACT

Introduction: Accurate and reliable clinical measurement of visual acuity (VA) is necessary to establish the needs for further clinical investigations. A simpler option for VA measurement is the use of smartphones, in which the measurement method is programmed in an application that enables automated and self-administered VA testing. **Aims:** This study aimed to investigate the validity of PEEK Acuity (PA), a smartphone's application for VA measurement, in testing children's vision, especially for vision screening programs. **Methodology:** Data were obtained from a vision screening program involving children aged 3–13 years. One hundred thirteen participants were included in the study (mean age 7.47±2.33 years old, 59 boys). The participants' VA was measured using the PA and Snellen chart in random order. Both eyes were tested, with 226 data points used in the statistical analysis. The Kolmogorov-Smirnov test revealed non-normal data. The VA between the PA and Snellen tests was compared using the Wilcoxon signed rank test. Test-retest variability was calculated for both tests using intraclass correlation (ICC) analysis. Spearman's rank correlation and the Bland-Altmann test were plotted to evaluate the agreement between tests. **Results:** The mean VA recorded using PA was 0.066±0.007 logMAR, while that recorded using Snellen was 0.103±0.009 logMAR ($z=-4.119$, $p<0.0005$, Wilcoxon signed rank test; ≈ two-letter differences). The ICC between the PA and Snellen was 0.641. Spearman's rank correlation revealed a significant correlation between PA and Snellen ($r=0.508$, $p<0.001$). **Conclusion:** There was a moderate correlation between the PA and Snellen scores. The PA application showed good agreement with conventional Snellen. Thus, smartphone applications such as PA may serve as an alternative to measure VA in children, especially in vision screening programs.

KEYWORDS: Visual Acuity, PEEK Acuity, Children's Vision, Vision Screening

INTRODUCTION

Visual impairment drastically affects a person's life, resulting in functional and psychological problems. Visual impairment lowers productivity, raises healthcare costs, and slows a country's economic growth (Wang et. al., 2014; Armstrong et al., 2012). More than two billion people have distance or near vision problems, with more than one billion being preventable with early detection (Flaxman et al., 2017). Clinically, the most important step in identifying visual problems may be the measurement of visual acuity (VA).

VA is the most common, yet the most important, visual function test performed on patients. VA measurements should be reliable and accurate, as VA is usually used to establish the need for further clinical investigations. The Snellen acuity chart was developed in the early 1860s and remains the most commonly used chart in clinical practice (Bailey et al., 2013). Nevertheless, the Snellen chart suffers from problems such as variable contour interaction, which affects the accuracy of threshold determination (Lovie-Kitchin, 2015). Although the Snellen chart may be lacking in optical inconsistency, it is arguably the most widely used because of its accessibility in hospitals and primary care settings and the degree of familiarity among clinicians (Perera et al., 2015). The Early Treatment Diabetic Retinopathy Study (ETDRS) acuity chart may provide a better VA measurement by overcoming Snellen's limitations. Despite the accuracy of the ETDRS chart, its cost, larger chart size, longer testing time, and longer testing distance may reduce its use in clinical settings (Lovie-Kitchin, 2015; Han et al., 2019). Both Snellen and EDTRS acuity testing require trained personnel to administer the tests. The need for a better acuity test that improves convenience, cost, and accuracy is important for tackling visual problems and preventing visual impairment and irreversible blindness (Bastawrous et. al., 2015; Siktberg et al., 2021).

Conventional VA testing may require patients to be in a clinic with highly trained personnel to perform the test. These become barriers for testing VA in screening programs and testing vulnerable patients such as children, the elderly, indigenous people, and those with impaired mobility. A promising approach to address this issue is to use mobile smartphones. Advancements in smartphone technology have enabled its application in medical practice (Perera et al., 2015). Being a staple technology in modern life, smartphones are accessible to many. VA testing applications in smartphones allow self-

administered testing, which improves accessibility and provides a solution to the aforementioned barriers.

There are a few vision-testing applications available, but PEEK Acuity (PA; Peek Vision Ltd, United Kingdom) has gained credible coverage in the literature (Han et al., 2019; Bastawrous et al., 2015; de Venecia et al., 2018). Nevertheless, the accuracy of this application, especially in its clinical use in children, has yet to be reported. In this study, we sought to identify the reliability of PA and establish its agreement with the conventional Snellen acuity chart, on testing children especially for vision screening programs.

METHODOLOGY

This cross-sectional retrospective study used data obtained from a mass health screening program on children in the Kuantan Pahang vicinity. The study was approved by the IIUM Research Ethics Committee (IREC No. KAHS 77/22). All guardians provided consent for the use of the data in this study.

Participants

A total of 113 participants (59 boys, 54 girls) were included in this study. The participants' age varies between three and 13 years, with a mean age of 7.47±2.33 years old. Both eyes were measured and used as data points. None of the participants had profound visual impairment and none were categorized as having low vision. The inclusion criterion was the ability of participants to comprehend instructions involving VA testing, whereas the exclusion criterion was any vision screening participants with missing data.

Visual Acuity Testing

The PA application is installed on various smartphones owned by multiple visual screeners. The screen brightness was set to 100% during testing. The PA follows the standard EDTRS chart design with a 5×5 grid optotype letter E displayed in one of four orientations (90°, 180°, 270°, and 360°) of varied sizes. The participants were given an "E" shaped cardboard to aid them in showing the direction of the E limb displayed on the phone screen. The visual screener held the smartphone two meters from the participant. The visual screener slid the smartphone's screen in the direction of the participant's response without looking at the screen to eliminate bias. This was done to reduce any verbal and nonverbal clues from the screeners, which may have biased the results. PA results were standardized to logMAR units. The test completion was indicated by sound and vibration alerts. All the instructions given to the participants were based on the directions provided by the application developer.

Snellen VA measurements were performed at a six-meter distance. The results were recorded as imperial Snellen units and converted to logMAR values. The conversion was conducted using the Snellen to logMAR calculator and by the Visual Impairment Network for Children & Young People (VINCYP) under the National Health Services (NHS) Scotland (NHS Scotland, 2022).

For all visual acuity tests, the presenting acuity was measured as habitual VA, with correction if worn. Participants were tested one eye at a time. The order of the tests (PA and Snellen) was not standardized. The tests were strictly performed or supervised by optometrists to ensure their precision and accuracy.

Statistical Analysis

Statistical analysis was conducted using IBM Statistical Package for Social Science Software (SPSS) (version 20.0; IBM Corp., Armonk, NY, USA). The normality of the data was investigated using the Kolmogorov-Smirnov test. Data were deemed non-normal; thus, non-parametric tests were used to evaluate the data. The mean and standard error of the VA for each method are reported. Acuity results

from PA and Snellen were compared using the Wilcoxon signed rank test. The validity of acuity between PA and Snellen was analyzed using the intraclass correlation coefficient (ICC) test. The test-retest variability of both methods was also calculated. Spearman's rank correlation coefficient was calculated to determine the agreement between PA and Snellen acuity. The Bland-Altman plot was used to demonstrate the consistency between PA and Snellen acuity. The significance level was set at $\alpha \leq 0.05$ (95%).

RESULT

The mean VA using PA was recorded as 0.066±0.007 log, while that using Snellen was 0.103±0.009 log (z=-4.119, p<0.0005, Wilcoxon signed rank test) (Table 1). Although the analysis showed a significant difference, the mean PA and Snellen VAs differed by approximately two logMAR letters only.

Table 1. Mean and standard deviation values of the PA and Snellen tests. The p value was indicated as significantly different and was calculated using the Wilcoxon signed rank test.

	PA (n = 266)	Snellen (n = 266)	z, p
VA (logMAR)	0.066±0.007	0.103±0.009	z=-4.119, p<0.0005

ICC analysis between PA and Snellen acuity yielded a coefficient value of 0.641 (95%CI:0.518–0.731, p < 0.001), indicating moderate reliability between the two tests. The Bland-Altman analysis indicated good agreement between the tests, with most data points concentrated within the 95% limit of agreement (LoA) (Figure 1). The logMAR acuity differences between PA and the Snellen chart are clinically acceptable for screening purposes as they lie within +0.037 logMAR (denoting a difference of about two acuity letters only).

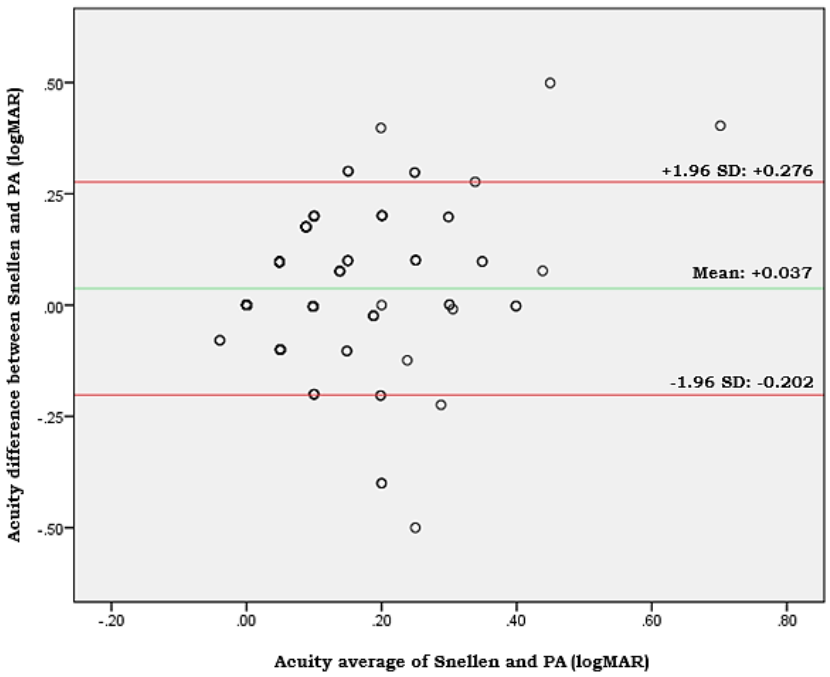


Figure 1 - Bland–Altman plot analysis of the agreement between PEEK Acuity (PA) and Snellen acuity. The y-axis marks the visual acuity differences between PA and Snellen acuity and the x-axis marks the acuity means of both tests.

The relationship between acuities yielded by PA and Snellen is shown in Figure 2. Spearman's rank correlation coefficient analysis revealed an r_s value of 0.508 ($p<0.001$), indicating a moderate positive correlation between Snellen and PA.

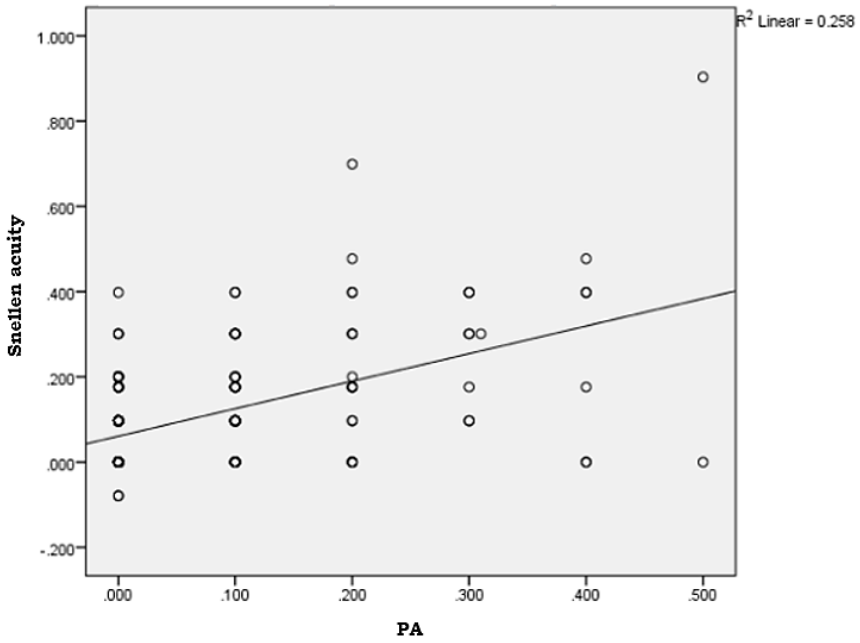


Figure 2 Spearman's rank correlation plot analyzing the agreement between the PA and Snellen acuity tests. An r-value of 0.508 indicated a moderate positive correlation between the tests.

DISCUSSION

The ubiquity of smartphones in modern life and their widespread use offers healthcare professionals an opportunity to improve the measurement of health-related outcomes. VA measurement using smartphone technology has proven its many benefits, particularly in low clinical settings, for communities that require testing and monitoring of their VA (Bert et al., 2014; Bastawrous et al., 2013). Many vision-testing applications are currently available, but only a few have been validated. Determining the accuracy, for instance, the self-testing VA application, is crucial because unreliable and inaccurate measurements may result in improper management and treatment of ocular disorders (Brady et al., 2015; Han et al., 2015).

This study aimed to test the reliability of the smartphone application PA to conventional Snellen acuity in testing children's VA. The VA obtained from the PA application was significantly better than that obtained using the Snellen acuity test (Table 1). VA obtained using PA seemed to yield better results than those obtained using the conventional Snellen test, albeit only by 0.038 logMAR. Even though the analysis indicated a significant difference, the 0.038 logMAR value only amounted to approximately two logMAR letters, which is arguably not clinically significant. External factors include illumination, contrast, glare, nature of the test object, distance, size of the retinal image, and visual efficiency (Lebensohn et al., 1993). Any ill-fitting factor could result in inaccurate VA measurements. For example, the acuity testing using the Snellen chart conducted in this study was using a printed version of the test. Such a setup is simple and probably ideal for vision screening purposes but may be lacking in illumination, resulting in a lower acuity response.

It is important to note that the findings of this study are in line with other studies in literature. It has been reported that PA tends to overestimate VA compared with other VA tests (Rono et al., 2018; de Venecia et al., 2018; Zhao et al., 2019). Overestimation of VA may result in higher acuity that may mask visual concern. Rono et al. (2018) reported a lower specificity using PA compared to the conventional Snellen tests, which resonated with the overestimation of patients' VA. de Venecia et al. (2018) in their

studies only reported a 48% sensitivity and 83% specificity, while Zhao et al. (2019) reported an average sensitivity and specificity of 80% and 96%, respectively. These two studies also indicated an overestimation of VA when using PA. Care must be taken when deciphering the results of PA to ensure the best management of a patient.

The ICC value with a 95% confidence interval has a value range of 0 to 1 and is divided into 4 value categories; (i) values below 0.5 indicate low reliability, (ii) between 0.5 to 0.75 suggest moderate reliability, (iii) between 0.75 to 0.9 indicates good reliability, and (iv) above 0.9 indicates exceptional reliability (Koo & Li, 2016). The ICC results of the current study indicate that PA and Snellen acuity tests have an inter-reliability of 0.641 (95% CI:0.518 – 0.731), which falls under the category of moderate reliability. Bastawrous et al. (2015) and Brady et al. (2015), who tested PA application against the ETDRS chart, concluded that there was a high degree of correlation between the two methods (95% CI, 0.05-0.10; p =0.08). In addition, Irawati et al. (2020) tested PA against the Snellen chart in participants who had leprosy. They concluded that PA is a reliable and repeatable screening tool that is as useful as the Snellen chart.

The agreement between the PA and Snellen tests was also investigated using the Bland–Altman plot. The VA measurement by these tests was consistent with one another, considering that the data points were mostly concentrated within the 95% of LoA (between +0.276 and -0.202 logMAR) and most were clustered near the mean difference value of 0.037. Spearman's rank correlation analysis indicated a significant positive correlation between the acuity results obtained using the tests (r_s =0.58, p<0.001). The results of the current study are consistent with those of Bastawrous et al. (2015), who demonstrated a much stronger correlation between tests. Although they separated their analysis according to the location of the test being conducted, both tests showed an r (at clinic) of 0.950 (p=0.08) and r (at home) of 0.902 (p=0.08). Their mean difference recorded were -0.078 log MAR (95% CI; -0.100 to -0.056) and 0.029 logMAR (95% CI; -0.007 to 0.065) for tests conducted at clinic and home, respectively.

Limitations of the Study

The current study had several limitations which warrant considerations in future studies. Firstly, the smartphones were not standardized in measuring the VA using PA. The screen projection by different smartphones may not be similar where it may affect image resolutions, and acuity responses (Han et al., 2019). Secondly, the participants of young children age ranged from three to 13 years old may yield different responses during the testing. Factors including cognitive level and test surrounding may have an impact on the VA results (Salthouse et al., 1996). Thirdly, the current study used the Snellen chart as opposed to a more standardized logMAR EDTRS chart. As the data were collected during a vision screening, employing EDTRS chart was not feasible as the test consumes more time for a vision screening. The Snellen test may be lacking in accuracy (Lovie-Kitchin, 2015), yet its usage in clinics is universal. Considering Snellen's popularity in a clinical setting, it is imperative to benchmark the PA application to Snellen.

Implications of the Study

The result of this study shows the feasibility of smartphone-based VA testing, specifically the PA, for use in vision screening programs. Care should be given in interpreting the VA obtained in children where overestimations may occur. The performance of PA in older patients is likely better based on the literature (Brady et al., 2015; Irawati et al., 2020) yet needs to be elucidated given the population and surroundings.

The ability to assess VA using smartphones is a game changer, especially given the alarming prevalence of myopia among younger generations and the rapidly growing elderly populations (Holden et al., 2016; Chew et al., 2018). With the availability of smartphones globally, such important vision tests can be self-administered at a meager cost, which in turn helps to reduce visual impairment (Free et al., 2013). Especially in settings where ophthalmic instrumentation or ophthalmic training is limited, the ability to reliably measure vision may improve the vision testing assessment in routine clinical practice.

Vision screening programs can be conducted easily with the availability of smartphones, and may also be conducted by untrained screeners (Siktberg et al., 2021).

CONCLUSION

The PA application in smartphones shows a promising potential to be used for visual screening on children, albeit the moderate agreement with the Snellen acuity test. The PA may yield a slightly better VA result relative to the Snellen acuity test. Yet, the simplicity, low cost, and quick testing may favor its usage in screening children's vision.

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RETINAL AND CHOROIDAL THICKNESS IN MYOPIC AND EMMETROPIC MALAY SUBJECTS

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ABSTRACT

Introduction: The elongation of eyeball which led to the increment of refractive error can cause pathological effects on the fundus. This is can be seen in myopic groups as their eyeballs are elongating which then affect the thickness of choroid and retina. The choroidal thickness (CT) and retina retinal thickness is highly influenced by refractive error. Depending on the refractive errors, some thinning areas of the choroid and retinal thickness would be varied. **Aim:** This study was carried out to assess the differences in retinal and choroidal thickness among myopic groups and emmetropic Malay subjects**. Methodology:** In this clinical cross-sectional study, 46 subjects (aged 19 to 24) with mean SER values of -0.10 ± 0.25 D for emmetrope, -1.69 ± 0.60 D for low myope, -3.92 ± 0.86 D for moderate myope, and -6.17 ± 0.63 D for high myope were examined. The retinal and choroidal thickness of the outer (perifovea) and inner (parafovea) macular layers at four separate locations, including the temporal, superior, nasal, and inferior quadrants, as well as the fovea itself, were measured using swept source optical coherence tomography (SS-OCT). **Results**: There were no significant inter-group differences in the foveal thickness and in the thickness of all the inner rings of the macula ($p > 0.05$). However, there were significant differences in the mean outer CT between the myopic groups and the emmetropes at the nasal quadrant ($F(3,43 = 6.15$, $p < 0.05$) and the inferior quadrant ($F(3,43) = 3.84$, $p < 0.05$). When compared to the emmetropic group, a Dunnet post-hoc test revealed that the outer CT in the nasal area was reduced in the low, moderate, and high myopia groups. In addition, compared to the emmetropic groups, the low and moderate myopia group had a reduced outer CT at the inferior region. **Conclusion:**

There are differences of CT between emmetropic and myopic Malay subjects however the retinal thickness does not vary.

KEYWORDS: choroidal thickness, retinal thickness, myopia, swept-source optical coherence tomography

INTRODUCTION

Myopia, a common refractive error, is impacting an increasing number of people. Myopia progression can lead to a variety of significant consequences, including blindness (Xiang & Zou, 2020). Holden et al. estimated in 2016 that 1.406 billion people (22.9 percent of the global population) had high myopia in 2000, and that 163 million people had high myopia in 2000. They also estimated that by 2050, there will be 4.758 billion persons with myopia (49.8% of the world's population), with 938 million of them having high myopia. This is a concerning figure, and more studies are required to determine how the increase in refractive error produced by the elongation of the eyeball affects the thickness of retina and choroid. Rudnicka et al. (2015) disclosed the differences in myopia prevalence based on ethnicity, age, environment, and gender in 2015. Myopia, for example, is most common in East Asians, and at the age of 10, the incidence was already 35%. At the age of 18, the incidence was as high as 80% in East Asians, while it was less common in Caucasians (23%) and black Africans (6%). Children in cities have a 2.6-fold higher chance of acquiring myopia than children in rural areas, while girls appear to have a 2-fold higher risk of developing myopia than boys, at least in Caucasians and East Asians.

This indicates that the solution for halting myopia progression should be implemented as soon as possible. One of the reasons to halt the myopia progression is pathological myopia. According to Ohno-Matsui et al. (2021), high myopia is defined by a high degree of myopic refractive error, whereas pathologic myopia is defined by the presence of typical fundus complications such as posterior staphyloma or myopic maculopathy that is equal to or more serious than diffuse choroidal atrophy. Although pathologic myopia is more common in eyes with high myopia, its repercussions, particularly posterior staphyloma, can occur in eyes with low and moderate myopia. Furthermore, the increase in refractive error is linked to the elongation of the eyeball, which affects the thickness of the retina and choroid. Therefore, this study was carried out to determine whether there were any differences between CT and retinal thickness in myopes and emmetropes.

MATERIALS AND METHODS

Myopic and emmetropic subjects were chosen from Kulliyyah of Allied Health Sciences, International Islamic University Malaysia (IIUM), Kuantan campus using a simple random sampling technique. The work was carried out in IIUM Optometry Clinic, IIUM Kuantan. The selected subjects were examined, and measurement was taken at the IIUM Optometry Clinic.

The inclusion criteria of the sample were based on the age range of 19 to 24 years, best spectacle-corrected visual acuity (BSCVA) of 6/6 or better and N6, and intraocular pressure (IOP) no greater than 21 mmHg. Subjects that were being selected were free from any ocular disease or surgery. The age of subjects is range from 19 to 24 years regardless of gender. Only Malaysian Malays were selected for the study. The onset of myopia is before the age of 16 years to ensure the myopia was axial in nature, i.e., the so-called juvenile-onset myopia (Chua et al., 2018; Kaiti et al., 2021; Williams & Hammond, 2019; Zadnik & Mutti, 2019). Exclusion criteria were: subjects with a history of intraocular or refractive surgery, retinal disease, glaucoma and other neurological diseases, anisometropia more than 0.50 D. Subjects who are undergoing treatment that could change the IOP and retinal thickness, eyes with abnormal OCT findings, OCT scan achieved with image quality less than eight and decentred image.

The study was carried out from March 2022 to June 2023. This research was approved by the Research and Ethics Committee for Medical Research (KAHS 74/22), IIUM and complied with the tenets of the Declaration of Helsinki. Informed consent was obtained from each subject before enrolment.

All subjects underwent evaluation of focimeter, autorefractor, distance visual acuity (VA), subjective refraction, slit-lamp examination, tonometry, and swept-source optical coherence tomography (SS-OCT). During clinical refraction, subjective refraction was performed and recorded as spherical equivalent refraction (SER). The SER is calculated by adding the sum of the sphere power with half of the cylinder power. Then, the subjects are classified as emmetropia (SER between +0.50 D and -0.50 D), low myopia (SER from -0.75 D to -2.00 D), moderate myopia (SER from -2.25 D to -5.00 D) or high myopia (SER greater than -5.00 D) (Williams & Hammond, 2019). Detailed information on OCT imaging is described in the S-S OCT manual. Data are presented in figures and false-colour topographic maps. The computer software analyses the image automatically.

In the study, the retinal structures were imaged using a commercial swept-source Topcon DRI-OCT Triton (Topcon Corporation, Tokyo, Japan). To create B and C-scan high resolution fundus images, this technology scans a narrow beam onto the retina with a central wavelength of 1 050 nm. The use of this near-infrared wavelength allows for a deeper penetration into retinal tissues, including the choroid and a portion of the sclera. On each eye, five B-scans centred on the fovea were obtained. The distance between adjacent scans was 0.15 mm. Each B-scan image was adjusted to 9 mm in length. A pixel in the image along the horizontal (vertical) direction corresponds to 8.79 m (2.02 m) in distance, according to the technical specifications. The retinal pigment epithelium (RPE) was chosen as the reference layer in this study. The technology automatically detects the RPE layer of each A-scan as the brightest signal in each B-scan. Once the RPE for each A-scan was determined, it was moved vertically to match the RPE across neighbouring columns in the B-scan. The RPE appeared as a "horizontal line" in this version of the OCT fundus image, while the rest of the morphological structures and layers maintained their size and relative position.

The CT was obtained from manual segmentation of fundus images from OCT B-scans. CT was measured from the RPE (outer border of the hyper-reflective line) to the inner sclera border. Measurement was taken on four locations which are central fovea (0 µm), 2250 µm nasal to the fovea (location N), 2250 µm (location T1) and 3375 µm (location T2) temporal to the fovea (Othman et al., 2012; Sezer et al., 2016; Fernández et al., 2022).

The retinal-macula thickness map was created by interpolating retinal thickness profiles from the six cross-sectional images using a colour scale. The Topcon Advanced Boundary Software (TABSTM) automatically analysed all scanning data and measured the thickness of the retina from the junction of the inner and outer segments of the photoreceptors to the inner limiting membrane. The macula was automatically divided into three concentric rings: the centre, inner, and outside rings, each measuring 1.0, 3.0, and 6.0 mm in diameter, as shown in Figure 1. The apparatus was centred on the foveal pit. The foveal, inner (parafovea), and outer (perifovea) macular regions were represented by the centre, inner, and outer rings, respectively. The Fast Macular Thickness OCT for emmetrope and myope are shown in Figure 2 and Figure 3, respectively.

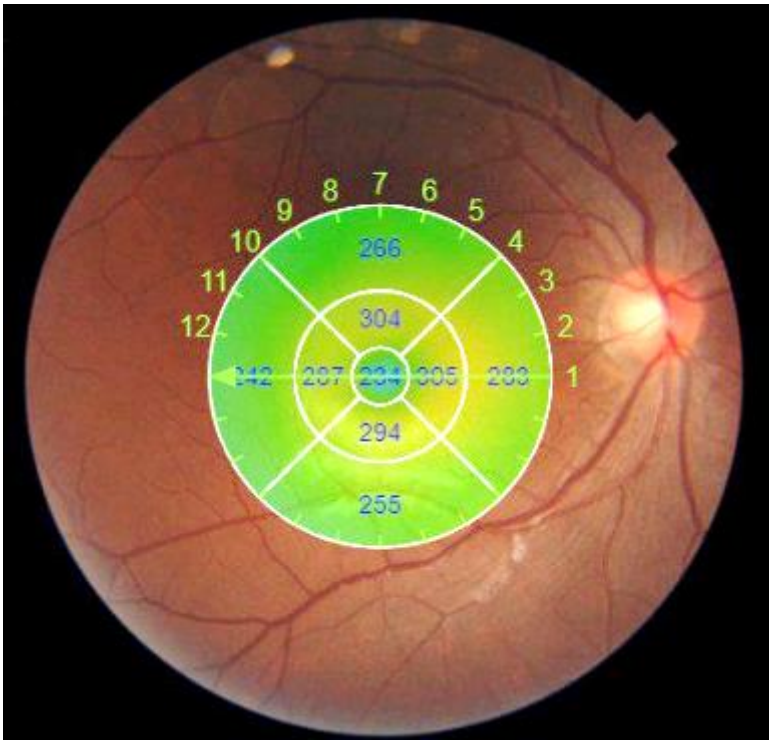


Figure 1. The Early Treatment Diabetic Retinopathy Study (ETDRS) grid of the OCT. The parafoveal region and the perifoveal region were further subdivided into superior, inferior, temporal, and nasal subfields, which consists of the OCT scanning image with resulting macular thickness and three concentric circles are formed 1.0, 3.0 and 6.0 mm in diameter around the central point of the fovea.

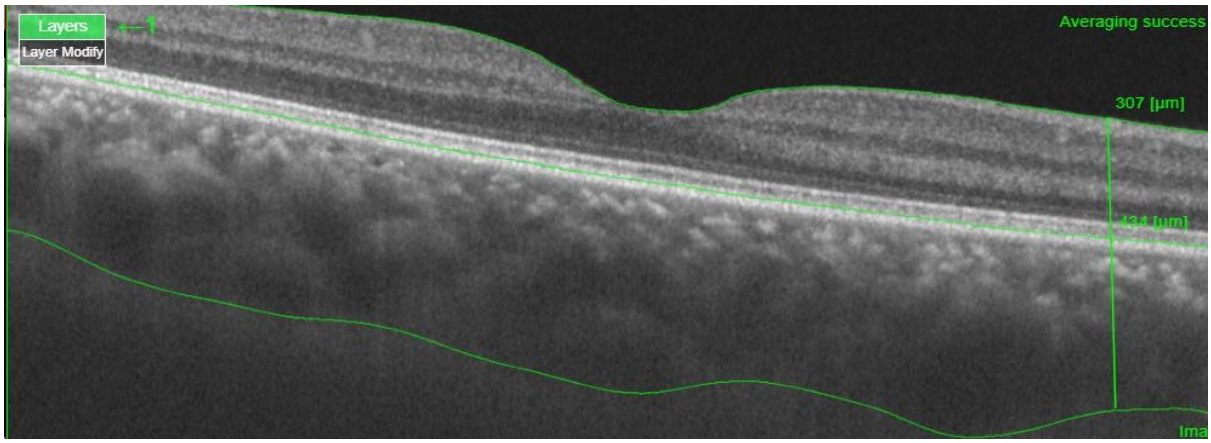


Figure 2. Fast macular thickness OCT scan from an emmetrope. Retinal thickness is measured anteriorly, from the inner limiting membrane (ILM) to the junction of the photoreceptor inner and outer segments (IS/OS) posteriorly. Meanwhile, choroidal thickness is measured from IS/OS to the junction of inner-scleral border.

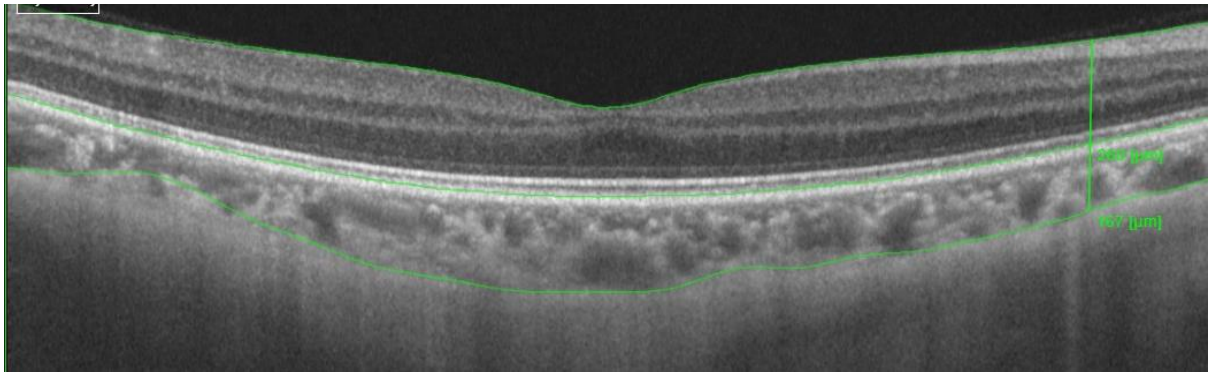


Figure 3. Fast macular thickness OCT scan from a myope. Retinal thickness is measured anteriorly, from the inner limiting membrane (ILM) to the junction of the photoreceptor inner and outer segments (IS/OS) posteriorly. Meanwhile, choroidal thickness is measured from IS/OS to the junction of inner-scleral border.

All data were analysed using the statistical package IBM SPSS version 22.0 for Windows (IBM SPSS, Armonk, NY, USA). A p-value of less than 0.05 was considered statistically significant.

RESULTS

Eighty-four (84) subjects in total were collected for measurement. However, only 46 subjects were chosen for statistical analysis. Thirty-eight (38) subjects were excluded because having the history of intraocular or refractive surgery, retinal disease, glaucoma, and other neurological diseases, anisometropia greater than 0.50 D, abnormal OCT findings, and astigmatism greater than 1.00 D.

The normal distribution of the data was analysed using the Shapiro-Wilk test of normality, skewness value and coefficient of variation (CV). As all the data were normally distributed, the one-way ANOVA test was used to compare the retinal and choroidal thickness between emmetropic and myopic Malay subjects. From the 46 eyes of the subjects enrolled in the study, there were 25 subjects categorised as emmetropia (SER -0.10 ± 0.25 D), 12 subjects were in the low myopia category (SER -1.69 ± 0.60 D), 6 subjects were moderate myopia group (SER -3.92 ± 0.86 D), and 3 subjects in the high myopia group (SER -6.17 ± 0.63 D). Foveal and regional retinal thickness measurements in each group are summarised in Table 1. There were no significant inter-group differences in the foveal thickness and in the thickness of all inner and outer rings of the macula ($p > 0.05$).

Table 1. Mean and standard deviation and one-way ANOVA results of retinal thickness in emmetropic and myopic groups

OCT Measurement	Emmetrope (n = 25)	Low Myope (n = 12)	Moderate Myope (n = 6)	High Myope (n = 3)	*p*-value
		Retinal Thickness (µm)			
Fovea	193.23 ± 38.24	208.17 ± 47.50	196.83 ± 21.76	205.33 ± 24.67	0.73
Inner Nasal	274.08 ± 27.84	285.92 ± 26.95	281.33 ± 6.06	290.67 ± 5.77	0.47
Outer Nasal	288.00 ± 23.97	282.50 ± 40.82	291.83 ± 23.20	277.67 ± 17.93	0.85
Inner Temporal	273.12 ± 23.30	282.00 ± 30.00	282.67 ± 16.51	245.33 ± 33.29	0.14
Outer Temporal	261.58 ± 20.09	249.25 ± 27.42	247.50 ± 20.67	252.00 ± 4.36	0.29
Inner Inferior	268.19 ± 39.12	278.08 ± 42.94	290.00 ± 9.70	284.33 ± 24.11	0.56
Outer Inferior	274.12 ± 20.84	273.08 ± 24.50	264.67 ± 4.84	261.67 ± 4.04	0.60
Inner Superior	290.35 ± 34.24	297.08 ± 33.84	300.00 ± 22.13	301.00 ± 5.20	0.85
Outer Superior	286.54 ± 24.86	285.08 ± 28.93	269.00 ± 23.61	267.00 ± 4.36	0.32

Whereas foveal and regional CT measurements in each group is summarised in Table 2. There were no significant inter-group differences in the foveal thickness and in the thickness of all the inner rings of the macula ($p > 0.05$). However, there were significant differences in the mean outer CT between the

myopic groups and the emmetropes at the nasal quadrant ($F(3,43 = 6.15, p < 0.05$) and the inferior quadrant ($F(3,43) = 3.84, p < 0.05$). The Dunnet post-hoc test revealed that the outer CT in the nasal area was thinner in the low, moderate, and high myopia groups than the emmetropic group. In addition, compared to the emmetropic groups, the low and moderate myopia group had a reduced outer CT at the inferior region.

Table 2. Mean and standard deviation and one-way ANOVA results of CT in emmetropic and myopic groups

OCT Measurement	Emmetrope (n = 25)	Low Myope (n = 12)	Moderate Myope (n = 6)	High Myope (n = 3)	*p*-value
		CT (µm)			
Fovea	326.25 ± 112.40	312.75 ± 75.46	257.83 ± 63.04	284.67 ± 11.68	0.45
Inner Nasal	315.19 ± 88.10	303.83 ± 75.41	248.33 ± 45.89	259.00 ± 39.05	0.24
Outer Nasal	298.92 ± 69.71	240.08 ± 48.89	214.83 ± 77.90	175.33 ± 12.58	<0.01
Inner Temporal	328.92 ± 98.23	319.92 ± 66.31	267.17 ± 76.96	283.33 ± 34.30	0.41
Outer Temporal	319.27 ± 86.95	273.17 ± 53.17	284.33 ± 29.53	308.67 ± 23.29	0.30
Inner Inferior	338.77 ± 69.68	292.17 ± 62.70	274.83 ± 55.46	276.67 ± 50.36	0.06
Outer Inferior	328.69 ± 77.72	267.83 ± 56.79	243.17 ± 32.46	288.00 ± 65.83	0.02
Inner Superior	312.69 ± 81.77	293.25 ± 63.67	304.67 ± 51.96	290.67 ± 51.32	0.87
Outer Superior	326.62 ± 78.15	320.17 ± 68.35	290.67 ± 39.17	303.67 ± 43.82	0.71

DISCUSSION

This study evaluated the variations in CT and retinal thickness in emmetropic and myopic Malay subjects. Our findings revealed that there is no influence on retinal thickness with increasing refractive error, with the exception of the CT, which decreased, notably in the outer nasal and inferior regions, with increasing refractive error.

Aydemir et al. (2021) found that myopia patients had thinner CT, retinal nerve fibre layer (RNFL), and macular layers than emmetropic and hyperopic patients. However, there were no appreciable differences in the average thickness of the retinal layer between the groups. This is also supported by a previous study done in 2020 by Heirani et al. that examined CT and refractive status and found that those with myopia had reduced CTs while people with hyperopia had greater CTs. This is also consistent with the study by Jin et al. from 2016, which found that the choroidal thickness was more significant in hyperopes and thinned in most regions in myopes. In addition, a study by Fernández et al., 2022 revealed that other works have reported minimal link between foveal thickness and axial length or refraction, not only in young eyes but even when middle-aged individuals' children and throughout a wide age range are involved. The same studies have shown that moderate to high myopia patients have thicker fovea than do non-myopic patients.

According to a study by Lee et al. (2021), the OCT type was the primary contributor of heterogeneity. It is hypothesised that CT values in healthy youngsters varied significantly between devices and were between 5.9 and 49.3 µm thinner on SS-OCT than on spectral domain OCT (SD-OCT). To our knowledge, our study is the first cross-sectional evaluation of the fundus performed on Malay patients utilising the SS-OCT. The OCT is well known as a viable method for capturing changes in the macular structure and gives the potential to image cross-sections of the retinal tissue in vivo. In our sample of emmetropic and myopic participants with a refractive error ranging from pl to -6.25 D, we used this "virtual" histology approach on living retinal tissue and discovered thinning of the choroid at the outer macula region (in two quadrants: nasal and inferior).

Our results show that there were no differences in the thickness of the fovea, inner (parafovea) and outer (perifovea) choroidal and retinal area between the emmetropic and myopic groups with the exception for outer CT at the nasal and inferior regions between emmetropic and myopic groups. This

is in agreement with a prior study by Lee et al., 2022, which found that choroidal thinning was more pronounced in the nasal and inferior areas with longer axial lengths.

Changes in CT may occur from the maintenance of vision clarity, according to the findings of several animal research. Because the image plane in myopic defocus is in front of the retina, a thickness of the choroid may push the retina in front of the image plane. Data from previous studies have demonstrated that, as part of this adjustment, CT prevents the entry of a variety of growth factors that serve as mechanical barriers and slows the growth of sclera (Lee et al., 2017). As a result, findings from both studies are congruent with findings from this study, which demonstrate that refractive error causes choroidal thinning in myopia in order to retain clear vision. This is compatible with the study's hypothesis that, in response to optical defocus, CT controls eye growth. They hypothesised that while CT can alter more easily than the eye can enlarge, repeated experiences of temporary choroidal thinning brought on by brief periods of hyperopic defocus, which is a suggested mechanism of myopigenesis, may cause ocular elongation by a mechanical or molecular mechanism (Nickla & Wallman, 2010). Thicker choroids represent a stronger physical barrier to chemical signals and growth factors travelling from the retina to the sclera, according to one of the explanations put up by the authors explaining this impact (Lee et al., 2022).

CONCLUSION

The findings of the current study, demonstrate that the outer CT at nasal and inferior areas reduces with increasing myopia. This thinned portion of the outer macula may be the initial structural alteration before any modifications to VA or other central visual functions.

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RETROSPECTIVE ANALYSIS OF BINOCULAR VISION ANOMALIES (STRABISMUS AND NON-STRABISMUS) IN A HIGHER EDUCATION OPTOMETRY CLINIC, KUANTAN, MALAYSIA FROM 2018 UNTIL 2021

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ABSTRACT

Introduction: Binocular single vision is required to see a single image with both eyes, so any disorders will impair visual function. It is supported by the normal visual apparatus, as well as sensory and motor systems. The anomaly on each component might lead to non-strabismus which are accommodation and vergence, as well as strabismus anomalies. **Aim:** This study was aimed to evaluate the retrospective data of non-strabismic and strabismic cases at International Islamic University Malaysia (IIUM) Optometry Clinic, Kuantan, Malaysia from 2018 until 2021. **Methodology:** A clinically based retrospective study was conducted, and all patients' files were thoroughly reviewed, and data collected were analyzed by different categories. The categories included demographic information such as age, gender, occupation, location, non-strabismus anomalies, including accommodation and vergence anomalies, as well as the type of strabismus. **Results:** The total sample size for the study was 91, with female participants accounting for 51.6 % of the total. The patients' ages ranged from 3 to 35 years (mean age: 12.03 ± 6.64 years), with one-third of them being under the age of ten. Most patients came from Pahang, with 57.1 % from the Kuantan district. 82 of the patients were still students, and the remaining of them worked as officers or non-officers. The most common cases were accommodation insufficiency, which affected 19.8 % of patients, while basic exophoria affected 9.9 %. Out of all strabismic patients, 67 patients had alternating exotropia at distance and near. **Conclusion:** Accommodation insufficiency, basic exophoria and intermittent exotropia dominated the binocular vision anomalies cases at the clinic. This data could be used in the clinic to forecast the trend of cases for the coming year. The awareness and prevention should be taken to reduce the number of cases especially on children.

KEYWORDS: Accommodation, vergence, strabismus, exophoria, exotropia

INTRODUCTION

Normal binocular vision can be achieved by simultaneous perception (O'Connor et al., 2010; South et al., 2019) as well as normal sensory and motor fusion (Paniccia & Ayala, 2015; She et al., 2021). These normal system results in superior three dimensional (3D) perception which is known as stereopsis, which is known as the hallmark of normal binocular vision (Kim et al., 2013; Wang et al., 2021). In order to achieve normal binocular vision, the eye visual system must have normal anatomy of visual apparatus (Bui Quoc & Milleret, 2014), normal sensory (Han, He, & Ooi, 2018) and normal motor (Niechwiej-Szwedo et al., 2017) systems. Anomalies in one or all eye visual systems could disrupt normal binocular vision which is known as binocular vision anomalies.

The anomaly of crystalline lens (Li et al., 2021) and disintegration between sensory and motor system of smooth ciliary muscle (Read et al., 2022) could lead to accommodation anomalies. Accommodation anomalies were classified as accommodation insufficiency, accommodation weakness, accommodation infacility, accommodation spasm, accommodation paralysis, and unequal accommodation (Darko-Takyi et al., 2016). Paniccia & Ayala, (2015) discovered that 39% of total 593 patients aged between 5 and 20 years old suffered accommodation insufficiency. In contrast, Paniccia & Ayala (2015) finding was not supported by Singh et al., (2020) whereby accommodative infacility was a common accommodation anomalies in 160 high school students. This similar trend of finding was also discovered by Wajuihian, (2022).

The anomaly occurs on the sensory and motor system at extraocular muscle could also lead to the vergence anomalies and strabismus (Kang et al., 2018). Wajuihian, (2022) conducted a study on 254 African patients aged 10 to 40 years to investigate the prevalence of vergence anomalies. It was found out that the most common vergence anomalies in the study population was convergence insufficiency. Similar findings was also discovered by Samsimon et al., (2020) whereby 23.4% of total 167 patients in a optometry clinic were having convergence insufficiency. Meanwhile, Nanjing Eye Study group conducted a study on 1986 children aged 48 to 60 months to evaluate the prevalence on the strabismus (Wang et al., 2021). Wang and co-author found that most of the subjects are having intermittent exotropia which consists of 4.89% of the total 167 patients.

However, the previous reported data was under explored for Malaysian populations. Therefore, this study was aimed to evaluate the retrospective data of non-strabismic and strabismic cases at International Islamic University Malaysia (IIUM) Optometry Clinic, Kuantan, Malaysia from 2018 until 2021.

MATERIALS AND METHODS

Data collection was conducted at IIUM Optometry Clinic, Kulliyyah of Allied Health Sciences, IIUM, Kuantan, Malaysia. Kuantan is a district in Pahang State which is located about 260-kilometer east capital city of Malaysia, Kuala Lumpur. It is also a city and the Pahang state capital. The district is located at the east coastal line and has its border with Terengganu state in the north.

All procedures conducted throughout the study were reviewed and approved by IIUM Research Ethics Committee (IREC) (IREC 2021-KAHS/DOVS01) and adheres to the tenets of the Declaration of Helsinki. This retrospective work was started in August 2021 and was completed in July 2022. All binocular vision anomalies patient records who received binocular vision treatment and therapy at IIUM Optometry Clinic from 2018 until 2021 were reviewed thoroughly. Patients who recorded agree to give consent to use their clinical data for research purposes in the patients' file were included in this study. Patients who were recorded having the history of ocular surface, ocular anterior and posterior, and systemic diseases, as well as active ocular allergy and ocular trauma, were excluded in this study.

The review process found that 91 patients attended the clinic throughout the period. Each patient file was labelled with a number and the collection of data was based on the labelled number for protecting their personal data. Demographic information, including patients' age, gender, the region, and state of residence, as well as type of binocular vision anomalies based on the clinician diagnosis, including a specific type of accommodation, vergence and strabismus anomalies were collected. The clinician diagnosis made for accommodative anomalies was based report from Singh et al., (2020). The clinician used the report from Khorrami-Nejad et al., (2018), Ma et al., (2019), Wang et al., (2021), and Zhang et al., (2021) to diagnose the vergence and strabismus anomalies. The collected data was inserted and analyzed using IBM®SPSS® Version 26.0. Descriptive analyses were calculated on all patients' demographic data and all types of binocular vision anomalies, including non-strabismic and strabismic types.

RESULTS

The study's total sample size was 91 individuals as demonstrated in Table 1 with 51.6 % being female. The patients ranged in age from 3 to 35 years (mean age: 12.03 ± 6.64 years). 71.5% of all 91 patients were 20 years old and below. 71.4% of total patients were coming from Pahang state, with 58.2 % coming from the Kuantan district community while the remainder (13.2%) from other districts. About 16.5% of the total patients originated from Terengganu state. Meanwhile, 82 patients (90.1%) were students and the remaining worked as officers and non-officers.

Table 1 Demographic data

Description N = 91	Mean (SD)	Minimum	Maximum	Frequency	Percentage (%)
Age (Years)	14.52 (7.50)	3	35		
0 –10				34	37.4
11 – 20				31	34.1
21 – 30				23	25.3
31 – 40				3	3.3
Ethnics					
Malay				87	95.6
Chinese				3	3.3
Others				1	1.1
Gender					
Male				44	48.4
Female				47	51.6
Origin of Patients					
Kuantan				53	58.2
Other district in Pahang state				12	13.2
Johor				1	1.1
Kedah				1	1.1
Kelantan				1	1.1
Kuala Lumpur				1	1.1
Penang				1	1.1
Perak				3	3.3
Selangor				2	2.2
Terengganu				15	16.5

Accommodation anomalies

All the necessary tests were performed on the patients with accommodation disorders. There was a higher incidence of patients with accommodation insufficiency in terms of accommodative dysfunctions (19.8 %), followed by accommodation excess, accommodation infacility and accommodation weakness. Table 3 summarized all the findings with the least number of patients having accommodation weakness.

Table 3 Data of accommodation anomalies

Type of accommodation anomalies (N = 91)	**Frequency**	**Percent (%)**
Accommodation excess	11	12.1
Accommodation infacility	3	3.3
Accommodation insufficiency	18	19.8
Accommodation weakness	2	2.2
NA	23	25.3
Normal	34	37.4

*NA: not applicable

Ocular alignment anomalies

Battery tests were done before deciding with a proper diagnosis. Table 4 showed the category for vergence anomalies, where 9.9 % of patients had basic exophoria, aside from patients with normal and not applicable (NA) data. Among all patients, 67 were strabismic, with intermittent exotropia having the highest prevalence as depicted in Table 5.

In each category, not applicable (NA) data was completely disregarded. This was caused by insufficient information being received to diagnose the patients and some of them had more profound anomalies such as strabismus, several accommodation tests were not performed on that situation yet.

Table 4 Data of vergence anomalies

Type of Vergence Anomalies (N = 91)	**Frequency**	**Percent (%)**
Normal	10	11.0
Convergence insufficiency (CI)	3	3.3
Convergence excess (CE)	1	1.1
Divergence excess (DE)	1	1.1
Basic esophoria	3	3.3
Basic exophoria	9	9.9
NA	64	70.3

*NA: Not applicable

Table 5 Prevalence of strabismic binocular disorder

Type of tropia		Frequency	Percent (%)
Normal		7	7.7
NA		17	18.7
Esotropia			
	Accommodative esotropia	2	2.2
	Divergence weakness	2	2.2
	Convergence excess	1	1.1
	Alternating	5	5.5
	Constant	6	6.6
	Other type	2	2.2
Exotropia			
	Constant	16	17.8
	Intermittent	26	28.6
	Alternating	13	14.3

DISCUSSIONS

Since the location of IIUM Optometry Clinic is in Kuantan district, most patients came from its district and other districts in Pahang state. However, 16.5 percent of total patients were living in Terengganu state. Due to the geographical location nearby Kuantan district, it might be convenient for the patients coming from the state to seek treatment at the clinic.

The result shows that 37.4% of total 91 patients were 10 years old and below. This age group are tendency to have strabismus if the signs of the eye deviation and anomaly of visual apparatus are left untreated (Hemptinne et al., 2020). The critical period for neuro-visual development occurs at this age of group which is between 18 to 24 months of life (Dennis et al., 2013) and the development of visual system becomes slow or matured after first seven years of life (Birch, 2013). Any anomaly of visual apparatus, as well as sensory and motor system could lead to amblyopia which is caused by visual deprivation due to lack of visual experience (Birch, 2013) and subsequently, leading to strabismus and binocular suppression (Scholl et al., 2013). Therefore, serious action is suggested to be taken by parents to bring their child for eye examination to prevent any visual anomalies in the age group which eventually results in strabismus and binocular suppression.

In the present study, it was found that the three most common accommodation anomalies at IIUM Optometry Clinic were accommodation insufficiency (19.8%), accommodation excess (11.0%), and accommodation infacility (3.3%). The finding was also agreed with a conducted in Ghana (Abdul-Kabir et al., 2015). Abdul-Kabir and the team conducted the study on 204 junior high school students, and it was discovered that about 32% of the total subjects were having accommodation insufficiency while 26% for accommodation infacility. A similar pattern was also reported by Samsimon et al. (2020) whereby the accommodation insufficiency patients consist of 26.3% of total patients came to optometry clinic, followed by accommodation excess (18.0%) and accommodation infacility (7.8%). Accommodation

insufficiency became most prevalent cases in accommodation anomalies might be due to academic demand of reading and writing (Abdul-Kabir et al., 2015). Moreover due to movement control order during COVID-19 pandemic in 2020 (Elengoe, 2020), the near work task might become exaggerated, especially on the digital devices (Trott, Driscoll, Irlado, & Pardhan, 2022) and subsequently could lead to the anomaly.

In terms of vergence anomalies, convergence insufficiency is the most prevalent problem (Trieu & Lavrich, 2018). A study was conducted in Puerto Rican pediatric population aged between 5 and 20 years, 593 patient records were reviewed between years 2004 and 2012 (Paniccia & Ayala, 2015). Patients with strabismus, amblyopia, nystagmus, vertical deviation, corneal pathology, retinal pathology, lens pathology, or any other parameter outside of population requirements were excluded. Paniccia and Ayala discovered that about 12.6% of total 593 patients were having convergence insufficiency, followed by convergence excess (9.1%). The identical pattern was also explored by Atiya et al., (2020). Atiya and co-author conducted a study on 66 ophthalmologist trainees (mean age: 29.3 ± 3.27 years) who had experience in surgical procedure attending a surgical training program at a tertiary eye care center. Convergence insufficiency was still recorded as the most common problem among the ophthalmologist trainees, which was 22% of the total subjects, followed by convergence excess (3%). However, the pattern of outcome was not demonstrated in this present study, whereby basic exophoria is recorded highest prevalence, followed by convergence insufficiency, and basic esophoria. This finding was in line with a study result in China which conducted on 415 Chinese participants aged between 21 and 38 years (Ma et al., 2019). Basic exophoria was seldom stated the most common diagnosis in previous prevalence studies with reported prevalence rates of 0.3% to 5.1% (Ma et al., 2019).

Intermittent exotropia cases dominated the strabismus anomalies among patients attending IIUM Optometry Clinic from 2018 until 2021. The discovery was identical with a study conducted in Hong Kong (Zhang et al., 2021). Zhang and the research team conducted a cross-sectional study involving 4273 children aged 6 to 8 years old. Only 133 children were diagnosed having strabismus. It was found that the 65 children were having intermittent exotropia, followed by constant exotropia (54 children), constant esotropia (12 children), and pure vertical strabismus (4 children). However, the finding in both investigations was contradicted with a study conducted in Iran (Khorrami-Nejad et al., 2018). The data was collected on 1174 patients aged between 0 to 18 years old from 2018 until 2014 at Farabi Hospital, Tehran, Iran. They found that accommodative esotropia accounted largest percentage, which was 25.04%, followed by intermittent exotropia, nonaccommodative esotropia and partially accommodative esotropia, with 12.09%, 11.24% and 10.39%, respectively (Khorrami-Nejad et al., 2018). This could be postulated that the western region of the World might have more esotropia cases while exotropia cases could commonly be demonstrated in eastern region.

CONCLUSIONS

In a nutshell, accommodation insufficiency and exophoria were suggested to dominate the non-strabismic anomalies among patients, especially for schoolchildren, teenagers, and work forces. Intermittent exotropia was suggested to be more prominent strabismus in eastern region of the World, while the number of esotropia cases, particularly accommodative esotropia might be enormous in the western region. These outcomes and discussions could be utilized as reference for the better management of non-strabismic and strabismic cases in future.

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THE STATUS OF MYOPIA REFRACTIVE ERROR FROM 2018 UNTIL 2021 AMONG AGED 30 TO 35 YEARS OLD IN A PRIVATE OPTOMETRY PRACTICE, DUNGUN, MALAYSIA: RETROSPECTIVE DATA

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ABSTRACT

Introduction: Myopia or also known as near-sightedness is a common visual impairment. Myopia usually started in children and the changes does occur to individuals across age groups. It is tightly linked or commonly related among young individuals which are children and teenagers. Study or research regarding the refractive error changes among adults especially among pre-presbyopia age is under-explored as past research does not collect data for the changes among individuals aged more than 30 years. **Aim:** To evaluate the myopia refractive error changes among adults aged 30 to 35 years old at a private optometric practice, Dungun district, Terengganu state, Malaysia from 2018 until 2021. **Methodology:** This retrospective study was conducted at ArRayyan Optometry, Dungun, Terengganu. All patient record aged 30 to 35 years old from 2018 until at the practice were reviewed. Patients with record having history of ocular surgery as well as ocular and systemic diseases were excluded. The onset of myopia was stipulated at 14 years old. Demographic and mean spherical equivalent refractive error (SER) were collected and analysed. **Results:** Fifteen generally healthy myopic participants mean age of 33.07 ± 1.79 years were met the criteria stipulated. There was a statistically significant increment in myopia refractive error changes in adults aged 30 to 35 years old (p<0.001). **Conclusion:** Myopia refractive error changes could not only occur in children and teenagers but could also demonstrate in adults aged 30 to 35.

KEYWORDS: myopia, pre-presbyopia, adults, sphere equivalent refractive error, refractive error

INTRODUCTION

Myopia or also known as near-sightedness is a common visual impairment as it affects an individual vision when looking at distance as the accommodation of the eye is relaxed (Smith & Walline, 2015) and the refractive error to define it is at least -0.50DS or more (Holden et al., 2015). It becomes major concern globally especially in East and South East Asia regions (Lam, et al., 2012; Mak et al., 2018) whereby it's condition is associated with an increased risk of several ocular diseases including retinal detachment, glaucoma, cataract, visual impairment, and blindness (Huang et al., 2015). Holden et al., (2016) stated that almost 30% of world populations are having myopia and the trend are expected to increase up to 50% of global population in 2050.

Myopia refractive error changes do occur to individuals across age groups. Verkicharla et al., (2020) discovered that the total means of the refractive error changes ranged from -0.07 ± 0.02 D (standard error) to -0.51 ± 0.02 D (standard error) across age groups, with children aged 6–10 years seeing the greatest annual change in refractive error, while adults aged 26–30 years experiencing the least. Similar pattern was also found by Polling et al., (2022). Children with spherical equivalent refraction (SER) -3 D at 10 years were all having high myopic (SER -6D) in their adult age. Meanwhile, children with SER between -1.5 D and -3 D at 10 years had a 46.0 percent risk of high myopia. Children with SER between -0.5 D and -1.5 D had a 32.6 percent risk of high myopia. However, the rate of increasing SER becomes slow in line with the increment of age, whereby the refractive error stabilizes at the age of 15 years.

Although the pattern of myopia refractive error has already reported in previous studies, the pattern of changes is under explored among populations aged 30 to 35 years old. Therefore, this study was aimed to evaluate the myopia refractive error changes from 2018 until 2021 among aged 30 to 35 years old.

MATERIALS AND METHODS

Data collection was conducted at ArRayyan Optometry, Dungun District, Malaysia. Dungun is a coastal district in Terengganu State which is located about 350 kilometres from Kuala Lumpur. Majority of the Dungun population is Malay which makes up about 97.3%, while Chinese, Indian and other population form 2.1%, 0.2%, and 0.4% (*Department of Statistics Malaysia*, 2020). Majority of areas in the district are rural. Most of the population in the district involves in petroleum industry activity since Dungun is located next to Kerteh, known as the petroleum and gas refinery area. However, there are still small pocket of the population take part in fishery, farming, and small trading.

Ethical approval for this study was obtained from International Islamic University Malaysia (IIUM) Research Ethics Committee (IREC) (IREC 2022-KAHS/DOVS/5). The sample size was measured using G*Power© version 3.1.9.4 software, Universität Düsseldorf. The effect size was chosen at 0.40 value, alpha error probability was 0.05, and power of study was 0.80. Number of measurement as well as number of groups were four, respectively. F-test with repeated measure ANOVA option was chosen and the minimum subjects calculated through the software to achieve 80% power of study was 12. This retrospective work started in September 2022 and ended in August 2023. Patient record aged 30 to 35 years old from 2018 until 2021 at ArRayyan Optometry were reviewed thoroughly and the refractive error data were taken. Onset of myopia was set between fourteen and 20 years old because the changes of refractive error is slowing down at the stipulated age (Trier et al., 2008). Patients with hyperopia, emmetropia ranged from +0.50DS until -0.25 DS and astigmatism more than -2.00DC were excluded. Patient with record having systemic diseases which include diabetes mellitus, hypertension and cardiovascular problem, active ocular allergy, refractive eye surgery, ocular trauma, cataract, and other media opacities, consume any drugs as medication, pregnancy, lactating, as well as neurological injury which may impact the eye system were also excluded in this study.

The review of the data in the practice discovered fifteen patients met the inclusion and exclusion criteria as stipulated. All patients were undergone non-cycloplegic refraction from 2018 until 2021 and the objective refraction using retinoscopy, as well as subjective refraction were conducted by an Optometrist in the practice who did not involve in this study. The patient file was labelled in number to protect the personal data information. The demographic data including age, ethnicity, and gender were collected. The spherical equivalent refractive error (SER) data on each eye for each patient was collected and SER was calculated based on Holladay et al., (2021) report. The data were analysed utilizing IBM®SPSS® Version 26.0. Descriptive analyses were calculated on all patients' demographic data while repeated measure analysis of variance (ANOVA) was used to compare the SER on right (RE) and SER on left eyes (LE) from 2018 until 2021 respectively. The p-value less than 0.05 is considered significant finding.

RESULTS

As described in Table 1, mean of age for all 15 patients were 33.07 ± 1.79 years with the highest frequency recorded at the age of 33 and 35 years (26.7% each). Female recorded the highest percentage for gender (66.7% of total patients), while all patients recorded from 2018 until 2021 were Malay (100%).

Table 1 Demographic data

Description N = 15	Mean (SD)	Frequency	Percentage (%)
Age (years)	33.07 (1.79)		
30		2	13.3
31		2	13.3
32		0	0
33		4	26.7
34		3	20.0
35		4	26.7
Gender			
Male		5	33.3
Female		10	66.7
Ethnic			
Malay		15	100
Chinese		0	0
Indian		0	0
Others		0	0

Table 2 Comparison of SER on the right eye (RE) from 2018 to 2021

SER on RE N= 15	Mean (SD)	*p*-value
SE RE 2018	-2.92 (1.36)	< 0.001**
SE RE 2019	-3.00 (1.36)	
SE RE 2020	-3.50 (1.40)	
SE RE 2021	-3.68 (1.32)	

*SD: standard deviation

**$p < 0.05$

Repeated measure analysis of variance (ANOVA) shows that all the p-values for the SER of right and left eyes were less than 0.05, indicating that there was statistically significant increase in the SER mean from 2018 to 2021. Table 2 and 3 demonstrates the significance level and the mean of SER for the RE and LE from 2018 until 2021.

Table 3 Comparison of spherical equivalent on the left eye (LE) from 2018 to 2021

SER on LE N = 15	Mean (SD)	*p*-value
SE LE 2018	-2.92 (1.25)	
SE LE 2019	-2.98 (1.25)	0.004**
SE LE 2020	-3.42 (1.31)	
SE LE 2021	-3.58 (1.29)	

*SD: standard deviation
**$p < 0.05$

DISCUSSION

Several studies have shown the possible correlation between near work and the progression of myopia, especially in young individuals which are children and teenagers. Myopia is closely related to the Asian community. The developed countries of East Asia are aware of the current myopia epidemic (Mak et. al., 2018). Certain theories propose that extended periods of near work might cause eye strain and exhaustion. Consequently, these factors could induce the elongation of the eyeball, which potentially contributes to the development and increment of myopia. The relationship between near work and hyperopic defocus is thought to be explained by a poor accommodative response in juvenile myopia (Huang et al., 2015)

In present study, the mean SER of patients on each eye respectively from 2018 to 2021 were compared. The findings showed that the SER of the myopic patients did show significant increment annually. The changes of SER on each eye in 2019, compared to the baseline data in 2018, was almost significant whereby the range of increment is about -0.06 to -0.08D. However, the changes of SER on each eye in 2020 was significant, whereby there was an increment about -0.50D compared in 2019. In contrast, the rate of changes in 2020 did not materialize in 2021. The changes recorded were about -0.16 to -0.18D. The refractive error changes of myopia in adults in the present study could be influenced by several factors which may include heredity, environmental factors such as excessive or less hours spent in outdoor activities, occupational considerations, and lifestyle choices. Increased dioptre hours of near work may lead to an increase in the prevalence of myopia since near work activities were linked to myopia (Huang et al., 2015). Nevertheless, since the onset of myopia among patients were categorized as late onset juvenile myopia, the significant increment of refractive error recorded in 2020 might be due to the situation induced by COVID-19 pandemic that changes the way of life at that time.

COVID-19 pandemic has had a huge impact on people's daily or routine activities, particularly their screen-time routines. To stop COVID-19 from spreading across the

country in Malaysia, the Movement Control Order (MCO) was put into effect on 18th March 2020 and remained in effect through 28th April 2020 (Elengoe, 2020). People turned to digital entertainment for relaxation during the pandemic as there were few opportunities for outdoor activities and social meetings which led to increased usage of streaming services for movies, TV shows, and online games. Increasing the amount of time spent outside considerably slowed the advancement of myopia, according to three studies that investigated the relationship between outside time and myopia (Sherwin et. al., 2012). Social media, social networking sites and messaging applications become even more important for maintaining contact with friends and family during times of lockdown and social distancing and to maintain social interactions, people spend more time on websites and social apps such as Facebook, Instagram, Twitter, WhatsApp, and others. Screen time plays a crucial function in bridging the communication gap between teens and their wellbeing to aid in their adjustment to these new norms (Amran & Jamaluddin, 2022).

Numerous people had to adjust to new ways of working, learning, and socialising from home as limitations on mobility and social gatherings were put in place to stop the virus from spreading. Most adults had to work from home and some of them lost their jobs. Increased time spent indoors and a shift to remote activities, screen time has significantly increased globally. Virtual meetings and video conferencing through online platforms by using gadgets such as laptops, computers and smartphones became the new norm as offices were closed and workers working from home. Communication with coworkers, clients, and business partners increased on online platforms.

CONCLUSION

Results of this study showed that myopia refractive error changes do not only occurs to children and teenagers, but it also may occur among adults as environmental factors which are excessive near work and less outdoor activities also could contribute to the increment of myopia SER especially in COVID-19 and movement control order era. Myopia refractive error changes in adults is extremely important, just as it is in children. The refractive error changes are frequently linked to younger age groups, however its effects on adults shouldn't be disregarded. Adults spend most of their lives working and participating in many activities; thus, the refractive error changes of myopia can have a significant impact on their quality of life. Therefore, with this finding, it is hoped that it can assist for further thorough research and attention to myopia refractive error changes in adults to create efficient preventive and management plans as well as measures for enhancing this population's visual health and general quality of life.

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THE TREND OF OPTOMETRIC DIAGNOSES AND THEIR MANAGEMENT IN THE IIUM OPTOMETRY CLINIC

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ABSTRACT

Introduction: The study aimed to identify the type and frequencies of optometric diagnoses in IIUM Optometry Clinic, Indera Mahkota Campus (IMC) in Semester 2 2016/2017. The relationship between age, gender and ethnicity with the three most common optometric diagnoses in IIUM Optometry Clinic has been studied. The management given in IIUM Optometry Clinic was also recorded. **Methods:** The study involved 223 subjects aged between 1 to 80 years old and gender independent. This study used universal sampling and retrospective design. Age, gender, race, diagnosis, and management of patients were noted from the case records. Some of the patients had more than one diagnosis. Hence, the diagnoses were more than the number of patients examined. **Results:** The top three classifications of optometric diagnoses were refractive problems (217, 45.2%), ocular diseases (198, 41.2%) and vergence problems (26, 5.4%). From these three classifications, they were divided into their own specific diagnoses in which myopia (96, 20.0%) was found to be the most common diagnosis followed by dry eyes (91, 19.0%) and convergence insufficiency (14, 2.9%). From the chi-square test, the results revealed a significant association between age with myopia (p=0.029) and dry eyes (p=0.022). The three most common management given were refractive management (226, 43.8%), prescribing artificial tears (77, 14.9%) and patient education (71, 13.8%). **Conclusions:** In conclusion, since refractive errors remain the leading cause of global visual impairment, better intervention strategies can be planned and implemented, especially in visual screening. A higher occurrence of certain cases can encourage optometrists to be very competent in managing the case.

KEYWORDS: optometry cases, optometry clinic, diagnosis

INTRODUCTION

Often, it was said cases managed by the students are stereotyped. Hence, this study was conducted to know about the trend of optometric diagnoses and their management in IIUM Optometry Clinic in Semester 2 2016/2017. Knowledge of the trend of optometric diagnoses could provide some overview of how often the students in IIUM Optometry Clinic could encounter the diagnoses. Thus, this can be helpful in planning the management. The trend of common specific disorders and problems may help practitioners and students to contemplate who is at a higher risk for a disorder and to better diagnose any pathological problem (Elam & Lee, 2013). This study also gave information about the management given in IIUM Optometry Clinic. Thus, a standard of procedures (SOP) can be produced or updated for the common optometric diagnoses in the IIUM Optometry Clinic.

Previous studies have done studies about the trend of optometric diagnoses in other eye care centres. For example, in the State College of Optometry, New York, optometrists found and diagnosed many refractive error problems (Soroka et al., 2006). Increased prevalence of myopia had been found during the late teens and 20s due to genetic and environmental factors (Williams et al., 2015). A study by Reddy, Tajunisah, Low & Karmila (2008) mentioned that the most common eye problems seen in University of Malaya Medical Centre were cataract (385, 32.9%), glaucoma (274, 23.4%), uncorrected refractive errors (126, 10.8%), diabetic retinopathy (113, 9.7%), visual impairment (105, 9.6%) and

blindness (11, 0.9%). Another study by Lara et al. (2001) reported that 22.3% of patients presented in the general clinic population with accommodation and convergence excess as the two most common disorders. A study by Garza-León et al. (2016) reported that dry eyes had become one of the most common eye diseases and the main cause for patients to seek prevention and treatment.

This current study also focused on the management provided in the IIUM Optometry Clinic. Since the management of optometric diagnoses varies among practitioners, a standard of procedure would be very useful as clinical practice guidelines to be referred to. A clinical practice guideline produced by the Ministry of Health Malaysia comprises management for glaucoma, diabetic retinopathy, post-operative infectious endophthalmitis and retinopathy of prematurity. During the run of this study, IIUM Optometry Clinic also very recently came out with several SOPs for clinic flow and management to be used internally.

MATERIALS AND METHODS

This study was conducted in IIUM Optometry Clinic, Indera Mahkota Campus (IMC), Kulliyyah of Allied Health Sciences, IIUM Kuantan, Pahang. It was a retrospective study and utilised a universal sampling technique, where all the records of patients that attended IIUM Optometry Clinic in Semester 2 2016/2017 were retrieved and reviewed. Only signed informed consent records were included as participants in this study.

Data Collection and Analysis

Data recorded by Optometry students on all patients who underwent optometric examination at IIUM Optometry Clinic (IMC) in Semester 2 2016/2017 had been retrieved and reviewed. Each optometry student in IIUM would record all the patients' results during the eye examination in a standardised form. The results had been kept as patients' records. In this study, age, gender, race, diagnosis, and management of patients were noted from the case records. Some of the patients had more than one diagnosis, and others also had more than one management. Hence, the total number of cases and management was more than the number of patients examined. The total number of diagnoses and management had been counted manually and inserted into the data collection form.

The obtained data had been keyed into Statistical Package for the Social Science (SPSS) for analysis. Statistical analysis was performed by using SPSS Version 12.0.1 for Windows. In all tests, a p-value of less than 0.05 was considered to indicate statistical significance.

RESULTS

The Trend of Optometric Diagnoses in IIUM Optometry Clinic (IMC) in Semester 2 2016/2017

Figure I shows refractive problems as the most common classification of optometric diagnosis seen in this study (217, 45.2%) followed by ocular diseases (198, 41.2%), vergence problems (26, 5.4%), accommodation problems (18, 3.8%), other diagnoses-discomfort/disability glare, bad dispensing, colour vision defect and migraine (10, 2.1%), visual disturbances- amblyopia, nystagmus and optic tract lesion (7, 1.5%) and strabismus (4, 0.8%).

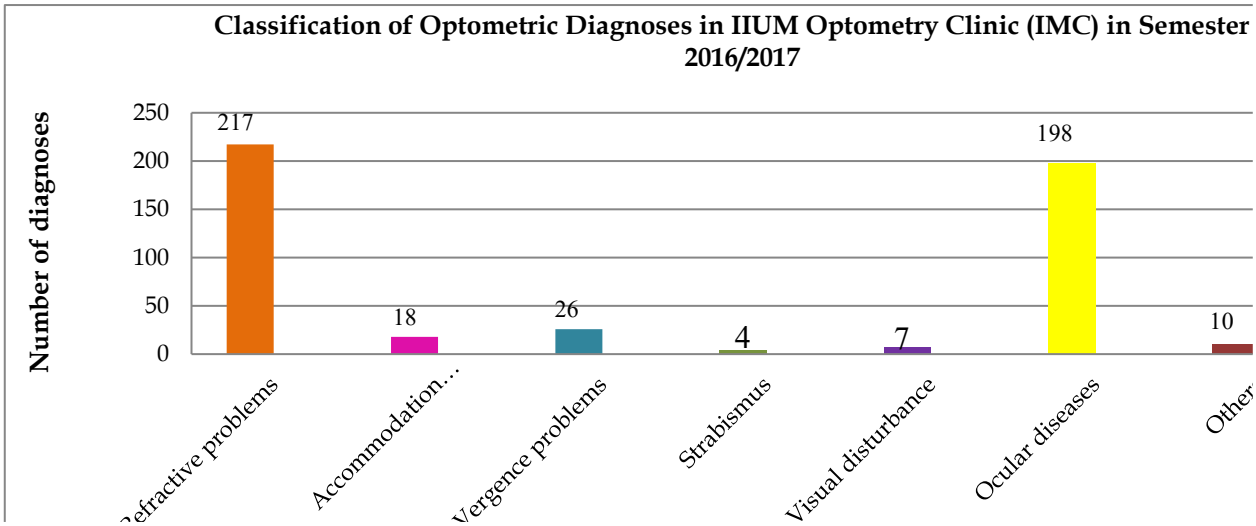


Figure I Classification of Optometric Diagnoses in IIUM Optometry Clinic (IMC)

The top three classifications of optometric diagnoses which were refractive problems, ocular diseases and vergence problems, had been divided into their specific diagnoses to get the results for the three most common optometric diagnoses. From the total of 480 diagnoses, myopia (96 cases, 20.0%) was the most common diagnosis followed by dry eyes (91, 19.0%) and convergence insufficiency (14, 2.9%) (Table I).

Table I Type and Frequencies of Optometric Diagnoses in IIUM Optometry Clinic (IMC)

OPTOMETRIC DIAGNOSES	**NO. (%)**
Refractive Problems	**217 (45.2%)**
Myopia	96 (20.0%)
Hyperopia	12 (2.5%)
Emmetropia	55 (11.5%)
Astigmatism Alone	21 (4.4%)
Anisometropia	12 (2.5%)
Antimetropia	3 (0.6%)
Presbyopia	18 (3.8%)
Accommodation Problems	**18 (3.8%)**
Accommodation Insufficiency	12 (2.5%)
Accommodation Excess	2 (0.4%)
Accommodation Infacility	3 (0.6%)
Accommodation Weakness	1 (0.2%)
Vergence Problems	**26 (5.4%)**
Basic Esophoria	4 (0.8%)
Basic Exophoria	1 (0.2%)
Divergence Weakness	2 (0.4%)
Divergence Excess	1 (0.2%)
Convergence Insufficiency	14 (2.9%)
Convergence Excess	3 (0.6%)
Hyperphoria	1 (0.2%)

Strabismus	**4 (0.8%)**
Visual Disturbances	**7 (1.5%)**
Amblyopia	5 (1.0%)
Nystagmus	1 (0.2%)
Optic Tract Lesion	1 (0.2%)
Ocular Diseases	**198 (41.2%)**
Chalazion	6 (3.0%)
Trichiasis	2 (1.0%)
Dry Eyes	91 (46.0%)
MGD	12 (6.1%)
Allergic Conjunctivitis	2 (1.0%)
Bacterial Conjunctivitis	1 (0.5%)
Papillary Conjunctivitis	12 (6.1%)
Conjunctival Concretion	7 (3.5%)
Pinguecula	5 (2.5%)
Pterygium	6 (3.0%)
Conjunctival Cyst	1 (0.5%)
Corneal Neovascularization	2 (1.0%)
Superficial Punctate Keratitis	7 (3.5%)
Corneal Staining	5 (2.5%)
Keratoconus	3 (1.5%)
Arcus Senilis	1 (0.5%)
Cataract	14 (7.1%)
Iris Pigmentosa	1 (0.5%)
Iris Synechiae	1 (0.5%)
Retinal Haemorrhage	1 (0.5%)
Retinitis Pigmentosa	1 (0.5)
ARMD	1 (0.5%)
Glaucoma	15 (7.6%)
Papilloedema	1 (0.5%)
Others	**10 (2%)**
Glare (Disability and Discomfort Glare)	5 (1.0%)
Bad Dispensing	3 (0.6%)
Colour Vision Defect	1 (0.2%)
Migraine	1 (0.2%)

The Association of Demographic Data with Common Optometric Diagnoses in IIUM Optometry Clinic (IMC)

The association of age, sex and ethnicity with myopia, dry eyes and convergence insufficiency were analysed using the Chi-square test in Tables II, III and IV.

Table II Association of Age, Sex and Ethnicity with Myopia

Variable	Myopia		p-value
	Present (n = 96)	Absent (n = 127)	
	n (%)	n (%)	
Age:			
Below 40	90 (93.8)	107 (84.3)	*0.029
Above 40	6 (6.3)	20 (15.7)	
Sex:			
Male	24 (25.0)	42 (33.1)	0.191
Female	72 (75.0)	85 (66.9)	
Ethnicity:			
Malay	92 (95.8)	119 (93.7)	0.508
Chinese	4 (4.2)	7 (5.5)	
Others	0 (0.0)	1 (0.8)	

*significant, $p < 0.05$

Myopia shows a significant association with age whereas no significant association was found with sex and ethnicity.

Table III Association of Age, Sex and Ethnicity with Dry Eyes

Variable	Dry eyes		p-value
	Present (n = 91)	Absent (n = 132)	
	n (%)	n (%)	
Age:			
Below 40	75 (82.4)	122 (92.4)	*0.022
Above 40	16 (17.6)	10 (7.6)	
Sex:			
Male	27 (29.7)	39 (29.5)	0.984
Female	64 (70.3)	93 (70.5)	
Ethnicity:			
Malay	86 (94.5)	125 (94.7)	0.564
Chinese	5 (5.5)	6 (4.5)	
Others	0 (0.0)	1 (0.8)	

*significant, $p < 0.05$

Dry eyes show a significant association with age whereas no significant association was found with sex and ethnicity.

Table IV Association of Age, Sex and Ethnicity with Convergence Insufficiency

Variable	Convergence insufficiency		p-value
	Present (n = 14)	Absent (n = 209)	
	n (%)	n (%)	
Age:			1.000
Below 40	13 (92.9)	184 (88.0)	
Above 40	1 (7.1)	25 (12.0)	
Sex:			1.000
Male	4 (28.6)	62 (29.7)	
Female	10 (71.4)	147 (70.3)	
Ethnicity:			0.876
Malay	13 (92.9)	198 (94.7)	
Chinese	1 (7.1)	10 (4.8)	
Others	0 (0.0)	1 (0.9)	

Convergence insufficiency shows no significant association with age, sex and ethnicity.

Management of Optometric Diagnoses in IIUM Optometry Clinic (IMC)

In Figure II, refractive management (226, 43.8%) was the most common management that had been given to the patients followed by prescribing of artificial tears (77, 14.9%), patient education (71, 13.8%), referral for further test (33, 6.4%), follow-up care (30, 5.8%), advised on ocular hygiene (30, 5.8%), co-management (27, 5.2%), vision therapy (21, 4.1%), and other management (1, 0.2%). Meanwhile, Table V shows the specific type of management given.

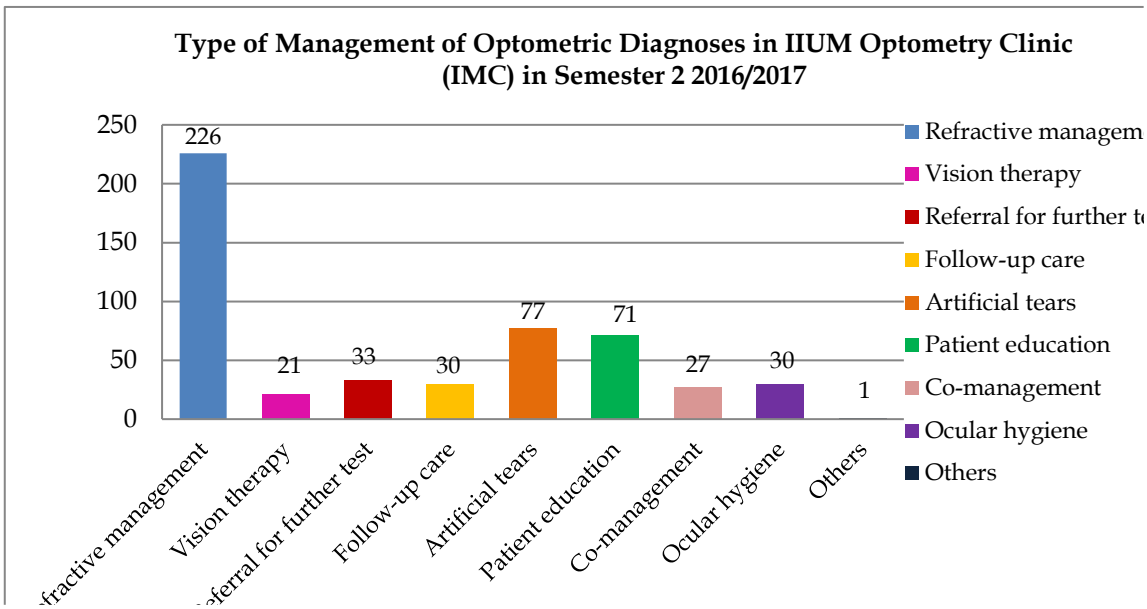


Figure II Type of Management of Optometric Diagnoses in IIUM Optometry Clinic

Table V Specific Type of Management of Optometric Diagnoses in IIUM Optometry Clinic

Classification	Specific Type of Management
Refractive management	New prescription
	No prescription
	Continue current prescription
Binocular vision	Vision therapy
Referral for further test/management	Refractive assessment (cycloplegic)
	Anisometropia assessment
	Dry eyes assessment
	Glaucoma assessment
	Keratoconus assessment
	Binocular vision assessment
Follow-up care	Visual acuity
	Accommodation and vergence
	Monitor progression
	Monitor compliance
Dry eyes symptoms	Artificial tears
Patient education	Patient education
Co-management	With ophthalmologist
	With medical officer
Ocular hygiene	Warm and cold compression
	Lid hygiene
Others	Epilation

DISCUSSION

Optometry diagnosis trend

Myopia was found to be the most common optometric diagnosis in IIUM Optometry Clinic (IMC), seen in Semester 2 2016/2017. This was supported by Goh, Abqariyah, Pokharel and Ellwein (2005), in which myopia was the most prevalent among the other types of refractive errors in the school-age population in the Gombak district. However, according to Wen et al. (2013), there was a significant number of hyperopic patients in both Asian and non-Hispanic white children, but the prevalence decreased after the infancy stage and then increased during late adulthood. Nevertheless, refractive errors remain by far the leading cause of major global visual impairment (Pascolini & Mariotti, 2012). This current study revealed that there was a significant association between age and myopia in the population. This result was supported by Williams et al. (2015) in which there was an increment in the prevalence of myopia during the late teens and 20's with the peak prevalence of myopia found during the age of 25–29 years old. However, there was no significant association between sex and ethnicity with myopia that had been found in this study. On the contrary, a study by Goh, Abqariyah, Pokharel and Ellwein (2005) found that myopia was higher in females than males. In addition, a study by Pan et al. (2013) revealed that the Chinese population were most affected by myopia compared to the Malay and Indian population.

Dry eyes were the second most common optometric diagnosis in IIUM Optometry Clinic (IMC) and the most common diagnosis among ocular diseases. A significant association was found between age and dry eyes in the population. The percentage of dry eyes in patients below 40 years old was higher compared to patients above 40 years old. However, if the total of patients with dry eyes was evaluated within the population of more than 40 years old, it was found that more than half of the patients above 40 years old had been diagnosed with dry eyes. Females and increasing age were found to be risk factors for dry eye disease (Mohd Ali et al., 2011). Even so, no significant association was found between sex and dry eyes in this current study. Besides dry eyes, a study by Reddy et al. (2008) included cataracts and glaucoma among the most common eye problems at the University of Malaya Medical Centre. However, in this study, even though glaucoma and cataracts were the second and third most common ocular diseases after dry eyes, they only accounted for 7.6% and 7.1% among the ocular diseases respectively compared to dry eyes which accounted for about 46% in the population. Cataracts and glaucoma were included as age-related eye diseases (Voleti & Hubschman, 2013). However, the current study only had 26 patients above 40 years old, which is insufficient to show any prevalence of age-related eye diseases, including diabetic retinopathy and age-related macular degeneration.

Another common optometric diagnosis in IIUM Optometry Clinic was convergence insufficiency. Convergence insufficiency is the most prevalent dysfunction among accommodative and binocular problems (Garcia et al., 2016). Since there was only a total of 14 patients with convergence insufficiency, no significant association was found between demographic data and convergence insufficiency. This result was supported by Hashemi et al. (2017), which showed no statistically significant association of age and gender with the diagnosis of convergence insufficiency. On the contrary, Rouse et al. (1999) stated that ethnicity was significantly associated with convergence insufficiency with Hispanic, Asian, white and black people as the study populations.

Types of optometry management

The management given within the study period was classified into nine categories. Refractive management was given depending on the type of refractive errors and patients' needs. A new prescription was prescribed to patients who presented with symptoms and showed improved acuity and comfort. Patients without any complaints and have optimum acuity were advised to continue wearing their current spectacle.

Meanwhile, most patients with accommodation/vergence problems had been prescribed new prescriptions and vision therapy and were asked to attend the follow-up care session. Examiners would advise and educate those who presented with no symptoms with visual hygiene. Even

though some of the patients came to IIUM Optometry Clinic with no specific symptoms, a comprehensive eye check-up must be performed. This is because a significant number of new diagnoses have also been found in asymptomatic patients, thus affecting the management (Irving et al., 2016).

The most common management for ocular diseases was prescribing artificial tears to manage dry eyes. For patients diagnosed with any ocular diseases at an early stage and asymptomatic, often the management given was patient education and visual hygiene. They also had been advised to come for follow-up care to monitor the progression of the ocular diseases. Co-management with ophthalmologists and other healthcare practitioners was also part of the optometric management at IIUM Optometry Clinic.

Besides that, to confirm the diagnosis, some of the diagnoses such as dry eyes, glaucoma and keratoconus had been referred for further assessment. These diagnoses would be further investigated and evaluated through the diagnostic procedures in the IIUM Optometry Clinic. Therefore, through various forms of diagnostic procedures performed, it can be seen here that optometrists play an important role as primary eyecare practitioners.

CONCLUSION

The three most common optometric diagnoses in IIUM Optometry Clinic (IMC) during Semester 2 2016/2017 were myopia, dry eyes and convergence insufficiency. In relation to that, the most common management given was refractive management, followed by prescribing artificial tears and patient education. Therefore, knowledge of the trend of optometric diagnoses is helpful for resident optometrists, especially the optometry students in training, to prepare themselves for the common cases possibly encountered in the clinic. It is helpful that the practising optometry students, including optometrists, are competent in managing the high occurrence cases. A proper and complete referral to other healthcare providers can be conducted to avoid incorrect diagnosis and unnecessary treatment (Nari et al., 2017). A standard of procedure (SOP) was produced and can be updated for the common optometric diagnoses in the IIUM Optometry Clinic.

The limitation of this study is that it did not specify the demographic of the patients attending the clinics which may be predominantly the university students and staff of IIUM.

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AUDITORY TRAINING PROGRAM FOR INDIVIDUALS WITH POST-LINGUAL HEARING IMPAIRMENT: A SCOPING REVIEW

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ABSTRACT

Introduction: Auditory training (AT) is an important area in aural rehabilitation that benefits individuals with post-lingual hearing impairment using amplification devices. The main benefit in targeting the auditory training program is to increase the quality of life by holistically reducing the hearing-loss-induced deficits of function through a combination of sensory management, instruction, perceptual training, and counselling. It also stimulates a successful listening using a training stimulus that engage the process for the role of cognition in auditory training, specifically executive processes such as attention switching and updating of memory. Such approach will need a meaningful training program for users to be able to generalize them in everyday life. This study is aimed at reviewing auditory training program in literatures for individuals with post-lingual hearing impairment with respect to the ***designs*** and ***parameters*****. Methods:** Pubmed, Science Direct, Scopus and Pro Quest (medical and health) databases were searched using English keywords; *hearing loss, auditory training, hearing aids, cochlear implants, perceptual learning, aural rehabilitation, auditory rehabilitation, adult*. Papers were selected from year 2013 to 2018 and papers from grey search were included if the paper has been quoted as important to learn further about AT program used in paper accepted from databases. 209 papers were identified from the databases. After removing duplications and screening of the inclusion criteria, a total of 24 papers were accepted; 21 papers from databases search and three papers from grey search. All selected papers were reviewed by four reviewers. This study adopted Preferred Reporting Items for Systematic Reviews and Meta-analysis extension for Scoping Review (PRISMA-ScR). **Results:** The results described 15 auditory training programs from 24 papers with each program has an exceptional ***design*** but shared practically the same ***parameters***. The AT program ***designs*** includes; 1. sample size, 2. hearing status, 3. hearing devices, 4. hearing age, 5. measurement test, 6. training sequence, 7. training durations, 8. training frequency, 9. length of training, 10. location of training, 11. training delivery style; either computer based or face to face, with trainer or self-training and individual or group training, 12. findings and 13. retention effects. The ***parameters*** used in auditory training program contains; 1. training activities, 2. training theme, 3. communication strategies, 4. methods, 5. approaches, 6. mode, 7. auditory skills, 8. speech stimulus, 9. sound stimulus and 10. complexity of training. **Conclusions:** Auditory training program for individuals with post-lingual hearing impairment was described in specific designs? and parameters to achieve its goal. The finding of this study could be used as a general guideline to develop the content and structure of future auditory training program.

KEYWORDS: Scoping review, auditory training, adult hearing loss, post-lingual hearing impairment

INTRODUCTION

Post-lingual deafened or post-lingual hearing impairment was described by Lazard et al. (2014) as a deafness appears after language acquisition and stabilization, the sensitive period of maximal plasticity has elapsed and major brain specializations are fixed. Researchers such as Hughes et al. (2018), Lin et al. (2013) and Strawbridge et al. (2000) emphasis on the alarming sequalae of sensory neural hearing loss (SNHL) among post-lingual person that might include cognitive impairment and dementia. While Turunen-Taheri et al. (2019) stated that SNHL leads to brain atrophy and neuroplasticity that may be detrimental to auditory rehabilitation and believed that the use of hearing aids may slow or improve this pathology. Therefore, the individuals with post-lingual hearing impairment require a reorganization of their current listening capabilities. This reorganization enables them to maintain their social habits without changing their communication mode to sign language which involves adapting to their hearing handicap, which is constrained by both anatomical and functional factors (Lazard et al., 2014). Blamey & Alcantara (1994) explained that a person with post-lingual hearing impairment may need auditory training with specific aims to minimize the hearing impairment consequences.

Auditory training (AT) is an important area in aural rehabilitation for post-lingual hearing-impaired person. Sommers (2016) and Beier et al., (2015) pointed out that auditory training is a strong ally for the auditory rehabilitation which benefits the hearing impaired individuals with amplification devices. They stressed that the comprehensive aural rehabilitation program will have better potential benefit when auditory training is included in the program. The two main benefits of the auditory training program are; 1. to improve users' participation in daily activities and 2. to increase the quality of life by holistically reduce the hearing-loss-induced deficits of function through a combination of sensory management, instruction, perceptual training, and counselling (Boothroyd, 2007). These two objectives aim to create effective listening conditions for hearing-impaired adults by utilizing a training stimulus proposed by Ferguson and Henshaw (2015). This training stimulus is designed to engage cognitive

processes, particularly executive functions such as attention switching and memory updating, underscoring the fundamental role of cognition in auditory training. The resulting AT module should constitute a meaningful auditory training program that users can apply in their daily lives. Hence, the development of an AT program should address the user experience improvement in everyday communication skills to illustrate the effectiveness of the AT program (Sweetow and Sabes, 2010).

Many hearing care professionals believe that auditory training cannot be fit into their routine clinical protocols because they believe that it is too expensive and time-consuming (Tye-Murray, 2016). This scoping review aimed to examine the AT programs that are available in literatures to find the best AT program protocol that may minimize the time-consuming and monetary issues in delivering AT. The scoping review will be visualizing the AT program content that is efficient and also that can be fit into the routine clinical protocols.

The Need of Scoping Review to Produce an Auditory Training Program Design

A scoping review is a mean for examining the trends in currently available AT programs, as recommended by Tye-Murray (2016). The aim is to provide audiologists and hearing care professionals with new strategies to achieve the goals for delivering a good quality hearing healthcare.

Valente (2015) recommended guidelines for the audiologic management of adult hearing impairment by, which emphasize the importance of understanding patients' specific communication needs and setting realistic expectations for interventions. The need for this scoping review is to create an AT program **design** that adheres to Valente's recommendations, primarily because there is currently no universally recognized gold standard for AT programs documented in the literature. The AT program design will cover factors such as program duration, frequency, length, location (computer-based or face-to-face), and involve a trainer or self-training as well as to be conducted individually or in groups. The design will also serve as a guide for audiologists and hearing care professionals to conduct future AT programs that it is tailored to patients' specific needs to measure the benefits of amplification outcomes accurately.

The outcomes for precise measurements of treatment are crucial for developing evidence-based clinical practice guidelines. However, as noted by Zhang et al. (2014), the provision of auditory training and the choice of training type (e.g.: computer-based or face-to-face) should be individualized. In a systematic review on the impacts of aural rehabilitation on the quality of life among older adults, Michaud and Duchesne (2017) found that no overarching trends emerged in the study due to the limited clinical applicability of the results. They found out that their systematic review findings were inconclusive because the assessment tools used to measure AT progress were lack of sensitivity and the reported interventions for adult hearing impairment lacking complete validity markers, leading to a risk of bias. The scoping review will provides recommendations for the guidelines for an AT program design and to raise awareness among trainees and trainers on the importance of conducting AT programs for individuals with post-lingual hearing impairment. Subsequently, it will also emphasize on the need for an updated AT program design to help both trainees and trainers in achieving the maximum benefit from AT programs.

Cardemil et al. (2014) have indicated that the use of hearing aids and individualized communication programs in adults as interventions can positively improve listening abilities? and speech perception. The AT programs, as part of auditory rehabilitation strategies, also have potentials to enhance the quality of life (Cardemil et al., 2014). This underscores the necessity for a scoping review to describe a comprehensive and practical auditory training program design for hearing healthcare professionals and patients. This scoping review is essential to gather evidences regarding the effectiveness of auditory training programs, specifically in assessing the variables outlined in the expected AT program design. It intends to create a structured AT program that can be assessed and audited externally to prevent assessment bias. The goal of this research is to produce a set of AT program designs. Based on these designs, an auditory training program should allow users to utilise informed choices by discussing their strengths and areas for auditory skill improvement with a clinician. This approach is expected to have a high impact and convenient to? both providers and recipients of hearing healthcare services.

The Need to Do Scoping Review on The Parameters That Defined an Effective Auditory Training Program

The AT program **parameters** explain the methods, approaches, modes, auditory skills, speech stimulus, sound stimulus and complexity of training used for individuals with post-lingual hearing impairment.

However, at present, there are no established parameters for an AT program that can serve as a reference for the development of such a program. For example, the current research review trend was focusing on auditory training program efficacy and benefits on a very specific areas or explain only prominent area. Michaud and Duchesne (2017) reviewed the effects of aural rehabilitation on quality of life in an older adult population, Beier et al. (2015) reviewed on auditory training benefits, Lawrence et al. (2018) reviewed the efficacy of auditory training on cognition, Henshaw and Ferguson (2013) reviewed on efficacy of auditory training on speech intelligibility, cognition and communication abilities and R. Sweetow and Palmer (2005) reviewed on efficacy of auditory training on communication skills. Therefore, this scoping review intended to compile all parameters used in the previous AT programs that may benefit for producing a new AT program.

According to Clark et al. (2008), Boothroyd (2007) and Hull (2014), audiologic management for hearing-impaired adult has a huge area that need to be included in the intervention such as, sensory management, auditory training, counselling. The auditory training itself also has various training components that may be administered on patient based on their needs. While Sommers (2016) stated that an individual auditory training at home on tablet-based devices with game-like formats will dramatically improve the ease and flexibility of administering auditory training and maintain the training over extended periods of time. However, the training gains could not be generalized outside the training materials. Sommers (2016) again stated that auditory training might be most effective if it is done using the voice of a specific individual who the trainee wants to understand, such as a spouse or a teacher. This dilemma showed the importance to compile all parameters in auditory training program to be acted as a guideline to produce a comprehensive auditory training program.

Each parameter in auditory training programs will be documented to understand the mechanism of the auditory training. This study will get a clear idea regarding the structures used in most auditory training programs available because auditory training program has wide area to target. The information gathered in this scoping review is hoped to explain the AT parameters available in the literatures to develop an AT program. Therefore, this study is essential to help both trainer (hearing health care) and trainee (patients or subjects) to achieve any specific goals in AT program.

The main objective is to review auditory training program available in literatures. While the specific objectives are; 1. to identify the auditory training **design** (durations, frequency, length, location, computer based/face to face, with trainer/self-training, individual/group) used in the individuals with post-lingual hearing impairment auditory training programs? and 2. to identify the auditory training program **parameters** (methods, approaches, modes, auditory skills, speech stimulus, sound stimulus and complexity of training) used in the individuals with post-lingual hearing impairment auditory training programs.

METHODOLOGY

The scoping review study was drafted using the Preferred Reporting Items for Systematic Reviews and Meta-analysis extension for Scoping Review (PRISMA-ScR) by Tricco et al. (2018). In this research, audiologists and hearing healthcare professionals who perform auditory training will be recognized as 'trainer' whilst the person with post-lingual hearing impairment will be known as 'trainee'.

Eligibility criteria

The eligibility criteria to accept or reject paper in this research are derived from suggestion made by Moher et al. (2009) to use PICOS; with reference to 1. **P**articipants; adults aged above 18 years old (based on definition of adult given by WHO (2010), with any degree of hearing loss using hearing aid(s) and/or cochlear implant(s) and/or any listening device(s) and also a normal hearing subject uses hearing impaired simulation device. 2. **I**nterventions; Interventions included in this study are all auditory training program available in English or Malay. To exclude program which has no publication to validate the scientific merit, to exclude paper with no intervention for auditory training program (e.g., paper with general information about auditory training program only) and also to excludes review-only paper. 3. **C**omparisons; Comparison with a control group or repeated measures (pre and post training comparison). However, if the paper has significant relation with this scoping review, it will be accepted and recognize under 'grey search'. 4. **O**utcomes; Outcomes measures related to listening skills, speech intelligibility, cognition and communication (either behavioural measures or self-reported outcomes) will be included in this studyand 5. **S**tudy design of a paper**;** The study designs accepted are

randomized controlled trials, nonrandomized controlled trials, cohort studies, repeated measures studies (pre and post training comparisons), case studies, reliability test and validity test.

Selection of paper

The paper search was done through four databases; **Pubmed, Science Direct, Scopus, Pro Quest (medical & health)**. Only papers from year **2007 to 2017** have been included in this study. **Grey Search papers** has also been included since it has significant relation to the papers accepted from databases. For example, the grey search paper was quoted from accepted paper as important to learn further about AT program.

The keywords used for database search include the *hearing loss, auditory training, hearing aids, cochlear implants, perceptual learning, aural rehabilitation, auditory rehabilitation, and adults.* They were selected based on the objectives and literature review of adult auditory training program.

The selection of sources of evidence has been done by a team consist of one speech-language pathologist (Reviewer 1, the main author), one audiologist with Ph.D. (Reviewer 2, second author), one audiologist (Reviewer 3) and one undergraduate audiology student (Reviewer 4). The decision whether to accept or remove a paper was under the prerogative of the reviewers through discussions and meetings.

All the articles were processed in three phases. The first phase is the identification process whereby all paper's titles were screened and identified using searched keywords from all databases (*hearing loss, auditory training, hearing aids, cochlear implants, perceptual learning, aural rehabilitation, auditory rehabilitation, adults)*. Accordingly, the title of the papers were screened for any duplications. During this phase, 209 papers were identified, and 10 duplicates were removed.

During the second phase, 199 Abstracts of the papers were screened by the reviewer 1 and 3. Both of the reviewers then agreed to removed 154 papers as the papers did not meet with eligible criteria of this study. Therefore, a total of 45 papers were further reviewed in the next phase.

The third phase was done by Reviewer 1 and 2 on 45 selected papers. In this phase, a full-text screening was done and both reviewers decided to exclude 24 papers from 45 selected paper and to include another three papers from grey search. These three papers were included because the documents were referred for final selection to explain the auditory training program used in their research. Finally, a total of 24 papers were included in this study. The selection process is shown in figure 1.

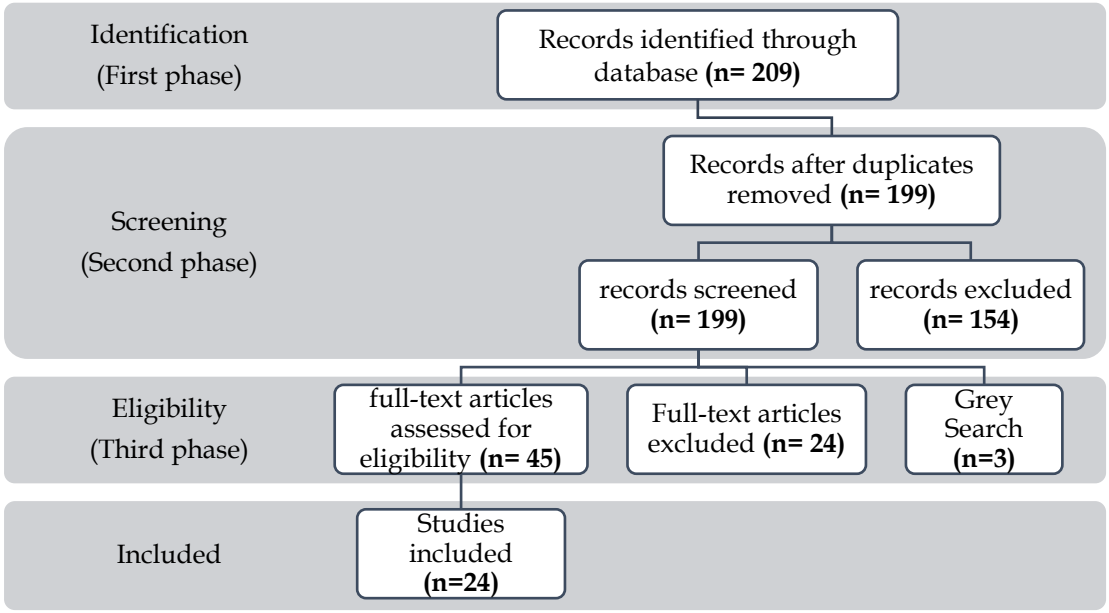


Figure 1 The Findings of Papers Searching

Data charting

The data charting process uses thematic analysis process by Braun & Clarke (2006) which was further explained in Maguire & Delahunt (2017) to induce the content of auditory training program. The process of determining the themes involved six steps; 1. Familiarizing with data, 2. Generating initial codes, 3. Searching for themes, 4. Reviewing themes, 5. Finalizing themes and 6. Defining themes.

All 24 papers have been given identity number (ID) from ID01 to ID24 to be recognized distinctively. From 24 papers, 15 auditory training programs has been identified. Some papers were using the same AT program, hence only 15 AT program from 24 papers. Each of the program has been given another ID to be explained and recognized. The ID is uniquely distinctive from paper ID, which identifiable from P01 to P15 (P is stand for program).

The data charting process were shown in Figure 2. Panels in the team who did full-text review were Reviewer 1 (the main author), Reviewer 3 and Reviewer 4. The reviewers read and re-read all papers to get a clear notion about the entire body of data as suggested by Maguire and Delahunt (2017). If the reviewers found any unfamiliar corpus, a consultation from related professional to better understand the paper was conducted. The consultation is to familiarize with any terms and concepts introduced in the paper to fathom the key ideas. data including bibliographical information, aims and results from the 24 papers were reviewed and extracted independently by all the reviewers. The key ideas known as code has been identified and themes has been generated. The team checked the data and had several meetings to find agreement on the findings. Early impressions and immediate thoughts were recorded to form an initial framework for further process.

Generating initial codes is the first stage by organising the coding process in a meaningful and systematic way using the ***main category***. The main category is formed from the research questions and familiarization process. Initially, team has construed three main categories using theoretical thematic analysis (Maguire & Delahunt, 2017). The initial categories were suggested based on objectives and abstract screening. They are; 1. Research background, 2. Auditory training program and 3. Outcomes measurements. The main category will serve as an outline to generate preliminary ideas about codes in full-text review. The category was tested for applicability in all 24 papers where the researcher generates codes from every segment of text that seemed to be relevant to specifically address the research question (Maguire & Delahunt, 2017).

Based on these three categories, a potential code has been derived; an outline to further induced codes from papers. In this stage, even though the category has been set, the reviewers used open coding process. The codes searching is not solely bound to the category, but it will also not astray away from the category. These two ways are to outline a strategic searching system to achieve goals. The codes were compared, discussed and modified one by one, moving from one paper to another. The process has been done by hand, working through hard and soft copies of the papers using pens and highlighters.

A theme is characterised by its significance with the codes and definitions (Braun & Clarke, 2006). The preliminary themes were identified from the initial codes. The reviewers examined the codes and found a clear fit together codes into a theme. Further reviewing the codes, the team agreed to refine the category and formed them into two main categories; 1. Auditory Training Program Design and 2. Auditory Training Program Parameters

All initial themes derived were reviewed, modified and associated with each theme in all 24 papers. The team considered whether the data really did work in the context of the entire data set (Maguire & Delahunt, 2017) then the theme have been accepted. However, four conditions may happen during this process; 1. The themes do not make sense, 2. The data does not support the themes, 3. The themes overlap, 4. Themes within themes. For each condition, the researcher has to enlist three action to treat the data. The decision either to remove, put in other related themes or to form new theme. All of this decision based on discussion among team members.

All 251 codes were translated into themes and sub-themes by thorough and comprehensive review across all 24 papers. Themes were checked against each other and backed by the data of the original papers to be harmonised with key ideas. In the process, the theme has undergone a treatment if they experienced the four conditions, 1. The themes do not make sense, 2. The data does not support the themes, 3. The themes overlap and 4. Themes within themes. The treatment was 1. To remove the

themes, 2. To move to any other related themes and 3. To form new themes or sub themes. This process is to produce a coherent, consistent and distinctive themes (Cruzes & Dybå, 2011).

Final themes were compared across all papers and interpreted into a model of two higher-order themes; 1. Auditory training program design and 2. Auditory training program parameters. The model of higher-order themes has 23 themes and 77 sub-themes. They were checked against research question and found to be able to describe themes relationship clearly.

This is the final refinement of the themes which aiming to identify the essence of what each theme is about (Braun & Clarke, 2006). The team's panel has to analyse the themes with each of the themes has been given a name and definition. Definition of each name was based on description appeared in dictionary, description suggested in literature (all references were stated) and a newly developed name which fits themes described in the papers. The definition which was accepted should be appeared and harmonised with the key concepts presented in the papers.

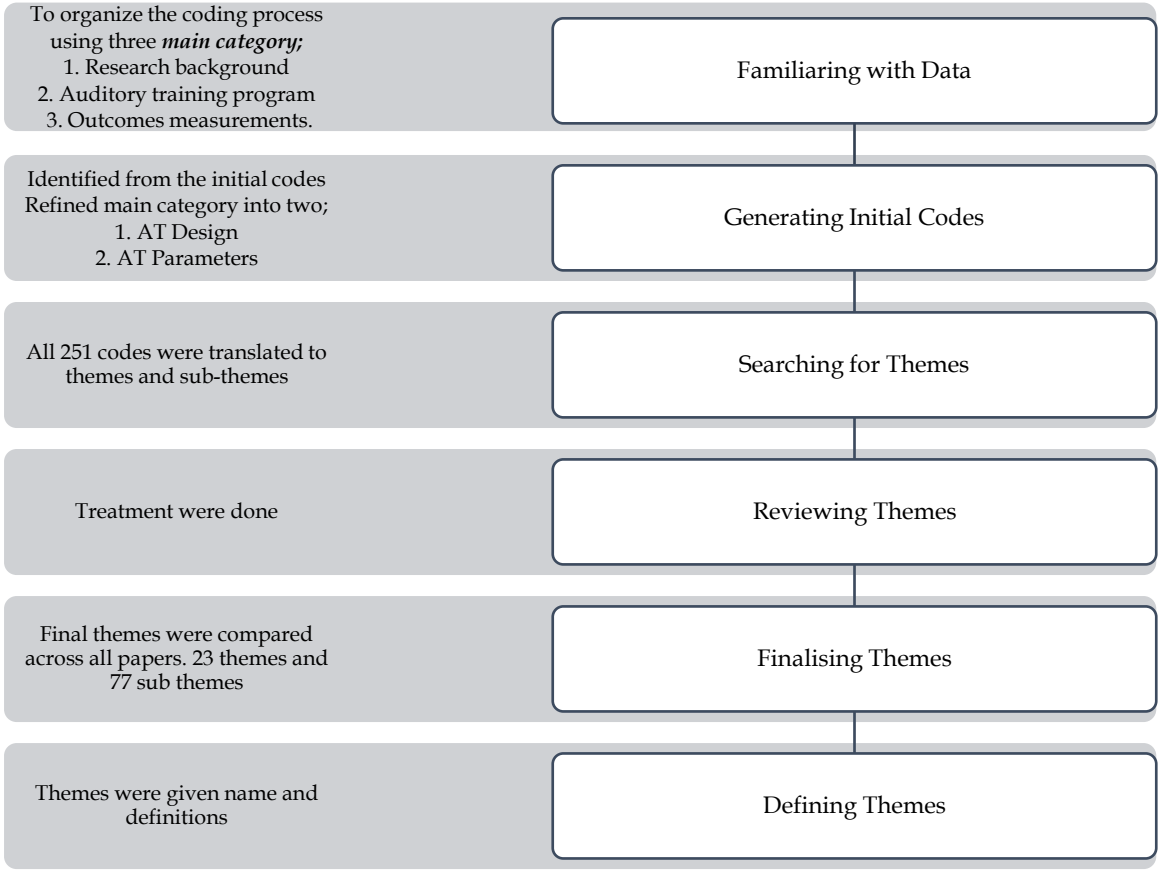


Figure 2 Data Charting Process

RESULTS

Results of Auditory Training Design (N=24)

The auditory training designs of selected studies are presented in table 1. The auditory training designs are including the; 1. author(s) and year of the paper published, 2. total sample Size (N) that indicate the number of subjects included in the research, (i.e.: the total number of participants in training and control group, 3. hearing status showing hearing devices used and hearing age, 4. auditory training name or description (if the program was not given a specific name), 5. measurement test used in the research, 6. research sequence and procedure 7. training duration and frequency, 8. training location (either at home or in laboratory), 9. auditory training delivery style (either computer based, with trainer, individual or in group, 10. findings of the papers (either positive findings; when the results showed better performances with AT program and negative findings; when the results showed regression findings, no differences findings, or findings which are not available) and 11. retention effect, if available. In this part, each of all 24 papers has been identified based on the ID number.

In general, studies on auditory training show large variation in terms of sample size (between n= 2 to n=279). However, 75% (18 out of 24 studies) of the study utilized sample size less than 100 participants

(< 100 participants). Studies that used large sample size (> 100) normally governed to the efficacy using self-training computer-based with audiologist as supervisor as shown in a several numbers of studies including, ID01, ID06, ID10, ID11 and ID23.

On the study compliance, 83% (20 out of 24 studies) of the study showed 100% compliance rate where all subjects recruited at the beginning had completed the whole research process. The lowest compliance rate recorded is in study ID 14 with 22 subjects complied from 49 subjects recruited because most of the subjects did not meet the inclusion criteria of the study.

13 out of 24 papers (54%) in this review have compared the improvement of the AT program between groups; a training group and a control group with 8 papers have 1:1 ratio of subjects in both groups (similar number of participants in the training and the control groups). The other 5 papers have training have higher number of participants in the training group than in the control group. 11 papers have not compared their research with control group.

71% of the study in this research used subjects with hearing loss (17 out of 24 papers) and another seven (29%) research used normal hearing subjects. The hearing loss range was mostly mild to moderate hearing loss subjects. Least papers (14 out of 24 studies) used severe to profound hearing loss subjects because most papers in this review were investigated hearing aids user.

Regarding hearing age, 58% of the study (14 out of 24 studies) did not specify the hearing age. The studies that showed hearing age were randomly from one month to 44 years.

In this review, three types of measurement have been used; standardized test, newly developed test or combination of these two types of measurement. The standardized tests were administered to measure either speech-perception, hearing handicap-perception or cognitive-performance. While the newly developed test was done to measure the specific area trained in the programs, for example The build-a-sentence Test developed in Customized Learning Exercise for Aural Rehabilitation (clEAR) by Tye-Murray et.al. (2008).

Research sequence and procedure is to show how the research and training has been conducted in each studies. Nine models of procedure were found in 24 papers; 1. PTP (pre-training, training, post-training), 2. PTPP (pre-training, training, post-training 1, post-training 2), 3. PPTPP (pre-training test 1, pre-training test 2, training, post-training 1, post-training 2), 4. PPTP (pre-training test 1, pre-training test 2, training, post-training test), 5. PTMP (pre-training test, training, mid-training test, post-training test), 6. PTMPP (pre-training test, training, mid-training test, post-training test 1, post-training test 2), 7. PPTMPP (pre-training test 1, pre-training test 2, training, mid-training test, post-training test 1, post-training test 2), 8. FPTP (familiarization, pre-training test, training, post-training test), and 9. FPTPG (familiarization, pre-training test, training, post-training test, generalization).

Pre-training and post-training measured the same outcome measures and tested according to the research's sequence and procedure. Training part was given to all subjects if the research has no objectives to compare between training and control group. The process of familiarization and generalization is to get the subjects to be familiar with training content or to use the training content in everyday life. Based on this review, 33% of studies used PTP sequence in their study (eight out of 24).

Each AT was design to be in a specific time duration per session, with specific frequency of training and in stipulated length of time. 33% studies (8 out of 24 studies) conducted training less than ⩽30 min and 31 to 60 min per session with 38% of studies (9 out of 24 studies) were conducted between 10 and 20 session in ⩽4 weeks.

This review found out that 63% of studies (15 out of 24 studies) were done in laboratories as compared to homes. While training delivery style explained AT either in computer based, face-to-face (F2F), with trainer, self-training (ST) individual or group showed 13 programs are computer- based program with only two program used face-to-face program. The programs were mostly focused on speech-perception training which 11 programs trained in speech, two programs trained in musical perception and one in environmental sounds. Only one program trained in cognitive-perception. Based on this review, 70% of the training (17 out of 24) were self-training and 79% of the studies (19 out of 24 studies) were done individually

Research findings in each paper has been classified either positive findings, no differences findings or findings which is not available. Positive findings are when the training has showed a significant better

training effect. 67% of the studies showed positive findings for their training (16 out of 24 studies). However, seven papers found no differences between pre and post training.

The retention effect is to see if the training is remained as a post-training. Only ten papers studied the retention effect which eight paper showed retention effect and two paper showed no retention effects. A total of 12 papers did not carry out research on retention effect and two are still on-going. Therefore, the result was not available.

Table 1 Descriptive Summary Of The Auditory Training Design

ID	Author and year	Sample Size		Hearing Status			AT Name or Description	Measurement Test	Research Sequence/ procedure	Duration, frequency and length of training	Location Home (H) Laboratory (L) Auditory Training Delivery Style Computer based/ Face-to-face/ with trainer/ self-training (ST) individual / group)	Findings + (positive, ND (No differences), NA (Not Available)	Retention
		Total (N) Total subject complies	Training group Control group	Hearing Status	Hearing Devices	Hearing Age							
1	Saunders et al. (2016)	243 243	206 73	Mild to Mod	HA	4wk to 6mo ⩾6mo	Listening & Communication Enhancement (LACE)	**Standardized test** Word-in-Noise-test (WIN) (Wilson et al. 2003; Wilson & McArdle 2007) NU-6-word lists (Wilson et al. 1994) Modified NU-20 test (Olsen & Carhat, 1967) Wechsler Adult Intelligence scale 3rd Edition, WAIS-III (Wechsler, 1997) The Low Predictability Sentences performance on the multi-SNR R-SPIN (Wilson et al. 2012) Abbreviated Profile of Hearing Aid Performance (APHAP) (The; Cox & Alexander 1995) Hearing Handicap Inventory (HHI) for the elderly and adults (Ventry & Weinstein 1982; Newman et al. 1990)	Pre-training test 1: Inclusion assessment Pre-training test 2: Baseline (within 6wk of pre-test 1) Training: 2wk to 4wk Post-training test 1: Immediate post training: Within 2wk of the end of the training period. Post-training test 2: 6mo post training: occurred 6mo to 8mo following	30 min 10-20 sessions 2wk to 4wk	H Computer based ST Individual	ND	No 6mo

2.	Tye-Murray et al., 2017)	47 47	47 0	HL (NS)	HA	NS	Customized Learning: Exercises for Aural Rehabilitation (clEAR) formerly known as: I Hear What You Mean	**Standardized test** Transfer-Appropriate Processing (TAP) style measure of improvement (Barcroft et. al., 2011b, 2016) The Build-a-Sentence test (BAS) (Tye-Murray et al., 2008)	Pre-training test Training: • The spaced group; began training within 1wk of completing the Pre-test, • The massed group; started at the 8th wk Post-training test 1 Post-training test 2: 3mo after the post-training test 1	60 min 20 sessions 5th wk and 10th wk	L Computer based ST Individual	ND	Yes 3mo
3.	Rishiq et al. (2016)	24 24	12 12	Mild to Mod	HA	NS	ReadMyQuips (RMQ)	**Standardized test** The Multimodal Lexical Sentence Test for Adults (MLST-A) (Kirk et al., 2012)	Pre-training test 1: on the day of hearing aid fitting Pre-training test 2: after 4wk of hearing aid use prior to RMQ training Training or no training: 4wk Post-training test 2: after 4wk of RMQ training or no training	30 min 20 sessions 1 to 4wk	L: 1wk (first) H: 3wk Computer based T: 1wk ST: 3wk Individual	ND	No 4wk
4.	Preminger & Ziegler (2008)	50 47	>16 ⩾16	HL (NS)	HA	⩾3m	Audiologic Rehabilitation Classes	**Standardized test** City University of New York (CUNY) AB Isophonemic Word Lists (Boothroyd, 1984; Boothroyd, Hnath-Chisolm, Hanin, & Kishon-Rabin, 1988) CUNY Topic Related Sentences (Boothroyd et al., 1988) Hearing Handicap Inventory (HHI) for the elderly and adults (Ventry & Weinstein 1982; Newman et al. 1990) World Health Organization Disability Assessment Schedule II (WHODAS II) **Newly developed test** Class evaluation form: A subjective class evaluation form	Pre-training test: 2-wk prior first class Training or no training: 6wk Post-training test 1: 2-wk after training or no training Post-training test 2: 6mo after training or no training	60 to 90 min 6 sessions 6wk	L F2F Two trainers Group	ND	Yes 3m
5.	Shafiro (2008)	7 7	7 0	NH	None	NS	Environmental Sounds Training	**Newly developed test** Tested using the entire stimulus set (40 sound sources, 4 exemplars each, for a total of 160 stimuli)	Pre-training test Training Post-training test	30 min 5 sessions 2wk	L Computer based ST	+	NT

											Individual		
6.	Loebach et al. (2010)	144 144	96 48	NH	CI	NS	Speech Processed Training	**Newly developed test** Transcribe 20 spectrally degraded meaningful sentences	Familiarization Pre-training test Training Post-training test Generalization	NS	L Computer based ST Individual	+	NT
7.	Driscoll et al. (2009)	66 66	66 0	NH	CI	NS	Musical Instruments Training	**Newly developed test** Music Background Questionnaire (MBQ) Paired Associate Memory Test (PAT) Instrumental Simulation Recognition Test	Pre-training test: 1st wk Training: 5wk training Mid-training Test: 3rd wk of training Post-training test 1: 5th wk Post-training test 2: 7th wk	12 minutes 15 sessions 5wk	H Computer based ST Individual	+	Yes 7w
8.	Shafiro et al. (2015)	14 14	14 0	Mild	CI	⩾12m	Environmental Sound Training	**Standardized test** The Familiar Environmental Sound Test (FEST) (Shafiro, 2008; Shafiro et al., 2012) Consonant-Nucleus-Consonant (CNC), monosyllabic word recognition test (Peterson & Lehiste, 1962) Speech-in-Noise (SPIN-R) sentence test (Elliott, 1995)	Pre-training test 1 Pre-training test 2: (1wk interval from pre-test 1) Training: (4wk) Post-training test 1 Post-training test 2: (1wk after training)	40 to 60 min 8 sessions 1wk	H Computer based ST Individual	ND	Yes 1w
9.	Preminger & Meeks, (2010)	72 72	36 36	Mod	HA and CI	⩾3m	Audiologic Rehabilitation Classes	**Standardized test** Hearing Handicap Inventory (HHI) Elderly (Ventry and Weinstein, 1982) Modified HHI-Adult (Newman et al, 1990) Modified HHI-Spouse (Newman and Weinstein, 1988) 10-item Perceived Stress Scale (PSS) (Cohen and Williamson, 1988) Philadelphia Geriatric Center Positive and Negative Affect Rating Scale (Affect Rating Scale, or ARS) (Lawton et al, 1992) Communication in the Marriage Primary Communication Inventory (PCI) (Navran, 1967)	Pre-training test: 4wk before AR program Training: AR Class for 4wk Post-training test 1: within 2wk after completing AR program Post-training test 2: 6mo after training	90 min weekly	H F2F Trainer with and without spouse	ND	Yes 6m
10		240	240		HA	⩾3m		**Standardized test**	Pre-training test		L: 6 sites	NA	NA

	Miller et al. (2015)		0	Mild to mod			Speech Perception Assessment and Training System (SPATS)	The Win (word-in-Noise-test; Wilson & McArdle 2007) Quick Speech-in-Noise Test (Killian et. al, 2004) CID Monosyllabic Word Test in Quiet and in Noise (Hirsch et.al. 1952) Connected Speech Test (listen Only) (Cox et.al. 1987 and 1988) Connected Speech Test (Look and Listen) (Cox et.al. 1989) The abbreviated profile of hearing aid performance (APHAP) (Cox & Alexander 1995) **Newly developed test** Speech-Perception Tests (Speech Perception Assessment and Training System–Related)	Training: (30 hours) Post-training test 1 Post-training test 2: after 2-3mo post training	90 to 120 min 15 to 20 sessions	Computer based Trainer Individual		
11	Smith et al. (2016)	279 263	193 70	Mild to Mod	HA	<6m ≥6m	Listening & Communication Enhancement (LACE)	**Standardized test** Word-in-Noise-test (WIN) (Wilson et al. 2003) Hearing Handicap Inventory (HHI) for the elderly and adults (Ventry & Weinstein 1982; Newman et al. 1990) The abbreviated profile of hearing aid performance (APHAP) (Cox & Alexander 1995)	Pre-training test 1 Pre-training test 2: baseline Training: immediate after pre-test 2 Post-training test 1: immediate after training Post-training test 2: 6-month	30 min 10-20 sessions 2 to 4wk	H Computer based ST Individual	+	NA
12	Tyler et al. (2010)	12 12	6 6	Mild to Profound	CI	3y – 8y	Speech-in-noise and Localization Training	**Standardized test** Nucleus-consonant monosyllabic words (CNC) (Tillman and Carhart, 1966) CUNY sentences (Boothroyd et al, 1985) Hearing in Noise Test (HINT) sentences (Nilsson et al, 1994) Everyday sounds localization test (Dunn et al, 2005) **Newly developed** Real-world listening test for localization and recognition	Pre-training test: 38-96mo post-implantation Training: 1 to 3mo Post-training test	30min Frequency at own control 4 to 12wk	H Computer based ST Individual	+	Yes 7m
13		77	38		None	NS		**Standardized test**	Pre-training test	60min	H	+	NT

	Anderson et al. (2012)	77	39	Mild to profound			The Brain Fitness™ Cognitive Training	Quick Speech-in-Noise Test (Killian et al. 2004) **Newly developed test** Two subtests of the Woodcock–Johnson Tests of Cognitive Abilities The Integrated Visual and Auditory Continuous Performance Test Electrophysiology test	Training Post-training test	40 sessions 8wk	Computer based ST Individual		
14	Rao et al. (2017)	38	11	Mild to Mod	HA	4w	ReadMyQuips (RMQ)	**Standardized test** Cortical late event-related potentials (ERPs) Hearing in Noise Test (HINT) sentences (Nilsson et al, 1994)	Pre-training test Training (4 weeks) Post-training test	30min 20 sessions 4wk	L: 1wk H: 4wk Computer based T: 1wk ST: 3wk Individual	+	NT
		22	11										
15	Yu et al. (2017)	2	2	Mild to Mod	HA	NS	ReadMyQuips (RMQ)	**Standardized test** Multimodal Lexical Sentence Test for Adults (MLST-A; Kirk et al., 2012) **Newly developed test** Functional magnetic resonance imaging (fMRI)	Pre-training test Training: HA uses for 8wk and one subject receive 4wk training Post-training test	NS	L Computer based ST Individual	+	NT
		2	0										
16	Fu & Galvin (2007)	13	13	HL (NS)	CI	Several years	Computer-Assisted Speech Training (CAST)	**Standardized test** HINT sentence recognition thresholds in steady, speech-shaped noise IEEE21 sentence recognition in quiet **Newly developed test** Multitalker vowel recognition in quiet Multitalker consonant recognition in quiet	Passive learning: • Pre-training test (baseline): every 3mo • adaptation period: 18mo • Post-training test: Retesting every 2wk Active 1. Pre-training test (baseline): at least 2wk 2. Training: 1mo or longer 3. Post-training test: Retesting every 2wk	60min 20 sessions >4wk	H Computer based ST Individual	+	NT
		13	0										
17	Petersen et al. (2012)	24	15	Severe	CI+HA	NS	The Musical Ear-Training	**Newly developed test**		60min	H and L	+	NT

		24	9					Musical instrument identification (MII) Melodic contour identification (MCI) Pitch ranking (PR) Rhythmic discrimination (RD) Melodic discrimination (MD) The Hagerman speech perception test (HAG) An emotional prosody recognition test (EPR)	Pre-training test (baseline): within 14dy after CI switch-on Training or no training: 6mo Mid-training test: within 3mo training or no training Post-training test: after training or no training	24wk	Computer based and F2F ST and with Trainer Individual		
18	Wayne & Johnsrude (2012)	144	144	NH	None	NS	Perceptual Learning of Degraded Speech Training	**Newly developed test** Word-report task	Pre-training test Training Post-training test: testing (report) after each training item (given 25s for report after each sentence during both training and test)	NS	L	ND	NT
		144	0								Computer based Trainer Individual		
19	Krull et al. (2012)	30	24	NH	CI or CI+HA	NS	Talker-identification Training	**Newly developed test** Sentence-recognition using two lists of sentences (in quiet and in noise) Emotion-recognition performance using 100 tokens in quiet	Pre-training test (first day) Training (4 days) or no training Post-training test 1 (at day 4) Post-training test 2 (after 30 days)	4 sessions 45 to 60min 4dy	L	+	Yes 1m
		30	6								Computer based ST Individual		
20	Richie & Kewley-Port (2008)	14	7	NH	None	NS	Vowel identification Training	**Newly developed test** Closed-set vowel identification test (vowels in CVC context) An open-set monosyllable word recognition test An open-set sentence recognition test (Central Institute for the Deaf Everyday Sentences)	Pre-training test: First day. designed to assess the participants' untrained auditory–visual speech perception abilities Training: 6 sessions or no training Post-training test: final day of testing.	60min 6dy	L	+	NT
		14	7								Computer based ST Individual		
21	Loebach et al. (2009)	48	24	NH	None	NS	Speech Processed Training	**Newly developed test** Environmental sound identification Talker- gender identification Talker discrimination	Familiarization (brief) Pre-training test Training Post-training test	1 session	L	+	NT
		48	24								Computer based ST Individual		
22	Sweetow & Sabes (2007)	65	65	HL (NS)	HA	6m to 44y	Listening & Communication	**Standardized test** Quick Speech-in-Noise Test (Killion et al. 2004)	Group One (immediately trained) Pre-training Test: Baseline Training: 4wk	20 sessions 30min	H	+	Yes 8w
		65	0								Computer based		

							Enhancement (LACE)	Hearing Handicap Scale for the Elderly (HHIE) (Ventry & Weinstein 1982; Newman et al. 1990) Communication Scale for Older Adults (CSOA)	Mid-training test Post-training test 1 post-training test 2: 4wk after post-test Group two (crossover period subjects): Pre-training test: Baseline Pre-training test (after 4wk from baseline) Training: 2wk Mid-training test Post-training test Post-training test 2: 4wk after post-test 1	4wk	ST Individual		
23	Tye-Murray et al. (2011)	>100	>100	HL (NS)	HA	NS	I Hear What You Mean	NS	NS	60min	L	+	NT
		>100	0								Computer based ST Individual		
24	Miller et al. (2007)	65	65	HL (NS)	NS	NS	Speech Perception Assessment and Training System (SPATS)	NS	NS	NS	L	+	NT
		65	0								Computer based ST Individual		

Results of The Auditory Training Program Parameters (N=15)

Table 2 shows the parameter found from 15 programs, consists of 1. Training activities, 2. Training theme, 3. Communication Strategies, 4. Methods, 5. Approach, 6. Mode, 7. Auditory Skills, 8. Speech Stimulus, 9. Sound Stimulus and 10. Complexity of training.

In every auditory training program, they have a specific training activity; with? different type of activities conducted in each training. A total of 11 studies conducted training activity by "choosing a response from a choice on screen after listening to auditory stimuli". Among the training activities conducted in the studies were "to complete modified crossword puzzles after listening to video recordings of quips", "face-to-face activities with trainer to do analytic and synthetic exercises", "to transcribe by typing on keyboard after listening to auditory stimuli", "to complete multiple-choice questions on personal computer after listening to auditory stimuli" and "music-training session by professional music teacher".

This research work has reviewed themes used for AT in each study paper and found out that most of the studies did not specify themes for their training but instead explained the materials used in their training. As such, this study categorizes the research themes in four training groups; 1. Topics, 2. Sounds, 3. Spoken Language and 4. Song. The topics used in the studies varies from multiple subjects such as health issues, money matters, exercise, restaurant, travel, family, sports, history, art and science. The sounds included are? human, animals, environmental and musical instruments. In addition, spoken language also included and covered all speech-language chunk from phonotactic, syllable and sentences. Selected songs were nursery rhymes and well-known folk songs.

In helping the subjects to achieve auditory skills after attended the AT, most research used various communication strategies such as using helpful hints or clue, interactive communicative strategies and giving support or encouragement to subjects to continue the training. However, seven programs (P06, P08, P10, P11, P13, P14, P15) did not specify any communication strategies.

From literature, AT method was defined by two trainings: analytic training or synthetic training. However, this study showed only one program used analytic and synthetic methods in the training. Other 14 program did not specify any methods used.

Most of studies did not state clearly what type of approach (either bottom up or top-down approach) that they used in their programs. Only four programs stated they used bottom up or top-down approach, but another three programs stated they "increased difficulties when correct response were given and decreased difficulties when wrong response were given:".

Three modes of auditory training were found from 15 programs namely; auditory-only (AO), auditory-visual (AV) and visual-only (VO). Some programs combined the mode with visual aid or feedback (VAF). In general, AT programs used AO with VAF.

Five auditory skills focused and targeted found in 15 programs; discrimination, identification, comprehension, auditory memory and localization.

Eleven speech stimuli were targeted in 15 programs; vowel, phoneme, syllable, word, spondee, sentence, paragraph, narrative, nursery rhymes, song and speech. Speech stimuli is based on the language of the speaker.

There was also program that targeted sound stimulus; environmental sounds stimulus and melodic contour. However, majority of the AT programs (nine out of 15) did not used any sound stimulus.

A total 17 parameters on how stimulus was presented in training named 'complexity of training' has been found in 15 programs which presented from most audible to least audible in training include; 1. Background noise (absence/ presence) found in nine programs, 2. Distance (close/ distance) found in three programs, 3. Repetition (repeated/ once) found in 12 programs, 4. Length of Utterance (short/ long) found in eight programs, 5. Complexity of utterances (simple/ complex) found in six programs, 6. Rate of utterances (slow/ individual) found in seven programs, 7. Suprasegmental (emphasis/ little or no emphasis) found in eight programs, 8. Segmental (emphasis/ little or no emphasis) found in six programs, 9. Target position (end/ middle / initial) found in one program, 10. Set (close/ open) found in five programs, 11. Speaker Familiarity (familiar/ unfamiliar) found in five programs, 12. Authenticity of sounds (degraded/ undegraded) found in four programs, 13. Sounds Origin (live/ recorded) found in 15 programs, 14. Learning Effect (adapted/ new) found in ten programs, 15. Learning Style (active/ passive) found in 13 programs, 16. Stimulus presentation (in-sequence/ random) found in seven programs and 17. Stimulus Context (in-context/ out of-context) found in five programs.

TABLE 2 DESCRIPTIVE SUMMARY OF THE AUDITORY TRAINING PROGRAM PARAMETERS

ID	AT Name	ID	Training Activities	Training theme	Method	Approach	Mode	Auditory Skills	Speech Stimulus	Sound Stimulus	Complexity of Training
P01	Listening and Communication Enhancement (LACE) (Sweetow and Sabes, 2006)	1, 11, 22	to choose a response from a choice on screen after listening to auditory stimuli	Topics health issues money matters exercise	NS	-when correct: increase difficulties -when wrong: decrease difficulties	Auditory-only and auditory-visual with visual aid/ feedback	identification comprehension auditory memory	word sentence speech	none	background noise length of utterance complexity of utterances rate of utterances speaker familiarity authenticity of sounds sounds origin learning effect learning style stimulus presentation stimulus context
P02	Customized Learning: Exercises for Aural Rehabilitation (clEAR) formerly known as: I Hear What You Mean Tye-Murray, Sommers, & Barcroft, 2011)	2, 23	to choose a response from a choice on screen after listening to auditory stimuli	Topics restaurant travel family sports	NS	bottom-up and top-down	Auditory-only with visual aid/ feedback	identification discrimination comprehension	phoneme word sentence paragraph	none	background noise repetition length of utterance complexity of utterances target position set speaker familiarity sounds origin learning effect learning style stimulus presentation stimulus context
P03	ReadMyQuips (RMQ; http: sensesynergy. com/)	3, 14, 15	to complete modified crossword puzzles after listening to video recordings of quips	NS	NS	bottom-up and top-down	Auditory-only, Visual-only and Auditory-visual with visual aid/ feedback	identification discrimination comprehension	syllable word narrative	none	background noise distance complexity of utterances rate of utterances segmental sounds origin stimulus presentation

P04	Audiologic Rehabilitation Classes (Preminger and Ziegler, 2008)	4, 9	Face to face activities with trainer Analytic exercises: to discriminate and identify phonemes synthetic exercises: (topic will be introduced for each exercise), i. answering questions about presented paragraph and ii. repeating sentences (varies in length)	NS	Analytic and synthetic	NS	Auditory-only and Auditory-visual	discrimination identification comprehension	phoneme syllable sentence paragraph	none	background noise distance repetition length of utterance speaker familiarity sounds origin learning style stimulus presentation stimulus context
P05	Environmental Sound Training (Shafiro, 2008)	5, 8	to choose a response from a choice on screen after listening to auditory stimuli	Sounds human and animal vocalizations and bodily sounds mechanical sounds of interacting inanimate solids water-related sounds aerodynamic sounds electric and acoustic signalling sounds	NS	NS	Auditory-only with visual aid/ feedback	dentification	none	environmental sounds	repetition authenticity of sounds sounds origin learning effect learning style stimulus presentation
P06	Speech Processed Training (Loebach, Pisoni and Svirsky, 2009)	6, 21	to transcribe by typing on keyboard after listening to auditory stimuli	Songs and Spoken Language familiar nursery rhymes 140 meaningful Harvard sentences contained five keywords e.g., the ripe taste of cheese improves with age. 60 meaningful sentences contained four keywords e.g., fresh bread smells great environmental context in four categories: general home, kitchen, office, and outdoors	NS	NS	Auditory-only and auditory-visual with visual aid/ feedback	discrimination identification comprehension	sentence nursery rhymes	environmental sounds	repetition rate of utterances speaker familiarity authenticity of sounds sounds origin learning effect learning style

P07	Musical Instruments training program (Driscoll et.al, 2009)	7	to choose a response from a choice on screen after listening to auditory stimuli	Sounds three simple melodic patterns from 8 musical instruments; flute clarinet saxophone trumpet trombone violin cello piano	NS	NS	Auditory-only with visual aid/ feedback	dentification	hone	environmental sounds	repetition sounds origin learning effect learning style
P08	Speech Perception Assessment and Training System (SPATS) (Miller et.al., 2007)	10, 24	to choose a response from a choice on screen after listening to auditory stimuli	Spoken Language the sentence module; contains spoken words (target words) in the onset, nucleus or coda e.g., if a target word was "pat", a foil might be "brat", "path" or "pit syllable constituent module; 45 onsets, 28 nuclei and 36 codas (onsets in word initial syllables, of nuclei in the stressed syllables of words, and of the word-final codas)	NS	bottom-up and top-down	Auditory-only with visual aid/ feedback	discrimination identification comprehension	sentence narrative phoneme syllable word	none	background noise repetition length of utterance complexity of utterances suprasegmental segmental set sounds origin learning effect learning style stimulus context
P09	Speech-in-noise and Localization Training (Tyler et.al. 2010)	12	to choose a response from a choice on screen after listening to auditory stimuli	Spoken Language and Sounds 12 spondee words sounds: fog horn, car horn, crowd cheering, drums, door knock, ocean waves, police siren, train, applause, bugle, cat meowing, children laughing, elephant trumpeting, motorcycle engine, bell ringing, and warning siren	NS	-when correct: increase difficulties -when wrong: decrease difficulties	Auditory-only and auditory-visual with visual aid/ feedback	localizations comprehension	spondee	environmental sounds	background noise distance repetition suprasegmental set sounds origin learning effect learning style stimulus presentation

P 1 0	The Brain Fitness™ cognitive Training (Posit Science Corporation, San Francisco, California)	13	to complete multiple-choice questions on personal computer after listening to auditory stimuli	Topics history art science	NS	NS	NS	comprehension auditory memory	syllable sentence	none	background noise repetition suprasegmental set sounds origin stimulus context
P 1 1	Computer-Assisted Speech Training (CAST) program developed at House Ear Institute	16	to choose a response from a choice on screen after listening to auditory stimuli	Spoken Language vowel and consonant contrasts were trained, using monosyllable words (ie, "seed" versus "said" versus "sad" versus "sawed")	NS	bottom-up and top-down	Auditory-only with visual aid/ feedback	Discrimination Identification comprehension	phoneme syllable word sentence speech	melodic contour	suprasegmental sounds origin learning style
P 1 2	The Musical Ear-Training Program (Petersen et.al. 2012)	17	Music-training session by professional music teacher to choose a response from a choice on screen after listening to auditory stimuli	Spoken Language and Sounds singing: to vocalize and imitate short phrases with a range of vowels. playing: to imitate short phrases and to play well-known folk and children's songs with a limited range of notes on the piano. listening: to identify and distinguish simple well-known monophonic melodies played on piano.	NS	-when correct: increase difficulties -when wrong: decrease difficulties	Auditory-only with visual aid/ feedback	discrimination identification comprehension	phrase song vowel	melodic contour	repetition length of utterance complexity of utterances rate of utterances suprasegmental segmental sounds origin learning effect learning style stimulus presentation

P13	Perceptual Learning of Degraded Speech Training (Wayne and Johnsrude, 2012)	18	to choose a response from a choice on screen after listening to auditory stimuli	Spoken Language 30 simple, declarative sentences with a range of lengths (6 to 13 words per sentence) sentences were assigned to six sets of five sentences each, such that they were matched item by item for number of words, spoken duration, naturalness, and imageability	NS	NS	Auditory-only and auditory-visual with visual aid/ feedback	identification comprehension	word sentence	none	repetition length of utterance complexity of utterances rate of utterances suprasegmental segmental authenticity of sounds sounds origin learning effect learning style
P14	Talker-identification Training (Krull and Luo, 2012)	19	to choose a response from a choice on screen after listening to auditory stimuli	Spoken Language 320 sentences (80 sentences x 4 lexical categories each). key words in each sentence are controlled for word frequency (i.e., how often the word occurs in english) and neighborhood density (i.e., the number of phonemically similar words). key words belong to one of four lexical categories representing orthogonal combinations of word frequency (high or low)	NS	NS	Auditory-only with visual aid/ feedback	dentification	word sentence	none	background noise repetition length of utterance rate of utterances suprasegmental segmental sounds origin learning style

P15	Vowel identification Training Program (Richie and Kewley-Port, 2008)	20	to choose a response from a choice on screen after listening to auditory stimuli	Spoken Language 10 english vowels /i, i, e, e, æ, a, ã, o, o, u/ in isolated monosyllables presented in a variety of cvc contexts; either some real words, such as bib /bib/, and phonotactically plausible nonwords, such as beeb /bib/ the words were composed of cvc, cvcc, and ccvc strings. the words were balanced for the 10 vowels; in the set of 40 words, there were four instances of each vowel. 10 sentences spoken by the female talker and a different 10 sentences spoken by the male talker were used.	NS	NS	Auditory-only with visual aid/ feedback	discrimination Identification comprehension	vowel syllable sentence	none	background noise repetition length of utterance rate of utterances suprasegmental segmental set speaker familiarity sounds origin learning effect learning style

DISCUSSION

This study has covered a total of 24 papers from 2007 to 2017 and 3 papers from grey search. The grey search papers have been included due their significance in describing the programs used; Listening and Communication Enhancement (LACE) (R. Sweetow & Henderson Sabes, 2007), I Hear What You Mean or Customized Learning Exercise for Aural Rehabilitation (cIEAR) (Tye-Murray et al., 2011) and Speech Perception Assessment and Training System (SPATS) (Miller et al., 2007). Other established programs found in the study include; ReadMyQuips (RMQ) (Rishiq et al., 2016), The Brain Fitness™ Cognitive Training (Anderson et al., 2012) and Computer-Assisted Speech Training (CAST) (Fu & Galvin, 2007). Other nine studies are newly developed programs covering; Audiologic Rehabilitation Classes (Preminger & Ziegler, 2008), Environmental Sound Training (Shafiro, 2008), Speech Processed Training (Loebach et al., 2009), Musical Instruments Training (Driscoll et al., 2009), Speech-in-noise and Localization Training (Tyler et al., 2010), The Musical Ear Training (Petersen et al., 2012), Perceptual Learning of Degraded Speech Training (Wayne & Johnsrude, 2012), Talker Identification Training (Krull et al., 2012) and Vowel Identification Training (Richie & Kewley-Port, 2008).

Based on findings of the scoping review, this study envisaged that AT program can be explained in two categories, the AT designs and parameters. The AT designs consisted of sample size, hearing status, measurement test, research sequence, duration, frequency, length of training, location of training, AT delivery style (either face-to-face, with or without trainer, individual or group training), findings and retention effect. The AT parameters on other hand included AT name, training activities, training theme, method, approach, mode, auditory skills, speech stimulus, sound stimulus and complexity of training.

The sample size in each study was varied from 2 to 279 subjects. Even with small sample size, the study was able to show positive findings as found from study by Rao et al. (2017) whereby, two subjects were able to conclude the other subjects trained using RMQ with marked improvement in their speech perception in noise when tested with Hearing in Noise Test (HINT). This was due to the comparisons made, in-between before and after training within subjects. There were also small sample size studies that compare between training group and control group. Study by Richie & Kewley-Port (2008) has compared between these two groups used seven subjects for each group also able to conclude a positive finding; vowel improvement in auditory-visual speech recognition under difficult listening conditions. A bigger sample size was used in study by Saunders et al. (2016) where they compared between 279 subjects in training group with 263 subjects in control group. This has enabled to result in a positive finding. As such, this can be concluded that AT program effectiveness can be proven even with small number of sample size. This conclusion is based on the premise that a program's impact can be evident and statistically significant even if the number of participants in the study is limited. Small sample sizes can still yield valuable insights and contribute to the understanding of the program's effectiveness, especially if the results are consistent and statistically significant, though larger sample sizes may enhance the robustness and generalizability of findings

One consideration needs to be taken when measuring the effectiveness of an auditory training program is the pre-training performance/ baseline. Saunders et al. (2016) suggested that the subjects with poorer baseline will yield a greater gain when tested using Words-in Noise test (WIN), Hearing Handicap Inventory for Adults/Elderly (HHIA/E) or Abbreviated Profile of Hearing Aid Performance (APHAP). This implies that individuals with lower initial hearing abilities may experience more significant improvements due to greater room for improvement before they reach their maximum potential as compared to the individuals with higher initial hearing abilities with smaller room of improvements. This may introduce bias in assessing the effectiveness of auditory training programs, as individuals who already have a certain level of ability might show improvement, but not necessarily yield greater improvements due to their initial abilities. It highlights the need to consider baseline abilities and their impact on the assessment of program effectiveness. This can be done through the use of normalized gain in measuring the effectiveness of an auditory training program. Normalized gain allows for a fair evaluation by considering the starting point of each participant and ensuring that improvements are measured accurately relative to their initial abilities (Coletta & Phillips, 2005).

With regard to hearing status, 17 studies used subjects with hearing loss ranging from mild to profound hearing loss. Tyler et al. (2010) stated that a systematic hearing training is viable for subjects with hearing loss from mild to profound hearing loss by improving the subjects binaural hearing in noise and localization. However, most studies used subjects with mild to moderate hearing loss (8 studies) and explained why from this review, it was found that most of the devices used was hearing aids because Ferguson et al. (2015) stated that hearing aids are most effective for those with mild to moderate hearing loss. There were also studies that investigate on normal hearing subjects using simulations devices to represent hearing-impaired subjects. The findings on using normal hearing subjects revealed that it will be practical and useful to generalize for the hearing-impaired subjects to undergo an auditory rehabilitation (Gfeller et al., 2015 and Loebach et al., 2009). Therefore, the study using normal hearing subjects has been included in this scoping review since the result has shown significant implications to hearing-impaired subjects and it enabled to be used to design a new AT program. When we look at hearing age, most studies did not state the subjects hearing age. Only 11 studies use hearing age as part of their study ranging from one month to 44 years. However, a minimum of 4 weeks of hearing age is recommended to be included in research to allow acclimatization to hearing devices (Saunders et al., 2016 and Rishiq et al., 2016). This has give suggestion to this study to not specified the hearing age as one of the inclusion criteria.

Standardized test, newly developed test for the research work or a combination of both measurements were done to measure the AT performances of each study. Standardized test that has been used were Word-in-noise test (WIN) (Miller et al., 2015; Saunders et al., 2016 and Smith et al., 2016) Handicap Inventory (HHI) (Preminger & Meeks, 2010 and Saunders et al., 2016) Hearing-in-noise Test (HINT) (Fu & Galvin, 2007; Rao et al., 2017 and Tyler et al., 2010), The Abbreviated Profile of Hearing Aid Performance (APHAP) (Miller et al., 2015; Saunders et al. 2016 and Smith et al., 2016) and Multimodal Lexical Sentence Test for Adults (MLST-A) (Yu et al., 2017 and Rishiq et al. 2016). The newly developed tests were needed to contemplate the essence of the training in different perspective following the study methodology. Shafiro (2008), Driscoll et al. (2009), Loebach et al. (2010) and Petersen et al. (2012) used the training stimulus itself to test subjects' performances. According to R. Sweetow and Palmer (2005), it is essential that auditory training programs utilize a measurement system that is highly sensitive and capable of accurately gauging the program's effectiveness. This sensitivity ensures that the measurement is precisely aligned with what the program is intended to assess and evaluate. Thus, when developing a new auditory program, incorporating the training stimulus as the tools to measure the effectiveness of the program can be considered. The incorporation of training stimulus and a purpose-built assessment tool, may not only evaluate the effectiveness of the program but also its ability to address specific auditory training goals and objectives.

The training sequence in each study was dependent on the objectives of their research. For example research by Shafiro et al. (2015), Tyler et al. (2010) and Rao et al. (2017) used 30 minutes per session training with pre-training test, training and post-training sequence; targeting to see the effect of the training by comparing pre and post training findings. While study to investigate retention effect have conducted second post-training test, for example in study by Saunders et al. (2016) and Smith et al. (2016), they did second post-training test after six months of the training. There were also researches that have conducted another test upon pre-training test to see baseline of all subjects as shown in study by Shafiro (2008) and Rishiq et al. (2016). While study by Loebach et al. (2009, 2010) introduced familiarization step before pre-testing to attain acclimatization on the training materials to all subjects to avoid bias. Therefore, this study review suggested that all training should be well prepared for the research sequence based on the research objectives to achieve anticipated goal.

Based on research, most study (91%) are leaning to use computer-based program or computer-based style. R. W. Sweetow & Sabes (2007), (Fu & Galvin, 2007) and Shafiro et al. (2015) stated, study that used self-training computer-based is cost effective in terms of money and time. While, study by Preminger & Meeks (2010) and Preminger & Ziegler (2008) that used face-to-face style focused on the study of group and with spouse to evaluate the quality of life among hearing impaired adult. In conclusion, we may suggest that computer-based program are more cost and time effective, but the use of traditional face-to-face training serves the closeness to real-life situation; using real voice, real setting and real feedback from trainer. Therefore, this study suggested to develop a face-to-face training for

new program to ensure the trainer could deal with the trainees emotional and practical aspect of AT. The training should be also held in clinical setting or laboratory to maintain all variables that may affect the training. This is based on suggestion made by Boothroyd (2007) that adult aural rehabilitation should optimize auditory function by controlling the listening environment in training and the need to have counselling to deal with emotionally and practically among individual with post-lingual hearing loss.

Regarding training duration, frequency and length of training, most study stated that they set their study in such a specific stipulated time based on two reasons; 1. They determined training duration, frequency and length of training based on research protocol (Rishiq et al., 2016) or 2. They integrated their studies with duration to finish the AT program which already stated in previous study (Richie & Kewley-Port, 2008). Based on findings of scoping review for most studies, the ideal training duration, frequency and length for face-to-face training around 30 to 60 minutes, minimum ten sessions in four to 12 weeks are recommended.

The variables of nine parameters explained that the strategy in each program should be; 1. Training activities, 2. Training theme, 3. Method, 4. Approach, 5. Mode, 6. Auditory skills, 7. Stimulus (speech or sound) and 8. Complexity of training. All parameters should be set according to research objectives, or the AT program aims. An established program such as cIEAR (Tye-Murray et al., 2011), LACE (R. W. Sweetow & Sabes, 2007) and SPATS (Miller et al., 2007) has specific parameters and conducted in laboratory. The suggestion has been made not only to answer the importance of having traditional style for AT program, but to help both trainee and trainer to achieve the best possible outcomes when conducting a standardized AT program.

CONCLUSIONS

The main objective of this scoping review is to review auditory training program in literatures and investigate the program trend. To achieve its specific goals the auditory training program has been designed meticulously through reviewing 24 papers included in this study and identifying 15 auditory training programs with each program has an exceptional ***design*** but shared practically the same ***parameters***. Saidi & Castro (2021) believed that auditory training, when chosen specifically according to each patient's needs, can enhance speech understanding.

The AT program ***designs*** explained; 1. sample size, 2. hearing status, 3. hearing devices, 4. hearing age, 5. measurement test, 6. training sequence, 7. training durations, 8. Training frequency, 9. length of training, 10. location of training, 11. training delivery style; either computer based or face to face, with trainer or self-training and individual or group training, 12. findings and 13. retention effects.

The parameters are the structure that scaffold the program that make auditory training as it meant to be. Therefore, the parameters that build an auditory training program need to be produced uniformly but tailored to the individual who needs it. The ***parameters*** used in auditory training program contains 1. Training activities, 2. Training theme, 3. Communication strategies, 4. methods, 5. approaches, 6. mode, 7. auditory skills, 8. speech stimulus, 9. sound stimulus and 10. complexity of training.

Research finding is optional to use as a guideline to develop an auditory training program designs and parameters. However, the designs and parameters should be carefully chosen for each individual with hearing impairment to heighten the improvement gain which benefit both trainer and trainee.

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SCOPING REVIEW ON AVAILABLE DELIVERY SYSTEMS OF SHORT INTERFERING RNA (SIRNA) THERAPY TO TREAT CARDIOVASCULAR DAMAGE DURING COVID-19: A STUDY ON HUMAN AND ANIMAL MODELS

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ABSTRACT

Background: Short-interfering RNA (siRNA) has the potential to treat a variety of diseases by silencing specific genes. It is currently being considered as an alternative method to treat cardiovascular damage that developed after the Covid-19 infection. If the damage persists for an extended period of time, it will lead to several other cardiovascular problems such as myocarditis. Application of compatible delivery systems can overcome the immunogenicity caused by the off-target reactions and sensitive interaction of siRNA with other cells. Therefore, the purpose of this scoping review was to identify effective delivery systems of siRNA therapy for treating arising cardiovascular problems during Covid-19 based on current studies. **Methods:** The search applied appropriate keywords involving three online databases: PubMed, Scopus, and ScienceDirect. The article selection was based on Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guideline and all articles published between 2010 and 2022 that met the inclusion and exclusion criteria were considered. **Results:** A total of six articles were discovered. Only one study used human cells, while the other five studies used animal models to investigate the effectiveness of distinct types of siRNA in silencing gene expression related to specific cardiovascular damage, which are ischemia-reperfusion injury, myocarditis, myofibroblast, venous thrombosis, and atherosclerosis. The methods of siRNA delivery involved the application of naked siRNA, specific-targeting nanocomplexes, and extracellular vesicles, which were administered through chemical transfection, intravenous injection, and subcutaneous injection. **Conclusion:** Both *in vivo* and *in vitro* approaches have their respective compatible delivery methods and administration routes for each type of siRNA.

KEYWORDS: delivery system, Covid-19, short interfering RNA, siRNA, cardiovascular

INTRODUCTION

Covid-19 has impacted various organs, especially the sites with angiotensin-converting enzyme 2 (ACE2) receptors as the binding site or the cellular pathway for the SARS-CoV-2, such as the heart, lungs, kidney, liver and brain. According to Zaim et al. (2020), Covid-19 infection has different paces of fatality between body systems. The respiratory system was affected in 17% of patients, with 65% experiencing rapid deterioration. Other than that, the loss of renal function might be observed one week after infection. Meanwhile, the prolonged silent damage to the cardiovascular system has led to a number of non-survivors, including 24% with coronary heart disease, 48% with hypertension, and cardiovascular risk factors of 31.4% with diabetes mellitus and 9.0% due to smoking. Overall, most body systems exhibit symptoms within a few days following the infection except for the cardiovascular system. Many Covid-19 patients are exposed to the risk of long-covid damage asymptomatically. The term "long-covid" refers to the damage that develops post-infection of Covid-19, which may take up to weeks until months. All patients who received one dose of the vaccination, received all of the vaccine

doses, and previously tested positive for SARS-CoV-2 had an increased risk of myocarditis (Patone et al., 2021). Meanwhile, patients may have a reduced risk of pericarditis after vaccination but an increased risk if they are past positive patients. Lastly, the risk of developing cardiac arrhythmia only decreased upon the first dose, but it increased after the second dose or had a previous Covid-19 history. From the data, it can be inferred that vaccinated people still have the risk of developing cardiovascular problems.

Recently, gene silencing RNA or known as short-interfering (siRNA) therapy has been explored as a potential alternative to overcome the problem. However, it is exposed to the possibility of immunogenic reactions and toxicity during the process (Medeiros et al., 2021). Hence, a thorough analysis of the delivery systems is crucial to prevent toxicity between the biomaterials used, siRNA genes and the target sites or its surrounding cells. Several studies were conducted to examine the impact of various delivery systems for siRNA therapy. However, there is still a limited understanding of which delivery systems are suitable and available for treating Covid-19 using the siRNA.

This scoping review aims to provide an evidence-based analysis of the available studies on delivery systems that can be used to treat cardiovascular problems and reduce complications during COVID-19. The present review summarises effective delivery system used for cardiovascular damage, comprised of the type of siRNA used for silencing specific gene, as well as suitable method of delivery and its route of administration.

MATERIALS AND METHODS

Study Design

A scoping review was performed by gathering evidences based on the published research articles on the same topic of interest; delivery systems used to treat cardiovascular damages. The framework involved the construction of research objectives based on the research problems, selection of articles that met the goals of this review, screening process to ensure the conformation of inclusion and exclusion criteria and the availability of full-text articles.

Search Strategy

The literatures were chosen from three online databases that were reliable in providing data relevant to the medical and health research, which were PubMed, Scopus, and ScienceDirect. The database search included papers from 2010 to 2022 comprising of the combination of following keywords; 'delivery system', 'vehicle', 'biomaterial', 'transport', 'biomaterial', 'short-interfering RNA', 'siRNA', 'RNA interference', 'RNAi', 'Covid-19', 'Coronavirus 2019', 'SARS-CoV-2', 'cardiovascular', 'heart' and 'cardiac'. In addition, Boolean operators AND and OR were applied to assist in the finding of specific articles related to the study.

Inclusion and Exclusion Criteria

Several criteria were devised and considered during the selection of relevant papers for this scoping review. Articles that did not meet the inclusion criteria outlined in Table 1 were excluded from the study.

Table 1 Inclusion and exclusion criteria for article selection

Inclusion Criteria	Exclusion Criteria
a) Published research articles were written in English. b) All articles must be published between 2010 and 2022. c) Qualitative and quantitative studies. d) Papers related to delivery systems of short interfering RNA (siRNA) and cardiovascular damage. e) The search consists of specific keywords.	a) Publish research articles were written in non-English version. b) Articles were published before 2010. c) Chapter of books, reviewed articles, proceeding, conference presentation, dissertation, and discussion papers. d) Absence of abstract and full-text articles e) Papers were not relevant to the objectives of the study.

Selection Procedures

The selection of articles was based on Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guideline (Moher et al., 2009). Articles published between 2010 and 2022 were extracted from online databases and screened. After removing duplicates from multiple databases, the selection of articles was subjected to title and abstract screening to identify any irrelevant studies. Then, all full-text articles of the remaining papers were retrieved. Following that, the information in those articles were examined thoroughly to analyse the data on the delivery systems of siRNA therapy in treating cardiovascular problems in Covid-19 patients. Throughout the screening process, articles that violated inclusion criteria and conformed with exclusion criteria will be excluded. The selection procedures are displayed in the PRISMA flow diagram shown in Figure 1.

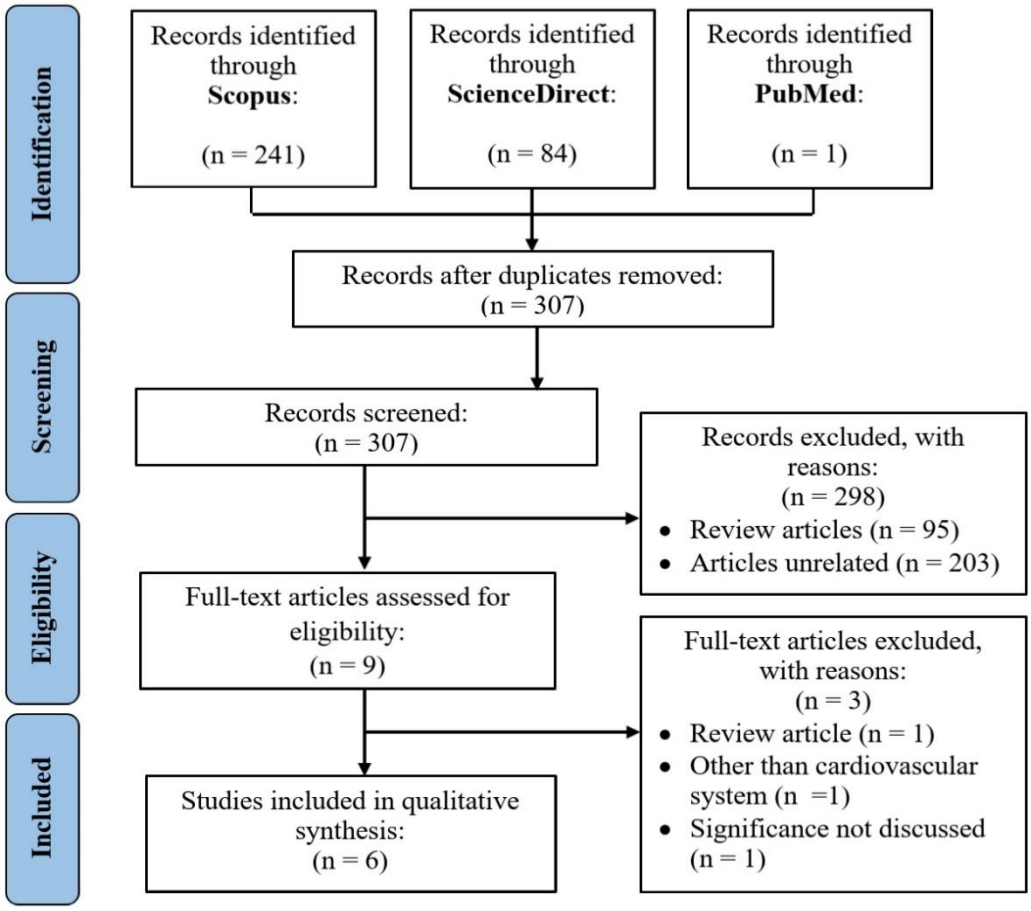


Figure 1 PRISMA flow diagram (Moher et al., 2009)

Data Extraction

The findings from the final full-text articles that passed the screening processes for the scoping review were extracted, analysed, and presented using tables. The tables have included important information about final full-text articles comprising the author's name, year of publication, method of study and subjects or models involved in the studies. The main findings of this scoping review are the characteristics of the delivery systems used in siRNA therapy in treating cardiovascular problems among Covid-19 patients, which comprised of the types of cardiovascular damage, type of short-interfering RNA, methods of delivery, routes of administration and impacts of the delivery system used.

RESULTS AND DISCUSSIONS

The selection of articles is summarised in the Figure 1. A total of 326 articles were discovered through Scopus, ScienceDirect and PubMed databases. After removing 19 duplicates, 307 remaining articles were assessed for the title and abstract screening. A total of 298 irrelevant articles were eliminated including 95 review articles and 203 articles unrelated to siRNA delivery in treating cardiovascular damage. To evaluate compliance with the inclusion and exclusion criteria, the full texts of the remaining publications were retrieved and reviewed. Three papers that met the exclusion criteria were excluded,

including a review and an article on the use of siRNA in the respiratory system. Finally, only six articles remained and specifically focused on the siRNA delivery for cardiovascular problems. The findings from the final full-text articles were synthesised and tabulated in Table 2.

Both *in vitro* and *in vivo* approaches used the same type of siRNA and method of delivery but different study model and route of administration for each cardiovascular damage. As shown Table 2, each cardiovascular damage utilised 6 distinct types of siRNA. Among the 6 final articles, 2 articles used each method of siRNA delivery, consisting of naked siRNA, specific-targeting nanocomplexes and extracellular vesicles. In all *in vitro* studies, chemical transfection was used as the route of administration, while intravenous and subcutaneous injections were used in *in vivo* studies. Table 3 summarised the effectiveness of each delivery system in all six final articles through positive recovery or changes observed in respective cardiovascular damage tested on.

The application of siRNA to treat cardiovascular problems of the heart, veins, and arteries has been investigated. Myofibroblast is an activated fibroblast that functions as a healing mechanism in response to cardiac injury, such as myocarditis and myocardial ischemia-reperfusion injury (MIRI). However, excessive myofibroblast deposition can result in fibrosis (Baum and Duffy, 2011). Successful treatment of myocarditis using siRNA in a study by Woods et al. (2021) provides a huge discovery in the post-Covid situation because myocarditis is one of the most vulnerable cardiovascular diseases. Increased risks were recorded in all categories, including people with complete vaccine doses, one vaccine dose, and patients with a history of being infected with Covid-19 (Patone et al., 2021). Venous thrombosis and atherosclerosis are common vascular damages, with both conditions interfering with blood flow to the heart and become a highly potent factor in the development of ischemia-reperfusion injury among patients (Frank et al., 2012).

According to Dana et al. (2017), the application of siRNA therapy can degrade the complementary mRNA and interfere with the protein translation and expression of the targeted gene. Among the studies reviewed, only CD147 siRNA has been experimented on human cells, while others are animal models. Incorporation of the αSMA protein and F-actin is vital in the formation of fibrosis. Woods et al. (2021) found that CD147 siRNA caused a lack of uniformity in αSMA protein formation, thus, impaired its contractility and restrained contact with F-actin. In myocarditis treatment, the receptor for advanced glycation and products siRNA (siRAGE) suppressed the continuous synaptic action that can cause inflammation (Christaki et al., 2012). It prevented the infiltration of inflammatory cells by lowering the level of pro-inflammatory cytokine, Interleukin-6. Hou et al. (2022) and Wang et al. (2022) used vascular adhesion molecule-1 siRNA (siVCAM-1) and siRNA against MOF (siMOF) to treat ischemia-reperfusion injury, respectively. Blood restoration of ischemic tissues triggers tumour necrosis factor-α (TNF-α) and induces recruitment of neutrophils to the site. Inhibition of neutrophil adhesion by VCAM-1 siRNA prevented the inflammation of vessels (Sager et al., 2016). The application of siMOF to histone acetyltransferase KAT8 or MOF prevented excessive production of reactive oxygen species (ROS) by suppression of ROS synthesising enzyme transactivation, hence reducing oxidative stress and the inflammatory response of cardiomyocytes (Yu et al., 2018). A research by Biswas et al. (2012), the toll-like receptor 3 (TLR3) siRNA has prevented venous thrombosis by inhibiting the TLR3 signal in activating tissue factors that cause hypoxemia and fibrin deposition in lungs. In atherosclerosis, Smad2/3 siRNA supressed the Smad2/3 signalling pathway that can trigger fibrosis, induce cell apoptosis and promote the formation of fat deposition in arteries (Comarița et al., 2022).

A naked siRNA is free from chemical modification and involves the localised injection of a solution containing non-complex siRNA sequences into the targeted areas. Findings by Woods et al. (2021) and Bhagat et al. (2020) found that localised direct injection of naked CD147 and naked TLR3 siRNA on primary human fibroblast culture and mice respectively have successfully impaired the expression of targeted genes. According to Zhang et al. (2016), the presence of ribonucleases may reduce the half-life to less than 1 minute. Specific-targeting nanocomplexes have been re-designed according to the suitability of surrounding tissues and the drug composition. Endothelial cell-targeting and ROS-ultrasensitive nanocomplexes, as well as polycations macrophage-targeting nanocomplexes, have demonstrated high potential in treating cardiovascular damage in both *in vitro* and *in vivo* testing. (Hou et al., 2022; Wang et al., 2022). Extracellular vesicles can be easily found as the sources mainly originate from the body cells such as T cells and dendritic cells. According to Raposo and Stoorvogel (2013), the mechanism of the extracellular vesicle is through endocytosis, and it encapsulates the drugs in vesicles before fusing with the target tissues through integration with the plasma membrane. The encapsulation has protected the drug cargo from being off-target reactive.

The delivery of siRNAs for *in vitro* experiments is through two types of chemical transfection, which are cationic lipids and cationic polymers. The mechanism of transfection is through endocytosis followed by the release of siRNA. Lipofectamine is the most widely utilised cationic lipid because its random Brownian motion manages to avoid active transport along microtubules, hence preventing metabolic breakdown (Cardarelli et al., 2016). In active transport, siRNAs may degrade within acidic lysosomal compartments due to the long-range motion, and the solid binding perinuclear accumulation of siRNA reduces the number of plasmids transported to the nucleus of the target sites. Meanwhile, poly(L-lysine) and Poly[2 (Dimethylamino)ethyl Methacrylate] (PDMAEMA) are the most commonly used cationic polymers (Lächelt and Wagner, 2015; Englert et al., 2018). In *in vivo* studies, siRNA is administered intravenously through the tail vein since artery has very high pressure of blood flow and may cause blood loss through the punctured site. Meanwhile, subcutaneous injection is preferable when the target area is the surrounding fats. However, it has a lower rate of absorption as only a few blood vessels present in the subcutaneous layers (Kim et al., 2021).

The limitation of this review is the inclusion of minimal number of journal articles relatively, as PubMed, Scopus, and ScienceDirect databases offered a limited number of relevant studies on the delivery systems of short-interfering RNA in treating disorders of the cardiovascular system. Furthermore, the research methodologies employed in different studies are inconsistent, as some studies only performed one method, either *in vitro* or *in vivo* study. Therefore, the effectiveness of certain siRNA in treating cardiovascular damage is dependent primarily on the findings of one study approach. Additionally, only one article related to Covid-19 cases is found, which is the use of CD147 siRNA on human fibroblast culture while the other are based on animal studies.

Recommendations for future siRNA study: (1) Analysis of the method used to assess the effectiveness of the delivery system. (2) In-depth discussion on mechanism for each delivery method for comprehensive comparison between different delivery systems such as its interaction with target sites and surrounding cells. (3) Compare the effectiveness of each delivery system in both *in vivo* and *in vitro* methods, to examine whether respective delivery system is effective across cultures and living models, especially human models like human cardiovascular cell culture. (4) Provide an in-depth analysis of the correlation and significances between the route of administration and delivery method applied in treating specific cardiovascular diseases.

CONCLUSION

Considering the rising prevalence of cardiovascular damage associated with Covid-19, this review comprehensively analyses the potential of siRNA therapy as a viable solution for this critical issue. Although the findings are primarily derived from experiments on human cell culture and animal studies, they hold significant relevance. The effective siRNA delivery systems could significantly contribute to mitigating complications related to cardiovascular damage during and post Covid-19 era. Each siRNA used to treat cardiovascular damage has its own delivery system consisting of a delivery method and administration route. The method of delivery for siRNA is modified according to the sensitivity of the target site or organs. Meanwhile, a different route of administration is implemented according to the location of the target site to enhance the efficiency of the delivery method applied to fuse with the cells or release the siRNA. The delivery systems are modified through the paired combination of delivery methods and administration routes to ensure the compatibility of siRNA and target sites and silence targeted genes in both *in vitro* and *in vivo* methods without causing toxicity. While these methods have not been directly employed during the pandemic, their potential utility remains evident. Given the persistent rise in cardiovascular disease, even beyond the Covid-19 context, these findings serve as a cornerstone for future research and development in addressing the challenges posed by cardiovascular damage.

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Table 2 Effective delivery systems used in treating various cardiovascular damages

Journal Reference	Cardiovascular Damage	Type of siRNA	Method of Delivery	Study Model	Route of Administration
Woods et al., 2021	Myofibroblast	CD147 siRNA	Naked siRNA	Primary Human Fibroblast culture	Chemical transfection (Cationic lipids)
Hou et al., 2022	Ischemia reperfusion injury	Vascular cell adhesion molecule-1 siRNA (siVCAM-1)	Endothelial cell-targeting and ROS-ultrasensitive nanocomplexes comprised of PLGA NPs decorated with cRGD-poly(ethylene glycol) (PEG)-modified, ditellurium-crosslinked PEI (RPPT)	Rats	Intravenous injection
				Rat cardiac microvascular endothelial cells (RCMECs)	Chemical transfection (Cationic polymers)
Bhagat et al., 2020	Venous thrombosis	Toll-like receptor 3 (TLR3) siRNA	Naked siRNA	Mice	Intravenous injection
Kim et al., 2021	Myocarditis	Receptor for advanced glycation end products siRNA (siRAGE)	Cardiac-targeting peptide (CTP) expressing sEVs (C-sEV)	Rats	Intravenous injection
				H9C2 cells (alternative of cardiomyocytes)	Chemical transfection (Cationic lipids)
Wang et al., 2022	Ischemia reperfusion injury	siRNA against MOF (siMOF)	Polycations macrophage-targeting nanocomplexes (NCs): Man-COOH/BPAE-SS/siMOF (MBSs) NCs	Mice	Intravenous injection
				RAW 264.7 cells (mouse monocyte macrophages)	Chemical transfection (Cationic polymers)
Comarița et al., 2022	Atherosclerosis	Smad2/3 siRNA	Subcutaneous adipose tissue stem cells extracellular vesicles (EVs), or bone marrow mesenchymal stem cells EVs	Hamsters	Subcutaneous injection

***Method of study:** ☐ *in vivo* ☐ *in vitro*

Table 3 Main findings from the application of delivery systems

Method of siRNA Delivery	Effectiveness Status	Result	Reference
Naked CD147 siRNA	Effective	Arrangement of F-actin is not altered, impaired the contractility in myofibroblast as it has irregular formation of αSMA protein that prevented incorporation of F-actin and αSMA, and. Fibrosis is inhibited.	Woods et al., 2021
Endothelial cell-targeting and ROS-ultrasensitive nanocomplexes (NCs) comprised of PLGA NPs decorated with cRGD-poly(ethylene glycol) (PEG)-modified, ditellurium-crosslinked PEI (RPPT)	Effective	Inhibition of neutrophil infiltration has lessened the post effects of MIRI in both *in vitro* and *in vivo*; reduction in the size of infarcted area, muscle degeneration, cardiac fibrosis, and cardiomyocyte apoptosis.	Hou et al., 2022
Naked Toll-like receptor 3 (TLR3) siRNA	Effective	Inhibition tissue factor activity that can cause hypoxemia leading to venous thrombosis.	Bhagat et al., 2020
Cardiac-targeting peptide (CTP) expressing sEVs (C-sEV) for the delivery of RAGE-targeting small interfering RNA (siRNA) (siRAGE)	Effective	Compared to N-sEVs, the efficiency of cardiac-targeting *in vivo* are 4 folds higher while 2 folds higher through *in vitro* and no toxicity is present.	Kim et al., 2021
Polycations macrophage-targeting nanocomplexes (NCs): Man-COOH/BPAE-SS/siMOF (MBSs) NCs	Effective	Reduced the post-RI effects by alleviating the production of reactive oxygen species (ROS); cardiomyocytes degeneration, fibrosis and apoptosis.	Wang et al., 2022
Smad2/3 siRNA with subcutaneous adipose tissue stem cells extracellular vesicles (EVs) or bone marrow mesenchymal stem cells EVs	Effective	Compared to typical atherosclerosis, a significant reduction is seen in (1) The total cholesterol, triglycerides, and LDL cholesterol in arteries, (2) the thickness of arteries and (3) The expression of NF-kB transcription factor in both aortic and thoracic arteries.	Comarița et al., 2022

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MAGNETIC RESONANCE IMAGING AND HYBRID IMAGING APPROACHES FOR ASSESSING COVID-19 DISEASE PROGRESSION AND STAGING: A SCOPING REVIEW

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ABSTRACT

Introduction: The outbreak of novel coronavirus (SARS-CoV-2) in Wuhan, China, occurred in December 2019. The World Health Organisation (WHO) named it coronavirus disease-19 (COVID-19). Common clinical signs of COVID-19 include fever, coughing, shortness of breath, myalgia, and exhaustion. While the RT-PCR test remains the gold standard for diagnosis, false-negative results are prevalent. Chest radiography and CT scans, which primarily focus on lung abnormalities, can complement RT-PCR in diagnosing and monitoring the disease. This study explores the roles of MRI, PET-CT, and SPECT-CT as diagnostic imaging modalities for COVID-19, aiming to improve clinical diagnosis and patient management. **Methods:** A scoping review was undertaken by systematically searching a number of databases, including PubMed, Scopus, and Google Scholar. The search was done using relevant keywords such as COVID-19, MRI, hybrid imaging, PET-CT, SPECT-CT, progression, and staging. Our study primarily focused on articles that emphasise the significance of imaging techniques for assessing COVID-19 disease progression and staging, following specific inclusion and exclusion criteria. **Results:** Fourteen relevant articles were reviewed. Medical imaging modalities, such as MRI, and hybrid techniques like PET-CT and SPECT-CT can effectively identify abnormalities caused by COVID-19 in patient images. However, they may not always distinguish overlapping pneumonia specifically associated with COVID-19. **Conclusion:** In conclusion, MRI, PET-CT, and SPECT-CT can provide complementary diagnostic images for understanding the progression and staging of COVID-19. These imaging modalities enhance patient management and follow-up, offering valuable insights into the disease's impact on the body.

Keywords: COVID-19, MRI, Hybrid Imaging, PET-CT, SPECT-CT, Progression, Staging

INTRODUCTION

In late 2019, the world received a shocking alert from the Health Ministry of China about a mysterious outbreak of pneumonia cases in the city of Wuhan, located in the Hubei District of Central China. This challenging health crisis initially unfolded at the Hua Nan Seafood and wet animal wholesale market, but what made it even more puzzling was the fact that it began affecting locals who had no direct exposure to this market (Harapan et al., 2020). At the start of the year 2020, the market was promptly closed in response to the unfolding situation. A mere week later, scientists identified the causative agent as a novel betacoronavirus, closely related to the infamous SARS-CoV and a group of bat-borne SARS-like coronaviruses (Mackenzie & Smith, 2020). Initially dubbed "novel coronavirus" (nCOV), it was subsequently officially named coronavirus disease 2019 (COVID-19) by the World Health Organisation

(WHO). It is also commonly referred to as SARS-CoV-2, which is derived from severe acute respiratory syndrome coronavirus 2 (Singhal, 2020).

The COVID-19 outbreak rapidly escalated, causing significant loss of life and wreaking havoc on economies worldwide. The first deaths occurred in China, where the China National Health Commission meticulously recorded them up until January 22, 2020 (Rothan & Byrareddy, 2020). However, this deadly virus soon transcended borders, spreading to countries like Italy, European nations, and the United States, where the number of confirmed cases surged relentlessly (Pascarella et al., 2020). As of May 10, 2023, the World Health Organisation (WHO) has reported a staggering 756,903,278 confirmed cases of COVID-19, with 6,927,378 tragic fatalities worldwide (World Health Organisation, 2023) as shown in Table 1.

Table 1. Confirmed COVID-19 cases on the globe by 10 May 2023 (WHO 2023)

Region	**Confirmed Cases**
Europe	276,136,217
Western Pacific	203,172,588
Americas	192,581,201
South-East Asia	61,120,704
Eastern Mediterranean	23,364,240
Africa	9,527,564

Initial local health concern soon escalated into a global pandemic, with COVID-19 reaching 213 nations and independent territories around the world (Chamola et al., 2020) as shown in Table 1. The rapid spread of this highly contagious and transmissible disease led the WHO to declare COVID-19 a pandemic, a declaration that has reshaped the course of modern history and continues to pose profound challenges to the global community (Pascarella et al., 2020).

The COVID-19 pandemic has posed unprecedented challenges to healthcare institutions on a global scale. The sheer magnitude of cases overwhelmed testing capacities, primarily relying on polymerase chain reaction (PCR) tests, which are both time-consuming and expensive. Moreover, the prevalence of both false positive and false negative outcomes in polymerase chain reaction (PCR) testing is widespread, hence necessitating the exploration of alternate diagnostic approaches. A review study conducted by Nor Fitri, and Sayed (2023) and reported that the diagnostic accuracy of plain X-ray, CT, and ultrasound modalities can vary depending on factors such as the stage of the disease, the expertise of the healthcare provider, and the specific equipment and protocols used. Additionally, the sensitivity of these modalities may change over time as new research and guidelines emerge. Moreover, alternate advanced imaging technologies such as MRI, PET-CT, and SPECT-CT may offer further supplementary insights into the pathophysiology and severity of COVID-19-related illnesses. In addition, the implementation of alternate strategies in situations where polymerase chain reaction (PCR) testing is inadequate or inaccessible can play a significant role in a complete understanding of COVID-19 and its progression and management.

Therefore, this review study explores the significance of advanced diagnostic imaging techniques, such as MRI, PET-CT, and SPECT-CT, in the diagnosis, assessment, and management of COVID-19.

METHODOLOGY

In this research endeavour, a thorough article selection process was conducted across various online databases, such as PubMed, Scopus, and Google Scholar. The focus was on the COVID-19 pandemic and its relationship with medical imaging techniques like MRI, PET-CT, and SPECT-CT. Boolean queries, including "AND," "OR," and "NOT," were employed to refine search results effectively.

The keywords used in the search included COVID-19, MRI, hybrid imaging, PET-CT, SPECT-CT, progression, and staging. Only English-language, full-text articles published between 2019 and 2023 were considered for inclusion to ensure that the sources used in the study were both relevant and up-to-date. Moreover, the articles should be relevant to the COVID-19 pandemic and medical diagnostic imaging techniques like MRI, PET-CT, and SPECT-CT.

Data extraction was meticulously carried out in accordance with the inclusion criteria, with Microsoft Excel serving as the organising tool. The extracted data encompassed details such as author(s), year of publication, title, and findings from the article.

Furthermore, we adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis methodology throughout the review process to ensure transparency and rigour in the selection of articles for the study.

RESULTS

In this review we employed PubMed, Scopus, and Google Scholar, databases to search for relevant online articles. The initial search yielded a total of 103 relevant studies/articles. Microsoft Excel was then used to manage and identify duplicate materials, resulting in the removal of 10 duplicate items. Following this, the remaining 93 articles underwent a thorough screening process based on their titles and abstracts, with a focus on their relevance to the research topic. After this screening, 37 articles remained for further review. The 37 articles were subjected to additional scrutiny, which involved a more detailed assessment of their content. During this phase, 23 articles were excluded due to insufficient justification, a lack of essential information, or the absence of full-text articles. Consequently, only 14 articles were deemed suitable for inclusion in the research, shown in Table 2.

Table 2. Summary of articles included in this study

Title	Imaging modalities	Roles in Managing COVID-19	References
A Comprehensive Survey of COVID-19 Detection Using Medical Images	MRI	Resolves characteristic features Alternative for imaging high-risk group	Mohammad et al., 2023
Characterization of COVID-19-Related Lung Involvement in Patients Undergoing Magnetic Resonance T1 and T2 Mapping Imaging: A Pilot Study	MRI	Resolves characteristic features	Camastra et al., 2022
Imaging of COVID-19: CT, MRI, and PET	MRI PET-CT	Resolves characteristic features Alternative for imaging high-risk group	Fields et al., 2021

		Monitoring disease progression	
Magnetic resonance imaging features of coronavirus disease 2019 (COVID-19) pneumonia: The first preliminary case series	MRI	Resolves characteristic features Monitoring disease progress	Torkian et al., 2021
Chest MRI of patients with COVID-19	MRI	Resolves characteristic features Alternative for imaging high-risk group	Vasilev et al., 2021
The Clinical Utility of Molecular Imaging in COVID-19: An Update	PET-CT	Resolves characteristic features Progression of disease	Elsakka et al., 2023
FDG PET/CT imaging features and clinical utility in COVID-19	PET-CT	Assess pulmonary disease Staging of the disease	Yeh et al., 2021
FDG-PET/CT imaging during the Covid-19 emergency: a southern Italian perspective	PET-CT	Assess the extent of the disease Staging of disease	Maurea et al., 2020
FDG-PET/CT of COVID-19 and Other Lung Infections	PET-CT	Malignancy evaluation and staging Resolves characteristic features	Eibschutz et al., 2022
Diagnostic Value of Imaging Modalities for COVID-19: Scoping Review	PET-CT	Assessing progression and staging of disease Assessing and monitoring of lung disease	Aljondi & Alghamdi, 2020
A comprehensive review of imaging findings in COVID-19 - status in early 2021	SPECT-CT	Assessing the progression and staging of the disease Assessing and monitoring of lung disease Resolves characteristic features	Afshar-Oromieh et al., 2021
Lung Scientigraphy for Pulmonary Embolism Diagnosis in COVID-19	SPECT-CT	Assessing and monitoring of	Roux et al., 2021

Patients: A Multicenter Study		lung disease Assess pulmonary changes	
Ventilation/perfusion SPECT/CT findings in different lung lesions associated with COVID-19: a case series	SPECT-CT	Resolves characteristic features Assessing the progression and staging of the disease Assessing and monitoring of lung disease	Cobes et al., 2020
Investigation of perfusion defects by Q-SPECT/CT in patients with mild-to-moderate course of COVID-19 and low clinical probability for pulmonary embolism.	SPECT-CT	Assessing and monitoring of lung disease	Ozturk et al., 2021

Effectiveness of Magnetic Resonance Imaging in Detecting COVID-19

The investigated literature reveals that MRI demonstrates significant promise as a diagnostic tool for COVID-19, with a high level of accuracy in detecting associated lung abnormalities. Fields et al. (2021) found MRI to have a sensitivity of 91.7%, a specificity of 100%, a positive predictive value of 100%, and a negative predictive value of 95.2%. Various MRI sequences, including T2-weighted sequences like half-Fourier acquisition single-shot turbo spin echo (HASTE), turbo spin echo (TSE), fast imaging with steady-state precession (FISP), and turbo inversion recovery magnitude (TIRM), enhance the precision of COVID-19 lung abnormality identification. The T2-weighted TSE-TIRM sequence is particularly effective in highlighting lesions associated with oedema, a common feature of COVID-19 disease. MRI can distinguish between subacute bleeding-induced changes in signal intensity and consolidation due to fibrous structures. Additionally, MRI is shown to be comparable to CT scans in detecting ground-glass opacities (GGOs) and consolidative lesions associated with COVID-19.

Despite its potential, MRI has limitations in COVID-19 diagnosis, including susceptibility to signal loss due to physiological factors (respiration and heartbeat), lower spatial resolution, and longer examination times. These factors may restrict its practicality in certain clinical settings (particularly in emergency). Further research and validation are needed to determine the optimal role of MRI in COVID-19 diagnosis and management.

PET-CT in Diagnosing and Monitoring of COVID-19

The primary radiotracer used in FDG PET-CT is 18F-labelled fluorodeoxyglucose (18F-FDG), which effectively highlights metabolic activity in inflamed areas. PET-CT in diagnosing and monitoring COVID-19 pneumonia yields several significant results and implications; like PET-CT, are better than traditional imaging methods for figuring out how COVID-19 is getting worse, how well treatment is working, and what the prognosis is (Elsakka et al., 2023).

Furthermore, PET-CT can show the immune response of the host to COVID-19 by showing the presence of inflammatory cytokines, alveolar macrophages, and neutrophils in the lungs (Yeh et al., 2021). This can aid in identifying COVID-19 and assessing its severity. Moreover, PET-CT demonstrates the potential to detect COVID-19 in asymptomatic individuals, even before symptoms appear (Eibschutz et al., 2022). This early detection could lead to timely interventions and reduced virus transmission.

PET-CT is highly sensitive in detecting COVID-19-related changes, it may lack specificity, potentially leading to false-positive results (Fields et al., 2021; Elsakka et al., 2023). Caution is needed when interpreting findings, especially in patients with underlying health conditions. PET-CT has clinical implications for understanding COVID-19 disease trajectories and evaluating treatments for patients with persistent respiratory symptoms. It can uncover findings that standard tests might miss, guiding more targeted treatments (Eibschutz et al., 2022). In addition, clinical decisions regarding the use of PET-CT in COVID-19 diagnosis and monitoring should prioritise patient safety and effectiveness, considering both the benefits of early detection and the limitations in specificity.

PET-CT holds promise as a valuable tool in diagnosing and monitoring COVID-19 pneumonia. It provides unique insights into disease progression and the immunological response. However, its lower specificity requires careful consideration when interpreting results. The results underscore the need for additional research and clinical validation to fully comprehend the role of PET-CT in COVID-19 management, especially across different patient populations and disease stages. Therefore, continued research and clinical validation are essential to maximising its potential in patient care.

Significance of SPECT-CT in diagnosing COVID-19

COVID-19 patients often experience coagulopathy, characterised by microthrombosis and venous thromboembolism. Studies by Cobes et al. (2020) and Roux et al. (2021) support this finding. Pulmonary embolism (PE) occurs in COVID-19 patients, predominantly in peripheral lung regions, suggesting microvascular thrombus formation due to vascular injury, different from traditional PE. Lung ventilation-perfusion (V/Q) scintigraphy, as described by Roux et al. (2021), is a valuable tool for diagnosing PE in COVID-19 patients, relying on wedge-shaped perfusion mismatch defects. Cobes et al. (2020) found that COVID-19-related lung lesions did not change the V/Q single-photon emission computed tomography (SPECT) patterns in COVID-19 cases. However, V/Q SPECT-CT remains reliable for identifying thromboembolic disorders in these patients. In COVID-19 pneumonia patients, Afshar-Oromieh et al. (2021) saw different ventilation SPECT patterns even though pulmonary parenchymal perfusion was the same. This highlights the complexity of COVID-19 lung involvement and the need for advanced imaging techniques.

In summary, the literature provides insights into COVID-19's multi-organ impact, with a focus on coagulopathy and PE. It underscores the importance of V/Q scintigraphy and SPECT-CT in diagnosing PE in COVID-19 patients and highlights the unique patterns seen in these individuals. These findings contribute to our evolving understanding of COVID-19 and can aid clinicians in early thromboembolic complication detection and management.

DISCUSSION

Role of MRI, PET-CT, and SPECT-CT in Detecting, Progression, and Staging of COVID-19

Magnetic Resonance Imaging (MRI)

Magnetic resonance imaging (MRI) is a non-invasive diagnostic tool known for creating detailed images of the human body without using harmful radiation. However, it is underutilised in diagnosing COVID-19 compared to alternatives like CT scans and lung ultrasound due to its longer examination time and higher cost. Instead of that the literature suggests that MRI can be a valuable tool for diagnosing COVID-19 pneumonia. Studies mentioned, such as Fields et al. (2021) and Muhammad et al. (2023), indicate that MRI shows a high sensitivity, specificity, positive predictive value, and negative predictive value when compared to CT scans. These findings suggest that MRI can accurately identify pulmonary lesions associated with COVID-19.

The various MRI sequences, such as T2-weighted sequences like HASTE, TSE, FISP, and TIRM, which are effective in identifying lung infiltrations. Additionally, it mentions that the T2-weighted TSE-TIRM sequence is particularly useful for detecting oedema, which is a common feature of COVID-19

pneumonia. This information suggests that specific MRI sequences can enhance the precision of the COVID-19 diagnosis. MRI can distinguish between different types of lesions in COVID-19 pneumonia. For example, it can differentiate consolidation linked to fibrous structures due to the relatively "short" T2 component. This ability to differentiate lesions may aid in understanding the stage and severity of the disease.

Furthermore, ground-glass opacities (GGOs) and consolidative lesions are detectable with MRI in a manner similar to CT, according to Ates et al. (cited by Fields et al., 2020). This finding is significant because GGOs are a common radiological feature of COVID-19 pneumonia. Additionally, the literature suggests that MRI findings are generally in agreement with the positions of consolidations seen on CT scan images. This concordance between MRI and CT findings further supports the use of MRI in assessing COVID-19-related lung abnormalities.

The literature acknowledges several limitations of using MRI for COVID-19 diagnosis. These include signal deprivation due to physiological factors like respiration and heartbeat, lower spatial resolution, and longer examination times. These limitations need to be considered when deciding whether to use MRI for COVID-19 assessment. Despite the challenges posed by signal deprivation, time and cost, MRI has the potential to play a significant role in diagnosing and understanding COVID-19 susceptibility in patients with cardiac conditions. Its ability to provide high-quality images can help healthcare professionals better visualise and comprehend the anatomical and functional performance of various organs affected by COVID-19. This is particularly crucial for patients with pre-existing cardiac conditions who are at higher risk for severe complications (Di Dong et al., 2021).

There are ample opportunities for research in this area, including assessing various diagnostic imaging techniques and thoroughly examining organ impairment and disease mechanisms in COVID-19 patients. Such research can lead to improved diagnostic and treatment strategies for individuals with cardiac conditions, helping to reduce the risk of severe COVID-19 complications.

In conclusion, the discussed studies and findings suggest that MRI can be a valuable imaging modality for diagnosing and assessing COVID-19. It offers high sensitivity and specificity and can provide detailed information about pulmonary lesions and their characteristics. However, it is essential to acknowledge its limitations and consider the specific clinical context when choosing between MRI and other imaging techniques like CT for COVID-19 diagnosis and evaluation.

Positron Emission Tomography-Computed Tomography (PET-CT)

Positron emission tomography-computed tomography (PET-CT) with 18F-2-fluoro-2-deoxy-D-glucose (FDG) has become a highly sensitive diagnostic tool for early detection and monitoring of infections, and inflammations. Eibschutz et al. conducted a study in 2022 that highlighted the potential of PET-CT as a primary modality for diagnosing non-cancerous diseases, particularly lung infections. In addition, the literature emphasises the use of 18F-FDG as the commonly used radiotracer in PET-CT, which reveals metabolic activity in inflamed areas.

Elsakka et al., 2023 stated that PET-CT, is superior to conventional imaging for diagnosing illness progression, treatment surveillance, and prognosis in individuals with COVID-19. Further, the immunological host response to COVID-19, such as the release of inflammatory cytokines and the accumulation of alveolar macrophages and neutrophils in the lungs, can be seen through FDG uptake (Yeh et al., 2021). This indicates that FDG PET-CT may help in identifying COVID-19.

Research published by (Fields et al., 2021; Elsakka et al., 2023) reports increased FDG uptake in the lungs of individuals with COVID-19, with maximum standardised uptake (SUVmax) values ranging from 4.6 to 12.2. The literature suggests that FDG uptake tends to increase as the disease progresses but decreases with virus elimination and the emergence of immunity.

Moreover, PET-CT can detect ground-glass opacities (GGOs) with enhanced metabolic activity in a peripheral, basilar, and posterior dominant pattern, often overlapping with consolidation (Eibschutz et al., 2022). Further, the study has reported the utility of PET-CT in detecting COVID-19 in asymptomatic individuals, even before the onset of symptoms. PET-CT showed higher SUVmax values in the lungs of infected individuals compared to controlled subjects (Fields et al., 2021; Eibschutz et al., 2022; Elsakka et al., 2023).

The literature acknowledges that while 18F-FDG PET-CT is very sensitive in evaluating COVID-19, it may have poor specificity. This suggests that it can detect COVID-19-related changes but may not always distinguish them from other conditions (Fields et al., 2021; Elsakka et al., 2023).

The articles mention that PET-CT can help understand the disease trajectory of COVID-19 and evaluate treatments for individuals with persistent respiratory symptoms. It also suggests that staging PET-CT scans may reveal unintentional findings that standard test scans might miss, potentially leading to further treatment (Eibschutz et al., 2022).

In summary, the published work highlights the potential of 18F-FDG PET-CT as a sensitive imaging technique for identifying and monitoring COVID-19 pneumonia, particularly in its early stages. However, it also acknowledges the need for caution due to the technique's poor specificity, especially in populations at risk, like oncology patients. Further research and clinical evaluation are necessary to fully understand the clinical utility of FDG PET-CT in managing COVID-19.

Single Photon Emission Computed Tomography-Computed Tomography (SPECT-CT)

The COVID-19 pandemic has presented numerous challenges to healthcare professionals, with a growing body of evidence highlighting the virus's multi-organ impact with a significant focus on coagulopathy. It indicates that this coagulopathy is a prominent feature of the SARS-CoV-2 disorder. Coagulation abnormalities are in the form of micro thrombosis and venous thromboembolism. To address the diagnostic challenges posed by PE in COVID-19 patients, alternative imaging techniques have been explored, especially when contrast-enhanced CT scans are not feasible, such as in cases of renal failure. Studies carried out by Cobes et al. (2020), Roux et al. (2021), and Afshar-Oromieh et al. (2021) support this conclusion.

A promising approach is ventilation/perfusion single photon emission computed tomography (V/Q-SPECT), with a particular emphasis on the perfusion (Q) component. This method helps minimise the risk of COVID-19 transmission and offers an alternative to low-dose Q-SPECT-CT. Focusing on perfusion, lung scintigraphy allows for a full analysis of pulmonary abnormalities, such as holes in the parenchyma, pleura, and chest lining. It works well with CT scans and other imaging methods. In patients with minimal clinical suspicion for embolism, perfusion scintigraphy has proven to be a reliable method for excluding it. In addition, the lung ventilation-perfusion (V/Q) scintigraphy describes the characteristic features of PE, such as wedged-shaped perfusion mismatch defects, which are perfusion abnormalities with normal ventilation. It is important to note that the majority of PEs brought on by COVID-19 occur in peripheral areas. This suggests that thrombus formation takes place at micro vascular levels due to vascular injury, rather than migrating to the pulmonary vascular area. Ozturk et al. (2021) are referenced to support this observation. Cobes et al. (2020) reported on five cases of COVID-19 individuals with distinct V/Q SPECT-CT patterns and features. Notably, they discovered that COVID-19 pulmonary lesions had no impact on the identification of thromboembolic disorders.

Regions affected by COVID-19, especially during the initial phase with ground glass opacities, often exhibit maintained perfusion with minimal or no reduction in ventilation. However, as the disease progresses, alveolar fillings and parenchymal anomalies can lead to impaired perfusion, with perfusion anomalies matching the ventilation. This observation is attributed to Cobes et al. (2020). Afshar-Oromieh et al. found in 2021 that COVID-19 pneumonia patients with ground glass infiltrates can show heterogeneous ventilation SPECT patterns with maintained perfusion in the pulmonary parenchyma.

The literature suggests that perfusion patterns may vary among patients, reflecting concurrent CT infiltrate findings.

The findings of the study underscore the significant impact of coagulopathy in COVID-19 patients, leading to micro thrombosis and venous thromboembolism, particularly pulmonary embolism. It cites studies to support findings related to the detection of PE and the characteristics of ventilation-perfusion abnormalities in COVID-19 pneumonia. Understanding these aspects is crucial for managing and treating COVID-19 patients, especially those at risk of thromboembolic complications.

Extensive research has validated the diagnostic accuracy and treatment efficacy of lung scintigraphy-based approaches. Large-scale studies show that lung scintigraphy is a good way to find out if someone has a pulmonary embolism. It does this mainly by finding perfusion problems or defects along with normal ventilation.

Lung scintigraphy, with a focus on perfusion, is a valuable diagnostic tool in the context of the COVID-19 pandemic, where pulmonary embolism has emerged as a critical concern. This approach aids in early and accurate detection while reducing the risk of COVID-19 transmission during imaging procedures. (Afshar-Oromieh et al., 2021; Roux et al., 2021; Ozturk et al., 2021; Cobes et al., 2020) show how important lung scintigraphy-based approaches are for treating COVID-19 patients who might have a pulmonary embolism.

This review study looked at how important diagnostic imaging techniques like magnetic resonance imaging (MRI), positron emission tomography-computed tomography (PET-CT), and single photon emission computed tomography-computed tomography (SPECT-CT) are in diagnosing and treating coronavirus disease 2019 (COVID-19). In our current global landscape, where the prevalence of this disease continues to challenge healthcare systems, it is crucial to continually explore and harness the potential of medical imaging modalities to enhance clinical strategies. Traditionally, chest CT scans have been the standard imaging method for managing COVID-19 patients since the inception of the pandemic. However, our investigation, alongside previous studies, has illuminated the comparable capabilities of chest MRI, PET-CT, and SPECT-CT in detecting the abnormalities associated with COVID-19. While these modalities are not considered primary diagnostic tools for identifying and distinguishing pulmonary COVID-19, their utility in the context of the disease is noteworthy. Our findings highlight that MRI exhibits similar sensitivity to CT scans in detecting and localising COVID-19, making it a viable alternative, particularly for high-risk individuals or cases where CT is contraindicated. Meanwhile, PET-CT, despite its limitations in specificity, offers high sensitivity for pinpointing COVID-19-related abnormalities and tracking disease progression. Though there is currently limited evidence and research specifically focused on identifying COVID-19 pneumonia through SPECT-CT images, these images have shown promise in detecting abnormalities through the observation of perfusion and ventilation defects. While these modalities may not be firmly established for COVID-19 patients, their ability to identify disease-related abnormalities and provide supplementary insights into disease progression and staging holds significant potential for improving patient management and prognosis. In essence, as the medical community continues to deal with the multifaceted challenges posed by COVID-19, the integration of MRI, PET-CT, and SPECT-CT into diagnostic and monitoring protocols presents a promising avenue. These techniques, although not the primary choices, can play vital roles in the wide-ranging care and understanding of COVID-19 patients, ultimately contributing to more effective strategies for diagnosis, management, and treatment of this global health crisis. Further research and clinical validation are essential to harnessing their full potential in the fight against COVID-19.

CONCLUSION

This comprehensive study explored the valuable roles of advanced diagnostic imaging techniques such as MRI, PET-CT, and SPECT-CT in diagnosing and managing COVID-19. Traditionally, chest CT scans have been the standard, but this review reveals that MRI can provide similar sensitivity to CT scans,

making it a viable alternative, especially for high-risk individuals or cases where CT is not suitable. PET-CT, despite limitations in specificity, offers high sensitivity for identifying COVID-19-related abnormalities and tracking disease progression. Additionally, SPECT-CT shows promise in detecting abnormalities related to COVID-19, particularly in observing perfusion and ventilation defects. These modalities may not be primary diagnostic tools, but they offer supplementary insights into disease progression and patient management. As the medical community continues to address the challenges of COVID-19, integrating MRI, PET-CT, and SPECT-CT into diagnostic and monitoring protocols can contribute to more effective strategies for diagnosis, treatment, and management of this global health issue, although further research and clinical validation are essential to fully harnessing their potential.

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UNDERSTANDING FOOD THERMOGENESIS: A NARRATTED REVIEW

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ABSTRACT

The thermic effect of food (TEF) is the amount of energy required for the digestion, absorption, and metabolization of the food. Various statements appear in the literature such as diet-induced energy or diet induced thermogenesis (DIT) or simply thermogenesis. The thermic effect of food is also known as the specific dynamic action of food (SAF). In simple terms food thermogenesis refers to heat/energy used during the digestion of food consumed. The thermic effect refers to the energy expenditure that occurs during the digestion, absorption, and metabolism of food. When we consume food, our body needs to expend energy to break-down and process the macro-nutrients, resulting in an increased metabolic rate. The macro-nutrients are the key players of the energy balance, however, to extract energy from it, the complementary nutrients such as minerals and vitamins presence is crucial to perform the tasks. This narrated review paper intends to discuss the thermogenic effect of various sources of food.

KEYWORDS: Food, Macronutrients, Mechanism, Induced, Thermogenesis

INTRODUCTION

Food thermogenesis refers to the heat induced with the consumption food sources also termed as diet induced thermogenesis (Harris et al., 2006). The process of converting food into energy is one of the energy expenditures processes in human or animal body. Energy expenditure is the energy used by the body to perform its routine obligatory functions or spontaneous physical activities (SPA) such as breathing and in addition, to that energy is used by organs to circulate blood to all parts of the body (Levine, 2005).

PROCESS OF ENERGY PRODUCTION

The process of energy production from food itself requires energy. The macronutrients (protein, carbohydrates, and fats) for example, one molecule of glucose requires two molecules adenosine triphosphate (ATP) to produce four molecules of ATPs. All the macronutrients, carbohydrate, protein, and fats provide energy to the body with the use of available energy in the form of ATPs (Leach, 1975). The carbohydrates containing foods such as rice, cereals, breads, pastas, and noodles provide four calories of energy per gram consumed. The carbohydrates ingested in the foods are converted into monosaccharides which are utilised for energy through various mechanisms (Donnelly & Finlay, 2015). The second source of energy other than carbohydrates is fat and it produces nine calories of energy per gram. The main function of fat is to maintain the body temperature and to provide protection to the soft organ of the body (Schutz, 2005). The energy extraction from food sources is elaborated for easy understanding elsewhere (Alberts, et al., 2002). The process is longer than carbohydrates because fat needs to be hydrolysed into smaller forms which are fatty acids and glycerol. The glycerol part is converted into glucose via gluconeogenesis and after that the glucose is used for energy. Theoretically, the longer is the process of metabolism, the higher is the amount of energy needed (Swinburn & Ravussin, 1994). Like carbohydrates, protein also contains four calories per gram However, protein has more crucial function than supplying energy to the body such as building muscles, replacement/regeneration of dead cells, synthesis of enzymes and hormones etc. The only situation like extreme starvation energy is generated from protein a condition where no carbohydrate and fats are available in the body for energy production (Grover & Ee, 2009). The process of converting protein into energy takes longer time unlike that of carbohydrate and fat which is to break down the protein under digestion into smaller units (amino acids). Amino acid undergo process of removing nitrogen before converted to glucose. For all these steps of producing energy is also required to carry out the process of releasing energy for the body use. The energy expenditure is dependent on gender, body size, body composition, genetics, and activity level of a person. The energy expenditure and energy consumption need to be balanced to have a healthy lifestyle and maintain healthy body weight. As an example, the grown-up man needs more energy than younger individuals due to variable tasks (Levine, 2005).

As mentioned earlier that the energy intake depends on the three macronutrients and to smaller extent from other sources like alcohol. However, it still depends on the net absorption and faecal losses. The absorption depends on the ingredients, food types, preparation of foods, and physiological/intestinal factors (Hall, et al., 2012). Therefore, the recommendation of energy is based on the individual body and lifestyles. Ideally it is best to balance the energy intake and energy expenditure keeping good control on the body weight gain and loss since it is always desired to lose or gain body weight. To reduce weight the energy expenditure is needed to be higher than energy consumed by an individual. The suggestion sound simple to be followed but the fact is that people have difficulty to restrain from food that is not needed by the body (Muller, et al., 2016).

MACRONUTRIENTS AND THERMOGENESIS

Thermogenic effect of food is very small in terms of percentages of the total daily energy expenditure of an individual which is in the order of fat < carbohydrates< protein respectively (Tappy, et al., 1996). However, it may vary due to the factors mentioned earlier specifically it would depend on the amount of carbohydrates, proteins, and fats. Let us consider the macronutrients thermic effect and metabolism. As mentioned earlier that protein has the highest thermic effect among the macronutrients and it require 20-30% of the calories for its digestion and metabolism (Tappy, et al., 1996). Carbohydrates have lower thermic effect compared to protein and typically around 5-10% of the calories for its digestion and metabolism (Tappy, et al., 1996). Dietary fat has the lowest thermic effect and requires usually 0-3% of the calories of the calories for its digestion and metabolism (Tappy, et al., 1996).

From the above discussion it is obvious that food rich in protein contents is higher in its thermogenic effects. Lean meats, skinless poultry, and fish are rich foods sources that have a higher DIT effect. Among the fishes the fatty fishes such as salmon, mackerel, and trout which are not only excellent

sources of quality protein but also contain omega-3 fatty acids, which are excellent for improving metabolism. Eggs are a source of protein and nutrients, contributing to the DIT effect of food. Many of experiments show that high protein diets lead to lower weight gain, lower respiratory exchange ratio, lower carbohydrate oxidation, and higher fat oxidation compared to low-protein diets (Whitehead, 1996, Mikkelsen, 2000, and Lippl 2010). The reason being for this is that when the diet is higher in protein lead to reduced postprandial hunger and desire to eat (Moon & Koh, 2020). This happen possibly by changing hormones for example it has been reported elsewhere that acute ingestion of protein suppresses appetite, decreases ghrelin, and augments cholecystokinin and GLP-1 (Kohanmoo, et al., 2020). The DIT of protein is dependent on the dose and type of protein, for example whey-protein is having higher thermogenesis because of the protein type, its turnover and oxidation (Kassis, 2019). As mentioned before, when diet contain more protein, it will cause more thermogenesis compared to the other macronutrients being the reason that protein synthesis requires ATP or energy. Therefore, the catabolism of amino acid causes an increase in thermogenesis. When there is deamination of amino acids ATP is formed with exception of threonine or serine deamination which results in net ATP formation with exception when serine and threonine are used for the synthesis of glutamine in the tissues. The formation of urea is a thermogenic using ATP as well as producing ATP from the metabolism of fumarate. In certain situations when the other macronutrients are least/not available in the diet then the amino acid are used for glucose synthesis (gluconeogenesis) which is long process and using energy or in other words it induces thermogenesis (Bender, 2012). In short using amino acids utilization for the purpose of energy must pass through several reactions which use energy and therefore it makes the protein to be more thermogenic compared to carbohydrates and fats which needs least amount of energy upon metabolism. The thermogenetic foods are many and can be presented in different groups of foods such as green vegetables, fruits, nuts, meat, and spices/herbs (Bo, et al., 2020). In the following sections we discuss the thermogenic food sources.

FOOD SOURCES AND THERMOGENESIS

Meat is basically complex in structure with connective tissues and fibres which need degradation/breakdown both mechanically/enzymatically in the digestive tract for its absorption and metabolism. This complexity means that the body needs to work harder to break down and absorb the nutrients from meat, leading to increased energy expenditure. While the thermic effect of meat may have some metabolic benefits (weight reduction), it is essential to consume a balanced diet that meets the individual's nutritional needs that aligns to the health goals. Additionally, individual responses to dietary components can vary, so what works best for one person may not be the same for another. It is worth noting that poultry eggs have DIT like other protein in food. The DIT of the individuals depends on metabolic states, the type of foods consumed, the way it is prepared, the composition of the food consumed (Karst, et al., 1984). Poultry can be used as DIT food for health benefits like maintaining body weight, sense of fullness (satiety) and having good, varied food would be the healthiest options (Keogh, & M Clifton, 2020).

Among the various food sources fish is moderately induce DIT the reason being the type of protein and fish-oils (Yamazaki, et al., 2021). Like other protein-rich foods, fish requires the body to expend energy during digestion and metabolism. It's important to note that the thermic effect of fish can vary depending on factors such as the type of fish, preparation method (e.g., grilled, baked, steamed), and the overall composition of the meal in which the fish is consumed. Additionally, the total thermic effect of diet is influenced by the combination of all the foods consumed (Nielsen, et al., 2019).

Dairy products such as yogurt is higher in protein contents and is good source of probiotics, which can enhance metabolism and improve digestive health (Hursel, & Westerterp-Plantenga, 2011). There are several mechanisms by which it might be responsible for the DIT consuming milk protein (Veldhorst, et al., 2008).

Green leafy vegetables are rich sources of fibres, minerals and vitamins which might be promoting DIT (Opazo-Navarrete, 2021). The capsaicin and capsiate found peppers like capsicum or chili peppers increase the metabolism and promote calorie burning which is suggested in the weight management (Ludy et al., 2012). The celery is lower in calories but requires energy to chew and digest, leading to

thermogenesis and good for fat burning (Mohsenpour, et al., 2023). It is an excellent source of Apigenin, hesperidin, luteo-lin, quercetin, and rosmarinic acid are flavonoids (Priecina & Karklina, 2014) and minerals, such as sodium, potassium, magnesium, calcium, vitamins such as beta carotene, vitamin C and higher amounts of fibres (Fazal & Singla, 2012). Sweet Potatoes is a rich source of complex carbohydrates and is an excellent factor for thermogenesis which provide sustained energy release, contributing to thermogenesis (Qin, et al., 2022). The nutrients in sweet potato cause faeces bulk improve blood lipids, insulin sensitivity and gut microflora (Alam, et al., 2016 and Neela & Fanta, 2019). The starch which is often known as resistant starch cause reduction in total cholesterol and LDL cholesterol concentrations (Nichenametla, et al., 2014). Furthermore, it is a rich source of minerals, vitamins (A, B, C), anthocyanin, β-carotene, and fibres (Neela & Fanta, 2019 and Obomeghei, et al., 2020).

Legumes and pulses such as black beans, kidney beans, and chickpeas are high in fibres and protein, also rich in complex carbohydrates thus increasing the DIT and food satiety (Yin, et al., 2022 and Kristensen, et al., 2016).

Several fruits such as berries like blueberries, strawberries, raspberries, and apples contain dietary fibres and antioxidants that can enhance metabolism and improve health with low caloric densities with higher DIT (Abdul Hakim, et al., 2019 and Horgan, et al., 2022).

Certain fat sources like avocado and olive oil are considered healthier rich in monounsaturated fats that can alter metabolism and satiety. In other words, both contain healthy antioxidants that promote metabolic health (Segovia-Siapco, 2021 and Carvajal-Zarrabal, et al., 2014). Dry fruits such as almond, apricot, pine nuts, brazil nuts, chestnut, cashew nut, peanuts, betel nuts, walnuts, hazelnuts, almonds, pistachios figs, raisins, prune, dates, plums, dried coconut, and sunflower, flax, sesame, pumpkin, chia, and poppy seeds are healthy sources of fats and fibre contributing to DIT and satiety (Ros. 2010 and Alasalvar, et al., 2020).

Whole grains such as quinoa and others are DIT foods due to complex composition and the metabolic processes involved in digesting and utilizing it (Karl, et al., 2017). The reason behind this is that these have higher complex carbohydrate contents including starch and dietary fibre. It is reported that whole grain increases the balance of protein in the body which is happening due to increased protein turnover (Mey, et al., 2021).

Spices and herbs such as cinnamon, turmeric, ginger, lemon grass curry leaf and many more contains bioactive compounds which induce thermogenesis and enhance metabolism and improve insulin sensitivity (Viuda-Martos et al., 2011 and Wang, et al., 2023). For example, turmeric contains curcumin, which has anti-inflammatory and metabolic benefits, supporting thermogenesis and ginger contain gingerol known for its potential to increase metabolism and DIT (Zhang, et al., 2021). Ginger is often considered thermogenic due to its natural compounds that can promote heat production and increase metabolism in the body. Ginger contains several bioactive compounds, with the most notable one being gingerol (Mao, et al., 2019). Gingerol is known for its various health benefits, including its potential thermogenic properties (Mansour, et al., 2012). In addition, there are also herbs and spices those are higher in their thermic effect. The hot chillies/peppers and black/white peppers both are having ability to produce heat via sweating while eating the taste of spicy food. This is all because the existence of capsaicin and piperine in the peppers (Nagy, 1999).

Chilies peppers in particular black peppers are DIT spice due to piperine presence in it. It is causing the spiciness and stimulating flavour. It is the active component in it and is also found in less quantity in white and green peppers. It also has capsaicinoids, luteolin, and quercetin (Batiha, et al, 2020). It induces thermogenesis and burns calories therefore reducing body weight (Zheng, et al., 2017). Garlic contain allicin and some other components which are its active and among them allicin is the most prominent one. It is released upon crushing or chopping, and it is responsible for the strange aroma (Bar, et al., 2022). Garlic is DIT spice in the food, it improves metabolism, blood hyperglycaemia/insulin

sensitivity, appetite, weight, fat metabolism, contains antioxidants and reduce oxidative stress (Sunanta, et al., 2023).

Beverages such as green tea, coffee contain caffeine and catechins that can boost metabolism and cause DIT (Stubbs & Whybrow, 2004). Apple cider vinegar help stabilize blood sugar levels and improve insulin sensitivity and affect energy balance (Ousaaid, et al., 2020).

CONCLUSIONS

This review paper explored the thermogenic effect of digesting protein, carbohydrates, and fats. Among the macronutrients protein require higher amount of energy followed by carbohydrates and fats. The thermogenesis of food is depending upon its composition. The higher the protein the more is the thermogenesis. The increase in thermogenesis also occurs due to the complexity of structure and other food components with in it. The other food components such is beverages, spices, and herbs in which there are antioxidants as well as bioactive compounds induce DIT.

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A SYSTEMATIC REVIEW OF THE GREEN TEA EFFECTS ON ANTHROPOMETRIC PARAMETERS OF PCOS PATIENTS

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ABSTRACT

Introduction: Polycystic Ovarian Syndrome (PCOS) is a prevalent endocrine illness affecting reproductive-aged women that is characterized by irregular menstruation periods, infertility, hirsutism and obesity. Natural therapies, such as extract green tea supplementation, have recently received interest owing to their possible therapeutic properties. However, only a few studies linked green tea with PCOS patients. Hence, this study aimed to review the effects of green tea on anthropometric parameters of patients with polycystic ovarian syndrome (PCOS). **Method:** Articles were identified through PubMed, Science Direct, Scopus and Google Scholar electronic databases based on PCOS OR "polycystic ovar* syndrome" AND "green tea" OR "*Camelia Sinensis*" AND "anthropomet* parameters" OR "weight" OR "body mass index (BMI)" keywords and were included if they met the following criteria: in-vivo studies, female, studies of green tea, PCOS patient, English paper and article from year 2006 until 2023. The reviewing process was conducted according to the Preferred Reporting Items for Systematic and Meta-Analyses (PRISMA 2020) method. **Results:** A total of 34 relevant abstracts were screened and 5 full-text articles were reviewed. The findings found that green tea have a significant effect in reduction of weight, BMI, waist circumference and body fat percentage. The recommended daily dose is ranging from 500 mg to 540 mg while the working duration is 12 weeks. **Conclusions:** Green tea supplementation may have some potential advantages for weight loss and maintenance in those with polycystic ovarian syndrome (PCOS) depending on the amount and period of consumption. Nonetheless, more clinical studies are needed to corroborate these findings and identify the proper use of abstract green tea as an additional treatment for PCOS control.

KEYWORDS: Green tea effect, Anthropometric Parameters, PCOS

INTRODUCTION

Camellia Sinensis is a Theaceae plant that grows as an evergreen shrub and small tree. Green tea, a popular beverage, is made from its leaves and leaf buds (Ayyadurai & Deonikar, 2021). This plant may also be used to make tea, including black and oolong tea. Camellia Sinensis is widely farmed, accounting for about 3 million hectares of agricultural land in China. It is the world's second-most drank beverage and a good source of dietary flavonoids (Ayyadurai & Deonikar, 2021). Green tea powder is created by steaming, pan-frying, and drying the leaves. This powder is recognized for its advantages and flavour and is used in a variety of culinary preparations. Green tea is not only eaten as a beverage but it is also advertised as a nutritional supplement and weight reduction. It has significant health benefits due to its antioxidant, anticarcinogenic, and neuroprotective properties (Paiva et al., 2020). In recent years, there has been a rise in interest in green tea in Western nations, particularly among older citizens. Green tea has been shown to increase mood, attentiveness, and cognitive performance in studies. Its health advantages are mostly related to its powerful natural antioxidants (Huynh, 2016).

Polycystic ovarian syndrome (PCOS) is a condition in which the ovaries create an overabundance of androgens, which are male hormones found in modest levels in women. It is characterized by small cysts on the ovaries, although some women with the syndrome may not have cysts and others do. It is produced by increased testosterone synthesis from the ovaries and/or adrenal glands, which is affected by variables such as steroidogenesis changes and hyperinsulinemia (Witchel et al., 2019). PCOS is a prevalent endocrine illness in reproductive-aged women that affects 6-25% of women before menopause. Infertility, hirsutism, acne, hair loss, insulin intolerance, and obesity are all the symptoms. According to studies, PCOS patients are more likely than the general population to be overweight or obese, with an increasing proportion of obesity cases among PCOS patients (Mombaini et al., 2017).

Despite extensive research, limited studies were found on the effect of green tea with anthropometric parameters of PCOS patients. Therefore, this study aimed to review the effects of green tea on anthropometric parameters of patients with polycystic ovarian syndrome (PCOS).

METHODOLOGY

This systematic review applied the Preferred Reporting Items for Systematic and MetaAnalyses (PRISMA 2020) method which was conducted by using the PRISMA 2020 flow diagram (Page et al., 2021). Articles were identified through databases by determining the search phrases that are related to research questions. Several databases were used which included PubMed, Science Direct, Scopus and Google Scholar. Following the identification of articles using databases, the articles were screened by their title. Then, the abstract was reviewed by two independent reviewers for the remaining articles.

The key characteristics of the target population that the researchers employed to address their study topic are referred to as inclusion criteria. Inclusion criteria include factors related to geography, clinical settings, and demographics which were PCOS OR “polycystic ovar* syndrome” AND "green tea" OR "Camellia Sinensis" AND “anthropomet* parameters” OR “weight” OR “body mass index (BMI)”. The articles were recorded, exported, and screened using EndNote software to remove data duplication. Once the duplicates have been removed, the remaining full-articles were assessed for their eligibility which was determined by its full-text. After the screening process, full-text articles that did not meet the inclusion and exclusion criteria were excluded from the study. Finally, the remaining data after discarding the full-text articles that did not match the criteria were included in the systematic review.

All papers that meet the inclusion criteria in the systematic review were appraised rigorously by two critical appraisers. Based on the appraisal result, the finding can be used to guide the study's synthesis and analysis. The quality assessment includes studies that were being evaluated for bias risk in order to validate their quality. This evaluation was carried out by using the Joanna Briggs Institute (JBI) critical appraisal instrument (JBI 2020). Overall, the risk of bias was low in the four studies; randomized double-blind placebo-controlled trial and randomized placebo-controlled trial, randomized clinical trial and randomized double-blind clinical trial (Alghamdi, 2020; Carina et al., 2006; Farhadian et al., 2020; Mombaini et al., 2017; & Tehrani et al., 2017).

RESULTS

This search engine has come out with 34 total identified articles particularly Scopus (n=12), PubMed (n=15) and Cochrane (n=7). 9 studies were excluded because of duplication. Then, articles were screened based on the title and abstract, which results in removal of 10 articles due to irrelevant title and abstracts. The remaining 15 articles are selected to assess for the full text. Among the 15 studies, 10 articles were excluded due to exclusion criteria during abstract screening. A total of 4 articles are removed because it is a review article while two articles are excluded because it is an animal study. The review is focusing on anthropometric parameters hence, one article is excluded due to focusing on cardiometabolic function instead of anthropometric measurement. The data cannot be derived because of no access to the full article hence, 2 articles were excluded from this review. Finally, 5 remaining articles were included for the review with the published year range from 2006 until 2020. Figure 1 shows the flow diagram used for identifying, screening and including the articles to validate the findings in this review. Then, the findings from these articles were summarized in Table 1.

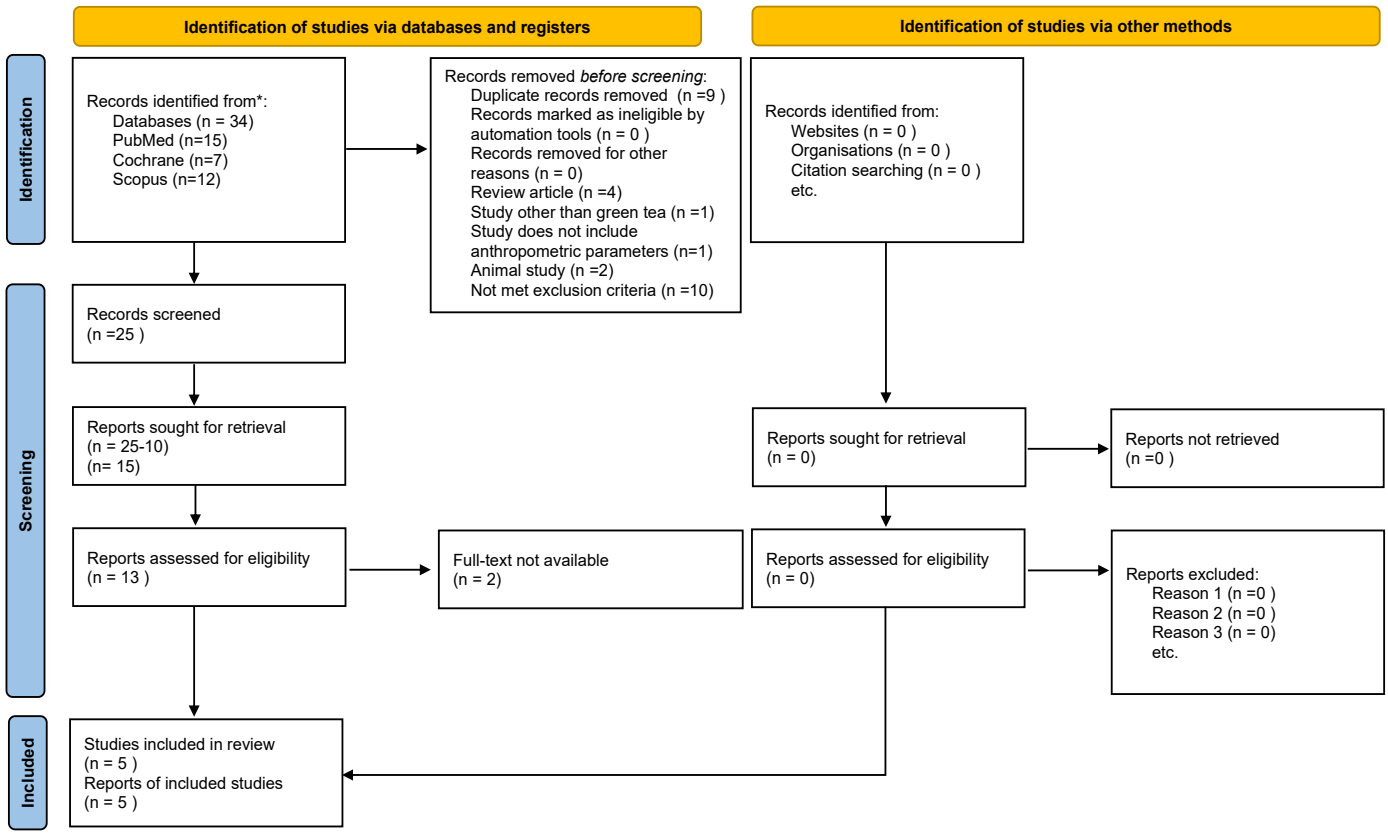


Figure 1: PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers.

Table 1: The dose, duration and effects of green tea supplementation on PCOS patients.

No	Author/year	Sample size/population	Study design	Research Findings		
				Duration of green tea supplementation	Dose of green tea supplementation	Effect of green tea intake on anthropometric parameters
1.	Mombaini E, Jafarirad S, Husain D, Haghighizadeh MH, Padfar P. (2017)	Fifty patients with PCOS, screened from a gynecology clinic. However, five subjects withdrew because of gastrointestinal complications and being pregnant. Hence, only forty-five patients completed the study (intervention group, green tea: n = 22, placebo group: n = 23)	Randomized double-blind placebo-controlled trial	45 days	Four tablets of green tea (Green Teadin, Dineh Co., Tehran, Iran) containing 500-mg green tea (C. sinensis L.) leaf powder.	Green tea supplement caused a significant reduction in weight, BMI, WC, and body fat percentage after the intervention period in the green tea group.
2.	Chan C.C., Koo M.W., Ng E.H., Tang O.S., Yeung W.S., Ho P.C. (2006)	Criteria for the subject: (1) age between 25 and 40 years (2) body mass index (BMI) 228 kg/M2 (3) diagnosis of PCOS Overall, thirty-four obese Chinese women with PCOS were involved in this study. They are eventually randomized into either the green	Randomized Placebo-Controlled Trial	3 months	2% Lung Chen tea freeze dried powder, which contained an equivalent of 540mg epigallocatechin gallate (EGCG) made into six capsules to be taken in three divided doses daily.	(1) Green tea consumption does not seem to exert a beneficial effect on glucose and lipid metabolism. (2) Green tea supplementation did not significantly reduce body weight in obese PCOS women.

		tea (n = 18) or placebo (n = 16) groups. However, two patients discontinued the treatment in the green tea group after 2 months because of emotional stress from family and work. Besides, another patient stopped the capsules consumption after the first week because she had no confidence in the capsules.				
3.	Tehrani H.G., Allahdadian M., Zarre F., Ranjbar H., Allahdadian F. (2017)	70 overweight and obese women aged between 20 and 40 years old and suffering from PCOS from a gynecological clinic of Isfahan city, Iran. They are divided into two groups. Experimental group is those who took green tea as Green Teadin tablet produced by DINEH IRAN; the group of pharmaceutical, hygienic & food industries. However, 5 patients were removed from the experimental group and control group respectively. Hence, only 30 patients were present in each group at the end of the study.	Randomized clinical trial	12 weeks	500 mg green tea capsules to be taken twice a day The green tea pills were produced by Dineh Industries of Iran (as Green Teadin) by grounding the green tea leaves and poured into capsules as green tea capsules.	Green tea consumption has positive effects on weight loss of women suffering from PCOS. It is reported that the ingredients of green tea can have a significant effect on weight loss, but additional mitigators such as caffeine intake and race can also play a role.

4.	Farhadian M., Barati S., M. Mahmoodi M., Barati Mosleh A., and Yavangui M. (2020)	45 women among 18–35 years of age with PCOS They are divided into 3 groups, (1) The green tea group was treated by green tea tablets. (2) The metformin group was treated by metformin tablets. (3) The control group received only placebo.	Randomized double-blind clinical trial	3 months	500mg of green tea tablets, three times a day.	The results showed that the average of all anthropometric indices such as weight, BMI, and waist and hip circumference was significantly reduced in the group receiving green tea as herbal medicine, and this reduction trend was statistically significant.
5.	Alghamdi, S.A. (2020)	85 PCOS women with obesity have been included and selected from Capital city of Kingdom of Saudi Arabia. The mean age of the PCOS women are 32.1±11.2 while the calculated BMI is 33.1± 8.6. For this study, 100% Saudi women were involved with 71.7% is known to be having family history of obesity.	Cross-sectional study	Daily	Not assigned.	Not assessed.

Based on 5 articles included in this review, the study design of 4 articles were randomized double-blind placebo-controlled trial, randomized placebo-controlled trial, randomized clinical trial and randomized double-blind clinical trial. All these study designs are classified as second level of evidence, whereas it can be considered as high-quality evidence. Only one study, which is a cross-sectional study, belongs to the fourth level of evidence.

In study by Mombaini et al. (2017), fifty patients with PCOS that have been screened from a gynecology clinic are chosen whose meet the criteria of PCOS patient. However, five subjects withdrew in the middle of research because of gastrointestinal complications and being pregnant resulting from consuming the green tea supplementation. Hence, only forty- five patients completed the study which consists of intervention group, green tea (n = 22), and placebo group (n = 23) (). Followed by a study by Chan et al. (2006), thirty-four obese Chinese women with PCOS were involved in this study. They are eventually randomized into either the green tea (n = 18) or placebo (n = 16) groups. The criteria that must be fulfilled where the participants must be 25 until 40 years old with body mass index 22.8 kg/m^2. Based on a study from Tehrani et al. (2017), seventy overweight and obese women aged between 20 and 40 years old who are suffering from PCOS from a gynecological clinic of Isfahan city, Iran were selected. They were divided into two groups, experimental group and control group. Experimental group is given green tea in the form of Green Teadin tablet produced by DINEH IRAN; the group of pharmaceutical, hygienic & food industries. However, before the study ended, 5 patients were removed from the experimental group and control group respectively. Hence, only 30 patients were present in each group at the end of the study. Another study includes forty-five women aged 18 to 35 years of age who suffer from PCOS (Farhadian et al., 2020). They were divided into 3 groups consisting of green tea group; treated by green tea tablets, metformin group; treated by metformin tablets, and control group; received placebo as treatment. Lastly, the study from Alghamdi, (2020), eighty-five PCOS women with obesity were included and selected from the Capital city of Kingdom of Saudi Arabia. The mean age of these PCOS women is 32.1±11.2 while the calculated BMI is 33.1± 8.6. For this study, 100% Saudi women were involved with 71.7% is known to behaving family history of obesity.

Moreover, a study from Mombaini et al., (2017) reports that their participants consume the green tea supplement within 45 days in order to complete the study. It shows a positive effect on the reduction of weight, BMI, waist circumferences and body fat percentage. On the other hand, three studies stated that the duration of green tea supplementation applied to their studies is 3 months or 12 weeks (Carina et al., 2006; Tehrani et al., 2017; & Farhadian et al., 2020). This timeline may allow for a better evaluation of the benefits of green tea on PCOS symptoms and general well-being. Overall, the range of green tea supplementation was 500 mg to 540 mg ((Mombaini et al., 2017; Carina et al., 2006; Tehrani et al., 2017; & Farhadian et al., 2020). There was no specific diet followed by any of the participants during the study. However, the study from Alghamdi et al., (2020) does not assign any doses of green tea in their study.

Based on a comprehensive analysis of the readings, all of the included studies are very likely to provide consistent outcomes. The findings imply that integrating green tea administration has the potential to help people with polycystic ovarian syndrome (PCOS). The results shows that the green tea group lost weight, BMI, waist circumference, and body fat following the intervention period.

DISCUSSION

Overall, green tea administration leads to weight reduction in people with polycystic ovarian syndrome (PCOS). There is a significant reduction in weight (Mombaini et al., 2017; Tehrani et al., 2017; & Farhadian et al., 2020), BMI (Mombaini et al., 2017; & Farhadian et al., 2020), waist circumferences (Mombaini et al., 2017; & Farhadian et al., 2020), and body fat percentage (Mombaini et al., 2017) following the intervention period in the green tea group. Green tea's weight reduction processes may be explained by its catechin polyphenol and caffeine content, which leads to sustained catecholamine activity and increased levels of norepinephrine. This will result in an increase in energy expenditure and fat oxidation, indirectly leading to reduction of body weight (Mombaini et al., 2017). However, Chan et al. (2006) reported that, no substantial improvement in glucose and lipid metabolism as well as no significant effects in body weight reduction among their subjects.

Findings show that determination of effective dose and working duration of green tea supplementation in PCOS patients involves careful evaluation of several criteria, including the precise aims of supplementation, individual patient characteristics, and the available research. According to Mombaini et al., (2017) Tehrani et al., (2017) & Farhadian et al., (2020) there is significant result in anthropometric parameters of PCOS patients prescribed with green tea supplementation with dosage of 500mg or 540mg green tea supplementation.

The dosage of green tea is crucial in prescribing it to patients. Findings from Dostal et al. (2015) found side effects associated with high doses of Green Tea Extract (GTE) capsules. In their study, 538 out of 1075 women were given GTE capsules containing 1315 mg ± 116 total catechins per day, with 843 ± 44 mg as EGCG. The results showed that participants with higher GTE doses experienced more side effects like nausea, indigestion, diarrhea, constipation, and vomiting compared to the placebo group. However, these symptoms cannot be solely attributed to green tea. This is evidenced by other studies from Nantz et al. (2009) and Widlansky et al. (2007) whereby even though lower doses of green tea were administered (300 mg of EGCG and 200 mg of GTE with >45% as EGCG), yet rash incidences were still reported. Thus, individual tolerance levels may vary, and even lower doses can have side effects

Study from Mombaini et al. (2017) discovered that a positive effect also can be obtained with a shorter length of green tea drinking. Participants in this trial who took green tea supplements at a comparable average dosage as in the previous studies showed substantial results after only 45 days of intervention. The best length of green tea intake for PCOS patients may differ based on individual responses and unique health circumstances. While some people may see considerable benefits in a very short period of time, others may take a longer period such as 3 months or 12 weeks of supplement administration to achieve apparent results.

The reviewed papers also have physical attributes that could be discussed. Majority of the studies were conducted in Iran, followed by Saudi Arabia and Hong Kong. Despite being a famous drink and food products, there is limited study available on the beneficial effect of green tea on PCOS patients. Hence, it is critical to carry out more study in depth to ensure that the unrevealed benefits of green tea among Malaysians are discovered.

CONCLUSION

In conclusion, this systematic review provides evidence on the potential significance of green tea in the context of weight management for PCOS. Green tea supplementation dose varies according to disease. A daily dosage of 500 mg to 540 mg is indicated for PCOS individuals. Furthermore, green tea consumption for 3 month or 12 weeks is recommended to see prominent changes in weight loss among PCOS patients. Based on this review, green tea may contain bioactive compounds such as catechins, flavonoids, and polyphenols, which have demonstrated anti-obesity properties and the ability to promote fat oxidation.

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THE RELATIONSHIP OF VITAMIN B6 (PYRIDOXIN) AND POSTPARTUM DEPRESSION: A SCOPING REVIEW

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ABSTRACT

Introduction: Postpartum depression (PPD) is one of the mental disorders that has a negative impact on a mother's feelings after birth and causes them to lose interest in living their daily lives, primarily due to the chemical imbalance in the brain. Vitamin B6, or known as pyridoxine, is believed to be one of the chemicals in the brain which is involved in emotional regulation. However, the mechanism of action is unknown. Thus, the aim of this study is to review the influence of vitamin B6 and its relationship with the onset of PPD. **Methods:** Keywords "vitamin B6" and "vitamin B" and "pyridoxine" and "nutrition" and "PPD" and "perinatal depression" were employed in PubMed, SpringerLink, BioMed Central Journal and ScienceDirect. The screened articles were chosen based on their suitability for the topic of interest and published in English between 2000 and2023. The articles were chosen in accordance with PRISMA, and their eligibility was determined using inclusion and exclusion criteria. **Results:** A total of 3404 articles had been obtained initially and the resulting five articles met the criteria. It was revealed that the relationship between deficiency of vitamin B6 and PPD is still ambiguous. Two articles suggested the intake of vitamin B6 to an adequate level can be helpful to reduce the risk of PPD. In contrast, there are three studies that proposed that low vitamin B6 levels are not associated with PPD, hence increasing its intake during this period is found to be irrelevant. **Conclusion:** In conclusion, this review indicates that further investigation is warranted to determine the exact effect of vitamin B6 and its mechanism of action in emotional regulation. It is hoped that this benefits the mothers in prevention and treatment of PPD, thus improving the quality of their life.

KEYWORDS: postpartum depression, pyridoxin, vitamin B6

INTRODUCTION

Postpartum depression (PPD) is characterised by newly given birth mothers who experienced mood swings and other depressive symptoms. It is the period after birth when the mothers are in their most vulnerable state, especially during the first month after childbirth (Cernadas, 2020). The PPD symptoms are observed around a month after birth and could be prolong due to factors such as financial difficulties or low level of awareness regarding health and safety after pregnancy and birth (Cernadas, 2020). Women with a history of depressive and anxiety disorders, as well as those who experienced premenstrual syndrome (PMS) are most likely to develop this type of depression after childbirth. In addition, women who have obstetric risk factors such as emergency caesarean section, lack of social

support and experience of domestic violence, as well as mothers with unhealthy lifestyles, including lack of exercise, are also prone to develop PPD (Hanna, 2022). Although the exact cause of PPD remains undefined, multiple factors such as genetics, hormones, psychology, as well as social life have been observed to contribute to its development (Mughal et al. 2022).

It is well known that the pathophysiology of PPD is attributed to the dysregulation of reproductive hormones, such as oestradiol and progesterone. Apart from that, changes in the specific components of the endocrine system, such as the hypothalamic-pituitary-adrenal axis (HPA) have also been suggested in the onset of PPD. These changes lead to the under-secretion of catecholamines, resulting in an inadequate stress response Moreover, the central nervous system also plays a significant role in the onset of depression. Depression can occur when there is a disturbance in certain parts of the brain responsible for regulating stress and emotions (Mughal et al., 2022). According to Kris-Etherton et al. (2021), it was reported that inadequate nutrition can cause mood disorders due to a lack of nutrients that play crucial roles in the neuroendocrine system. For example, important nutrients including tryptophan, vitamin B6, vitamin B12 and folic acid are necessary to produce neurotransmitters such as serotonin and dopamine, which are mainly involved in mood regulation (Kris-Etherton et al., 2021). Crucial micronutrients such as vitamin D, fatty acid, and vitamin B during pregnancy and after birth period have a significant role in the onset of PPD. These micronutrients deficiencies have been observed to affect the psychoneuroimmunology of the mothers, which may cause them to develop PPD during this vital and fragile period (Ellsworth-Bowers and Cowin, 2012).

One of the crucial vitamins that could affect the balance of neurotransmitters in the nervous system is vitamin B6 (Berkins, 2021). Vitamin B6 is "the generic name for six compounds with vitamin B6 activity: pyridoxine, pyridoxal, pyridoxamine and their respective 5′-phosphate esters, pyridoxal 5′ phosphate (PLP)and pyridoxamine 5′ phosphate (PMP) which are the active coenzyme forms of vitamin B6". Similar to other vitamins in the B vitamin family, vitamin B6 acts as a coenzyme in a variety of physiological processes, and most of them are protein metabolisms. Therefore, the vitamin B6 deficiency has a significant physiological effect such as the onset of depression and anxiety in general. Meanwhile, in a study by Berkins et al. (2021) about the association between vitamin B6, B12 and folate deficiency and depression among vegetarians, they observed that there are positive associations between these nutrients' deficiency and the mood disorder, which proves that under-intake of vitamin B6 lead to depression. To date, the relationship of vitamin B6 with specific depression like PPD is unknown. Therefore, this review aimed to explore the relationship between vitamin B6 and PPD. The findings are hoped to be a motivation towards more clinical and non-clinical investigation as a strategy to prevent or lower the risk of PPD.

METHODOLOGY

Identification of Relevant Studies

This study aimed to gather a comprehensive selection of pertinent articles from various databases, including PubMed, SpringerLink, BioMed Central Journal and ScienceDirect. The study employed keyword searches; vitamin B, vitaminB6, pyridoxine, nutrition, postpartum, depression, PPD, perinatal depression. Search results were enhanced by combining terms with the Boolean operators AND, OR, and NOT. Furthermore, this scoping review was conducted according to the Joanna Briggs Institute (JBI) methodology for scoping reviews (Peters et al., 2020). The JBI methodology of scoping review is a method of evidence synthesis, and this methodology follows the established methodological guidance, Preferred Reporting Items for Systematic Reviews and Meta-Analysis extension for Scoping Reviews (PRISMA-ScR) guidelines (Munn et al., 2022).

The selection of papers that were involved in this study followed the inclusion and exclusion criteria. The articles that were qualified to be included in this review were the papers that mainly or in an aspect of mentioning the relationship between vitamin B6 and PPD. The articles that were chosen were limited to only being published from 2000 until 2023 and should be written in English only. Apart from that,

the papers had to be full paper publication and publication types such as index and non-index journals were also included. Meanwhile, the articles which did not pertain to the topic of vitamin B6 and PPD, published before the year 2000, articles that could not be accessed in full-text and articles that were not written in English were excluded from this review.

Selection of Relevant Studies

The screening of the articles was divided into two phases. The first stage was by searching the keywords on the databases and screening based on the titles and abstracts of the articles to filter out any ineligible papers to be included in this study. Next, any duplicates found from the articles were removed. The second stage was by evaluating the articles in full-text form to verify that the articles fulfil the inclusion criteria to participate in this scoping review and must be excluded if they meet any of the exclusion criteria. The final articles that were selected were further included in the study and have undergone data extraction.

Data Selection

After the articles were approved to be included in this study, the data related to the effect of vitamin B6 imbalance which led to PPD to occur as well as data regarding the use of vitamin B6 to reduce the risk of PPD were extracted. The data was either numerical, such as level of vitamin B6 in plasma among postpartum mothers, or in words taken from the articles. The data extraction, or charting of the data, was done in a charting table to record the key information of the source including the author, reference and findings of the research objectives and questions. The key information that was recorded in the charting table include authors, title, year of publications, the origin of the study, study designs, results, and key findings related to this scoping review.

RESULTS AND DISCUSSIONS

A comprehensive search resulted in the identification of 3404 articles that were deemed relevant to the study. The number of articles remaining after the screening for duplicates was 2297, and a total of 60 articles remained after the screening based on the titles. After the abstract screening, a total of 15 articles remained. These articles were then assessed based on their full text to determine which articles would be included in the result. A few articles were removed due to not fulfilling the inclusion criteria and as a result, five articles met the established criteria for inclusion in the analysis. Figure 1 illustrates the procedures involved in selecting relevant articles based on PRISMA-ScR 2009 Flow Diagram.

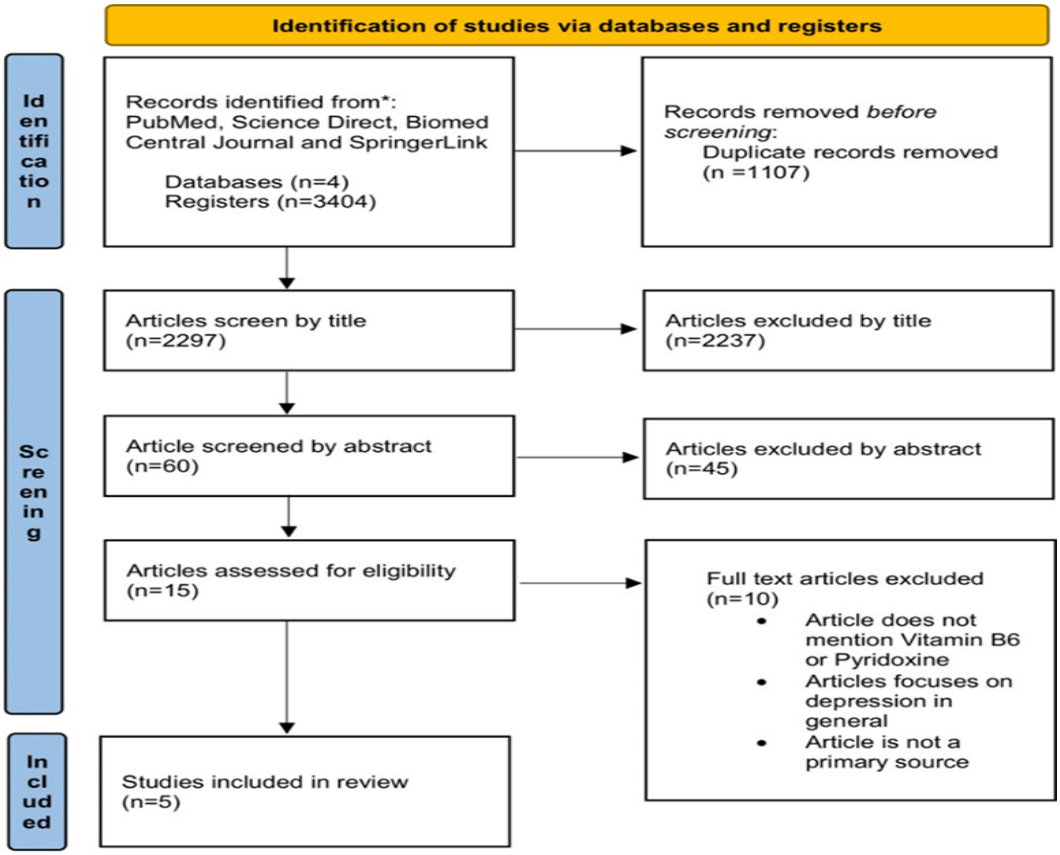


Figure 1 Selection of Articles based on PRISMA-ScR 2009 Flow Diagram

The Relationship of Vitamin B6 and PPD

According to Table 1, two out of five articles concluded that vitamin B6 has a significant influence on the onset of PPD (p<0.001), while the remaining three articles found no prominent association between vitamin B6 and PPD (p>0.05). All five articles emphasize the importance of nutrition among postpartum mothers regarding depression, considering the fragile period faced by the mothers during this time. The findings from the two articles regarding vitamin B6 and PPD are characterised by the decreased intake or level of this micronutrient among postpartum women, which led to the occurrence of PPD (Khodadad et al., 2021, Qiu et al., 2020). In addition, Qiu et al. specifically mentioned that fluoxetine (FLX) treatment could significantly disrupt the metabolism of vitamin B6, eventually inducing postnatal depression.

Meanwhile, it can be observed in another three articles where the inadequate intake of this vitamin does not contribute to the factor of postnatal depression. One of the studies concluded that the intake of pyridoxine pre-pregnancy and during pregnancy did not affect the occurrence of perinatal depression, while another study showed that subjects who consume vitamin B6 lower than the recommended range did not have a significant relationship with PPD. Additionally, one of the studies mentioned that there is no inverse relationship discovered between the intake of pyridoxine with the risk of PPD. To conclude, two of the articles, which consist of one randomised controlled trial and one preclinical experiment agreed that there is a significant relationship between vitamin B6 and PPD, meanwhile the other three articles which were all cohort studies disagreed with the relationship between vitamin B6 and PPD.

Table 1 Details of Selected Articles

Author/ Year	Title	Country	Study Design /sample size	Relationship with PPD
Miyake et al. 2006	Dietary folate and vitamins B12, B6, and B2 intake and the risk of Postpartum depression in Japan: the Osaka Maternal and Child health Study	Japan	Prospective Cohort Study (n= 865)	An inverse relationship between the intake of folate, cobalamin, or pyridoxine and the risk of PPD was not observed.
Khodadad et al., 2021	Can Vitamin B6 Help to Prevent PPD? A Randomised Controlled Trial	Iran	Randomised Control Trial; case group (=41), control group (n=40)	Vitamin B6 has a positive effect on reducing PPD scores among mothers at risk for PPD.
Blunden et al.,2012	Postpartum depressive symptoms: The B-vitamin link	United Kingdom	Cohort Study (n=2856)	Vitamin B6 intake before and during pregnancy is not associated with postpartum depressive symptoms.
Qiu et al., 2020	Postpartum fluoxetine increased maternal inflammatory signalling and decreased tryptophan metabolism: Clues for efficacy	Canada	In vivo Preclinical experiment, (n=47)	The changes in vitamin B6 metabolites because of fluoxetine treatment may be a representation of disrupted vitamin B6 metabolism.
Leung et al., 2013	Prenatal micronutrient supplementation and postpartum depressive symptoms in a pregnancy cohort	Canada	Cohort Study (n=475)	Vitamin B6 showed a nonsignificant trend with PPD although the subjects in this study consumed this vitamin lower than the recommended intake.

The Effect of Imbalance of Vitamin B6 In Mothers During Postpartum Period

The level of vitamin B6 is observed to be closely associated with PPD. The occurrence of PPD in relation to vitamin B6 is attributed to its inadequate level among postpartum women during this period, as has been proven in the article by Qiu et al. (2020). As has been proposed by several previous studies regarding the association of vitamin B6 with depression and anxiety, it can be confirmed that a similar mechanism is implied to PPD. Vitamin B6 plays a significant role in the production and biosynthesis of important neurotransmitters including serotonin and dopamine. Therefore, the insufficient levels of this vitamin among postpartum women are indeed an associated factor with PPD. According to Qiu et al. (2020), the fluoxetine treatment significantly decreases the plasma concentration of tryptophan as well as the components of pyridoxine, which proves that the metabolism of vitamin B6 is disrupted in the study. This is due to the role of pyridoxine as the important coenzyme for tryptophan metabolism. Hence, decreased levels of vitamin B6 plays a part in causing PPD to occur.

The Use of Vitamin B6 to Prevent the Onset of PPD

Based on the results obtained in a study by Khodadad et al. (2021), it is proved that vitamin B6 possesses an ability to reduce the chance of PPD onset among postpartum women. In the study, the Edinburgh postnatal depression scale (EPDS) was used to assess depression rates prior to and 1.5 months after the last intervention (day of pregnancy) as the primary outcome measure. From the statistical analysis provided by Khodadad et al. (2021), the mean post-intervention depression score of the case group is 4.2, which is significantly lower than the control group who has the mean of 10.4 ($p < 0.01$). This shows that vitamin B6 can be used to reduce the risk of PPD among the mothers. According to a study by Hanna et al. (2022), vitamin B6 has been observed as one of the supplements that is helpful in treating patients with depression, behavioural issues as well as migraine headaches. This is due to vitamin B6 being prominently involved in the production of neurotransmitters. Thus, it is suggested that vitamin B6 as one of the potential treatments for PPD. Due to the decreased level of vitamin B6 during pregnancy as well as during the postpartum period, increasing the intake of vitamin B6 is helpful to decrease the risk of PPD (Khodadad et al., 2021), especially in a population where nutritional deficiencies are prominent. Despite that, findings from a few papers involved in this study conflicted with this opinion.

According to Hvas et al. (2004), low levels of vitamin B6 may be associated with the onset of depression due to it being a coenzyme, particularly in the pathway of tryptophan-serotonin. Apart from that, low intake of vitamin B6 also has been found recently to be related to depression and anxiety in a study by Kafeshani et al. (2019). Hence, the effect of decreased levels of vitamin B6 in inducing depression in general has been known. Regarding PPD, which is also considered one of the types under the umbrella term of depression, its association with vitamin B6 also has been understudied due to there being less papers being published on this topic.

One of the papers included in this review, by Khodadad et al. (2021) specifically studied the ability of vitamin B6 in preventing the onset of PPD among postpartum mothers in a randomised control trial study. It was found that the group that was given vitamin B6 had a reduced depression score post-intervention while there was no significant difference in the placebo group post-intervention. In the same study, the level of pyridoxal 5'-phosphate, which is the active form of pyridoxine was specifically mentioned to be lowered during the second and third trimesters of the pregnancy and returned to its normal level when it reached the first month of the postpartum period. This may prove how the reduced level of plasma vitamin B6 may induce postnatal depression, as well as proving that vitamin B6 had the capacity to lower the risk of postnatal depression among women. According to the authors, this study was perhaps considered as the first study to investigate the effect of vitamin B6 on PPD prevention due to there being no other studies available at the time studying this topic. Meanwhile, the main limitations of this study were the confounding factors such as uncontrolled dietary vitamin B6 intake and physical activity.

Additionally, one of the studies included in this review done by Qiu et al. (2020) titled 'Postpartum fluoxetine increased maternal inflammatory signalling and decreased tryptophan metabolism: Clues for efficacy', supported the significant relationship of pyridoxine with PPD by studying the relationship of postpartum fluoxetine, maternal inflammatory signalling and tryptophan metabolism. Findings showed that the vitamin B6 influences the efficacy of FLX treatment during the postpartum period. The FLX treatment was found to decrease the plasma levels of tryptophan as well as the levels of pyridoxine components in the subjects. Due to the role of vitamin B6 as an essential coenzyme in the metabolism of tryptophan, therefore the metabolism of vitamin B6 was also disrupted by FLX. In addition, it was found that the disturbance of vitamin B6 metabolism due to the FLX treatment may cause the inefficiency of this treatment in treating depressive symptoms during postpartum, which also proves that the lower levels of vitamin B6 may induce depression in the postpartum period. This study was able to prove their hypothesis right, as well as identify two possible mechanisms that affected the treatment of PPD by FLX, one of them being the disruption of metabolism of tryptophan and vitamin B6. This study also suggested for further research on vitamin B6 as a biomarker for PPD in the future.

As mentioned in a study by Kris-Etherton et al. (2021) on nutrition and behavioral health disorders, vitamin B6 is involved in a lot of physiological processes in the human body, one of it is the production and synthesis of neurotransmitters. Therefore, the deficiency of vitamin B6 has been closely associated with the onset of mood disorders including depression. A severe deficiency of vitamin B6 can cause a few other conditions and some of it being mood disorders and cognitive decline. Additionally, they also mentioned that adequate levels of vitamin B6 can reduce the level of plasma homocysteine, which reduces the risk of depression. This fact is supported by Bremner et al. (2021), which showed that high concentration of plasma homocysteine may indicate insufficient methyl transfer reaction which causes inadequate synthesis of neurotransmitters, and eventually lead to depression.

Interestingly, findings from three articles showed that there was no significant relationship between vitamin B6 and PPD. Miyake et al. (2006) concluded pyridoxine (B6) along with folate (B9) and cobalamin (B12) intake was not related to the risk of PPD as observed in the subjects. From the questionnaire, 21 out of 865 participants were found to develop PPD. However, there was no significant relationship between vitamin B6 and PPD. These studies had a few methodological strengths including low possibility of recall bias or bias due to the relatively high rate of follow up, which was 86.3% and the participants came from the same residential background. However, this methodology could not control other confounding factors such as family psychiatric history and participants' lifestyle. Apart from that, the self-perception without clinical diagnosis from professional was one of the main weaknesses of this study.

Other findings were determined by Blunden et al. (2012) which supported the contradiction with the positive effect of vitamin B6 on PPD. The cohort study on PPD symptoms with vitamin B came up with a summary of there was no association between the intake of vitamin B6 during and after pregnancy with the symptoms of PPD. From this study, it was found that the dietary intake of vitamin B6 before, early and after pregnancy has no significant relationship with PPD. The results obtained from this study can be supported with a few strengths including using the largest sample size to date to study the relationship between nutritional status with postpartum depressive symptoms. Another cohort study by Leung et al. (2013) on prenatal micronutrient supplementation and postpartum depressive symptoms concluded a similar outcome. Among the 475 participants who managed to complete the EPDS questionnaire, 59 of them were found to have PPD. It was found that vitamin B6 was one of the vitamins that were consumed by the participants 90% above the recommended dietary allowance (RDA). It was also found that participants with low EPDS score consumed more vitamin B6 than participants with high EPDS score. However, vitamin B6 intake has no significant relationship with PPD. Further actions to support their initial findings were executed including the establishment of temporal relationship between supplement intake with postpartum depressive symptoms, as well as the repeated collection of supplement intake to ensure the valid average intake of the nutrients of the participants in this study.

CONCLUSION

In a positive note, vitamin B6 has shown to induce a therapeutic effect on reducing and preventing the risk of PPD during pregnancy and postnatal period in two selected studies. In contrast, three cohort studies disagreed with the positive relationship between pyridoxine and the onset of PPD. Thus, the relationship between vitamin B6 and PPD is still ambiguous because of the contradictory between the two opinions. Therefore, more studies focusing on the population of mothers who are prominently facing deficiencies of nutrient access, for example, in geographical regions which has high poverty rate or on mothers who are struggling with eating disorders, can be explored. Other important but under-studied micronutrients can be considered since it may also become one of the contributing factors to PPD. Importantly, understanding the mechanism of action of vitamin B6 or other nutrients and PPD may lead to prevention of this disease and improve the quality of life among mothers.

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PHYTOCHEMICALS OF *Tinospora crispa* WITH ANTICANCER AND ANTIVIRAL ACTIVITIES: A REVIEW

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ABSTRACT

Introduction: The discovery of new anticancer and antiviral agents from plants have drawn a lot of attention due to their vast spectrum of biological and therapeutic properties in which many evidences proved that the plants and plant-derived products are effective and safe for treating and managing various types of diseases and illnesses. Phytochemicals in plants are promising anticancer and antiviral agents which may improve the treatment efficiency and decrease the adverse reactions. *Tinospora crispa* plant is traditionally used to treat various types of illnesses and diseases. Many studies reported that *T. crispa* has anti-proliferative and anti-angiogenesis activities as well as antiviral activities. **Objective:** The purpose of the study was to compile and identify the phytochemicals of *T. crispa* with anticancer and antiviral properties. **Method:** The online databases that have been utilized in this study were Google Scholar, Science Direct and PubMed. The selection of articles was managed based on PRISMA 2009 and was assessed based on inclusion and exclusion criteria as specified. From total of 705 articles screened, 11 relevant articles were chosen. **Result:** *T. crispa* compounds with potential anticancer activity were tetrandrine and alkaloid, while *T. crispa* compounds with potential antiviral activities were berberine, 112ndrostane112ne-4-ne, 2-imino-1-(4-methoxy-6-dimethylamino- 1,3,5-triazin-2-yl), spiro[4,5] dec-6-en-1-ol, 2,6,10,10-tetramethyl, 3β-hydroxy-5- cholen-24-oic acid, 112ndrostane-17-one, 3-ethyl-3-hydroxy-(5α), camphenol, (−)- globulol, yangambin, nordazepam, trimethylsilyl derivative and benzeneethanamine. Meanwhile, the compounds that may have potential for both anticancer and antiviral activities were magnoflorine, β-amyrin, β-sitosterol and lupeol. **Conclusion:** This study found 52 compounds from *T. crispa*, including alkaloid, terpenes, phenolic compounds, glycosides and alcohol that exhibited anticancer and antiviral activities.

KEYWORDS: *Tinospora crispa*, Phytochemical, *Patawali*, Anticancer, Antiviral

INTRODUCTION

Cancer is a global major health problem which caused mortality worldwide with estimated 18.1 million new cases in 2018 and are likely to increase to 23.6 million cases by 2030 (Bray et al., 2018; Choudhari et al., 2020). According to World Health Organization (WHO), about 9.6 million people died from cancer in 2018 worldwide. Fernando and Rupasinghe (2013) stated that about 30% of cancers are caused by modifiable risks factors. The conventional treatment of cancer such as cancer chemotherapy and radiotherapy have caused high rate of mortality due to the adverse effect or toxic side effects. This is

due to the use of alkylating agents, antimetabolites, antitumor antibiotics, platinum analogs and natural anticancer agents (Fernando & Rupasinghe, 2013). The major disadvantages of chemotherapy are cancer recurrence, resistance of drug and also toxic effects on non-targeted tissues, limiting the use of anticancer drug and causing deterioration of patients' health (Choudhari et al., 2020).

Meanwhile, the alarming threat of viral diseases to humans are causing global concern around the world. Viral diseases create a significant risk to human health as viral infections are difficult to manage due to the mutative nature of the viral genomes (Yasuhara-Bell at el., 2010; Kapoor et al., 2017). Among the emerging diseases, the viruses that have caused viral diseases are human immunodeficiency virus (HIV), influenza, herpes simplex virus (HSV), Dengue virus, Chikungunya virus, Zika virus, Hepatitis A virus (HAV), Hepatitis B virus (HBV), Hepatitis C virus (HCV) and most recently, SARS-CoV-2 virus that causes coronavirus disease (Covid-19). Currently, due to the ability of the viruses to modify their genomes and become resistant to drugs, the development of effective treatments and antivirals against virus has become challenging (Irwin et al., 2016; Ghildiyal et al., 2020).

On the other hand, plants have been used by many researchers to explore effective therapeutics. Plant can be used as an alternative source of natural metabolite that confer potent anticancer and antiviral activities. In fact, some cancers are attributable to virus infections. *Tinospora crispa* plant is traditionally used to treat various types of illnesses and diseases. Many studies reported *T. crispa* as a natural antioxidant and as anticancer agent due to anti-proliferative and anti-angiogenesis activities against cancer cells (Mutiah et al., 2019; Liao et al., 2019). It showed antiviral activities against viruses such as dengue, Zika and Chikungunya viruses (Rakib et al., 2020; Ratanamokol et al., 2021). Therefore, this review was conducted to compile the phytochemicals in *T. crispa* and to determine the phytochemicals with anticancer and antiviral activities. Hence, this review will provide information that can be used in the future and further research related to specific phytochemicals and cancer types caused by virus.

MATERIALS AND METHODS

Study Design

A scoping review approach was conducted to compile the phytochemical of *T. crispa* that have anticancer and antiviral activities. The selection of articles was managed based on PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analysis) 2009, that consist of four main segments which are identification, screening, eligibility and included. To determine the eligibility of the studies, the population (P), intervention (I), comparison (C), outcome (O) and study design (S) (PICOS) framework was used (Table 1).

Table 1 PICOS Framework for Determining the Eligibility of Studies.

Criteria	Determinants
Problem	Phytochemicals, anticancer and antiviral activities
Intervention	*Tinospora crispa* compounds
Comparison	Not applicable
Outcomes	Primary outcome: Anticancer activity of *T. crispa* compounds Secondary outcome: Antiviral activity of *T. crispa* compounds
Study Design	Experimental studies, qualitative and quantitative studies, preclinical and clinical studies

Search Strategy

This study was conducted by searching and reviewing the relevant articles followed by summarized the selected articles. The online databases that have been utilised in this study were Google Scholar, Science Direct and PubMed. The database search comprised from January 2017 to April 2022 using the following search keywords: "*Tinospora crispa*", "patawali", "brotawali", "seruntum", "compounds", "compound", "phytochemical", "phytocompound", "anticancer", "anti- proliferation", "antiviral" and

"viral treatment". The Boolean operators (AND and OR) were used to specify and separate each search keyword.

Study Selection

The study selection process started with title screening, abstract screening and assessing the eligibility of the articles based on inclusion and exclusion criteria by author and co-author. During the title screening, any research paper that was not related to the topic of study was excluded. Then, the abstracts were screened to exclude any unrelated and irrelevant to the research objective. Lastly, the articles were assessed for full text access and were excluded if the articles not met the criteria as stated in Table 2. The accessible full-text articles were thoroughly reviewed.

Inclusion and Exclusion Criteria

The inclusion and exclusion criteria used in this study are listed in Table 2.

Table 2 Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
a) Articles must be published in English. b) Time frame of the relevant articles must be in between January 2017- April 2022. c) Qualitative and quantitative study. d) Experimental paper. e) Papers about *T. crispa* or anticancer or antiviral or *T. crispa* phytochemicals. f) Full-text article is accessible.	a) Review articles.

Data Extraction

The data extraction was reviewed and summarized in the table form from the final full text articles and journals. The table content of the data extraction comprises of author's name, year of publication, origin of the plant, part of plant, extraction solvent, assay method, positive activity outcome and extracted phytochemicals from the study. The result of data extraction gave a descriptive summary that validate the objectives of the scoping review study.

RESULTS AND DISCUSSIONS

Articles Found

From the search through online databases (Google Scholar, Science Direct and PubMed), initially, there were 705 articles were discovered. The total number of articles discovered from Google Scholar were 540, Science Direct were 133 and PubMed were 32 (Figure 1). The total number of 115 articles were excluded after the removal of duplicates and 590 articles remained. The number of articles were then reduced to 71, while the rest were rejected due to the unrelated titles. Then, 71 articles were further screened by the abstract, full text accessibility and based on inclusion and exclusion criteria, only 39 articles passed the inclusion criteria, while another 32 articles were excluded from this study.

The remaining 39 articles and journals were further reviewed. In the eligibility stage, 39 articles were further screened to ensure the reliability and validity of the research paper. It was recorded that 11 articles were included in this scoping review study, while other 28 articles were excluded due to relevant reasons. The justification of removal of each article is listed in Table 3. From the excluded articles, 12 of the articles were irrelevant due to the research did not specifically correspond to the objective of this study, 3 articles were non-laboratory study, 6 review study, 5 study did not utilize *T. crispa* in experiment, one unrelated study that did not represent the objectives of this study and one article that do not have access to full-text.

The final 11 articles were included for data extraction since the articles fulfilled the inclusion and exclusion criteria as listed in Table 4. Table 5 showed list of phytochemicals detected via different extraction method. Table 6 and Table 7 summarized the anticancer and antiviral activities of *T. crispa*, respectively.

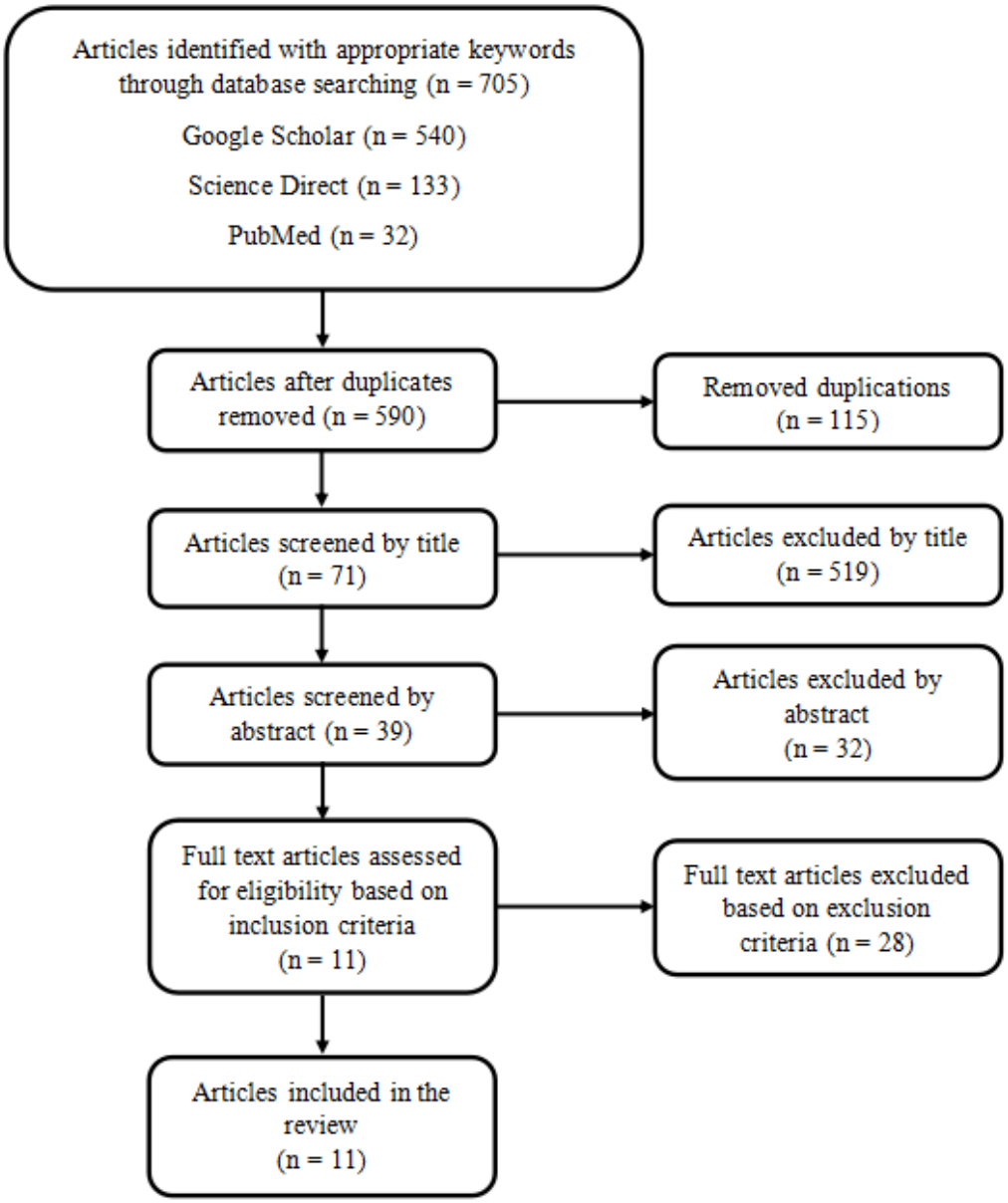


Figure 1 Result based on PRISMA flow diagram.

Table 3 Status of articles screened.

No.	Article titles	Rejection status
1.	Antioxidant capacities and total phenolic contents of 20 polyherbal remedies used as tonics by folk healers in Phatthalung and Songkhla provinces, Thailand	Article ***No. 1-12*** were rejected: Irrelevant due to the research did not specifically correspond to the objective of this study.

2.	Combination of cisplatin, *Hedyotis corymbosa* L. and *T. crispa* extracts as a new therapy for breast cancer cells 4T1 through in vitro induction and cell	
3.	Computational study and *in vitro* alpha-glucosidase inhibitory effects of medicinal plants from a Thai folk remedy	
4.	Exploring bioactivity potential of polyphenolic water-soluble lignin derivative	
5.	Function of selected natural antidiabetic compounds with potential against cancer via modulation of the PI3K/AKT/mTOR cascade	
6.	Hypoglycemia induced by *Plasmodium berghei* infection is prevented by treatment with *T. crispa* stem extract	
7.	*In vitro* protective effects of plants frequently used traditionally in cancer prevention in Thai traditional medicine: An ethnopharmacological study	
8.	Innocuousness of a polyherbal formulation: A case study using a traditional Thai antihypertensive herbal recipe in rodents	
9.	Metabolite detection and antibacterial activity of fungal endophytic extracts isolated from Brotowali (*T. crispa*) plants using TLC-bioautography assay	
10.	Natural plant products as potential inhibitors of RNA dependent RNA polymerase of Severe Acute Respiratory Syndrome Coronavirus-2	
11.	*T. crispa* leaves extract for the simple preparation method of CuO nanoparticles and its characterization	
12.	*T. crispa* methanolic crude extract activates apoptotic pathway of insulin resistant-HepG2 cell lines by improving the insulin sensitivity	
13.	Phytochemicals: Intellectual property rights	Article ***No. 13-15*** were rejected: The studies are not laboratory-based.
14.	Potent plants, cool hearts: a landscape of healing in Laos	
15.	Recent efforts for drug identification from phytochemicals against SARS-CoV-2: Exploration of the chemical space to identify druggable leads	
16.	Alkaloids	Article ***No. 16-21*** were rejected: They are review studies.
17.	Chapter six - Metabolic activation and toxicities of bis-benzylisoquinoline alkaloids	
18.	Elucidation of mechanisms of anticancer plant compounds against the tumor cells	
19.	Ethnomedicinal plant diversity in Thailand	
20.	Immunomodulatory properties of plants and mushrooms	
21.	Trends in diabetes care with special emphasis to medicinal plants: Advancement and treatment	
22.	Exploring bioactivity potential of polyphenolic water-soluble lignin derivative	Article ***No. 22-26*** were rejected: The studies did not utilise *T. crispa* in the experiment.

23.	Extracts of select endemic plants from the Republic of Mauritius exhibiting anti-cancer and immunomodulatory properties	
24.	Magnoflorine—Isolation and the anticancer potential against NCI-H1299 lung, MDA-MB-468 breast, T98G glioma, and TE671 rhabdomyosarcoma cancer cells	
25.	Synergistic or additive pharmacological interactions between magnoflorine and cisplatin in human cancer cells of different histological origin	
26.	The cardiac electrophysiology effects of higenamine in guinea pig heart	
27.	Interrogation of ethnomedicinal plants for synthetic lethality effects in combination with deficiency in the DNA repair endonuclease RAD1 using a yeast cell-based assay	Rejected. Unrelated to the objectives of this study.
28.	Probing PXR activation and modulation of CYP3A4 by *T. crispa* and *T. sinensis*	Rejected. Full text not accessible.

Table 4 Articles accepted for review.

No.	First author	Year	Title
1	Syarifah	2017	High performance liquid chromatography fingerprint analysis for quality control of brotowali (*T. crispa*)
2	Noman	2018	Crispenes F and G, cis-clerodane furanoditerpenoids from *T. crispa*, inhibit STAT3 dimerization
3	Ahmad	2018	Immunomodulatory effects of *T. crispa* extract and its major compounds on the immune functions of RAW 264.7 macrophages
4	Sharif	2019	Susceptibility of *Toxoplasma gondii* to ethanolic extract of *T. crispa* in Vero cells
5	Parveen	2019	Rearranged clerodane diterpenoid from *T. crispa*
6	Liao	2019	Tetrandrine interaction with ABCB1 reverses multidrug resistance in cancer cells through competition with anticancer drugs followed by downregulation of ABCB1
7	Mutiah	2019	Profile of anticancer activities of brotowali (*T.crispa* L.) plants of various regions in East Jawa
8	Parveen	2020	Development of a chemical fingerprint as a tool to distinguish closely related *Tinospora* species and quantitation of marker compounds
9	Haque	2020	Standardized ethanol extract of *T. crispa* upregulates pro-inflammatory mediators release in LPS-primed U937 human macrophages through stimulation of MAPK, NF-κB and PI3K-Akt signaling networks
10	Rakib	2020	Biochemical and computational approach of selected phytocompounds from *T. crispa* in the management of Covid-19
11	Ratanakomol	2021	Berberine inhibits Dengue virus through dual mechanisms

Table 5 Phytochemical identification from *T. crispa* plant.

No.	Author	Year	Origin	Part of Plant	Extraction Solvent	Extraction Method	Result	Phytochemical Extracted
1	Syarifah et al.	2017	Indonesia	Leaves and stems	Methanol	High performance liquid chromatography (HPLC)	Berberine was detected at retention time of 20.5 minutes in stem and leaves extracts of *T. crispa*.	Berberine
2	Noman et al.	2018	Bangladesh	Stems	Methanol	Vacuum-liquid chromatography (VLC)	The extract was separated into 46 fractions using mixtures of solvents - petroleum ether, CH_2Cl_2, EtOAc and MeOH. All compounds were obtained by using EtOAc-toluene.	Crispene F, Crispene G, Crispene D, Columbin, N-trans-feruloyltyramine, Cycloeucalenone, β-amyrin, Lupeol, β-sitosterol
3	Ahmad et al.	2018	Malaysia	Stem	80% ethanol	Thin-layer chromatography (TLC)	The extract was fractioned into alkaloid and non-alkaloid fractions by acid-base extraction method. $CHCl_3$ layer containing non-alkaloidal fraction (26.1 g) showed brown gummy residue, while for alkaloidal fraction (4.3 g) depict concentrated to a dark brown gummy residue.	N-formylannonaine, N-formylnornuceferine, Lysicamine, Magnoflorine, Syringin, 1-octacosanol
4	Sharif et al.	2019	Malaysia	Stem	99.9% ethanol	Phytochemical screening	Quantitative analysis of *T. crispa* extracts showed high quantity of phenolics (91.47 ± 1.2 mgGAE/g), followed by tannins, flavonoids, alkaloids	Flavonoid, Tannins, Phenolics, Alkaloid, Terpenoid, Saponins, Glycosides

							and the least is terpenoids (21.07 ± 3.2 mgGAE/g).	
5	Haque et al.	2020	Malaysia	Stems	80% ethanol	High performance liquid chromatography (HPLC) and LC-MS/MS analyses	Analysis of quantitative data showed that syringin and magnoflorine were found: 466.92 µg/mL and 281.21 µg/mL. LC-MS/MS results showed the presence of compounds from *T. crispa* extract.	Magnoflorine, Alkaloids, Flavones, Terpenes, Phenolic compounds, Tinorcodiside, Tinosponone, Columbin, Apigenin conjugate, Palmatoside, Syringin, Borapetoside A & C, Cordifoliside B & C, Palmarin, Jateorin
6	Parveen et al.	2019	Thailand	Stem	Methanol (8L)	Column chromatography (CC) over silica gel & High performance liquid chromatography (HPLC)	Extraction and isolation of compound using CC over silica gel. Extraction and isolation of compound using HPLC.	Tinocrispide, Baenzigeride A, Columbin, Borapetol A, Borapetoside B, Borapetoside C, Borapetoside F, (2R,5R,6R,8R,9S,10S,12S)-15,16-epoxy-2-hydroxy-6-O-(b-D-glucopyranosyl)-cleroda-3,13(16),14-trien-17,12-olid-18-oic acid methyl ester, (2R,5R,6S,9S,10S,12S)-15,16-epoxy-2-hydroxy-6-O-(b-D-glucopypranosyl)-cleroda-3,7,13(16),14-tetraen-17,12-olid-18-oic acid methyl ester, (-)-pinoresinol, Lysicamine,

								(6S, 9 R)-vomifoliol, N-trans-feruloyl tyramine, (-)-steponine
7	Parveen et al.	2020	United States of America	Whole plant	80% methanol	UHPLC-PDA-MS analysis	Quantitative analysis of ten compounds was achieved using UHPLC-PDA method.	Magnoflorine, Borapetosides B, N-trans-feruloyl tyramine, Borapetosides F, Borapetoside C

Table 6 Phytochemical of *T. crispa* with anticancer activity.

No.	Author	Year	Origin	Part of Plant	Extraction Solvent	Assay Method	Result	Positive Activity Outcome	Phytochemical Extracted
1	Mutiah et al.	2019	Indonesia	Stems	80% ethanol	MTT assay	Cytotoxic test showed the reduction of cell viability in MCF-7 breast cancer cells.	+ Anticancer	Alkaloid
2	Liao et al.	2019	China	Not mentioned in study	Not mentioned in study	MTT assay	Tetrandrine showed reduction in cell proliferation cell lines: SW620 and SW620/Ad300, KB-3-1 and KB-C2, HEK293/pcDNA3.1 and HEK293/ABCB1.	+ Anticancer	Tetrandrine

Table 7 Phytochemicals of *Tinospora crispa* with antiviral activity.

No.	Author	Year	Origin	Part of Plant	Extraction Solvent	Method	Result	Positive Activity Outcome	Phytochemical Extracted
1	Ratana-komol et al.	2021	United States of America	Not mentioned in study	100% dimethyl sulfoxide (DMSO)	Virucidal activity assay	All viruses (CHIKV, ZIKV and DENV 2) affected by high concentration of Berberine. About 1 log reduction of viral titer was reduced when virus was incubated with Berberine.	+ Antiviral	Berberine
2	Rakib et al.	2020	Bangladesh	Whole plant	Methanol (4L)	Molecular docking	All compounds from *T. crispa* interact with SARS-CoV-2 M^{pro} enzyme. Among those compounds, seven showed higher docking scores compared to control.	+ Antiviral	1. Imidazolidin-4-ne, 2-imino-1-(4-methoxy-6-dimethylamino-1,3,5-triazin-2-yl) 2. Spiro[4,5]dec-6-en-1-ol, 2,6,10,10-tetramethyl 3. 3β-hydroxy-5-cholen-24-oic acid, androstan-17-one

	4. 3-ethyl-3-hydroxy-(5α)
	5. Camphenol
	6. (−)-Globulol
	7. Yangambin
	8. Nordazepam
	9. TMS derivative
	10. Benzeneethan amine

Tinospora crispa phytochemicals extracted from the whole plant were magnoflorine, borapetosides B, borapetosides C, borapetoside F, N-trans-feruloyl tyramine. The phytochemicals extracted from the stem of *T. crispa* were crispene F, crispene G, crispene D, columbin, N-trans-feruloyl tyramine, cycloeucalenone, β-amyrin, lupeol, β-sitosterol, N-formylannonaine, N-formylnornuceferine, lysicamine, magnoflorine, syringin, 1-octacosanol, flavonoid, tannins, phenolics, alkaloid, terpenoid, saponins, glycosides, tinorcodiside, tinosponone, columbin, apigenin conjugate, palmatoside, syringin, borapetoside A & C, cordifoliside B & C, palmarin, jateorin, tinocrispide, baenzigeride A, borapetol A, borapetoside B, borapetoside F, (2R,5R,6R,8R,9S,10S,12S)-15,16-epoxy-2-hydroxy-6-O-(b-D-glucopyra-nosyl)-cleroda-3,13(16),14-trien-17,12-olid-18-oic acid methyl ester, (2R,5R,6S,9S, 10S,12S)-15,16-epoxy-2-hydroxy-6-O-(b-D-glucopypranosyl)-cleroda-3,7,13(16),14-tet-raen-17,12-olid-18-oic acid methyl ester, (-)-pinoresinol, lysicamine, (6S, 9 R)-vomifoliol and (-)-steponine. The major phytochemicals from leaves and stem of *T. crispa* was berberine.

T. crispa phytochemicals proven to have anticancer activity are alkaloid and tetrandrine. According to Mutiah et al. (2019), *T. crispa* has been acknowledged to contain alkaloid that was important for anticancer activity. The extraction of alkaloid from *T. crispa* stems using 80% ethanol showed cytotoxic effect on MCF-7 breast cancer cells. Bisbenzylisoquinoline alkaloid, tetrandrine that was extracted from *T. crispa* showed anticancer activity towards various types of cancer cell lines including human lung carcinoma, human colon cancer, human hepatoma and human leukemia (Liu et al., 2016). According to Liao et al. (2019), tetrandrine showed reduction in cell proliferation of KB-3-1 human epidermoid carcinoma cell line and multidrug resistant cancer cell line (Liao et al., 2019). Tetrandrine also inhibited the MDA-MB-231 breast cancer from growing by decreasing the tumor weight and volume significantly in mouse xenografts (Wang et al., 2020).

According to Ratanakomol et al. (2021), berberine showed antiviral activity against dengue virus (DENV), Zika virus and chikungunya virus. Berberine also depicts antiviral activity against respiratory syncytial virus by inhibiting the activation of p38 mitogen-activated protein kinase (MAPK) (Shin et al., 2015). Hung et al. (2019) mentioned that berberine was a potent inhibitor for hepatitis C virus. Interestingly, Rakib et al. (2020), reported the presence of phytochemicals in *T. crispa* such as imidazolidin-4-ne,2-imino-1-(4-methoxy-6-dimethylamino-1,3,5-triazin-2-yl), spiro[4,5] dec-6-en-1-ol,2,6,10,10-tetramethyl, 3.beta-hydroxy-5-cholen-24-oic acid, androstan-17-one, 3-ethyl-3-hydroxy-(5.alpha), camphenol, (−)-globulol, yangambin, nordazepam, trimethylsilyl (TMS) derivative and benzeneethanamine were proven to have antiviral activity towards Covid-19 virus by modifying the SARS-CoV-2 M^{pro} enzyme activity.

The phytochemical of *T. crispa* that have potential for both anticancer and antiviral activities are magnoflorine, β-amyrin and lupeol. There is evidence that magnoflorine extracted from *Berberis cretica* L. showed anticancer activity to some types of lung cancer while magnoflorine from *Coptidis rhizoma* showed anticancer activity to gastric cancer (Sun et al., 2020). Moreover, magnoflorine extracted from *Magnolia grandiflora* leaves also showed potent antiviral activity against herpes simplex virus type-1 (HSV-1) and it was stated that magnoflorine that was extracted from *T. cordifolia* has potential as antiviral agent against DENV-2 (Paul et al., 2021). The triterpenoids β-amyrin that was extracted from *Bombax ceiba* plant showed anticancer activity towards lung cancer cells (A-549) (Rehan & Shafiullah, 2021) and Hep-G2 liver cancer (Wen & Zeng, 2018). Interestingly, β-amyrin was proven have antiviral activity towards influenza A, herpes simplex virus (HSV) and hepatitis B virus (Parvez et al., 2018). The triterpenoids lupeol inhibited the proliferation of NSCLC cells (Min et al., 2019), human lung cancer cell (A-549) (Dwivedi et al., 2014) and MCF-7 breast cancer cells (Pitchai et al., 2014). Lupeol also showed anticancer activity towards human osteosarcoma cells (MNNG/HOS and MG-63) (Liu et al., 2016) and it also exhibited antiviral activity towards HSV (Flekhter et al., 2004; Parvez et al., 2018) and SARS-CoV-2 (Ali et al., 2020).

CONCLUSION

A total of 52 compounds from *T. crispa* were identified that consist of alkaloid, terpenes, phenolic compounds, glycosides and alcohol with 13 of them exhibited anticancer and antiviral activities. The discovery of links between phytochemicals of *T. crispa* with anticancer and antiviral activities may pave the way to further scientific research of phytochemicals and virally associated human malignancies.

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THE EFFECTIVENESS OF INTRA-ARTICULAR INJECTIONS FOR KNEE OSTEOARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

Introduction: Intra-articular (IA) injections have been used to reduce knee osteoarthritis (OA) pain. However, several side effects following the injections were reported and raised the question of whether IA injections were effective and safe. Hence, this study aimed to identify the most common type of IA injections used in treating knee OA and to determine its effectiveness, duration of pain relief and most common side effects. **Methods**: Online literature searches on PubMed, Wiley Online Library, and Cochrane Library were performed by using the keywords "intra-articular injection" AND "knee osteoarthritis" OR "knee OA" AND "randomised controlled trial" OR "RCT". Only randomised controlled trial studies that analysed the effects of intra-articular injections for knee OA patients and published in English were included. A total of 2823 articles were identified, 22 full-text articles were assessed, and six articles have been included in this study. National Institutes of Health (NIH) Quality Assessment Tools were used to evaluate the risk of bias in these six articles, and only four articles were included for meta-analysis. **Results**: The present data showed that intra-articular hyaluronic acid injection was the most common type of IA injection. However, only intra-articular corticosteroid injections (IACI) are effective for knee OA treatment. The pain relief duration provided by each intra-articular injection type varies between 1 month to 6 months. Side effects such as arthralgia and joint swelling were recorded following the administration of IA hyaluronic acid injection and IA stem cell injection, but not in the IACI therapy groups. **Conclusion:** Although IACI has been shown to reduce pain in patients with knee OA, the long-term consequences of IACI therapy in this population have yet to be confirmed.

KEYWORDS: intra-articular injection, knee osteoarthritis, randomised controlled trial, side effects

INTRODUCTION

Osteoarthritis (OA) is characterised by the gradual loss of articular cartilage and commonly affects the joints in the knees. The main symptoms of OA are joint pain and stiffness that will cause difficulties in moving. Globally, OA was estimated to be the fourth leading cause of disability and is highly associated with the ageing Asian population (Fransen et al., 2011). Other than age, overweight, obesity, and previous

knee injury are regarded as modifiable risk factors for the development and progression of OA (Ministry of Health Malaysia, 2013).

One of the non-surgical treatments for knee OA is intra-articular (IA) injections. IA injections are the administration of medication directly into the joint with the main purpose of alleviating pain. Several studies have indicated that IA injections can effectively relieve pain in individuals suffering from knee OA (Saturveithan et al., 2016; Tian et al., 2018; Xu et al., 2020). To date, there are several different types of IA injections, such as corticosteroid injections (IACI), hyaluronic acid (HA) injections, platelet-rich plasma (PRP) injections, and so on.

Different types of IA injections were used to treat knee OA depending on the severity of knee OA in every patient. Ayhan et al. (2014) reported that IACI relieves pain in moderate and severe knee OA, while intra-articular HA injection was administered to reduce pain in mild knee OA. On the other hand, a study conducted by Taniguchi et al. (2018) suggested that intra-articular PRP injection was a safe treatment for the Japanese with mild to moderate knee OA and effectively alleviated pain up to 6 months (Taniguchi et al., 2018). Despite its effectiveness, previous studies have also shown that the administration of these intra-articular injections needs to be repeated as they presumably provide a short-term pain relief effect only (Raynauld et al., 2003; Ayhan et al., 2014; Chen et al., 2019).

Cole and Schumacher (2005) claimed that there is no consistent data on the duration of pain relief after injection, even though the literature shows that many patients respond positively to intra-articular injection therapy. Not only that, the manifestation of side effects after receiving intra-articular injection among knee osteoarthritis patients was also considered a significant issue to be highlighted (Grillet & Dequeker, 1990; McAlindon et al., 2017). Hence, it raises the question of whether intra-articular injections are effective and safe for knee OA. Thus, the present study aimed to determine the effectiveness of intra-articular injections in treating knee osteoarthritis by using a systematic review and meta-analysis of randomised control trials on the effects of intra-articular injections among patients with knee OA.

MATERIALS AND METHODS

Identification

This study was based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The articles were retrieved from four databases, including Wiley Online Library, PubMed, and Cochrane Library. Boolean operators' AND' and 'OR' were employed with the combinations of the following keywords: "intra-articular injection*" AND "knee OA" OR "knee OA" AND "randomised controlled trial*" OR "RCT".

Screening and Eligibility

All identified articles were screened for duplication, and their eligibility was assessed based on the inclusion and exclusion criteria. The inclusion criteria were human study, randomised controlled trial (RCT), English journal, published or peer-reviewed journals and journal articles published within ten years, while the exclusion criteria were review or case report study, proceeding and dissertation.

Data Extraction and Collection

Extracted data from the selected articles were the first author's name, year of publication, place of study, number and demographic information of participants, types of IA injection, administration, side effects manifestation, the usage of other medications, importance outcome measures, and funding source. These

data were recorded independently by the first author (NFS), presented in the table form using MS Excel 2019 and validated by the corresponding author (ZZ).

Meta-Analysis

Meta-analysis was performed to statistically and critically evaluate the strength of the evidence presented between the intervention or treatment, IA injection and knee OA disease by combining the results of comparable studies. Meta-analysis was conducted according to the following steps: (1) frame a question (based on a theory); (2) read the individual papers' abstracts and titles; (3) extract information from a selected set of final articles; (4) construct a forest plot by estimating the summary effect size in the form of Inverse Variance and applying appropriate effects models; and (5) determine the degree of heterogeneity in these articles (Basu, 2017). The degree of heterogeneity was managed using a random-effect model and 95% prediction interval to determine the overall interval effect. The result of the meta-analysis was presented as a forest plot, which was constructed using RevMan software. It represents the estimates of effects for each type of intra-articular injection in relieving pain among knee OA patients and was interpreted by observing the direction of effect, mean differences, heterogeneity, and p-value for the overall effect (Sedgwick, 2015; Cochrane, 2021).

Risk of Bias

The NIH Quality Assessment Tool for Controlled Intervention Studies was used to assess the risk of bias in each selected study (Ma et al., 2020). This tool provides signalling questions (i.e., randomisation and allocation concealment, the similarity of compared groups at baseline, use of intent-to-treat (ITT) analysis, adequacy of blinding, the overall percentage of subjects lost to follow-up, and so on) to address the potential for bias. The overall quality of the included studies was assessed as good, fair, or poor.

RESULTS AND DISCUSSIONS

From 2823 records identified through database searching, 109 duplicate records were removed (Figure 1). In the screening stage, 2692 records were excluded based on the title and abstract. Twenty-two full-text articles were assessed for eligibility, and six studies were included in qualitative synthesis. Among the six included studies, four studies were included in the meta-analysis. Sixteen full articles were excluded at the eligibility stage based on the inclusion and exclusion criteria, and two journal articles were excluded from meta-analysis due to inadequate data.

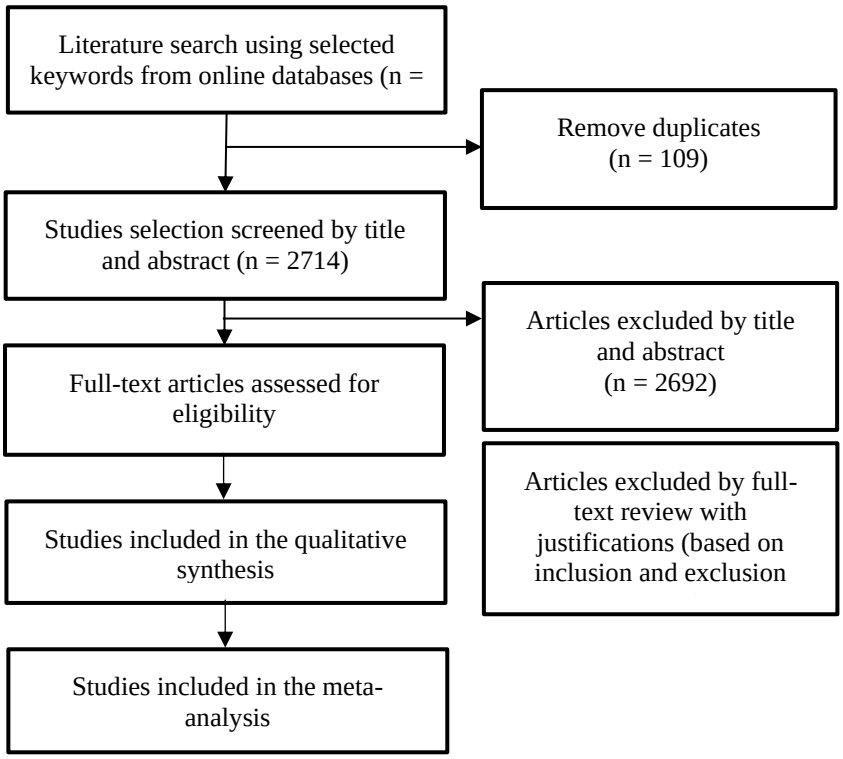


Figure 1 The flow of identification, screening, eligibility and included studies based on PRISMA guidelines.

Study Characteristics

Table 1 shows the characteristics of the included studies. Generally, all the included studies discussed the pain-relief effects of intra-articular injections within knee osteoarthritis patients, with one study from Turkey, Japan, South Korea, and Brazil and two from the USA. All the studies were conducted between 2017 and 2019 and consisted of one or two treatment groups. Moreover, all studies indicated that the duration of pain relief provided by each type of IA injection varies from one month (short-term) to nearly seven months (long-term). IA steroid injection, IA stem cells injection, and IA hyaluronic acid injection were proven to relieve pain from 1-3 months, up to 6 months, and from 6 to 6.5 months, respectively.

In addition, all the included studies used either the Visual Analogue Scale (VAS) or Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores to measure the pain scores after administering IA injections. Studies by Eker et al. (2017) and Takamura et al. (2019) indicated improved VAS/WOMAC mean scores for the IA injections vs. control (T = 2.8, CR = 4.8) and (T = 43.02, CR = 47.55), respectively. Meanwhile, a study conducted by Farr et al. (2019) demonstrated a reduction in VAS mean

scores vs. control for only one treatment group, i.e., IA stem cells injection (T = 44.38, CR = 61.02), but not in the IA hyaluronic acid injection group, (T = 68.69, CR = 61.02).

Other than that, a study conducted by Mendes et al. (2019) presented alleviated VAS and WOMAC mean scores vs. control for both treatment groups, IA Botox and IA hyaluronic acid injection. For IA Botox injection, the VAS mean score was (T = 3.8, CR = 4.0), and WOMAC mean score was (T = 30.3, CR = 34.4), while for IA hyaluronic acid injection, the VAS mean score was (T = 1.8, CR = 4.0), and WOMAC mean scores were (T = 23.3, CR = 34.4), respectively. Other studies (Lee et al., 2019; Petterson & Plancher, 2019) did not state their VAS/WOMAC scores but reported improved pain after the IA injection.

For the types of IA injections used, three out of six studies used intra-articular HA injections to treat knee OA (Farr et al., 2019; Petterson & Plancher, 2019; Takamura et al., 2019). Meanwhile, two studies used intra-articular corticosteroids and intra-articular stem cell injection to treat knee OA, respectively (Eker et al., 2017; Mendes et al., 2019; Farr et al., 2019; Lee et al., 2019). Only one study used intra-articular Botox injection as the treatment group (Mendes et al., 2019). Among all studies, two studies conducted by Petterson and Plancher (2019) and Lee et al. (2019) demonstrated the manifestation of side effects. The side effects are arthralgia (i.e., joint pain) and joint swelling or effusion following intra-articular injections—hyaluronic acid and stem cells.

Table 1 Characteristics of included studies

Study	Total Subjects M/F	Group	Age Mean (SD)	KL Grade	Type of IA Injection	Type of Administration	VAS Score Mean (SD)	WOMAC Score Mean (SD)	Duration of Pain Relief (month)	NSAIDs / Analgesic Usage	Side Effects
Eker, et al., 2017	52 28/24	T	65.15 (10.23)	2-4	CS	Repeated	2.8 (1.3)	-	3	Tramadol	-
		CR	69.73 (7.26)		Saline		4.8 (2.5)	-			-
Takamura, et al., 2019	311 124/187	T	61 (9.38)	2-3	HA	Single	-	43.02 (26.1)	6.5	-	-
		CR	62.8 (8.85)		Saline		-	47.55 (26.7)			-
Lee, et al., 2019	24 6/18	T	62.2 (6.5)	2-4	Stem Cells	Single	3.4 (1.5)	26.7 (13.3)	6	AO	AG JE
		CR	63.2 (4.2)		Saline		-	-			

M, Male; F, Female; T, Treatment; CR, Control; SD, Standard deviation CS, Corticosteroids; HA, Hyaluronic Acid; VAS, Visual Analogue scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index scale; NSAIDs, nonsteroidal anti-inflammatory drugs; AO, Acetaminophen; AG, Arthralgia; JE, Joint Effusion

Table 2 Characteristics of included studies (continue)

Study	Total Subjects M/F	Group	Age Mean (SD)	KL Grade	Type of IA Injection	Type of Administration	VAS Score Mean (SD)	WOMAC Score Mean (SD)	Duration of Pain Relief (month)	NSAIDs / Analgesic Usage	Side Effects
Mendes, et al., 2019	105 9/96	T1	62.5 (6.8)	2-3	Botox	Single	3.8 (2.4)	30.3 (15.2)	1	AO, Lidocaine	-
		T2	65.5 (6.9)		CS		1.8 (2.3)	23.3 (17.7)			-
		C R	64.6 (6.7)		Saline		4 (3.2)	34.4 (16.3)			-
Farr, et al., 2019	200 105/ 95	T1	55.9 (12.3)	2-3	Stem Cells	Single	44.38 (33)	-	6	-	-
		T2	55.4 (11)		HA		68.69 (36)	-			-
		CR	54.9 (9.9)		Saline		61.02 (32)	-			-
Petterson & Plancher, 2019	369 154 / 215	T	59.5 (8)	2-3	HA	Single	-	-	6	GS	AG, JE
		CR	58.7 (9.2)		Saline		-	-			

M, Male; F, Female; T, Treatment; CR, Control; SD, Standard deviation CS, Corticosteroids; HA, Hyaluronic Acid; VAS, Visual Analogue scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index scale; NSAIDs, nonsteroidal anti-inflammatory drugs; AO, Acetaminophen; AG, Arthralgia; JE, Joint Effusion

Risk of Bias

Table 2 shows the qualities of the included studies as assessed using the NIH Quality Assessment Tools of Controlled Intervention Studies. Based on this table, studies by Eker et al. (2017), Lee et al. (2019), Mendes et al. (2019) and Petterson & Plancher (2019) were rated as good because they are transparent enough to provide adequate or sufficient information, thus reducing the potential of bias that could create arguments towards their findings and helps to improve the articles' quality. Besides that, a study by Takamura et al. (2019) was rated as fair, and a survey by Farr et al. (2019) was rated as poor because they presented a moderate to low number of important information, which can lead to uncertainty in their findings.

Table 2 Risk of bias assessment on the included studies

Author/ Year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14	Overall result
Eker, et al. (2017)	✓	✓	✓	✓	✓	✓	✓	✓	–	×	✓	✓	✓	–	Good
Takamura, et al. (2019)	✓	–	–	×	✓	✓	–	–	–	–	✓	–	✓	–	Fair
Lee, et al. (2019)	✓	–	✓	✓	✓	✓	✓	✓	✓	×	✓	×	–	Y	Good
Mendes, et al. (2019)	✓	✓	✓	✓	✓	✓	×	✓	–	×	✓	✓	✓	✓	Good
Farr, et al. (2019)	✓	–	✓	–	–	–	×	×	×	✓	✓	✓	✓	–	Poor
Petterson and Plancher (2019)	✓	✓	–	✓	✓	✓	✓	✓	–	×	✓	✓	✓	✓	Good

Effectiveness of IA Steroid Injection

Figure 2 summarises pooled estimates for treatment effect—IA steroid injection in two subgroups of trials (Eker et al., 2017; Mendes et al., 2019) that were defined according to the characteristics of participants. Eker et al. (2017) and Mendes et al. (2019) had significantly more reductions in VAS/WOMAC scores with a 95% confidence interval of mean differences, -2.00 and -2.20, respectively. Overall, these studies were homogenous (p = 0.82) and showed a statistically significant reduction of knee pain with a mean difference of -2.08 (p < 0.00001).

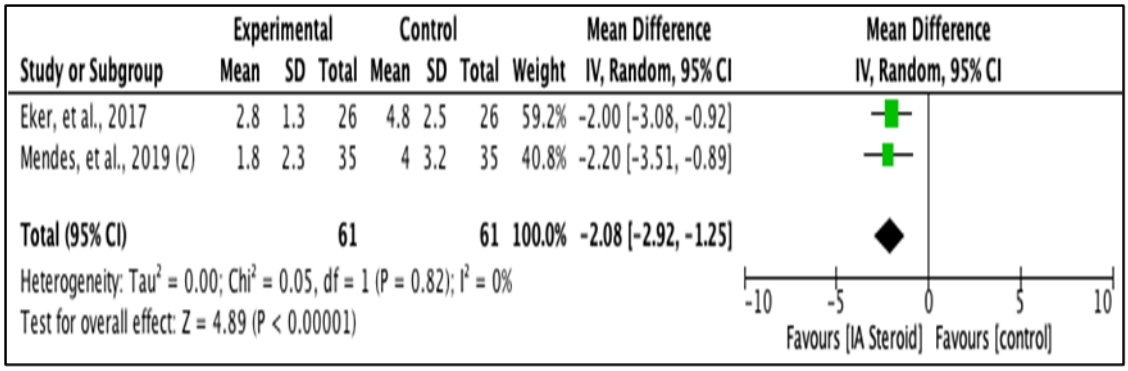


Figure 2 Results of Meta-analysis with 95% Confidence Interval comparing Intraarticular Steroid Injection and Control

Effectiveness of IA Hyaluronic Acid Injection

Figure 3 summarises pooled estimates for treatment effect—IA hyaluronic acid injection in two subgroups of trials (Farr et al., 2019; Takamura et al., 2019) that were defined according to the characteristics of participants. It was indicated that the study by Takamura et al. (2019) demonstrated an insignificantly reduced VAS/WOMAC score with a 95% confidence interval of mean differences, -4.53. In contrast, Farr et al. (2019) showed no reduced VAS/WOMAC score following IA hyaluronic acid injection, favouring the control group. Overall, both studies were heterogeneous ($I^2 > 50\%$), and the pooled estimates of the effect of IA hyaluronic acid injection in alleviating knee pain were not observed (p=0.93).

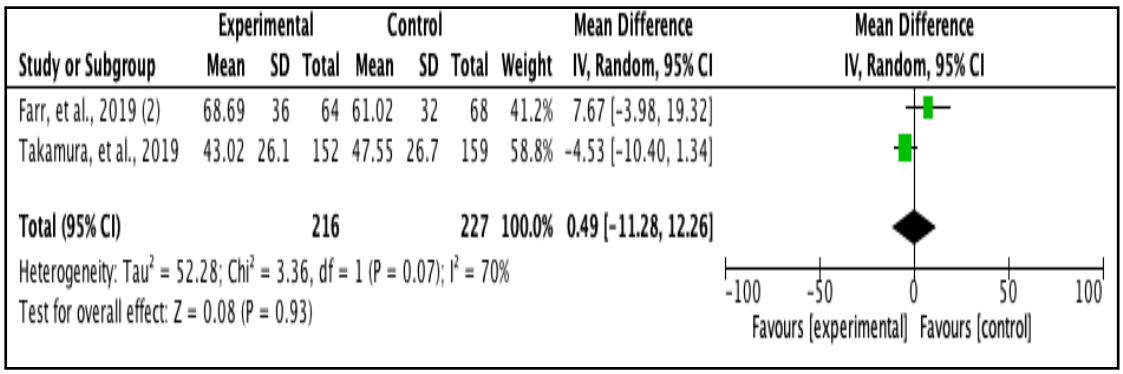


Figure 3 Results of Meta-analysis with 95% Confidence Interval comparing Intra-articular Hyaluronic Acid Injection and Control

Based on the meta-analysis, it was observed that intra-articular corticosteroid injection (IACI) at the suggested concentration had improved pain in patients with knee OA for over 1 to 3 months. The present findings are consistent with the previous studies, which offered short-term pain relief was observed up to one month after IACI (Ayhan et al., 2014; Juni et al., 2015; Wagner et al., 2015; Da Costa et al., 2016; He et al., 2017). Nevertheless, Raynauld et al. (2003) have reported that the long-term effectiveness of IACI could be achieved by frequent steroid injection. As reviewed in the present study, Eker et al. (2019) have shown that repeated administration of IACI significantly reduced the VAS pain scores up to 3 months post-injection. On the other hand, a single injection of IACI significantly reduced the VAS pain scores only up to 1 month after injection (Mendes et al., 2019). Perhaps the repetition administration of IACI could achieve cumulative benefit or restore benefit that has decreased, thus extending the duration of pain relief (Murthy et al., 2014).

Unlike IACI, IA hyaluronic acid injection had a heterogeneous finding and pooled estimates showed insignificant effects on alleviating pain among the patients with knee OA. Provided IA hyaluronic acid injection was found to be the most common IA injection used to treat pain in osteoarthritic knees; such insignificant pooled estimates resulted from the studies conducted by Farr et al. (2019) and Petterson and Plancher (2019). The former presented no reduced VAS pain scores in the IA hyaluronic acid group. At the same time, the latter was excluded from the analysis, though a significant reduction in VAS pain scores was observed due to some limitations. Two included studies (Farr et al., 2019; Takamura et al., 2019) are heterogenous because both studies indicated the contradictory direction of the IA hyaluronic acid treatment effect; Farr et al. (2019) showed negative treatment effect while Takamura et al. (2019) showed positive treatment effect. Other than that, the study by Farr et al. (2019) possessed a higher risk of bias (i.e., high withdrawal rate, poor study design and incomplete outcome data) compared to the study by Takamura et al. (2019). All these heterogeneity factors were deduced based on the guidance provided (Fletcher, 2007; Deeks et al., 2019), which were believed to be the contributing factors of insignificant findings.

In terms of duration, a single intra-articular hyaluronic acid injection resulted in adequate pain relief among individuals with osteoarthritic knees for over 3 to 6 months of follow-up (He et al., 2017; Suppan et al., 2017). Consequently, the findings of these studies are congruent with the current reviewed study of Takamura et al. (2019) and Petterson and Plancher (2019). Nevertheless, the wide range of pain alleviation duration (i.e., 3 – 6 months) of IA hyaluronic acid injection depends on the various types of HA employed, which include multiple formulations such as molecular weight and cross-linking (Aggarwal & Sempowski, 2004; Farr et al., 2019). Therefore, considering that IA hyaluronic acid

provided a longer duration of pain relief for knee OA, it is recommended to use intra-articular HA injection rather than IACI, which was found to relieve pain not more than three months (Askari et al., 2016).

For the side effects of IA injections, previous studies by Richards et al. (2016) and McAlindon et al. (2017) have found several side effects following intra-articular corticosteroids injection (IACI), namely systemic hyperglycemia, septic arthritis, and bone loss. Although the present systematic review did not find any side effects post-IACI injection in the selected studies, many reports in the literature suggest otherwise (Hauser, 2009; Wernecke et al., 2015; McAlindon et al., 2017; Zeng et al., 2019). In these reports, the side effects might manifest following its treatment for a long time. Repeated administration of IACI to sustain the pain relief for a longer timeframe (> 1 month) might induce severe side effects such as articular and bone loss. McAlindon et al. (2017) found that IACI resulted in more significant cartilage volume loss. Similarly, a larger and longer population study by Zeng et al. (2019) showed the worsening of radiographic OA in the IACI group compared to the control group. This side effect could happen due to the impact of corticosteroid itself decreasing osteoblast function, thus reducing the formation of new bone (Canalis, 2003; Briot & Roux, 2015).

On the other hand, according to a prior study by Honvo et al. (2019), IA hyaluronic acid does not appear to be linked to any safety concerns when used to treat OA. The findings of Honvo et al. (2019) are consistent with the current reviewed study of Petterson and Plancher (2019), which found that the intra-articular HA therapy group had a lower than 5% incidence of joint swelling and arthralgia. Similarly, Lee et al. (2019) also found no significant side effects in the IA stem cell injection group, further supporting the findings of previous studies (Peeters et al., 2013; Jo et al., 2014; Fodor & Paulseth, 2016; Khalifeh Soltani et al., 2019; Kim et al., 2019). Although there is no report of side effects, high-quality evidence is needed to confirm the therapeutic impact of IA stem cell injection, as few studies have identified cell malignancy as a potential risk of stem cell therapy (Suzuki et al., 2011; Zhang et al., 2020).

LIMITATIONS AND FUTURE STUDIES

To date, only the present study investigated the effectiveness of different IA injections for alleviating pain in patients with knee OA using meta-analysis approaches. Nevertheless, a few limitations have been discovered. First, the process of identification and screening articles has been done by one person only, which may increase the risk of bias during the reviewing process. Second, there were only two studies included in each meta-analysis. Although meta-analysis can be performed with at least two studies (Valentine et al., 2010; Ryan, 2016), it will still lead to some weaknesses, especially when the included studies are poor and have low quality. Third, using other oral or topical pain medications might also influence the findings of each selected study. Experimental studies on the effects of prolonged use of IACI, especially its association with bone resorption, are warranted in the future. In addition, other than alleviating pain, the potential use of IA stem cell injection in regenerating the osteoarthritic articular cartilage is interesting to explore as an alternative approach for knee OA treatment.

CONCLUSION

In conclusion, intra-articular HA injections are the most common type of IA injection used among patients with knee OA, followed by IACI. Moreover, the duration of pain relief for IA injections varies from 1 month to 6 months, depending on the types of IA injection and frequency of dosing. Side effects such as arthralgia and joint swelling manifested following administering IA hyaluronic acid and IA stem cell injection but were not reported in the IACI therapy groups. Although IACI has proven to be effective in alleviating pain among patients with knee OA, the side effects of prolonged IACI use in this population have yet to be determined.

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AUDITORY SENSORY GATING IN AUDITORY BRAINSTEM RESPONSE (ABR) WITH PSYCHOLOGICAL TASK IN AUTISM SPECTRUM DISORDER (ASD) CHILD: A CASE STUDY

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ABSTRACT

Studies related to auditory sensory gating have primarily focused on the higher processing center of the auditory system (frontal and temporal lobe), either using electroencephalography (EEG) or magnetoencephalography (MEG). There are limited studies investigating auditory sensory gating from the auditory brainstem region or descending pathways connecting the auditory cortex and brainstem, especially in the autism spectrum disorder (ASD) population. In this report, the auditory sensory gating function of an ASD child using auditory brainstem response (ABR) with a psychological task was compared to typically developing children. Two 10-years old children participated; one diagnosed with ASD and another a typically developing child. They underwent audiological assessment and had normal audiograms with type A tympanograms. The ABR with and without psychological tasks (congruent, incongruent, and neutral conditions) was then conducted. The ABR waveforms (amplitude and latency) and the Stroop variables (percentage score and response time of correct responses) differences were examined among the participants. This case report highlights the six important sensory gating features, i.e., percentage score, response time, facilitation effect, Stroop interference, cognitive interference, and interference concept between an ASD and typically development child. The findings are expected to contribute to future research in the same niche.

KEYWORDS: Case Reports; Auditory Brainstem Responses; Autism Spectrum Disorder; Sensory Gating; Psychological Inhibition

INTRODUCTION

Auditory Brainstem Response (ABR) is a well-known electrophysiology measurement founded by Jewett and Williston (1). Auditory Evoked Potentials (AEPs), including ABR, measure the electrical signals the central nervous system produces along the auditory pathway when stimulated by a stimulus (2). The ABR measures the earlier components of the path within the first 10 to 15 msec following a transient acoustic stimulus and the neural pathway mainly located at VIII nerve and the brainstem. (2). Clinically, ABR is commonly used to estimate the hearing threshold for difficult-to-test patients such as those with comorbidities and as a support for diagnosis. Furthermore, it acts as neurodiagnostic testing that measures impairment that may occur along the auditory pathway from the outer ear to the auditory brainstem.

ABR was used in neurophysiological research and has been studied continuously by scientists in different areas until today (3, 4). ABR's area of research includes those for cognitive and behavioural function, hearing screening, diagnosis, and prognosis of the disorders and development of behaviour and emotion regulation, also brain development from the neuroscience angle. Recently, study has been focused on understanding the sensory gating function using ABR as an assessment tool (3, 4). Sensory gating is defined as the situation when any redundant or irrelevant information obtained from the environment is filtered before being processed by the brain (5). Sensory gating is usually determined by the presence of responses at 50 msec after the presentation of the auditory stimulus, known as the P50 component. A previous study has used cognitive tasks while the ABR is recorded, and the authors hypothesised that attention and cognitive function might have a particular influence on the ABR waveforms (4). Brännström (3) also investigated cognitive function when presented with cognitive interference, namely Stroop Task (ST).

The ST measures the ability to inhibit cognitive interference but is also used for measuring attention and processing abilities as part of the cognitive function. There are different versions of ST, e.g., the original ST by Stroop in 1935, emotional ST, day and night ST, and counting digit ST (this version in this study). In the conventional ST (Stroop Color and Word Test), congruency exists when a word's meaning and font colour are identical (congruent). For example, the word "green" is printed in green ink. Incongruent is the complete opposite. That is, the word's meaning and the printed colour

does not correspond, e.g., "green" could be printed in red ink. In other words, participants must do a less automated job (i.e., naming ink colour) while suppressing the interference caused by a more automated task (i.e., reading the word). This difficulty in preventing a more automated process is known as the Stroop effect (Stroop, 1935).

Brännström (3) suggested that cognitive interference generated by the ST could trigger inhibition at the brainstem level to suppress information processing. The suppression could be present as a reduction of wave V amplitude (3). This suggests that wave V amplitude will be smallest in incongruent conditions as the brainstem receive the highest cognitive interference than in the congruent and neutral conditions. Based on this report, it can be inferred that the ABR may have the potential to be used as an assessment tool to diagnose sensory gating impairment in support of other evaluation methods such as the P50, P300, and N100 test (cortical auditory evoked potential, CAEP) as well as a parental or self-reported questionnaire.

Even though ABR shows potential in the study of sensory gating, there is a need to be more information on its ability as an assessment tool to measure sensory gating since the neural substrates for efferent pathways still need to be better understood. The information on the sensory gating function reported from the previous studies involves other electrophysiological test such as CAEP (6) and involves other mode of testing such as using magnetoencephalography (MEG) (6) instead the typical Electroencephalography (EEG) mode (6). These tests measure brain responses, focusing on cortical connection and spontaneous brain activities (7). In contrast, the ABR measures the vestibulocochlear (VIII) nerves up to the inferior colliculus of the midbrain (2).

In children with ASD, impairment to the sensory gating is usually observed as auditory hypersensitivity (8). ASD children exhibit sound hypersensitivity by covering their ears, dislike or have difficulty with a specific sound, may get startled and distracted easily, and may notice a sound that others did not. Studies reported that about 30% to more than 90% of the ASD population either ignore or overreact to familiar sensations (9).

However, as mentioned above, the scarce findings restrict our ability to understand the process of the auditory sensory gating function in the brainstem, which is very important for the future diagnosis of ASD. This case study explores the effect of auditory sensory gating on ABR with

psychological tasks in a child with ASD compared to a typically developing child by highlighting the essential features of this research area.

CASE PRESENTATION

Participant

This case study was conducted on a patient diagnosed with ASD recruited from a healthcare institution, while the typically developing child was recruited using a convenience sampling technique among parents who are volunteers. This study received ethical approval from the institution's research committee. Two children that fit the inclusion criteria, aged ten years old, were involved. Both children had passed their hearing assessment: precise otoscopy examination, normal audiogram, type A tympanogram, and presence of all acoustic reflexes. The exclusion criteria are having fever or flu, presence of comorbidity, and impaired understanding ability (important for understanding and following instructions). The parents have given full written and informed consent for participating and publishing this report.

ABR with psychological task (ST) procedure

Participants were seated in front of a laptop and were advised to remain still to reduce any noise and artefacts in the ABR. Before the test, the skin was prepared by applying Nu-Prep skin preparation gel (Weaver and company, Colorado, USA) to both sides of the high forehead, lower forehead, and mastoid. The disposable silver/silver chloride electrodes (Ambu A/S, Ballerup, Denmark) were placed in the prepared areas. When the patient was ready, the audiologist gave the instructions for ST verbally and in writing. For ST, they must count the digit/s displayed on the screen and respond as quickly and accurately as possible by pressing the correct number key on the numerical keypad. Trials in each ST condition were presented randomly (60 trials of neutral, 60 trials of congruent, and 60 trials of incongruent). These trials were presented on a laptop using the E-prime 3.0 software interface (Figure 1). Each trial was displayed for 4000 msec before the interface moved to the following trial. Participants were given practice before they proceeded with the actual task.

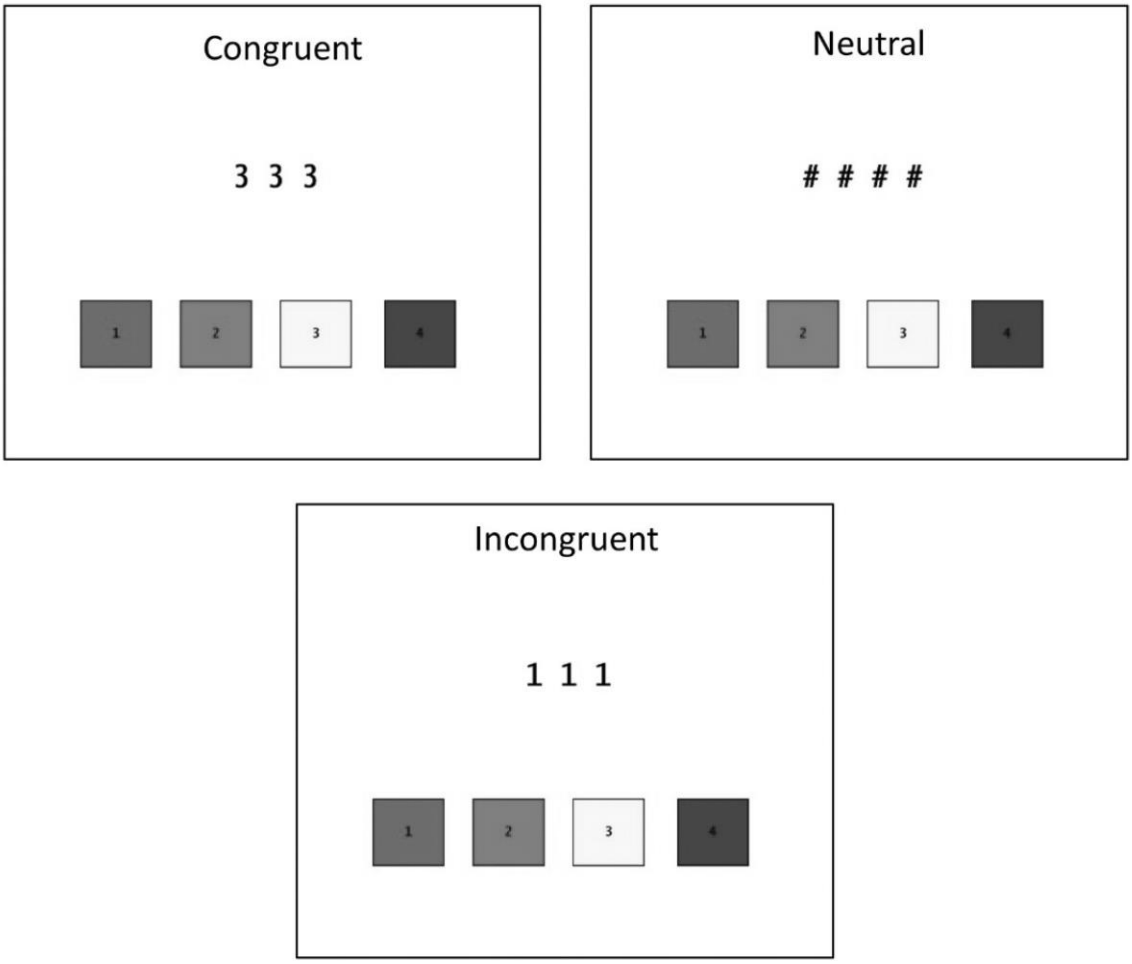


Figure 1: Stroop task condition (congruent, incongruent, and neutral) presented using E-prime 3.0.

The ABRs were recorded at the same time the participant did the ST. The ABR waveforms were recorded in the four conditions: 1) without ST (baseline), 2) neutral, 3) congruent, and 4) incongruent, and the sequence of the four conditions was randomized for both participants. The incongruent condition involves presenting numbers, but the digit display is different from the number of digits presented. For instance, the digit "2" might be written as "3 3". Participants are asked to identify the number of digit while ignoring the actual digit. The incongruence between the digits and number of digits creates cognitive conflict, as there's a tendency to automatically read the digit, which can interfere with accurately identifying the number of digits displayed. As for congruent condition, the digit and number are the same e.g., digit "2" is presented as "2 2". While neutral condition uses symbols instead of digits, for example "# #".

The ABR was elicited by presenting a tone burst of 1000 Hz at 70 dBnHL with a stimulus repetition rate of 33.1 Hz on the test ear (right) through an Eclipse ER-3A insertphone (Interacoustic A/S, Middlefart, Denmark). Meanwhile, white noise was presented as a contralateral masking noise continuously on the non-test ear (left) at 40 dBnHL below the stimulus presentation at the test ear. ABR testing was conducted using two-channel Eclipse ABR equipment (Interacoustic A/S, Middlefart, Denmark). The average response was filtered using a 100 – 3000 Hz band-pass filter to remove unwanted activities unrelated to ABR. The level of individual electrode impedance was maintained below < 5000Ω to ensure an optimal common mode rejection. Two ABR waveforms were recorded from each participant in each condition to check for repeatability.

Data analysis

ABR waveforms in each condition from all participants were analysed based on their presence or absence, the amplitudes and latencies. The cognitive interference of wave V amplitude for each participant was then determined by subtracting wave V amplitudes of ABR in incongruent conditions from wave V amplitudes of ABR in a neutral condition. In addition, the percentage reduction of wave V amplitude (%) was calculated to compare the participants.

For ST, the response time (msec) and percentage score (%) of correct responses from each condition was calculated using descriptive statistics. The response time and percentage score for each participant was calculated by averaging the value from 60 trials in each condition. Next, Stroop interference (measures inhibitory control) for response time and percentage score was determined by subtracting response time / percentage score in incongruent conditions from response time / percentage score in the neutral condition (3).

Typically developing children

A ten-year-old Malay girl came as a participant with her parents. History suggests no significant history related to childhood development, and she did not report any issues with hearing. The audiological assessment results were as follows; (i) a normal audiogram with normal audiometric hearing

thresholds, (ii) tympanometry with type A which suggests a normal middle ear function, and normal acoustic reflex thresholds at all stimulation and frequency bilaterally.

Referring to Table 1, ABR with and without psychological task suggested normal absolute latencies and the presence of wave V amplitudes in all conditions, with the largest amplitude found in the congruent and incongruent conditions. In contrast, the smallest amplitude was found in the baseline ABR (without psychological task). The cognitive interference obtained was 0.13, with a 38.88% increase in wave V amplitude from neutral to incongruent test conditions.

The percentage score is 100% in both congruent and incongruent conditions and 96.67% in the neutral condition. For the response time, the fastest time was obtained from the neutral condition, followed by incongruent and congruent. The Stroop interference for both percentages score and response time are 3.33 and 154.36 msec, respectively (Table 1).

Table 1: Summary of the ABR sensory gating result from a typically developing child and a child with ASD.

ABR with Stroop Task		**ASD**	**Typically development Child**
Baseline	Wave V amplitude	0.520	0.332
	Wave V latency	7.30	6.80
Congruent	Wave V amplitude	0.449	0.457
	Wave v latency	7.43	6.83
	Correct Response (%)	100	100
	Response time (msec)	1035.13	1018.40
Incongruent	Wave V amplitude	0.417	0.456
	Wave V latency	7.33	6.83
	Percentage score (%)	93.33	100
	Response time	1545.68	837.92

	(msec)		
Neutral	Wave V amplitude	0.457	0.326
	Wave V latency	7.37	6.90
	Percentage score (%)	96.67	96.67
	Response time (msec)	1247.82	683.55
Stroop Interference Percentage Score		297.86	154.36
Stroop Interference Response Time		-3.34	3.33
ABR Amplitude Cognitive Interference		-0.04	0.13

Child with ASD

A ten-year-old Malay girl with mild ASD was diagnosed by a psychiatrist when she was five. At the time of the appointment, she has a scheduled appointment with a psychiatrist and occupational therapist. The parent reported that she has no other comorbidity and no history of hearing problems. Her audiological assessment shows normal hearing, type A tympanogram suggesting normal middle ear function and presence of all reflexes bilaterally.

The findings from ABR show normal absolute latencies for wave V in ABR without and with the psychological task (congruent, incongruent, and neutral). The wave V amplitude was the largest from congruent and the smallest from incongruent. The cognitive interference of wave V amplitude was -0.04, with the wave V amplitude reduction of -8.75% was noted.

For the ST (Table 1), the percentage score and response time for congruent, incongruent, and neutral are 100% and 1035.13 msec, 93.33% and 1546.68 msec, 96.67%, and 1247.82 msec, respectively. Stroop interference response time is 560.06 msec, while the Stroop interference percentage score is -3.34.

Typically Development versus ASD child

ABR wave V amplitude and latencies in all conditions show a similar value between the two children. The amplitude of wave V is descriptively larger for the ASD child in the baseline and neutral conditions

and relatively similar in congruent and incongruent conditions compared to the typically development child. This suggest that the sensory gating ability is intact in both child when looking at the findings in congruent and incongruent condition. Also, the difference seen in baseline and neutral might be cause by individual variation. Comparing the findings with the norms, the latency of both children is within normal limits (10). The ABR of the study participants is also valid and reliable based on the robustness of wave V, as expected in typical tone burst ABR recordings (10).

Furthermore, wave V amplitude from neutral to incongruent test conditions was reduced in the ASD child compared to the typically development child with an increment of the wave V amplitude (Figure 2). As for cognitive interference, only the child with ASD shows a negative interference pattern. To ensure that the result obtained is not affected by noise interference, the value for Signal-to-Noise ratio (SNR), F at multiple points (Fmp), and residual noise level (RNL) was computed. The SNR, Fmp, and RNL of the ABR in each condition, in general, exceeded the recommended guideline of i) SNR > 3.0, 2) Fmp >3.1, and 3) RNL sufficiently low < 80nV (11).

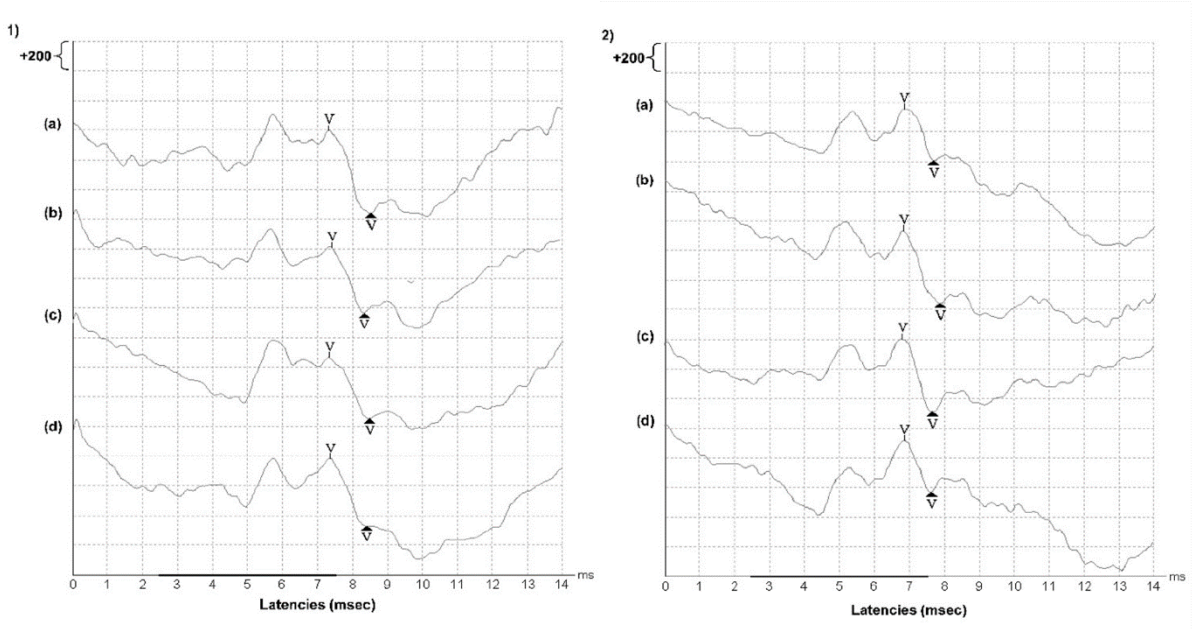


Figure 2: ABR waveform of (1) typically developing child and (2) autism spectrum disorder child in Stroop task condition; (a) baseline, (b) congruent, (c) incongruent, and (d) neutral.

The response time in all conditions was lower for the typically development child than for the ASD child. At the same time, the percentage score is almost similar between the children except for the incongruent condition in which the typically development child scores better than the ASD child. In Stroop interference response time, the typically development child has a smaller value suggesting that she had an excellent cognitive ability to respond better during the challenging task than the ASD child. Stroop interference percentage score also shows a higher value for the typically development child.

DISCUSSION

The information on auditory sensory gating in the brainstem is limited, especially among ASD children. Additionally, it is hypothesised that the ABR has great potential in its applicability as a measurement tool for sensory gating because it is associated with working memory and cognitive function (12). It prompts the investigation using ABR with psychological tasks among ASD children compared to typically development child. The data from this study suggests that the typically development child had a better cognitive response than the ASD child.

In previous ST studies for typically development children, the response time and percentage score decreased and increased respectively from the congruent condition to the neutral condition and finally to the incongruent condition (13). Contrary to this account, the typically development child in this study did not show the classical performance pattern for both ST measurements. To note, mental fatigue as a result from demanding task for a long period of time might influence the percentage score and response time which explain why the findings did not follow the classical pattern. Thus, looking at the normative data from Sulaiman's study (13), the value obtained is within range for normal children's norms in each condition, suggesting that the results are normal even if it did not follow the pattern. The individual result obtained in this study may coincide with some of the individual result in past study (12, 13). Therefore, a clinically significant in comparison to research significant may provide a different finding, which means even the finding is not significant statistically, but a real-life effect might be present that could not be measured due to factors such as sample size.

Furthermore, it can be observed that the typically development child had a better response time in all conditions than the ASD child that suggests better selective attention and sensory gating abilities. This is expected with prior studies (14) which suggest typically development to have faster response suggesting good cognitive ability to inhibit cognitive interference. However, this result also differs from other findings obtained from a prior study (15), which shows comparable results for the response time between typically development and ASD children. Yasumuru's (15) and Zhou (16) findings suggested no deficits in cognitive inhibition in ASD children as measured by the ST. The authors argue that the inhibitory control skills increase from three to six years (17); thus, by the age of seven years old, the inhibitory control is developed, which explains the no difference between ASD and typically development children in inhibitory control skill. Therefore, it is expected that there is not much difference in the response time between the ASD and typically development children. The large difference for incongruent condition partly may be caused by the variety in the spectrum of ASD. Some children may have issue in inhibitory control as compared to the other ASD children as shown by the individual participated in the present study.

On the other hand, facilitation effect was also observed in this study but only in ASD children. The facilitation effect is defined as the fastest Response for the congruent condition compared to the typically development child. The hyper-systemising theory of autism proposed by Baron-Cohen (18) explains that those with ASD have a higher systemising mechanism (SM); the brain processes the information to identify the pattern or law that governs the system. Due to the autistic traits, the ASD child will perform at its maximum or even better, resulting in them noticing the pattern of congruent condition earlier than the typically development child. Although similar to the point discussed in the previous paragraph, the difference is slight and requires further investigation to identify whether the difference is statistically or clinically significant.

Based on the normative value of Stroop interference obtained from a study by Olivia and colleagues (19), the result indicates that the typically development child has normal Stroop interference of correct response while the ASD child did not. A similar study measuring the inhibitory control as revealed by the Stroop interference is comparable to the typically development group suggesting unimpaired inhibitory control (20).

Cognitive interference, as mentioned previously, is the value of amplitude wave V in an incongruent condition minus the value of amplitude wave V in a neutral condition. The value obtained is assumed to be in a negative pattern as the amplitude of wave V in incongruent should be smaller than the neutral due to the suppression or inhibition of the cognition from the ST interference (13). The present finding suggests that the ASD child yielded a negative pattern compared to the typically development child. According to Brännström (3), a few of their normal participants had negative patterns, while others did not. Thus, the participants might not exhibit the negative pattern as the negative pattern is not a universally acceptable result that can be observed even in typically developing children. All the data obtained has a good recording (based on the value of FMP, RNL, and SNR as in the result section), suggesting that technical factors do not influence the results obtained; thus, the result is valid and reliable.

CONCLUSION

To conclude, the present case study highlights the essential features of the sensory gating between an ASD and typically development child: 1) Percentage of the correct response, 2) Response time of correct responses, 3) Facilitation effect, 4) Stroop Interference, and 5) Cognitive interference (ABR). The findings also expand the concept of interference from the ST and the suppression of wave V amplitude in ABR with the psychological task. Extensive research is required to explore this study's key features with a detailed analysis of each component. The information will help us understand the sensory gating mechanism and its relationship with ASD. It is recommended for this study to be extended in the future using a larger sample size using a fully randomized controlled trial experiment method that would allow the researchers to make generalization and to further understand the relationship and the causal-effect between the ST findings and ABR ST findings with ASD.

ACKNOWLEDGEMENT

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DECLARATION OF INTEREST

The authors declare no conflict of interest.

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Validation of Malay-Adapted Nordic Occupational Skin Questionnaire (NOSQ-2002/SHORT) As A Reliable and Specific Screening Tool For Occupational Skin Diseases

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ABSTRACT

Occupational skin disease is one of the most reported occupational diseases. Its prevention is important to ensure good health and quality of life of workers which can be achieved through screening, for which the Nordic Occupational Skin Questionnaire, NOSQ-2002/SHORT was developed. The questionnaire had been adapted and translated into Malay Language for use in Malaysia and other Malay-speaking communities. A cross-sectional pilot study was carried out to check the validity and reliability of the Malay-adapted NOSQ-2002/SHORT, using purposive sampling among a few factory workers in East-Coast Malaysia. The results showed that the finalized version of the Malay-adapted questionnaire has good validity and reliability, with the Cronbach alpha of 0.867. The specificity and negative predictive values were quite high, with the values of 86.0% (95% CI: 80.1, 90.8) and 96.9% (95% CI: 93.6, 98.5), respectively. Even though the sensitivity and positive predictive values were a bit lower at 72.2% (95% CI: 46.5, 90.3) and 34.2% (95% CI: 24.7, 45.2), respectively, it is still higher than previously reported questionnaire used to screen skin condition. In conclusion, the Malay-adapted NOSQ-2002/SHORT is valid and reliable as a screening tool for occupational skin diseases, in which it is inexpensive, simple, and quick to be used.

Keywords: Questionnaire, screening, occupational skin disease, reliable, specific

INTRODUCTION

It has been reported that significant number of workers from different industries are exposed to different irritants which predispose them to several conditions, including occupational skin diseases (OSD), which is one of the most common occupational diseases in many countries (Trotto, 2023; Susitaival et al., 2003). In Malaysia, even though only 436 cases of OSD were reported in 2020, but it constitutes 20.4% of all occupational diseases reported to the Social Security Organization (SOCSO) which is probably an under-reporting, considering the difficulties in confirming the diagnosis of OSD (SOCSO, 2020). It is important to note that these statistics are an increased from 228 or 9.6% cases of OSD reported in 2014 (SOCSO, 2014).

Malaysian government regularly carries out screening for occupational diseases through Occupational Health Surveillance program. The number of workers that need to be screened could be very large, and this could incur a lot of expense, not to mention time-consuming. There is a need for inexpensive and fast yet valid and reliable screening methods to ensure efficient and effective detection of diseases to improve its health outcome (Herman, 2006). One such method is the use of questionnaire, which can be a reliable and specific screening tool for OSD that can be utilized in any industries in Malaysia.

MATERIALS AND METHODS

Source of the questionnaire

Through literature search, brainstorming and discussion sessions with occupational health experts (OHE), it was noted that Nordic Occupational Skin Questionnaire (NOSQ-2002) is one of the questionnaires that is well-documented and commonly used in many countries for screening of OSD. Originally developed in English, NOSQ-2002 has since then been translated into many different languages (Susitaival, 2003; Flyvholm et al., 2002). With support from the

Nordic Council of Ministers, the Nordic Occupational Skin Questionnaire Group had developed the standardized tool, NOSQ-2002, to facilitate research on OSD and environmental factors exposures. Available in a long version to be used in research, and a short version for screening and monitoring of OSD, NOSQ-2002 was developed from experience in combination with several existing questionnaires on OSD (Flyvholm et al., 2002). Since the purpose of this study was to validate a fast and inexpensive screening tool for OSD, the NOSQ-2002/SHORT was adapted for use. Although the Nordic Council of Ministers holds the copyright to the NOSQ-2002 questionnaires, its use is free of charge provided it is not used commercially and available online (Flyvholm et al., 2002).

Adaptation of NOSQ-2002/SHORT into Malay Language

The NOSQ-2002/SHORT was translated from English into Malay language to facilitate its use among the workers in Malaysia. The forward and backward translation process has been conducted by experts in both English and Malay languages, to ensure that the translated questionnaire is acceptable and perform similarly as its original English version by maintaining the cross-cultural function and concept (Su & Parham, 2002). NOSQ-2002 had been verified in many studies, but to complete the validation process, the content validity was checked by several skin specialists and OHE. Content validity explains whether an instrument such as a questionnaire has sufficiently covered all the contents that is associated with a variable (Oluwole-Sangoseni et al., 2013). It is commonly practiced by the rational analysis of the instruments by experts who are familiar with the subject of research (DeVon et al., 2007).

Some changes were made into this Malay-adapted version, in which the images of human hands marked with eczema sites had been included in the items describing the area of eczema to assist the workers in answering the questionnaire. Furthermore, instead of asking when they last had eczema, item 3 of the Malay-adapted NOSQ-2002/SHORT requires the workers to identify whether they have eczema upon starting work at the current workplace. The question on atopic eczema from the original NOSQ-2002/SHORT was omitted because it was not suitable for current research purposes. The finalized Malay-adapted NOSQ-2002/SHORT questionnaire is available in the appendix.

Checking for the reliability and validity of the Malay-adapted NOSQ-2002/SHORT

Study design and area

A cross-sectional pilot study was carried out to check the validity and reliability of the Malay-adapted NOSQ-2002/SHORT. Several factories in East-Coast Malaysia were purposively selected based on the possible hazards found in these factories, to ensure the possibilities of getting positive cases through the screening so that sensitivity and positive predictive value (PPV) of the screening tool can be calculated. Johanson and Brooks (2010) suggested that 30 participants would be a reasonable minimum sample size for a pilot study.

Employees in selected factories had been invited to participate in this study by answering the Malay-adapted NOSQ-2002/SHORT. Afterwards, all the respondents were interviewed and examined by two Occupational Health Doctors (OHDs) to obtain a clinical diagnosis for the OSD. The clinical diagnosis was used as the gold standard to make a comparison between the calculated sensitivity and specificity, as well as the positive and negative predictive values of the screening tool. Then, the two OHDs discussed the cases to ensure that they came to a correct diagnosis for the respondents examined. In cases of any doubt, a skin specialist was consulted using the photos taken during the initial examination.

Statistical Analysis

The data was analyzed using the IBM SPSS Version 24 to determine the validity and reliability of the Malay-adapted NOSQ-2002/SHORT. Validity is the extent to which a measurement accurately measures what it is supposed to measure, while reliability is the repeatability of the measurement (Bolarinwa, 2015; Heale & Twycross, 2015). On that note, Cronbach alpha is one of the most used values to check the internal consistency reliability (ICR) of a tool, method or test (Bolarinwa, 2015; Tavakol & Dennick, 2011). The Cronbach alpha values between 0.70 - 0.95 are usually accepted as a good alpha value for a survey form, though values greater than 0.90 are less favorable as it could be due to the redundancies in the survey form (Tavakol & Dennick, 2011).

Additionally, corrected item-total correlation (ITC) value for each item was also analyzed to show the relevance of each item with the construct of the screening tool where the acceptable values are between 0.3 to 0.7 (De Vaus, 2004). It is interesting to note that the Questionmark blog (2013) claimed that "higher positive values for the item-total correlation indicate that the item is discriminating well between high- and low-performing participants". On the other hand, factor analysis was also done to obtain the loading factor value which shows the relationship of each item in the construct of the screening tool, where the value calculated is considered good if it is greater than 0.4 (Rahn, 2018).

To assess the validity of the Malay-adapted NOSQ-2002/SHORT, crosstab analysis using SPSS had been used to calculate the sensitivity and specificity of the screening tool, as well as the positive and negative predictive values (PPV and NPV, respectively), along with their 95% confidence intervals which were analyzed using a freely available software, MEDCALC Diagnostic test evaluation calculator (MedCalc Software, Belgium).

The U.S. Department of Health & Human Services (2015) defines sensitivity as "the proportion of persons with disease who are correctly identified by a screening test or case definition as having disease" and specificity as "the proportion of persons without disease who are correctly identified by a screening test or case definition as not having disease". On the other hand, PPV and NPV are defined as "the proportion of patients with positive test results who are correctly diagnosed" and "the proportion of patients with negative test results who are correctly diagnosed" (Altman & Bland, 1994). The sensitivity and specificity values are not dependent on the population undergoing the test so can be applied to any population. However, the PPV and NPV depend on the prevalence of the disease in the population being tested. If the prevalence of the disease is high in the population, the PPV will be higher but the NPV will decrease (Lalkhen & McCluskey, 2008).

Ethical consideration

The approval for this study was given by the Malaysian Department of Occupational Safety and Health (DOSH/No. Petender-(03)/04/2016/Rekod) and consent was also obtained from one of the authors of the original NOSQ-2002 through email correspondence. The employers of the workplace involved in this study were agreeable to the data collection, and they were explained regarding the purpose and processes of the study before they answered the questionnaire. The participations were voluntary, and confidentiality of the participants was kept safe where the results were presented in an aggregate form and any participant was not identified individually.

RESULTS

The validity and reliability of the Malay-adapted NOSQ-2002/SHORT are presented in Table 1 for corrected ITC and factor loading, and in Table 2 for sensitivity, specificity, PPV and NPV.

Cronbach alpha, corrected ITC and factor loading of the Malay-adapted NOSQ-2002/SHORT

For analysis purposes, only the items on aggravating factors were analyzed for Cronbach alpha, corrected ITC and factor loading (items 3 to 6). With the Cronbach alpha of 0.867, the ITC and factor loading for all items are more than 0.4 as shown in Table 1, it shows the Malay-adapted NOSQ-2002/SHORT has good validity and reliability of the questionnaire and the items.

Table 1: Validity and reliability of items in the Malay-adapted NOSQ[a]-2002/SHORT by corrected item-total correlation (ITC) and factor loading (n=79)

Items	ITC	Factor loading
3	0.556	0.717
4	0.756	0.874
5	0.814	0.908
6	0.756	0.874

[a]Nordic Occupational Skin Questionnaire

Sensitivity, specificity, PPV and NPV of the Malay-adapted NOSQ-2002/SHORT

In checking for the sensitivity, specificity, PPV and NPV of the Malay-adapted NOSQ-2002/SHORT, the gold standard used was the clinical diagnosis by OHDs, while the screening test was considered as positive when any respondent answered "yes" or "not sure" in item 1 or 2 which asked about the presence of previous or current hand eczema, respectively, in the presence of exposure to hazards in workplace (from the occupational section) or the aggravating factors. The results obtained are shown in Table 2. The specificity and NPV (86.0% and 96.9%, respectively) were higher as compared to the sensitivity and PPV (72.2% and 34.2%, respectively).

Table 2: Validity and reliability of Malay-adapted NOSQ[a]-2002/SHORT by sensitivity, specificity, PPV[b] and NPV[c](n=197).

			Diagnosis		
			Positive	Negative	Total
Screening	Positive	Number	13	25	38
		PPV[b] (95% CI[d])	**34.2% (24.7, 45.2)**	65.8%	
		Sensitivity (95% CI)	**72.2% (46.5, 90.3)**	14.0%	19.3%
	Negative	Number	5	154	159
		NPV[c] (95% CI[d])	3.1%	**96.9% (93.6, 98.5)**	
		Specificity (95% CI[d])	27.8%	**86.0% (80.1, 90.8)**	81.1%
		Total	18	179	197
		Prevalence	**9.1%**	90.9%	100.0%

(95% CI[d])	**(5.5, 14.1)**

[a]Nordic Occupational Skin Questionnaire [b]Positive Predictive Value
[c]Negative Predictive Value [d]Confidence interval

DISCUSSION

The use of questionnaire as a screening tool

In designing a good questionnaire, Stone (1993) described that it should be "appropriate, intelligible, unambiguous, unbiased, capable of coping with all possible responses, satisfactorily coded, piloted, and ethical". Despite their limited sensitivity and specificity which might not be comparable to laboratory or clinical tests, questionnaires have been used as screening tools, not only in the field of occupational health such as the NOSQ-2002, but also in another fields (Starvard et al., 1999; El Sayed, 2012; Tyagi et al., 2021; Ode et al., 2023; Rigal et, al., 2023). In the current study, the NOSQ-2002/SHORT was selected as a tool to screen for OSD because it is widely accessible, simple, and easy to be used by employers and workers. Furthermore, using questionnaires as a screening tool will incur minimal cost, especially for the smaller industries where limited budgets are available for such screening program. Additionally, a questionnaire can be carried out quickly with minimal disruption of the usual processes and activities in the workplace.

The validity and reliability of Malay-adapted NOSQ-2002/SHORT

The result from this study shows that the reliability and validity of the Malay-adapted NOSQ-2002/SHORT is quite good with the Cronbach alpha of 0.867, the corrected ITC of between 0.556 to 0.814 and the factor loading of between 0.717 to 0.908. On the other hand, the sensitivity, specificity, PPV and NPV were 72.2%, 86.0%, 34.2% and 96.9%, respectively. Even though the PPV is quite low, but as explained above, PPV value depends on the prevalence of the disease in the population. In this study, the resulting prevalence of OSD was quite low at only 9.1%, hence the low PPV. The results from this study, however, are quite comparable to the validity and reliability of questionnaire as a screening tool for OSD in other studies, as summarized in Table 3.

It can be seen from Table 3 that the sensitivity of the Malay-adapted NOSQ-2002/SHORT in current study (72.2%) is lower as compared to the Italian (86%) (Chiesi et al., 2016) and Spanish (96.5%) (Martí-Margarit, 2015) versions, but this could be due to the short version of NOSQ-2002 used in the current study. However, the current sensitivity is higher than a few previous studies (Meding & Barregård, 2001; Vermeulen et al., 2000). It is good to note that the specificity achieved in the current study is quite good at 86%, which is higher than the Spanish NOSQ-2002 (75.2%) and symptom-based questionnaire (Martí-Margarit, 2015; Vermeulen et al., 2000). High specificity means that it is almost assured that a negative screening test means the subject can be ruled-out from the disease or the person does not have the disease of concerned (Safari et al., 2015).

Table 3: Comparison of the validity and reliability of questionnaires as the screening tools for skin disease.

Screening tool used	Population studied	Cronbach alpha	Sensitivity	Specificity
Malay NOSQ[a]-2002/SHORT (current study)	Factory workers	0.867	72.2%	86%
Italian NOSQ[a]-2002 (Chiesi et al., 2016)	Patients	0.88 and 0.97	86%	89%
Spanish NOSQ[a]-2002 (Martí-Margarit, 2015)	Workers in cleaning company	-	96.5%	75.2%
Hand eczema in past 12 months (Meding & Barregård, 2001)	Car mechanics, dentists, and office workers	-	53-59%	96-99%
Symptom-based questionnaire (Vermeulen et al., 2000)	Rubber workers	-	71.4%	76.1%
Self-reported (Yngveson et al., 1997)	Schoolchildren	-	73%	99%

[a]Nordic Occupational Skin Questionnaire [b]United Kingdom

Current study used clinical diagnosis as the gold standard to base the sensitivity and specificity of the screening tool evaluated, similar to a number of other studies evaluating questionnaires to screen hand dermatitis, either as occupational-related or not (Meding & Barregård, 2001; Vermeulen et al., 2000; Yngveson et al., 1997). In many of these studies, the criteria for clinical diagnosis or positive cases from the questionnaire were not explicitly defined, which might create a problem due to the variability in interpreting the positive cases when the comparison between these studies are to be made (Susitaival, n.d.). To overcome this problem, Nordic Occupational Skin Questionnaire Group had come up with a standardized NOSQ-2002 for OSD and the UK Working Party had come up with a minimum set of discriminating criteria to diagnose atopic eczema (Susitaival et al., 2003; William et al., 1994). A standardized criteria to diagnose contact dermatitis, especially as an OSD could have been developed to minimize the variability to facilitate valid comparison between researchers.

CONCLUSION

With the Cronbach alpha, sensitivity and specificity of 0.867, 72.2% and 86.0%, respectively, the Malay-adapted NOSQ-2002/SHORT has good validity and reliability. It is inexpensive and suitable to be used as a screening tool for OSD in Malaysia or any Malay-speaking population. It can be applied easily and completed quickly in identifying OSD among workers, hence preventing it from becoming a chronic condition.

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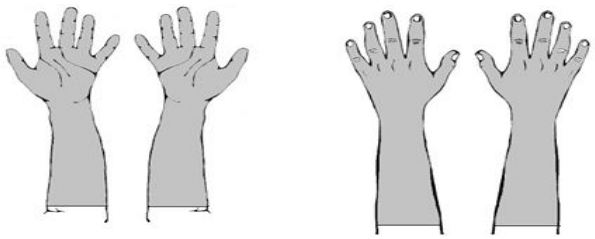
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Appendix: The Malay-adapted NOSQ-2002/SHORT

1. Pernahkah anda menghidapi ekzema tangan atau / dan pergelangan tangan atau / dan lengan bawah (kecuali pada pelipat siku)?
   Definisi ekzema: keradangan (kemerahan) pada kulit yang disertai dengan kekeringan kulit, lelehan, sisik atau keruping, dan menyebabkan pesakit rasa gatal dan tidak selesa
   ☐ Ya
   ☐ Tidak
   ☐ Tidak pasti



2. Adakah anda masih mengalami ekzema itu sekarang?
   ☐ Ya
   ☐ Tidak

Terus ke soalan berikut jika anda menjawab "Ya" atau "Tidak pasti" pada soalan 1 atau 2 di atas.

3. Adakah anda mula mendapat ekzema tersebut di atas apabila anda mula bekerja di tempat kerja sekarang?
   ☐ Ya
   ☐ Tidak
   ☐ Tidak pasti

4. Adakah anda perasan sentuhan dengan bahan tertentu, bahan kimia atau bahan-bahan lain **di tempat kerja anda** membuatkan ekzema anda semakin teruk?
   ☐ Ya
   Bahan apa? : _____
   ☐ Tidak
   ☐ Tidak pasti

5. Adakah anda perasan sentuhan dengan bahan tertentu, bahan kimia atau bahan-bahan lain **di luar tempat kerja anda** membuatkan ekzema anda semakin teruk?
   ☐ Ya
   Bahan apa? : _____
   ☐ Tidak
   ☐ Tidak pasti

6. Adakah ekzema anda bertambah baik apabila anda berada jauh dari tempat kerja biasa anda? Contohnya hujung minggu atau tempoh yang lebih lama.
   ☐ Ya
   ☐ Tidak
   ☐ Tidak pasti

THE RELATIONSHIP BETWEEN MEDIAN NERVE COMPRESSION IN THE CARPAL TUNNEL AND SLEEPING POSITION: A SYSTEMATIC REVIEW

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ABSTRACT

Median nerve compression is reported to be the most common nerve compression in the upper extremity, especially in the carpal tunnel. Carpal tunnel syndrome (CTS) is a condition where the median nerve is entrapped in the narrow passageway that is covered by carpal bones and ligaments which is called the carpal tunnel. Despite the common symptoms such as numbness and tingling sensation in the median nerve distribution, many studies have agreed to characterize nocturnal paresthesia as one of the CTS symptoms. These symptoms have been frequently reported to cause a sleep disturbance to the patients at night. According to recent research, sleeping position is reported to be the provocative factor to the symptoms, while some studies reported that alteration in sleeping position can reduce the symptoms. Hence, this study objectively aims to identify the relationships between median nerve compression in the carpal tunnel and sleeping position through a systematic review. This review followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) as the main guideline. This study retrieved all selected articles from online databases such as PubMed, Scopus and ScienceDirect and from other sources such as Google Scholar that were published from 2010 to 2022. The articles were screened through the titles and abstract and were further reviewed and evaluated for eligibility. Only four articles that meet the inclusion criteria were included in this study. The included articles were then assessed for the risk of bias by using Crowe Critical Appraisal Tools (CCAT). The data from the selected articles were then analyzed and extracted for the results. Our assessment suggests that lateral side sleeping is the most preferred sleeping position in CTS patients that increased the symptoms at night. This study has a limitation where least research articles were published that are concerned about the association between nerve compression and sleeping position despite the frequent complaint of the symptoms at night. It is suggested for the future researchers to include the possible associations such as pain intensity, BMI, nature of work, the use of night splint and preferred hand position during sleeping in their study.

INTRODUCTION

Peripheral nerve compression syndrome (PNCS) is a condition that can be described as a chronic irritation or pressure palsies in the area of anatomical constriction (Assmus, Antoniadis & Bischoff, 2015). Besides, it also can be defined as a condition where the nerve is entrapped at various anatomical locations in the extremities (Strohl & Zelouf, 2017). According to Mansuripur, Deren and Kamal (2013), Doughty and Bowley (2019), and Nicholls and Furness (2019), upper extremities entrapment neuropathies are a common form of peripheral nerve compression, especially within the carpal tunnel at the wrist area that compresses the median nerve which is also known as Carpal Tunnel Syndromes (CTS).

Median nerve neuropathy is the most common peripheral nerve compression in the upper extremities where the frequently reported cases of entrapment were in the carpal tunnel of the wrist (Assmus et al., 2015). The statistic showed that median nerve entrapment cases that occur at various sites along with the median nerve distribution are approximately about 7% to 10% (Boyd, Singh, Robin, & Sharma, 2021). It is reported that the median nerve can also be compressed in four locations of the elbow where are at the supracondylar process, the lacertus fibrosus, at the origin of the flexor digitorum superficialis (FDS) and between the head of pronator teres (PT) between the humeral and ulnar head which can trigger to pronator teres syndrome (PTS) (Hussain & Winterton, 2016). However, the cases are very rare to be compared with median nerve entrapment in the carpal tunnel of the wrist (Dididze, Tafti & Sherman, 2018).

Prevalence showed an estimation of 10% to 15% of the incidence risk of CTS in a lifetime and approximately 2% in developed countries (Hussain & Winterton, 2016; Doughty & Bowley, 2019). CTS is widely known as an occupational disorder that occurs especially in men and affects bilaterally in about 50% of cases (Hussain & Winterton, 2016). It is mainly reported to be involved with a repetitive movement of the wrist flexion and extension and may be due to vibration of the wrist through machinery tools (Mansuripur et al., 2013; Hussain & Winterton, 2016; Meyer, Lintingre, Pesquer, Poussange, Silvestre & Dallaudière 2018; Nicholls & Furness, 2019).

Generally, median nerve compression shared the same clinical manifestation with another nerve compression in the upper extremities which affects the sensory and motor innervation (Hussain & Winterton, 2016). The common symptoms were neuropathic pain, numbness, loss of sensory and weakness of the muscle that may progress to functional disability depending on the affected nerve distribution (Mansuripur et al., 2013). According to Hussain and Winterton (2016), most CTS patients reported having numbness and tingling sensation, hand clumsiness and nocturnal paresthesia. This neuropathic pain may also cause a sleep disturbance for a patient at a chronic stage.

Prevalence shows that patients who complained of having chronic pain with sleep disturbance range between 50% to 80% and the severity of sleep disturbance depends on the pain intensity (Ferini-Strambi, 2017). Nocturnal pain or night paresthesia are commonly characterized as one of the early symptoms of CTS (Nicholls & Furness, 2019). According to Ferini-Strambi (2017), the relationship between neuropathic pain and sleep disturbance is bidirectional. McCabe, Uebele, Pihur, Rosales and Atroshi (2007) reported in their literature that there is a possible association that sleeping position is the causative factor of CTS. Wahab, Sanya, Adebayo, Babalola and Ibraheem (2017) also supported the statement by suggesting in

their literature that sustained hand or arm position could be the causative factor of CTS.

However, McCabe et al. (2007) mentioned in their study that the relationship between the sleeping position as the possible causative mechanism of the nerve compression syndrome, mainly in CTS, is still less clear and needs further study. Thus, this study aims to systematically review and evaluate and highlight the relationship mainly between median nerve compression in the carpal tunnel and sleeping position besides evaluating any preferred sleeping position in CTS patients as possible management to reduce the pain.

Nocturnal paresthesia that awakes CTS patients at night can be such a disturbance for the patients as it reduces sleep quality in most patients (Patel, McCabe & Myers, 2012; Patel, Culbertson, Patel, Hashem, Jacob, Edelstein & Choueka, 2014; Karatas, Kutluk, Akyuz, Karaahmet & Yalcin, 2020). It is reported by Patel et al. (2012) that approximately 80% of CTS patients complained of waking up at night from experiencing paresthesia of the wrist. It is supported by Karatas et al. (2020) who also reported that bilateral CTS patients in their findings also showed significantly higher results of waking at night especially in mild to moderate cases. This showed that it is indeed the symptoms that are disturbing and affecting the patient's sleeping quality.

According to the study by Karatas et al. (2020), some CTS patients are reported to change their sleeping position at night which they find comfortable and less painful in the wrist. In addition, McCabe et al. (2007) and Patel et al. (2014) suggested that malposition of the wrist can increase within the carpal tunnel and trigger the CTS symptoms during sleep. However, even though many studies noted that nocturnal paresthesia are characterized as one of the CTS symptoms (McCabe et al., 2007; Wahab et al. 2017; Boyd et al., 2021), there are still fewer studies that take sleep management such as altering sleeping position as the possible management to reduce the symptoms in CTS patients besides other common management such as physical therapy, medication and surgery (Patel et al., 2014).

The purpose of the study is to find the relevant relationship between a sleeping position with median nerve compression in the carpal tunnel. This is because, most of the research papers are studied about the effect of CTS symptoms on sleep disturbance and sleep quality (Patel et al., 2012; Patel et al., 2014; Karatas et al., 2020). However, there is very little evidence that taking the sleeping position is the causative factor that triggers CTS symptoms at night or as possible management in reducing the symptoms.

METHODOLOGY AND STATISTICAL ANALYSIS

This research study was conducted by systematically reviewing the previously published research papers that mainly focused on sleeping positions in CTS patients. According to Aromataris and Pearson (2014), the goal of systematic reviews is to present a thorough, objective synthesis of numerous pertinent studies in a single document (as cited in Lockwood & Oh, 2017). In this project, Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) were used as the guideline to extract the data and produce a good report writing systematically. PRISMA guidelines provide 4 steps in the selection of published articles which include; identification, screening, eligibility and included studies (Figure 3.1).

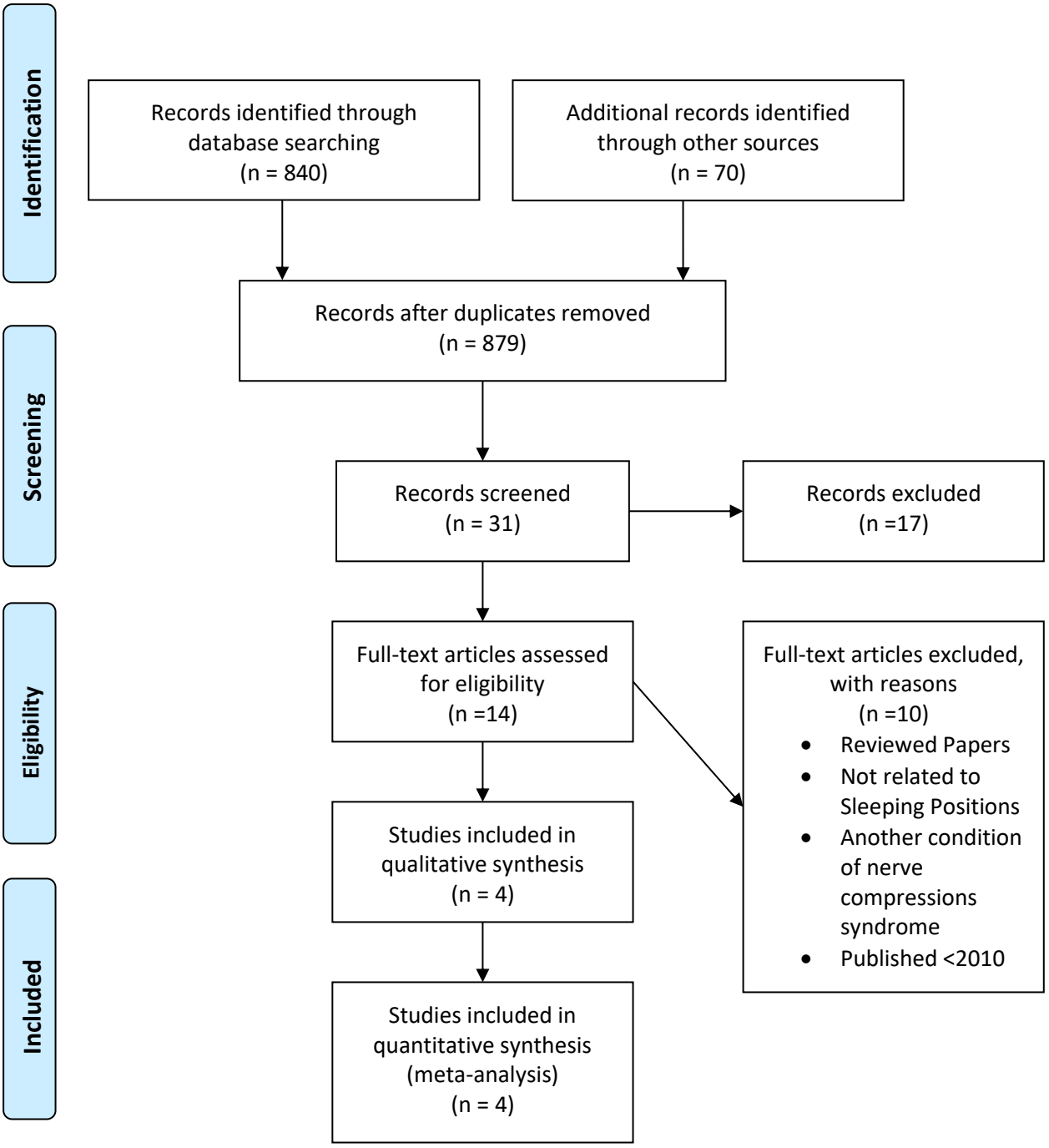


Figure 3.1 PRISMA Flow Diagram

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., & PRISMA Group*. (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Annals of internal medicine*, *151*(4), 264-269. https://doi.org/10.7326/0003-4819-151-4-200908180-00135

IDENTIFICATION

Online databases were used in the process of identifying and searching for the literature related to the topics. Online databases that were used to access the articles are PubMed, and Science Direct. Besides, other sources such as Google Scholar also is used to search the articles. During the article searching process, the Boolean Operators which are simple words like 'AND', 'OR', and 'NOT' were used in the combining words. The specific keywords used during the searching process in the study are "Carpal Tunnel Syndrome" AND "Sleeping Position" AND "Median Nerve Compression" OR "Median Nerve Entrapment" AND "Night Paresthesia" OR "Nocturnal Paresthesia". The number of the studies or articles found in the online databases and other sources were recorded to be screened.

SCREENING

The compilation of the selected studies is then screened to check for any irrelevant, duplication or redundancy of the articles. The articles were screened through the title and abstract to identify the correlation with the research objectives and research questions. Any irrelevant articles that did not meet the study objectives and research questions are excluded from the study. The remaining article that is relevant to the study objective and research question was to be reviewed and filtered by inclusion and exclusion criteria (Table 3.1). The reasons for the excluded articles were noted and the number of finalized articles was recorded.

Inclusion Criteria	Exclusion Criteria
Full-text articles	Non-assessable to full-text articles
Published within 2010-2022	Published < 2010
English language text	Non-English language text
Research studies	Reviewed articles
CTS patients with night paresthesia	Another peripheral nerve compression syndrome
Related to sleeping positions	Related to sleep disturbance or sleep quality

Table 3.1 List of inclusion and exclusion criteria

ELIGIBILITY

After the screening process, the selected articles were then evaluated to identify the eligibility of the research paper based on PICOS criteria (Population, Intervention, Comparison, Outcome and Study). According to Jain and Sharma (2016), PICOS criteria is an effective framework for reporting clinical characteristics, disease, intervention methods and group comparison. Any articles that meet the PICOS criteria will be finalized and included as review articles. The PICOS criteria are shown in (Table 3.2) below. A flow chart as shown in (Figure 3.2) is the process used to assess and select the relevant articles throughout the eligibility phase.

Population	Adult patients with Carpal Tunnel Syndrome (CTS)
Intervention	Preferred sleeping position that eases the symptoms
Comparison	Sleeping position that triggered the symptoms
Outcomes	Any reliable and valid outcome measures used to measure sleep and CTS symptoms
Study	Any experimental study related to CTS and sleeping position

Table 3.2 PICOS Criteria

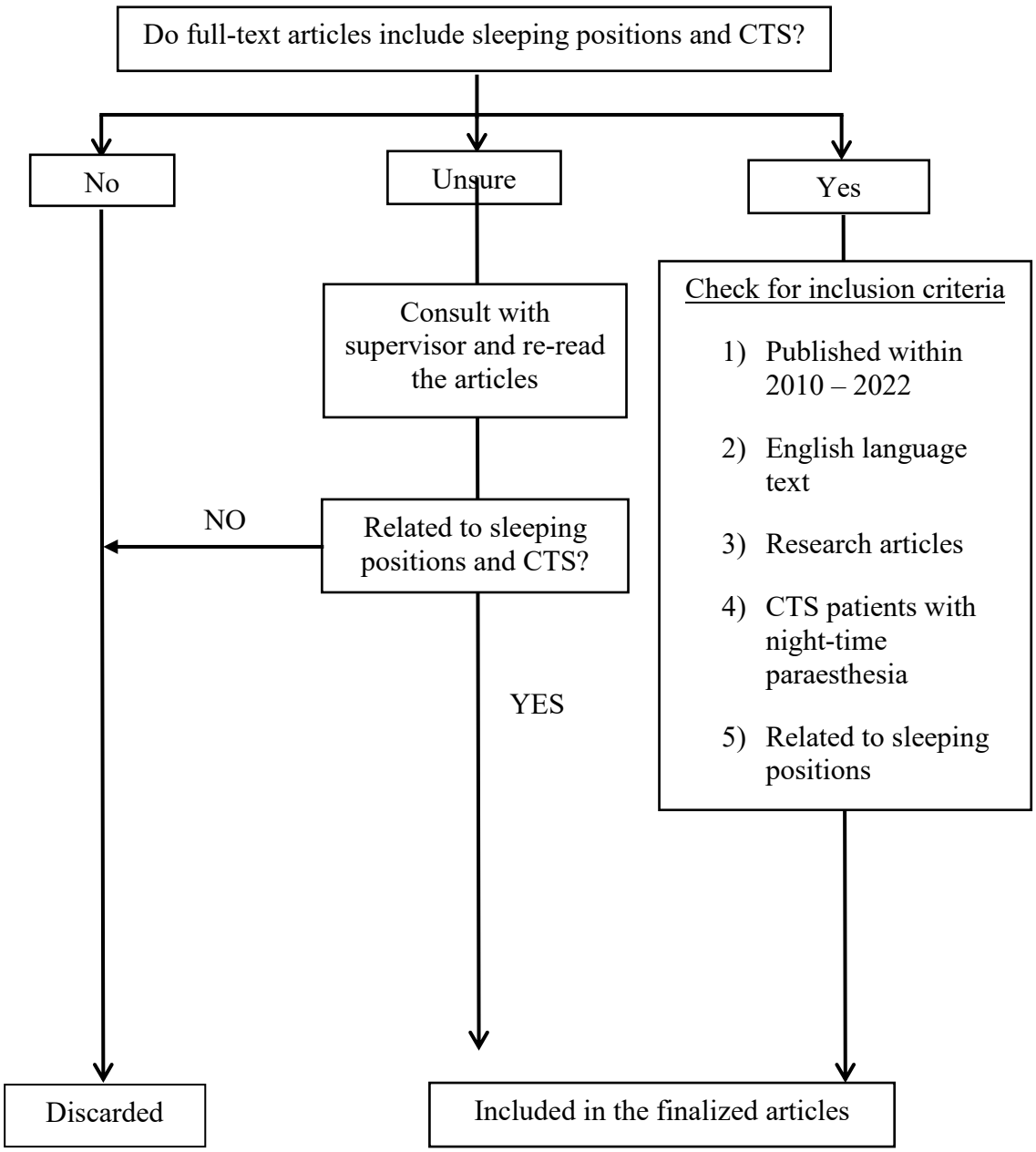


Figure 3.2 Flow chart of eligibility assessment

QUALITY OF ASSESSMENT

Critical appraisal is a structured method of evaluating research so that decisions can be made using the best evidence available (Crowe, Sheppard & Campbell, 2012). Hence, in this study, the quality of the finalized selected research paper is assessed by using the Crowe Critical Appraisal Tool (CCAT). In the CCAT checklist form, there are eight categories to be assessed which include preliminaries, introduction, design, sampling, data collection, ethical matters, results and discussion. Furthermore, Nicoll, MacRury, Woerden and Smyth (2018) stated that instead of focusing only on the overall study score, the CCAT highlights the value of measuring and documenting results for each of the areas. According to Crowe et al. (2011), CCAT was more reliable appraisal tools compared to informal appraisal of the research papers. Besides, CCAT assists researchers to analyze research papers more systematically and efficiently.

REPORTING RESULTS

The data from the selected relevant articles were presented in the form of a table adapted based on the Guidelines of Systematic Reviews by the American Occupational Therapy Association (AOTA), updated in December 2020. The data included in the table are the author and year of publication, title, study design, CCAT score, patients (number and inclusion criteria), results and outcomes of the studies.

RESULTS

STUDY SELECTION

This systematic review collected the articles from online databases such as PubMed (*n* = 11) and ScienceDirect (*n* = 829) which initially provided (*n* = 840) total number of articles. Besides, in other sources such as Google scholar, it yielded (*n* = 70) number of references. Hence, the subtotal of the overall identified studies was (*n* = 910) and (*n* = 879) of duplications were removed. Only (n = 31) articles are proceeded for screening through titles and abstract and (*n* = 17) articles were excluded with reasoning. The remaining articles were evaluated according inclusion and exclusion criteria as shown in (Table 3.1). From (*n* = 14) articles, only four articles that meet the inclusion criteria and were finalized to be included in the systematic review and the remaining articles were discarded.

STUDY CHARACTERISTICS

This study included a total of four articles that meet the inclusion criteria. The study design used in three out of four articles are cross-sectional study (Betlach et al., 2019; Iranmanesh et al., 2015; McCabe and Xue, 2010) while another remaining article used case-control study design (McCabe et al. 2011). All the articles included mainly studied the association of the preferred sleeping position in patients with CTS. (Table 4.1) listed the summary of the participants with inclusion criteria, main results, outcome measures and limitation of the included studies.

Table 4.1 Characteristics of the included studies

Author/Year Titles	Study design CCAT Score	Participants Inclusion Criteria	Main Results	Outcome Measures	Study Limitation
Betlach et al. (2019) Preferences in Sleep Position Correlate with Nighttime Paresthesias in Healthy People Without Carpal Tunnel Syndrome	Cross-sectional study 88%	*Participants* N = 396 *Inclusion criteria* Healthy Volunteers (above 23 years old) Patient populations Young adult population	*Significant findings* *a) Demographics* 1) Participants older than age 40 years are significantly frequent in experiencing nocturnal paresthesia (n = 33, 20.2%) compared to the age below than 21 years (n = 7, 5.0%) *Clinical insomnia is more likely to exhibit in those who frequently experience nocturnal paresthesia *b) Logistic Regression Analysis* 1) Frequently self-reported of nocturnal paresthesia were significantly associated with	*Insomnia Severity Index*	*Study Limitations* Limited evidence regarding sleep position as a potential cause of CTS Multifactorial disease using self-reported survey are not properly studied Lack of accuracy of the model that indicating potential risk factors for nighttime paresthesia in the survey Lack in assessing the relationship between the risk factors

			BMI (P < .001) and diagnosis of CTS (P = 0.001) compared to those who reported of rare occurrence of the symptoms 2) Frequent nocturnal paresthesia is significantly associated with the wrist in a flexed position during sleeping (P = 0.03) 3) Reduce in nighttime paresthesia is significantly associated with sleeping position specifically on lateral side sleeping (P = 0.003) *c) Subgroup Analysis* 1) Nighttime paresthesia is reportedly less significant in young adults below 21 years that preferred sleeping with straight wrist position compared to other preferred wrist positions (P = 0.015) 2) Increasing in nighttime paresthesia is significantly associated with young adults above 21 years old without	

			CTS diagnosis and with increase in BMI (P = 0.002) 3) There is a significantly less frequent event of nocturnal paresthesia that associated with sleeping in wrist straight position (P = 0.016) *Non-significant findings* 1) No significant association noted between preference of sleeping position and frequency of nocturnal paresthesia or with gender and BMI *Other Findings:* 1) Increasing age in the study population, increasing preference in sleep only on the lateral position (P = 0.003)		
Iranmanesh et al. (2015) Sleep position in patients with carpal tunnel	Cross-sectional study	*Participants* N = 540 (two groups) *Inclusion criteria* *n = 220 (patients)* 1) Patients with	*Significant findings* 1) Frequency of sleeping positions is significantly less in patients compared to control groups (P = 0.04)	*Electromyography* (used to confirmed CTS diagnosis for inclusion criteria)	*Study Limitation* Lack of case-control studies conducted related to sleeping positions and CTS Not include snoring as potential sleep disorder

syndrome	85%	unidentified cause of CTS 2) BMI < 30 3) Able to identify sleeping positions 4) Does not have any sleeping disorder 5) Not an alcohol or drugs addict *n = 320 (control)* 1) Healthy participants 2) Patients' relatives 3) Same age and sex with the patients	2) Right side CTS is significantly associated with sleeping positions compared to the left side CTS (P = 0.0001) *Non-significant findings* 1) Age and sex between two groups showed no significant difference 2) Severity of CTS has no significant association with sleep position (P = 0.07) *Other Findings* 1) Prevalence of CTS is significantly higher in lateral side sleeping compared to other sleeping positions		
McCabe et al. (2011) Preferred Sleep Position on the Side is Associated with Carpal Tunnel Syndrome	Case-control study 85%	*Participants* N = 206 (two groups stratified by age, gender and controlled BMI) *Inclusion Criteria* *n = 68 (patients)* 1) Patient who had	*Significant findings* 1) A significantly difference showed in men with CTS preferred side sleeping compared to control population (28.6%; P<0.001) 2) Women patients under age 60 years old significantly	*Katz-Stirrat Hand Diagram* *CTS-6 probability instrument* (reported by Graham, 2008) *CTS disease-specific symptom severity*	*Study Limitation* 1) Small sample size 2) Not include work attribution of CTS

		hand diagram score of "classic" or "probable" 2) Patient with complaint of numbness and tingling sensation of the hands mainly due to CTS 3) Have information gathered about sleep position before diagnosis and patient entry 4) CTS cases that are not caused by the anatomic factor *n = 138 (control)* 1) Patients from previous (2010) cross-sectional survey 2) Patients reported had no history of waking at night due to paresthesia	showed higher preference in side sleeping compared to participants without CTS (OR = 8.7, 95% CI 1.9-39.4, P = 0.05) 3) Women under age 60 years who preferred side sleeping were still showed a significant association to CTS after BMI adjustment (OR = 8.0, 95% CI 1.7-37.7, P = 0.016) *The association between CTS and lateral side sleeping remained significant with change of women age to 63 years and below *Non-significant findings* 1) There were no significant showed between presence of CTS and BMI in men *Other findings* *Control Populations* 1) Patients with no nocturnal paresthesia who preferred side sleeping (59.7%) were significantly less than	*score* (revised by Atroshi et al., 2007)

		3) Had selected preferred sleeping position from previous survey (2010)	patients with nighttime paresthesia who preferred side sleeping (75.7%) *The lateral side sleeping had a strong association with presence of CTS especially in men and women under age 60 years old		
McCabe and Xue (2010) Evaluation of Sleep Position as a Potential Cause of Carpal Tunnel Syndrome: Preferred Sleep Position on the Side is Associated with Age and Gender.	Cross-sectional survey 78%	*Participants* N = 247 *Inclusion Criteria* 1) Primary care setting's patients (used as control group for further case-control study)	*Significant findings* 1) Women showed higher significant in sleeping on lateral side with unadjusted OR 2.7 (P<0.001) 2) Women had significantly strong association between age and sleeping position compared to men (P<0.001) *Non-significant findings* 1) Age in men and sleeping position showed no significant association 2) No significant association showed between sleeping position and BMI 3) Lateral side sleeping and	*Insomnia Severity Index*	*Study Limitation* 1) Insufficient sample size 2) Inefficient in measuring sleep position 3) Limited in association

	insomnia score had no significant association	

***Note. BMI= Body Mass Index; OR= Odd Ratio; CI= Confidence Interval*

Table 4.2 Crowe Critical Appraisal Tool (CCAT) summary

Author/Year	CCAT Category								
	Preliminaries	Introduction	Design	Sampling	Data Collection	Ethical Matters	Results	Discussions	Total score, n (%)
Betlach et al. (2019)	5	5	3	4	5	3	5	5	36 (88%)
Iranmanesh et al. (2015)	4	5	3	4	5	3	5	5	34 (85%)
McCabe et al. (2011)	4	5	4	5	4	2	5	5	34 (85%)
McCabe & Xue (2010)	3	5	3	5	4	2	4	5	31 (78%)

BIAS ASSESSMENT

This systematic review used CCAT to assess the risk of bias on the four selected articles and the scores were summarized in (Table 4.2). Most of the data that has been evaluated met the requirement in all categories in CCAT. Among all the categories, the evaluation on the Ethical Matters was the lowest average score because most of the studies do not mention providing the informed consent from the participants which secure the privacy and confidentiality of the participant, funding and conflict(s) of interest in their studies. However, all articles do obtain the ethical approval in the researcher ethics for their studies.

The Design category was the second lowest average score because it evaluated the risk of bias of the studies. Nevertheless, it is recorded that the highest average score among all the categories were both Introduction and Discussion. Generally, only one study scored the total percentage of 78% (McCabe and Xue, 2010) while the other three studies scored above 80% of the total percentage. McCabe and Xue had the lowest score in the preliminaries compared to the other articles which affect the total percentage of their articles. This is because they did not provide informative details regarding their study in the abstract evaluation in the preliminaries category. However, according to the CCAT user guidelines, the total percentage score is to prevent papers that do well overall but poorly in one or more categories from being mixed in with papers that performed well across the board.

RESULTS

This systematic review included four studies that studied the association between sleeping positions in CTS patients. According to the data that has been summarized in the (Table 4.1), it showed that mostly the studies shared the same methods of study whereby, cross-sectional study and only one study used case-control study as the study design. Based on the data collection that has been made, it can be said that the selected participants were mostly patients with CTS from young adults to the elderly and healthy participants were selected as the control group.

The outcome measure that has been used as the measuring tools varies in every article. Only two studies by Betlach et al. (2019) and McCabe & Xue. (2010) were reported to use the same outcome measure which is *Insomnia Severity Index* in their studies in measuring participants' quality of sleep. The finding also noted that most of the studies shared the same limitation whereby they had difficulty in obtaining large sample size, lack of association with possible risk factors and limited evidence explaining sleeping positions and nerve compression.

Based on the findings from the first article which is written by Betlach et al. (2019), lateral side sleeping is the most common preferred sleeping position reported in the study as it is believed that the sleeping position reduced the nighttime paresthesia that was experienced by the participants. According to the demographic data of the study, it showed a significant difference between participants that frequently experienced nighttime paresthesia with increasing age. It can be concluded that as the age increases, the frequency of the individual experiencing nighttime paresthesia increases. It also noted that the more frequent the individual experiencing nocturnal paresthesia, the more likely the clinical insomnia will present.

According to the logistic regression analysis in the articles, participants who frequently reported to experience nighttime paresthesia were significantly associated with BMI and CTS diagnosis compared to participants who reported to have less occurrence of the symptoms. Besides, in the study it is noted that the symptoms had a significant association with wrist flexion during sleeping and that it is reported to decline significantly associated with lateral side sleeping. Hence it can be concluded that sleeping with the wrist in flexion position can provoke the symptoms, while the symptoms are reduced with sleeping in lateral position.

In addition, according to the subgroup analysis in the article, the findings demonstrate that nocturnal paresthesia can affect young adults above age 21 without CTS diagnosis and with higher BMI. The study also illustrated that the symptoms had less significant association in young adults below age 21 that are also preferred sleeping with straight wrist position. Besides, it is reported to have a significantly less frequent association between sleeping with the wrist in a straight position and nocturnal paresthesia. There were no further associations recorded between the preference of sleeping position, nocturnal paresthesia, gender and BMI in the study. Hence the main report that can be concluded from the findings is, as the age increased in the study population, the preference in sleep specifically on the lateral position increased.

In the study by Iranmanesh et al. (2015) that conducted a cross sectional study, it observed two groups of participants which divide the patients with CTS and healthy participants as the control group. The findings illustrated the frequency of sleeping position in patients was less significant compared to the control group. It is also demonstrated that patients with right side CTS were more likely to be affected with sleeping positions compared to the left side CTS. The study reported no significant difference in age and gender between the two groups and the sleeping position does not affect the severity of CTS. Iranmanesh et al. (2015) also highlighted in the study that lateral side sleeping showed a significant association with the prevalence of CTS.

McCabe et al. (2011) is the only study in this review that reported to conduct a case control study that include two group of participants whereby the participants for the case group are the new patients that is reported with CTS and the control group was selected from the patients that previously reported of having no history of nighttime paresthesia from the previous survey that was conducted by McCabe and Xue (2010). Compared to other sleeping positions, lateral side sleeping has been reported to be the most preferred sleeping position by CTS patients that is severalized by both age and gender in this study. The study demonstrated a significant difference in male CTS patients where they were more preferred side sleeping compared to control population.

Besides, it is reported that female CTS patients under the age of 60 were significantly associated with side sleeping compared to the participants without CTS. It is also noted that the preference of side sleeping in women under the age of 60 remained to be significantly associated with CTS even after BMI adjustment. With the change of women's age to 63 years and below, the association between lateral side sleeping and CTS also remained significant. However, the results illustrated the contrast in men where it is noted to have no significant association between the presence of CTS and BMI. In short, the study highlighted that presence of CTS especially in men and women under age 60 years old that also experience nocturnal paresthesia had a strong association with lateral side sleeping.

Finally, according to the findings by McCabe and Xue (2010) that conducted a cross-

sectional survey study illustrated that women had a higher significant association in the lateral side sleeping and age compared to men. The non-significant findings that were presented in the study are men had no significant association with sleeping position and sleeping position had no relationship with BMI. It is also noted that lateral side sleeping had no significant association with insomnia score. To conclude, the study demonstrated that women CTS patients was more preferred sleeping in side lying and were influenced by their age compared to men.

DISCUSSION AND CONCLUSION

The findings describe the most common sleeping position in patients with CTS that also showed a significant association with age, gender and BMI of the participants. Basically, the median nerve compression in the carpal tunnel that is called CTS is the most common neuro compression in the upper extremity (Patel et al., 2014; Meyer et al., 2018). Many factors and risk factors can result in CTS. The most reported cases were noted to be mainly associated with female gender with increasing age as the common risk factor of CTS (Assmus et al., 2015; Hussain & Winterton, 2016).

The symptoms of the neuropathic pain, numbness and tingling sensation in the wrist were initially treated through conservative management to control the pain and if the symptoms worsen, it will then refer to proceed with surgical management. However, the noted symptoms of nighttime paresthesia were usually managed by wearing a night wrist splint to ease the pain and were rarely to be managed through sleeping position alteration despite the common complaint of the symptom (Wahab et al., 2017). Through the review that has been made, the findings also showed the limitation in the previous study obtaining research papers that studied in this field.

All four research papers that have been included in the systematic review specifically discussed the association of sleeping position in the CTS patients that includes other possible risk factors that may affect the symptoms and mostly was conducted through cross sectional study and only one article that conducted case-control study. Since nocturnal paresthesia has been characterized as the common symptoms of CTS, the criteria were included as the inclusion criteria in all four articles. However, only research by McCabe et al. (2011) and Betlach et al. (2019) presented in detail regarding the association between nighttime paresthesia and sleeping position.

Yet, the findings were noted to be contrast in the both articles. According to McCabe et al. (2011), patients who preferred side sleeping are more likely to report that the position provokes the symptom, while Betlach et al. (2019) presented in their findings side sleeping position was reported to reduce the symptom at night. Besides, Betlach et al. (2019) also believed in their study that the symptoms presented in young participants is due to the variables of lifestyle, ergonomics and posture. The study also hypothesized that the pressure of the median nerve in the carpal tunnel is increased with certain hand position, for instance hand-fisted position during sleeping triggered the CTS symptom.

All of the four studies showed that lateral side sleeping is the most preferred sleeping position especially as it is increased in age. However, the findings presented in the four studies had different arguments but agreed that side sleeping position is closely related with nighttime paresthesia and CTS. Three studies reported by Iranmanesh et al. (2015), McCabe et al. (2011)

and McCabe and Xue (2010) discussed the contribution of the lateral side sleeping in provoking the symptoms of CTS at night. This goes with the theory discussed by Iranmanesh et al. (2015) their study whereby, extension and flexion of the wrist increased in lateral side sleeping which then caused the compression of the median nerve in the carpal tunnel and lead to the increase of the prevalence of the cases. This is supported by McCabe et al. (2011) which also had an almost similar theory where they believed the possibility of the wrist to deviate and positioned in wrist flexion and extension when sleeping on the lateral side would eventually increase the pressure in the carpal tunnel and provoke the pain.

In contrast, Betlach et al. (2019) argued in their study that lateral side sleeping with neutral hand position resulted in less frequent event of nocturnal paresthesia but agreed that with the theory that describe wrist in flexed position during sleeping resulted in frequent nocturnal paresthesia. Furthermore, Iranmanesh et al. (2015) also noted that the severity of CTS with sleeping position had no significant association. They just conclude that sleeping position can be the possible causative factor of CTS and the theory is supported by McCabe et al. (2011) and McCabe and Xue (2010).

According to the findings from the article review, it can be synthesized that lateral side sleeping is more likely to be associated with the women population compared to male. Only studies by McCabe et al. (2011) and McCabe and Xue (2010) provide detailed description findings of the association between sleeping position and gender with the variation of age. The study by Betlach et al. (2019) reported having no relationship between preferred sleeping position and gender, while the study from Iranmanesh et al. (2015) presented, age and gender between both groups in their study had no relationship associated.

McCabe et al. (2011) discussed in their article, the occurrence of CTS cases was most likely in men and women under age 60 years old with preference of lateral side sleeping. They noted in their study, the significant association between lateral side sleeping and CTS cases with the change of women's age to 63 and below was maintained. However, they also discussed in their study that women with CTS were less preferred in lateral side sleeping compared to the control populations in the study.

In contrast, the result from the previous study by McCabe and Xue (2010) reported only women patients showed a significant difference in lateral side sleeping and had a strong influence of age in sleeping position compared to men patients. They also reported having no significant association between men and sleeping position. Nevertheless, it can be concluded that CTS patients in both genders showed the preference of sleeping on the side as the age increases despite the occurrence of the symptom nocturnal paresthesia at night. This can be theorized that lateral side sleeping as the possible factor that provoke the symptom at night

In the literature by Betlach et al. (2019), participants aged 40 years and in young adults above age 21 years without diagnosis of CTS and with increase of the BMI were reported to experience nighttime paresthesia more frequently compared to the age of 21 years and below. The possible theory that can be concluded for the young adult aged 21 years and below that experienced the symptoms was due to the occurrence of different nerve entrapment in the upper extremity that may be caused by malposition of the arm and hand at night.

From the overall review, three articles were noted to include BMI measurement as the possible variable in their studies. However, the findings were presented with different results in every

studies. Based on the previous study by McCabe and Xue (2010), the findings showed no significant difference between BMI and sleeping position. In contrast, in the study by McCabe et al. (2011) found that with BMI adjustment, women under age 60 years who preferred sleeping on the lateral side had a significant association with CTS. Betlach et al. (2019) also agreed that the symptom of nighttime paresthesia was influenced by BMI and was associated with patients with diagnosis of CTS and young adults above agde 21 without diagnosis of CTS. In short, BMI may contribute as the possible variable causing the nerve entrapment in the upper extremity.

This review strongly concludes that sleeping position mainly in lateral side sleeping had a contribution in triggering CTS symptoms at night even though according to recent study by Betlach et al. (2019) lateral side sleeping is shown to ease the pain at night. However, from the overall review, it can be strongly concluded that lateral side sleeping was noted to be the most preferred sleeping position in patients with CTS either it triggered or ease the symptoms at night. Thus, this systematic review demonstrates the importance of recognizing sleeping positions as one of the possible risk factor or management to either provoke the symptoms of ease the pain in CTS patients as it is significantly associated with the symptoms of nocturnal paresthesia that has been recognized by most of the researchers as one of the common CTS symptoms (Mansuripur et al., 2013; Hussain & Winterton, 2016; Nicholls & Furness, 2019; Boyd et al., 2021).

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ASSOCIATION BETWEEN LEVEL OF FATIGUE AND PHYSICAL ACTIVITY OF POST-COVID-19 SURVIVORS AMONG IIUM KUANTAN COMMUNITY

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ABSTRACT

Introduction: Post-COVID-19 fatigue is symbolic in discussing long COVID. The new emergence of barriers might cause a deterioration in physical activity levels. **Objective**: This study aims to address the level of fatigue in post-COVID-19 survivors among the International Islamic University Malaysia (IIUM) Kuantan community and its association with the level of physical activity. **Method**: A cross-sectional study design was conducted on 75 IIUM Kuantan communities using a convenience sampling method based on the inclusion and exclusion criteria. All respondents answered a questionnaire on the demographic data, Fatigue Severity Scale (FSS) and a short-form version of the International Physical Activity Questionnaire (IPAQ-SF). Descriptive statistics, independent t-test and Chi-square test were applied to analyze the data. **Result**: The mean age of the respondents is 23.64±5.795, with an average mean score of FSS 4.242 (SD=1.097). The result shows a significant difference (p<0.001) between low and high fatigue groups with a high prevalence in the latter group. Gender (p=0.176) and recovery period post-COVID-19 (p=0.175) were not associated with fatigue levels. The result of the association between fatigue and physical activity level showed no significant relationship present, with a p-value of 0.703. **Conclusion**: Although there was no association found between fatigue and the physical activity level, the IIUM Kuantan post-COVID-19 community did experience high fatigue. Future prevention can target the correct populations and bring more research on fatigue with other factors such as quality of life (QoL) and functional status.

Keywords: fatigue, physical activity level, post-COVID-19

INTRODUCTION

Coronavirus disease (COVID-19), a global pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has led to 626 million confirmed cases and 6.5 million deaths (as of October 2022) (World Health Organization [WHO], 2022a). In Malaysia, 4.8 million confirmed cases were reported, and 36,458 lives succumbed to the infection (WHO, 2022a). The COVID-19 cases are still doing numbers over the years and despite the effort to fight off the symptoms in the acute phase, the survivors may have yet to battle another persistent state of ill health after the initial infection; known as long COVID symptoms (Nehme et al., 2021).

Malik et al. (2022) in their recent meta-analysis study showed that the effects of SARS-CoV-2 infections could last for weeks to months after the initial infection. The risks of getting post-COVID-19 fatigue are likely to affect females, patients with a longer duration of recovery process, old age, pre-existing depression/anxiety, pre-existing comorbidities, pre-existing autoimmune disease, parents with more children and those with higher levels of vitamin D or ferritin (Joli et al., 2022). Meanwhile, in terms of duration, it is said that patients who continued to experience post-COVID-19 fatigue between 4-12 weeks had higher levels of fatigue, as fatigue is likely to subside after 12 weeks post-infection (National Institute for Health and Care Excellence [NICE], 2022).

One of the post-COVID-19 complications that has attracted many researchers is the decreasing level of physical activity. Wright et al., (2022) found that the PA level did not seem to improve with the duration of long COVID. In a way, it may be caused by the residual symptoms felt by the survivors that hindered them from returning to pre-

COVID-19 activity levels. In some post-COVID-19 patients, there is a decline in physical and/or mental performance resulting from psychological, central and/or peripheral changes following COVID-19 disease (Rudroff et al., 2020). Aldhahi et al. (2022) demonstrated that the level of fatigue among recovered COVID-19 patients in Saudi Arabia may increase due to low physical activity. The relationship between fatigue and PA level is bidirectional, and the previous study did not explore on the opposite relationship (level of fatigue towards PA). Moreover, the relationship between fatigue in a specific population involving long COVID patients and the PA level is still limited. This study aims to address the level of fatigue in post-COVID-19 survivors among the IIUM Kuantan community and its association with the level of physical activity. This association may help to detect early barrier on physical inactivity among long COVID patients and the evaluation of fatigue is pivotal for post-COVID-19 treatment planning and prognosis.

MATERIALS AND METHODS

After obtaining the ethical approval from the Kulliyyah Postgraduate and Research Committee (reference no.: IIUM/310/14/11/2 ID No. KAHS 96/22), a cross-sectional study was conducted among the post-COVID-19 survivors (with no previous comorbidity and had recovered at least 4 weeks after the last infection with COVID-19) from the International Islamic University Malaysia (IIUM), Kuantan Campus. The self-administered questionnaire was disseminated through the social media platforms and divided into two parts:
Part A: Collection on the sociodemographic data of the respondents.
Part B: A validated structured questionnaire using (i) the Fatigue Severity Scale (FSS) which contains 9-item scale, and it rates the severity in terms of how fatigue affects PA, activities of daily living, and motivation. The cut-off point for FSS of ≥4 indicates high fatigue (Lerdal, 2014) and (ii) the short version of the International Physical Activity Questionnaire (IPAQ-SF) (Craig et al., 2003). It captures three different levels of PA intensity (vigorous, moderate, and walking) and sitting time over the course of the previous seven days. The statistical analysis data were done using the Statistical Package for the Social Science (SPSS) version 22 for Windows. The demographic data and level of fatigue were analysed by using the descriptive statistics. The levels of fatigue and its relationship with gender and phase of post-COVID-19 infection were evaluated and reported using the independent-sample t-test. Finally, the association between the level of fatigue and PA level was assessed using the Chi-Square test.

RESULTS

The total of respondents who completed this study was 75 post-COVID-19 survivors, consisting 24 males (32%) and 51 females (68%). The mean age of respondents was 23.64±5.795. The proportion of the occurrence of COVID-19 infection shows a large difference, once (92%) and twice (8%). Table 1 tabulates the characteristics of the respondents based on each variable.

Table 1 *Characteristics of the Respondents (n=75)*

Variable	Frequency	Percentage (%)

Gender:		
Male	24	32.0
Female	51	68.0
Age:		
19	6	8.0
20	4	5.3
21	10	13.4
22	32	42.7
23	14	18.7
31	1	1.3
34	2	2.7
35	1	1.3
37	1	1.3
40	1	1.3
41	2	2.7
50	1	1.3
Occurrence of COVID-19:		
Once	69	92.0
Twice	6	8.0
Last infection:		
More than 3 months	61	81.3
1 to 3 months ago	14	18.7

Level of fatigue

The second part of the questionnaire measured the level of fatigue in post-COVID-19 survivors among IIUM Kuantan community using the 9 items of the FSS questionnaire. In general, the population demonstrated a slightly high fatigue level post-COVID-19, as it is nearly passing the borderline (4.00). Among the respondents, the highest score obtained was 6.33 and the minimum score was 1.00. In comparison to age, the top three highest FSS mean score is among those aged 34 which is 5.056±0.056, followed by age 22 (4.483±0.179) and age 23 (4.246±0.308).

For the variable of occurrence in COVID-19, from 51 fatigue respondents, 90.2% who experienced a one-time COVID-19 infection were categorized under the fatigue group, while the respondents who had been infected twice acquired only 9.8%. The data shows that 68% of respondents (n=51) were under the category of high fatigue, and it widens the gap between the low fatigue group by 32% (n=24). This means that post-COVID-19 fatigue prevalence is high among the long COVID-19 of IIUM Kuantan community. There was also a significant difference ($p<0.001$) in the FSS score when comparing the low and high fatigue groups.

Relationship between gender and fatigue level

It was found that females have a higher number of high fatigue compared to males (37 vs 14), with similar findings in the low fatigue group where females are higher than males (14 vs 10) (Figure 1). For the FSS mean score, female respondents showed a higher score on FSS, 4.360±1.136, whereas male respondents only recorded a slightly lower score, 3.991±0.986. Further analysis showed there were no differences in gender when compared with their level of fatigue (*p*-value=0.176) (Table 2).

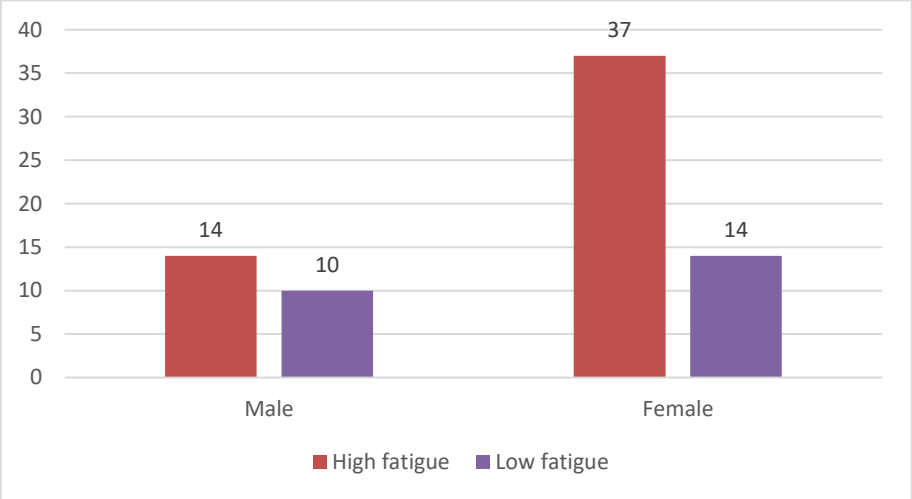


Figure 1: *Bar Chart on Frequency of High and Low Fatigue Groups in Genders (n=75)*

Table 2: *Comparison of Gender and Level of Fatigue using independent t-test* (n=75)

Variable	Male (n=24)		Female (n=51)		Mean differences (95% CI)	*t*-statistics (df)	*p*-value
	Mean	SD	Mean	SD			
FSS score	3.991	0.986	4.360	1.136	-0.369 (-0.907, 0.170)	-1.365 (73)	0.176

Relationship between the Phase of Post-COVID-19 Infection and Fatigue Level

The respondents were asked for two phases of the post-infection period: 1 to 3 months ago and more than 3 months ago. A total number of 61 respondents (81.3%) accumulated for the last COVID-19 infection more than 3 months ago while the remaining 14 respondents (18.7%) accounted for 1 to 3 months ago.

Looking at the high and low fatigue groups, descriptively, quite a high number of respondents reported high fatigue in the subgroup of "more than 3 months ago" as compared to "1 to 3 months ago" (43 vs 8). Meanwhile, in low fatigue groups, the subgroup of "more than 3 months ago" was also found to be higher than the subgroup of "1 to 3 months ago" (18 vs 8) (Figure 2). In finding the differences in the relationship between fatigue level and recovery phase post-COVID-19, the *p*-value was 0.175 (Table

3). Therefore, there was no significant difference between the last time of experiencing COVID-19 infection and fatigue level, despite the differences between the subgroups.

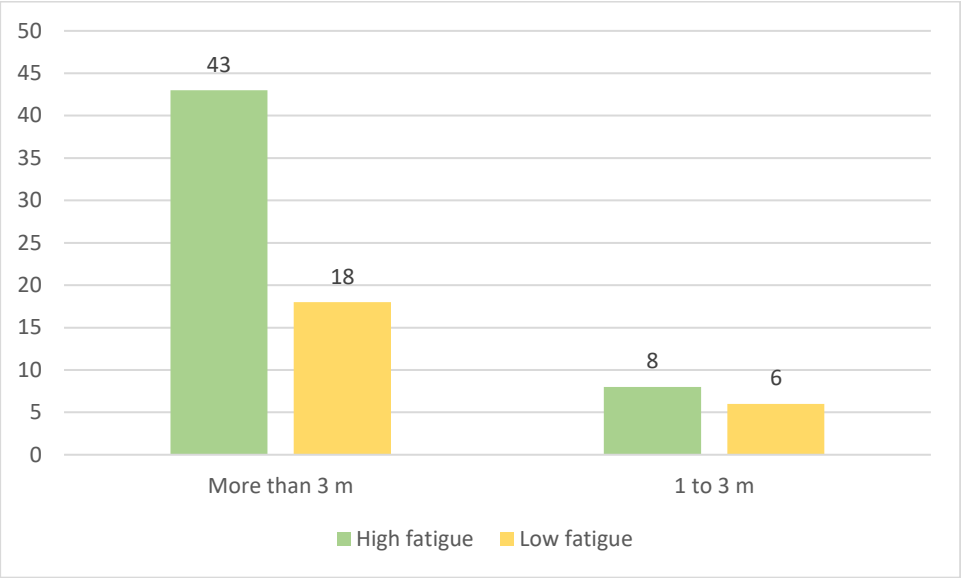


Figure 2: *Bar Chart on the Frequency of Low Fatigue and High Fatigue Groups in COVID-19 Occurrence (n=75)*

Table 3*: Comparison of the Post-COVID-19 Infection Phase and Level of Fatigue using independent t-test (n=75)*

Variable	**1 to 3 months** (n=14)		**More 3 months** (n=61)		**Mean differences (95% CI)**	***t*-statistics (df)**	***p*-value**
	Mean	SD	Mean	SD			
FSS score	3.881	1.075	4.324	1.094	0.443 (-0.201, 1.088)	1.371 (73)	0.175

Association Between Level of Fatigue and Physical Activity Level in Post-Covid-19 Survivors of IIUM Kuantan Community

For the physical activity level, a moderate level was achieved in almost half of the respondents (48%), followed by a vigorous level (38.7%), and lastly low level (13.3%). The result indicated a good habitual practice of post-COVID-19 IIUM Kuantan survivors towards PA. When comparing genders and PA levels, the majority of the females (52.9%) have moderate PA levels while in males, they were dominant in high PA levels (58.3%). Much to our surprise, there was no significant association found between fatigue and physical activity, with a *p*-value higher than α (0.703 > 0.05).

DISCUSSION

Consistent with the previous studies, the current result shows that post-COVID-19 fatigue was highly prevalent in long COVID patients, with the total respondents of 68% reported that they experienced this prominent symptom (Joli et al., 2022; Malik et al., 2022). In addition, it was found that the mean age of the respondents in this study is 23.64±5.795. Although older age could be a contributing factor to fatigue, this finding shows that being young is not an exception in getting post-COVID-19 fatigue. Davis et al. (2021) surveyed long COVID in young adults (age 18-39 years old) and identified fatigue as the most frequent symptom, forcing 22% of patients to cut their working hours in half, along with the inability to work. Hence, the young age group (age 18 to 44 years old) who in general are more active in physical activity (WHO, 2022b) are prone to post-COVID-fatigue relapses because being overly active may lead to muscle loss and consequently affect the acceleration of muscle fatigue. Practicing a good lifestyle is not harmful, but in long COVID people, muscle fatigue must be tackled first before returning to pre-morbid PA level or else it will worsen the fatigue symptom. Incorrect PA patterns can cause worsening of long COVID symptoms such as fatigue (Wright et al., 2022).

Relationship between Gender and Fatigue Level

This study attempted to find out whether there would be any differences in the fatigue levels among the male and female respondents. While reporting that there was no significant difference between gender and the level of fatigue (p=0.176), female respondents tend to have a higher level of fatigue as measured by the FSS score (4.360±1.136) as compared to males (3.991±0.986). In support of this finding, Boter et al. (2014) also found that gender is independent of the level of fatigue. Concurrently, Aldhahi et al. (2022) examined the fatigue severity among recovered COVID-19 subjects, and reported that females were prone to have high fatigue as compared to males. The existence of these gender-based differences may have its explanation. Sex hormones may come into play in discussing the development of high fatigue in females. Meanwhile, the inflammatory response, which is the associated factor in fatigue is different between males and female. The cytokine interleukin 6 (IL-6) found in persistent fatigue was said to be higher in females than males. In summary, females are prone to high fatigue because they are at risk of muscle fatigue, more exposed to long COVID symptoms, have more immune symptoms, and are associated with various diseases caused by hormonal changes. However, this current study has limitations in analyzing gender-based differences in post-COVID-19 fatigue. The more comprehensive and explorative study is required to further explore this relationship.

Relationship between Phase of Post-COVID-19 Infection and Fatigue Level

The study showed that there was no significant difference between the phase of post-COVID-19 infection and fatigue level. Furthermore, even the FSS mean score value shows the phase for “3 months ago” is higher than (4.324±1.094) the phrase “1 to 3 months ago” (3.881±1.075). This finding is in contrast with the initial finding by NICE (2022), which stated that the long COVID symptoms are supposedly to subside after 12 weeks post-infection.

Augustin et al. (2021) found that at a period of more than three months post-infection, 14.2% of their respondents complained of fatigue. This is supported by Goërtz et al. (2020), who did a study among 2,113 participants at three months following the onset of COVID-19 symptoms and found that fatigue is one of the most prevalent symptoms, impacting 87% of the participants. COVID-19 is the main factor for fatigue but with the presence of co-factors such as less sleep quality, mood disorders as well as abnormal illness beliefs and behavior (e.g. over-exercise to fight off the exertion) these might conjure a set of determinants in post-COVID-19 fatigue (Sandler et al., 2021).

Association Between Level of Fatigue and Physical Activity in Post-Covid-19 Survivors of IIUM Kuantan Community

There is no association found between fatigue and physical activity level among IIUM Kuantan post-COVID-19 survivors ($p=0.703$). To the writer's knowledge, there is no direct study that examined the association between fatigue and physical activity in a population of post-COVID-19 in Malaysia. The emergence of COVID-19 is quite new, and most of the research explored these two variables independently such as physical activity level and pattern alone without connecting the relationship with fatigue level.

Several researcher has found a relationship between fatigue and physical activity but in different populations. Özkeskin et al. (2021) conducted research in multiple sclerosis (MS) patients with and without a COVID-19 history. The findings showed that the PA level was lower in COVID-19 MS patients and fatigue has an association with the PA level, in which the author found that the PA level is lower when the fatigue level is higher. Meanwhile, Vieira et al. (2021) conducted a study among chronic obstructive pulmonary disease (COPD) patients and found that those with higher scores of fatigue have lower PA levels, though the relationship is weak. There is also a study that explores the middle age groups and the results are similar to the above (Liao et al., 2017). In explaining the older age association with fatigue-PA level relationship, Vetrovsky et al. (2021) stated that functional status in this age group was influenced by fatigue. Older adults who typically had higher levels fatigue took fewer steps/day. However, this current study did not include any respondents above 65 years old and had received fewer participants from different ranges of age. Therefore, this might conceal the fact that older age may be the contributing factor to the association between fatigue and physical activity level. It is understood that fatigue is likely to affect physical activity levels, considering the fact from the pathological view. The small sample size and an instrument of self-reported fatigue and physical activity in this study might explain the less accuracy in determining the relationship.

CONCLUSION

This study has shown that fatigue is highly prevalent in post-COVID-19 survivors among the IIUM Kuantan community despite the mean age being from young age, and a significant difference between high and low fatigue groups. It is noteworthy to mention that even though there is no significant difference in the fatigue level when comparing to gender and post-COVID-19 infection phase as well as no association between fatigue and physical activity level, there is an important finding that elucidated a clear relationship between these two variables. This study may suggest that future

researchers to look into the level of fatigue in different timeframes and comprehensive assessment by the clinician to come up with more meaningful data.

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EXPLORING PARTICIPATION OF IIUM KUANTAN STUDENTS IN WALKING AS A PHYSICAL ACTIVITY

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ABSTRACT

Introduction: Walking is one of the physical activities that benefits people of all ages. The main objective of this study is to determine the participation in walking among IIUM Kuantan students and comparison with other physical activities. **Method:** The study was conducted by distributing an online google form questionnaire to all undergraduate IIUM Kuantan students via an online survey. 80 of the respondents participated in the study based on inclusion and exclusion criteria. **Result:** The outcome of the research regarding frequency and duration of walking was within average number of 5 days per week and 30 minutes duration per day. **Conclusion:** The adherent to simplest physical activity such as walking needs to be empowered to ensure the long-term applicability and benefits. However, the gender differences portrayed no significant difference between male and female respondents in walking activity. In terms of physical activity, walking was found to have the highest participation among IIUM students as compared to moderate and vigorous physical activity.

Keywords: walking, physical activity, IIUM Kuantan

INTRODUCTION

University or college as a centre of knowledge is a place where students supposed to develop healthy habits. Nevertheless, majority of students exhibit a decrease in motivation for physical activity as soon as their age increases. This is commonly occurred among university students due to their preoccupation with daily tasks and less motivation to exercise (Alkhateeb et al., 2019). During the Coronavirus disease 2019 (COVID-19) pandemic era, most of the learning activities were conducted online thus limit the student's involvement in any physical activity. Even before the pandemic, there was strong evidence that most children and adolescents, specifically school-going adolescents aged 11–17 years, in many countries do not participate in sufficient physical activity (Bronikowska et al., 2021). According to Kanniyan (2015), walking is the most natural activity and the only sustained dynamic aerobic exercise, common to all. There is no need for any special knowledge or equipment. Any frequency of walking at any pace will expend energy and provide benefits mentally and physically. Hence, the younger generation is encouraged to include walking activities in their daily routine as the simplest form of exercise than any other physical intervention to keep healthy. Therefore, this research study aimed to determine the participation in walking as a physical activity among IIUM Kuantan students compared to the other physical activities. This endeavour is considered as vital to achieving this objective as there are numerous benefits to be gained just by walking instead of enhancing the students' motivation to engage with physical activity and not just focusing on academic matters alone.

MATERIALS AND METHODS

Study Design
The study design was a cross-sectional study. The participants in the cross-sectional study were selected based on the inclusion and exclusion criteria.

Subjects
The study was conducted at the International Islamic University Malaysia (IIUM) in Kuantan, Pahang Darul Makmur. The study consisted of undergraduate students of IIUM Kuantan. The inclusion criteria of the study were Year 1 to Year 4 undergraduate students from the six Kulliyyah age 18 years old and above. The students with walking difficulty or other lower limb deformity were excluded from the study.

Ethical Consideration
The study was approved by the Kulliyyah Postgraduate and Research Committee (KPGRC: KAHS98/22). The subject acknowledged that they have the right to withdraw from the study at any time. The result of the study is kept confidential and not to be disclosed unless required by the law.

Sample Size Calculation
The sample size was calculated using a single proportion formula, with a confidence interval of 95% and an expected proportion of 29.4% of walking adults (Fitzhugh & Thompson, 2009). The precision in the study was 10%. Withdrawal of participants from the study was expected and an additional 10% for incomplete data was added to the sample size.

The formula is as below with:

- $Z = 1.96$ ($\alpha = 0.05$, at 95% CI)
- $p = 0.294$, mean for adult walking for leisure time physical activity (Fitzhugh & Thompson, 2009)
- $q = 1-P$
- $\Delta = 0.10$ (precision 10%)

$n = (Z\alpha/\Delta)^2 (p)(q)$
$n = (1.96/0.10)^2 (0.294) (1-0.294)$
$n = 79.7378$
$n = 79.7378 +10\%$ (possible error)
$n = 79.8378$
$n \approx 80$

From the sample size calculation, the sample size for this study was about 80 students.

Sampling Method
The sampling method that was used in this study was convenience sampling. The data was collected by using an online google form questionnaire that consists of four sections which are the participant information sheet, informed consent form, demographic data, and International Physical Activity Questionnaire (IPAQ). The questionnaire from Van der Ploeg et al., 2010 was distributed among the undergraduate students of IIUM Kuantan from Year

1 to Year 4 through social media platforms such as WhatsApp and Instagram. The English language was used and divided into 2 parts:

a) Demographic data include age, gender, study program, department and year of study were recorded.
b) Short-Form International Physical Activity Questionnaire (SF-IPAQ)

IPAQ measures the number of days and duration of PA that was conducted for at least ten minutes each time at vigorous intensity, moderate intensity, and walking during the last seven days, respectively. Here, PA at vigorous intensity refers to those that make hard effort to conduct and make people "breathe much harder than normal". For instance, heavy lifting and fast bicycling. PA at moderate intensity refers to those that take moderate effort and make people "breathe somewhat harder than normal" moderate PA include carrying light loads and swimming at a regular pace. Walking is evaluated separately from PA at vigorous and moderate intensity in IPAQ but is generally considered low to moderate intensity. This paper focused on data collection from walking items in the IPAQ short form which assesses the frequency and duration of walking in the past 7 days. The respondents need to report the frequency and duration of participating in moderate-intensity and vigorous-intensity physical activity.

Statistical Analysis

The statistical analysis was done using the Statistical Package for the Social Science (SPSS) version 22 for Windows. Demographic data was analyzed by using descriptive statistics. Frequency and duration of walking activity, comparison with other physical activities and gender differentials was studied and reported using descriptive statistics and inferential statistics respectively. The parametric test of paired samples t-test was used to compare participation in walking with moderate and vigorous physical activity.

RESULTS

Demographic data

The total respondents were 83 in the research. The characteristics of the respondents are presented in Table 4.1. A total of 83 students aged 19-23 years old voluntarily participated in this study with no missing data. The mean age of the participants was 21.02 ± 1.288 years old. There were 73.5% of female and 26.5% of male participants in this study respectively. Most of the respondents were students of Year 4 with 45.8% followed by Year 1, 3 and 2 with 22.9%, 19.3% and 12% each respectively. Among the respondents, 36.1% were from Kulliyyah of Allied Health Sciences (KAHS), 27.7% from Kulliyyah of Pharmacy (KOP), 16.9% from Kulliyyah of Nursing (KON), 9.6% from Kulliyyah of Sciences (KOS), 7.2% from Kulliyyah of Dentistry (KOD) and 2.4% from Kulliyyah of Medicine (KOM).

Table 4.1: *Characteristics of the participants (n = 83)*

Variable	Frequency	Percentage (%)
Genders:		
Male	22	26.5
Female	61	73.5

Age:		
19	17	20.5
20	11	13.3
21	13	15.7
22	37	44.6
23	5	6.0
Year of study:		
1	19	22.9
2	19	12.0
3	16	19.3
4	38	45.8
Kulliyyah:		
KAHS	30	36.1
KOD	6	7.2
KOM	2	2.4
KON	14	16.9
KOP	23	27.7
KOS	8	9.6

Frequency and Duration of Walking

The one-week frequency of walking in the current study was analyzed using descriptive statistics. The data of the respondents are presented in Table 4.2. The results demonstrated weekly participation in walking varied among the respondents. Most of the respondents were walking for seven days or the whole week (37.3%). Only 3.6% were involved in walking for six days, 19.3% for five days and 9.6% for four days in a week. There was participation of 15.7% walking for three days, 4.8% and 8.4% for two days and a day each respectively. Among the respondents, only 1.2% were not engaged in walking in a week, and Table 4.3 shows the mean score for walking frequency by the respondents which is 4.83 ± 2.088. From this data, it can be concluded that the frequency of walking is approximately 5 days per week. Out of 83 respondents, the highest day participated in walking, which is seven days was obtained by 31 respondents while the lowest zero-day was obtained by one participant.

Table Error! No text of specified style in document.**.1**: *Descriptive statistics for walking frequency (day) per week of the respondents (n = 83)*

Days of Walking	Frequency (n)	Percentage (%)
0	1	1.2
1	7	8.4
2	4	4.8
3	13	15.7
4	8	9.6
5	16	19.3
6	3	3.6
7	31	37.3

Table Error! No text of specified style in document.**.2**: *Mean score of walking frequency (n = 83)*

Variable	Mean score of Walking Frequency (Days)	Standard Deviation
Days of Walking	4.83	2.088

Table 4.4 shows the descriptive statistics for duration of walking per day among the respondents. Among the respondents, the walking duration of 30 minutes per day has the highest percentage of participants which is 20.5%, followed by 19.3% for 60 minutes duration and 9.6% for 10,15 and 120 minutes of walking duration. For 20 minutes duration, there are 8.4% of respondents and 6.0% for 45 minutes. Besides, there are 4.8% for 40 minutes duration, followed by 3.6% for 90 minutes and 2.4% for 50 and 180 minutes of duration. Finally, there are 1.2% for 300-, 25- and 0-minutes durations of walking each respectively. Since the data is not normally distributed, the results are reported using the median score and interquartile range. The median score of walking duration per day is shown in Table 4.5 which is, 30.00 ± 40.00 minutes. Out of 83 respondents, the duration of 30 minutes has the highest respondents, which is 17.

Table Error! No text of specified style in document.**.3***: Descriptive statistics for duration of walking per day of the respondents (n = 83)*

Duration of Walking (Minutes)	Frequency (n)	Percentage (%)
0	1	1.2
10	8	9.6
15	8	9.6
20	7	8.4
25	1	1.2
30	17	20.5
40	4	4.8
45	5	6.0
50	2	2.4
60	16	19.3
90	3	3.6
120	8	9.6
180	2	2.4
300	1	1.2

Table Error! No text of specified style in document.**.4**: *Median score of walking duration (n = 83)*

Variable (n)	Median score of walking duration (Minutes)	Interquartile Range
Duration of walking (300)	30.00	40.00

Comparison Between Males and Females in Walking

In terms of walking frequency

The result of analysis comparing both genders regarding walking frequency per week is shown in Table 4.6. The one-week walking frequency was analyzed using independent samples t-test. According to Levene's test, this data meets the assumption of having equal variance (p = 0.846). From the statistical analysis, the comparison of p-value was done with the significance level (α) for 95% confidence level. The p-value for walking frequency was more than α (p>0.05) where the null hypothesis cannot be rejected. Thus, there are no significant differences in the mean of walking frequency between males and females (p = 0.613) even though females have a slightly higher frequency than males.

Table Error! No text of specified style in document.**.5**: *Comparison of walking frequency between males and females using independent t-test (n = 83)*

Variable	**Males (n=22)**		**Females (n=61)**		**Mean differences (95% CI)**	***t*-statistics (df)**	**p-value**
	Mean	SD	Mean	SD			
Walking frequency (Days)	4.64	2.105	4.90	2.095	-.265 (-1.303,0.773)	-.058 (81)	.613

In terms of walking duration

The result of the analysis comparing both genders regarding walking duration per week was analyzed using the Mann-Whitney Test since the data is not normally distributed. According to Levene's test, this data meets the assumption of having equal variance (p = 0.754). However, normality distribution is not assumed for both groups, males and females. Thus, we can only report the results using median score. The walking duration was varied among respondents and Table 4.7 shows the median score and interquartile range for males and females which is 150.00 ± 371 and 200.00 ± 255 each respectively. Since the p-value a (p>0.05), the null hypothesis cannot be rejected. Thus, there is no statistically significant difference between males and females even though the median score for female students was 200.00 ± 371, which was higher than male students, 150.00 ± 255 (U = 610.500, p = 0.532).

Table Error! No text of specified style in document.**.6**: *Comparison of walking duration per week between males and females using Mann-Whitney test (n = 83)*

Variable	**Male Median (IQR) (n= 22)**	**Female Median (IQR) (n= 61)**	***p*-value**
Walking duration (minutes)	150.00 (371)	200.00 (250)	0.532

Table Error! No text of specified style in document.**.7**: *Test statistics for walking duration (n = 83)*

	Walking Duration (Minutes)
Mann-Whitney U	610.500
Wilcoxon W	863.500
Z	-.625
Asymp. Sig. (2-tailed)	.532

Comparison Between Participation in Walking with Moderate and Vigorous Physical Activities Among IIUM Students

The comparison between participation in walking with other physical activities was analyzed using paired samples t-test to explore the differences between two numerical data: walking with vigorous physical activity and walking with moderate physical activity.

The statistical analysis is shown in Table 4.10 and Table 4.11. The p-value was compared with the significance level (α) for a confidence level of 95%. Based on the result, there is a significant difference between participation in walking with vigorous and moderate physical activity since p-value <0.001.

Based on the results, walking activity has the highest mean score (262.17 ± 303.034) compared to moderate (96.89 ± 143.388) and vigorous physical activity (66.69 ± 101.757). Even though there is a significant difference between participation in walking with other physical activities, moderate PA demonstrated higher mean of duration compared to vigorous PA. Therefore, it can be concluded that walking activity possesses the highest participation among IIUM students compared to moderate PA and vigorous PA while moderate PA has more participation compared to vigorous PA.

Table Error! No text of specified style in document.**.8**: *Comparison between participation in walking and vigorous physical activity by using paired samples t-test (n = 83)*

Variable	**Walking Activity**		**Vigorous Physical Activity**		**Mean difference (95% of CI)**	***t*-statistics (df)**	***p*-value**
	Mean	SD	Mean	SD			
Duration (Minutes)	262.17	303.034	66.69	101.757	195.482 (126.295, 264.669)	5.621 (82)	<0.001

Table Error! No text of specified style in document.**.9**: *Comparison between participation in walking and moderate physical activity by using paired samples t-test (n = 83)*

Variable	**Walking Activity**	**Moderate Physical Activity**	**Mean difference (95% of CI)**	***t*-statistics (df)**	***p*-value**

Duration (Minutes)	Mean	SD	Mean	SD	165.277 (92.349, 238.205)	4.508 (82)	<0.001
	262.17	303.034	96.89	148.388			

DISCUSSION

The respondents demonstrate walking frequency of approximately 5 days per week on average. 30-minutes walking duration is the average of participation among respondents. The students may practice walking for different purposes, and it mainly combined with leisure, study, transport, or work activities. The current results are probably due to walking is one of the easiest with great benefits of physical activities to do for leisure compared to the other physical activities. According to a study by the Sport Sciences for Health, walking is acknowledged as a sustainable type of exercise that may be performed without an expert's teaching, opening the door to the possibility of public health promotion (Wang & Boros, 2020). Besides, the preference for walking is because it can be done independently, costs little, allows the individual to determine the level of intensity, and is done around university area (Doyle et al., 2019). Additionally, weather can become a significant factor. Commonly, the students are more encouraged to walk on a sunny day. However, even though the distance to class or campus is appropriate for walking, students choose to take a bus or a car to avoid walking on rainy days (Ma et al., 2019). Thus, it may affect also affect the weekly frequency of walking especially in a raining or monsoon season.

This study also found that there is no statistically significant difference between males and females regarding participation in walking in terms of frequency and total duration per week. This current study is supported by Azevedo et al. (2017). Men appeared to have higher activity level than women in terms of moderate-intensity, vigorous-intensity, and total-leisure-time physical activity practice but walking was the only activity that have similarity among males and females. Men is more likely to cite fun, challenge, social acceptance, affiliation, competition, and strength and endurance as reasons for exercising. In contrast, women is more on preventing illness, maintaining good health, controlling weight, and appearance (Lauderdale et al., 2015). Both perceptions may be obtained from the benefits of walking. Walking is one of the physical activities that is suitable to be done in groups or in pairs. According to one study, both male and female university students in Canada preferred exercising with others outside of a structured class (Doyle et al., 2019). Both genders may have similar participation in walking due to the tendency of doing physical activities with friends.

The most likely reason walking was the most preferred type is that it is one of the easiest physical activities to perform, easy to maintain the pace, safe, has no cost associated with it, and does not require any special skills or equipment as compared to other physical activities, for instance, cycling. In contrast, other physical activities which are not provided on the campus such as Zumba classes and horse-riding commonly require specific skills where students will need to spend their money to learn from a qualified coach or instructor. Apart from that, another research study in different population stated that 78% of the obese adult preferred low-cost or no-cost PA over paid activities (Baillot et al., 2021). Furthermore, university students are often associated with hectic daily schedules, therefore, walking during leisure time is one of the easiest ways to maintain mental, emotional, and physical

health. Ma et al. (2022) proved that outdoor mindful walking enhanced the trait mindfulness levels, mood and quality of sleep-in university students.

The result from this research study is supported bv Alkhateeb et al. (2019) that found the most preferred physical exercise practiced during school and college years was walking with a percentage of 71.7% and 61.6% each respectively. Walking activity has the highest percentage of participants rather than other physical activities such as cardio (28.3%), weightlifting (16.8%) and swimming (14.6%). Similarly, the study from the previous years by the Bureau of Health Promotion, Department of Health (2012), reported that 42% of the Taiwanese population's most preferred choice of physical activity was walking. After all, walking is an activity practiced by many people for many years ago.

CONCLUSION

The study concluded that the frequency and duration of walking among the respondents is five times weekly and 30 minutes per day. There is no significant difference between males and females regarding participation in walking in terms of frequency and total duration per week. There is a significant difference between participation in walking with vigorous and moderate physical activity based on the IPAQ. Improvement and encouragement towards these students to increase their physical activity is still needed. It is imperative to improve not only our physical health but also our mental health.

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The Effects of Workplace Office Ergonomic Intervention on Work-Related Posture and Musculoskeletal Symptoms: A Systematic Review

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Abstract

Introduction: Office computer workers' sedentary lifestyles and improper posture increase the risk of musculoskeletal symptoms. Previous studies have conducted research regarding the effect of ergonomics on musculoskeletal symptoms, however, there is still some debate on which ergonomic interventions, either a combination of workstation adjustment and educational components or educational components alone give a positive effect on improving the posture and decreasing the musculoskeletal symptoms. **Objective:** This study was conducted to review the effects of ergonomic interventions; workstation adjustments, and/or educational components on work-related posture and musculoskeletal symptoms among office computer workers. **Method:** This review analysed articles from ScienceDirect, Taylor & Francis, The Cochrane Library, and PubMed between the year 2003 to 2023. The study screened articles, assessed eligibility using PICOS criteria, and assessed bias risk using RoB2 tools. The data was descriptively analysed. **Result:** Out of three studies that are included in this systematic review, two studies (one study on the effect of educational components alone; one study on the effect of workstation adjustment with educational components) showed a significant reduction in musculoskeletal symptoms, whilst another study (the effect of workstation adjustment with educational components) showed no significant effect on musculoskeletal symptoms. Besides, only one study (the effect of workstation adjustment with educational components) showed a positive effect on work-related posture. **Conclusion:** The result showed that there is a positive effect of ergonomic intervention on improving work-related posture and reducing musculoskeletal symptoms, however, it is still inconclusive due to the lack of studies being reviewed.

Keywords: Ergonomic Intervention, Workstation Adjustments, Educational Components, Posture, Musculoskeletal Symptoms

Introduction

Musculoskeletal symptoms are known as pain in the muscles, tendons, and nerves caused by repetitive, prolonged, and unnatural movement. As musculoskeletal disorders (MSDs) are among the most common occupational injuries and impairments in both developing and industrialized countries, the World Health Organization (WHO) has listed MSDs as the second most common work-related illness in 2013 (Safarian et al., 2018). Office computer work is one of the professions that contribute to musculoskeletal symptoms due to its nature of work. According to Calik et al. (2020), prolonged computer use in the workplace increases musculoskeletal issues among workers, with most experiencing problems after over 6 hours (Borhany et al., 2018). Lee et al. (2021) reported that prolonged use of computers with poor back posture, static neck position and repeated hand and wrist movements are common issues among office computer workers. Moreover, a lack of workplace ergonomics will eventually lead to musculoskeletal disease (Mansor et al., 2022).

Ergonomics is the study of adjusting jobs, equipment, and persons to one another for maximum safety and production (Mansor et al., 2022). It is essential to understand ergonomics to improve comfort and safety in the workplace. Ergonomic interventions include both

workstation adjustments and ergonomic training. These interventions involve rest breaks, physical activity, and adapting the workplace to the worker's anthropometric data. Workstation adjustments should be based on ergonomic recommendations, such as changing table height, chair height, screen height, and keyboard and mouse positions. Ergonomic training is also involved in this intervention, which includes workshops and follow-up educational programmes incorporating instructional videos, distributed pamphlets, and group activities. The education programme usually consists of customised email notifications. It is crucial to provide ergonomic training to workers to increase their understanding of workplace ergonomics and encourage them to apply this intervention in their work environment.

Amick et al. (2003) found that office ergonomic chairs and training resulted in less pain and discomfort during the workday compared to those who only received instruction or neither. Adjusting chair height and armrest with keyboard and mouse positions helps maintain neutral posture, reducing static muscular load and forearm flexor forces. A flexible back support allows for different torso positions while keeping hands in contact with the keyboard. This improves chair matching to upper body gravity, allowing for more reclining postures and less static strain on erector spinae. Lee et al. (2021) found that ergonomic intervention, including workstation adjustment, reduced neck, upper back, upper limb, shoulder, wrist, and hand pain, but not lower back and elbow pain.

Prolonged computer use in a sitting position can lead to musculoskeletal disorders and affect comfort and productivity. Lack of awareness about proper posture and neck and upper limb alignment can cause this issue to persist among office workers. Therefore, this study aims to reveal the effects of ergonomic interventions; workstation adjustment and/or education components on posture and musculoskeletal disorders among office computer workers.

Previous studies conducted by Esmaeilzadeh et al. (2012), Gerr et al. (2005) and Delshad et al. (2019) regarding the effect of ergonomics on musculoskeletal symptoms showed inconsistent results as some studies used both workstation adjustment and educational components as interventions, while some studies only used either one. Thus, the present study will systematically review the effect of ergonomic intervention, including workstation adjustment and/or education components on posture and musculoskeletal symptoms among office computer workers to improve their work performance and improve their comfort when performing their work.

Materials and Methods:

Study Design

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed in writing and reporting this systematic review. The steps applied in this guideline include identification, screening, eligibility, and included studies.

Identification

Online databases, which are PubMed, The Cochrane Library, Taylor & Francis and ScienceDirect were used in searching for the relevant articles. Boolean operators like 'AND' or 'OR' were applied. During the article's search, some keywords such as "ergonomic intervention", "workstation adjustment", "education", "posture" and "musculoskeletal symptoms" were used to identify relevant studies. The identified studies/articles then were recorded.

Screening

Relevant articles were screened to remove duplicate studies, and the remaining articles were flagged for inclusion. Then, the titles and abstracts of the remaining articles were screened based on the topic of this study to determine whether they should be retained or removed. Finally, the full texts of the selected articles were screened based on the inclusion and exclusion criteria presented in Table 1. The screening process including the reasons for the exclusion of articles and the number of articles remaining shown in Figure 1.

Table 1: Inclusion and exclusion criteria

Inclusion Criteria	Exclusion Criteria
• Studies involved office workers with prolonged computer use, aged between 18 to 60 years old. • Studies that used ergonomic intervention included adjustment of workstations and/or educational components. • Studies that report on the effect of ergonomic intervention on musculoskeletal disease throughout parts of the body include the neck, upper limb; shoulder, elbow, hand/wrist and back. • Studies with randomized control trial study design, which consist of control and experimental groups • Studies that have an initial assessment and follow up • Studies in which written in the English language • Studies listed from 2003 and above	• Studies only require the participant to fill out the questionnaire without giving any intervention to know the effect.

Eligibility Criteria

Article eligibility criteria were reviewed based on specific study characteristics; PICOS style, includes population, intervention, control, outcome, and study type. The PICOS criteria for this study are listed in Table 2.

Table 2: PICOS criteria

PICOS criteria	
Population (P)	Office workers with prolonged computer use
Intervention (I)	Ergonomic intervention; workstation adjustment and education
Control (C)	Other than workstation adjustment and education
Outcome (O)	Work-related posture and musculoskeletal symptoms
Study Design (S)	Randomized control trial study

Quality Assessment/ Risk of Bias

Before reporting the outcome, the Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) was used as a risk-of-bias assessment tool to obtain more precise and relevant results. This tool is relevant for assessing the risk of bias in randomized trials. This instrument included five domains, including: 1) randomization process, 2) deviations from planned interventions, 3) missing outcome data, 4) measurement of outcome and 5) selection of reported outcome.

Reporting Result/ Data Extraction

The information obtained from the selected articles was presented and tabulated in a table. The table consists of seven main components, including author/year, study design, risk of bias, participants, outcome measure, intervention, and study outcome.

Results:

Study Selection

In selecting the study, EndNote was used to store and organize the articles. Online databases were used to retrieve 394 articles, primarily from PubMed (n=41), The Cochrane Library (n=2), Taylor & Francis (n=39) and ScienceDirect (n=312). Three duplicate studies were identified and removed from the list, leaving 391 articles that were screened based on their title and abstract. After screening for the title and abstract, 373 articles were excluded because they were not related to this study. The remaining 18 articles were then evaluated according to the inclusion and exclusion criteria of this study. After the final screening, 15 articles were excluded, allowing the remaining 3 full-text articles to be included in this systematic review.

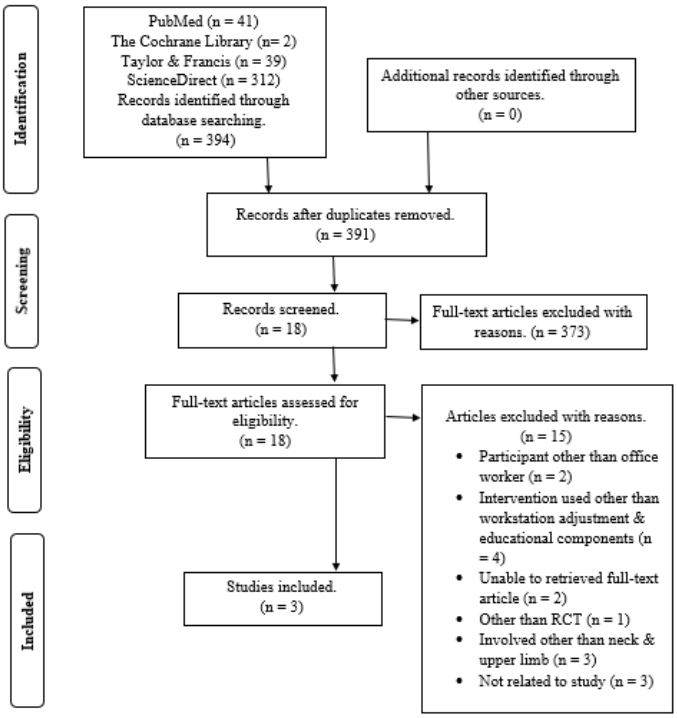


Figure 1: PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) flow diagram of each stage of the study selection

Description of Included Studies

Three articles were included in this study, and all the articles were randomized control trials (RCTs). The number of participants in these articles ranged from 87 to 375, and their ages ranged from 18 to 60 years old. All of them were office workers who used computers for prolonged periods; the time range was between 4 and 15 hours per day. Besides, the participants in the three articles had musculoskeletal symptoms at the beginning of the studies. In the study conducted by Esmailzadeh et al. (2012), the participant presented with musculoskeletal symptoms in the neck and upper extremities for which the VAS score was 3 within the past 12 months in the preliminary study, while in the study by Gerr et al. (2005), the participants were also presented with musculoskeletal symptoms in the neck, shoulder, and hand or arm for which the VAS score was less than 6. Other than that, the intervention used for these three articles were all ergonomic interventions; either the intervention includes both workstation adjustments and an education component like the study by Esmaeilzadeh et al. (2012) and Gerr et al. (2005) or the intervention that only include educational component alone like study by Delshad et al. (2019). The other characteristics include list of participants, interventions, outcome measures, and results were tabulated in Table 4.

Methodological Quality

The quality assessment of included studies was evaluated using RoB2: A revised Cochrane risk of bias tool for randomized trials and the result was reported in table 3. Based on the result, all the three articles were judged to have low risk of bias.

Table 3: Quality Assessment of Included Studies using RoB2

Study	Risk of Bias Domain					
	Domain 1: Bias due to randomisation	**Domain 2: Bias due to deviation from intended intervention**	**Domain 3: Bias due to missing data**	**Domain 4: Bias due to outcome measurement**	**Domain 5: Bias due to selection of reported result**	**Overall**
Delshad et al. (2019)	+	+	+	+	+	+
Esmaeilzadeh et al. (2012)	+	+	+	+	+	+
Gerr et al. (2005)	+	+	+	+	+	+

High Risk (×), Some Concern (-), Low Risk (+)

Discussion:

This systematic review reported three RCTs studies on the effects of ergonomic intervention on work-related posture and musculoskeletal symptoms among office computer workers. All participants in the three studies had musculoskeletal pain as symptoms that were assessed using VAS score. At the beginning of study, all participants are those with musculoskeletal pain. Participants in the studies by Esmailzadeh et al. (2012) and Gerr et al. (2005) were presented with musculoskeletal symptoms (neck and upper extremities) for which the VAS score was 3 and less than 6, respectively. However, the VAS score for participants' musculoskeletal pain was not stated at the beginning of the study that was conducted by Delshad et al. (2019).

Effect of Ergonomic Intervention on Musculoskeletal Symptoms

Out of three studies, two studies; Delshad et al. (2019) and Esmailzadeh et al. (2012) reported significant results of reduction in pain intensity while one study by Gerr et al. (2005) showed no significant pain reduction occurred throughout the study time range. Delshad et al. (2019) found that the participants from the intervention group who received workstation adjustment

and educational components such as presentation regarding ergonomic content and stretching practice did experience pain reduction after 6 months follow-up ($p < 0.001$) compared to the control group who did not receive any ergonomic intervention. Similarly, the study by Esmaeilzadeh et al. (2012) showed a significant reduction in intensity of pain at 6 months ($p < 0.001$) after receiving educational program (ergonomic training lesson) and ergonomic training brochure combine with workstation adjustment (based on OSHA recommendation) compared with the group who receive nothing. On the other hand, a study by Gerr et al. (2005) who also emphasized educational component such as discussion on proper posture combine with workstation adjustment (based on protective factor identified during preliminary analyses result from prospective study and recommendation by OSHA, NIOSH, and private industry) found no significant differences in the intensity of pain compared to non-intervention group.

The ineffectiveness of ergonomic intervention in reducing musculoskeletal symptoms among office computer workers may be due to presence of other factors that may trigger and make the symptoms become worsen. One of the factors include prolonged working hours per day which present in the participants involved in the study conducted by Gerr et al. (2005) where the time range of working hour was more than 15 hours compare to study by Delshad et al. (2019) who the worker spent only more than 4 hours and study by Esmaeilzadeh et al. (2012) only spent more than 3 hours. Park et al. (2022) in their study found that the chance of having musculoskeletal problems among workers who exposed to ergonomic risk factors steadily rose when working hours exceeded the typical hours of work which is more than 60 hours per week. Stanam et al. (2019) also found that the risk of getting musculoskeletal symptoms (neck pain, upper back pain, shoulder pain and wrist pain) increased as working hour using computer increased, with low exposure group (those working hour using computer < 4 hr/day) having a lower risk. Thus, it is proven that too prolonged working hours can increase risk of musculoskeletal symptoms, so the number of working hours per day must be considered to accurately measure the effect of ergonomic intervention.

According to Hoe et al. (2018), ergonomics refers to interactions among workers and other elements in the working environment, which includes physical, organisational and cognitive components thus this aspect has to be emphasized when doing an intervention to reduce risk of musculoskeletal symptoms among office workers. For organizational component treatment, it includes providing adequate workplace and rest time for the musculoskeletal system to recuperate from exhaustion, hence lowering the risk of long-term damage (Hoe etal., 2018). Thus, other than ergonomic intervention such as workstation adjustment and educational component, there are other factors that need to be emphasized such as the rest break as this factor might influence musculoskeletal symptoms. Putsa et al. (2022) has stated that office computer workers who work 150 min/week should take a break from extended sitting at work by shifting their posture from sitting to standing or walking every hour to avoid MSDs. Taking a break after 40 minutes of sedentary work with no body movement has been shown to be beneficial in altering muscle activity and relieving pain (Ding et al., 2020). As there is evidence that having a regular short rest break can reduce musculoskeletal symptoms, a combination between ergonomic interventions which is workstation adjustment and

educational components with having regular rest breaks by changing posture to standing and doing brief walking need to be emphasized.

Effect of Ergonomic Intervention on Work-Related Posture

For the effect of ergonomic intervention on posture, Esmaeilzadeh et al. (2012) found the intervention group had a significant reduction in postural abnormalities and improper equipment location after receiving educational program and workstation adjustment compared to the control group that were not given any intervention. However, the other two reviewed studies (Delshad et al., 2019 and Gerr et al., 2005) do not report the effect of ergonomic intervention on posture as their outcome. Thus, this shows that there is a lack of study evaluating the effects of ergonomic interventions on work-related posture, which causes further discussion of this issue could not be made.

There are few limitations that were found throughout this study. First, only a few articles were reviewed because there is still a lack of articles on RCT studies on the effects of ergonomic interventions on work-related posture and musculoskeletal symptoms. This limitation caused only one article in this systematic review that discussed the effects of ergonomic intervention on posture. Another limitation of this study was that only an instrument based on a questionnaire was used as a measurement for work-related posture, although there is a more advanced instrument to be used.

Conclusion:

This systematic review concluded that the positive effects of workstation adjustment and educational components of ergonomic intervention on improving work-related posture and reducing musculoskeletal symptoms are uncertain. Although there is a study that showed ergonomic intervention which includes workstation adjustment and educational components did improve the office worker posture, the evidence on this effect is still cannot be confirmed as only one RCT study analyzed work-related posture as an outcome. For the effects of workstation adjustment and/or educational component of ergonomic intervention on musculoskeletal symptoms, positive effect had been shown however, there is still uncertainty present as one of the studies that provide both workstation adjustment and educational component shows no significant reduction of musculoskeletal symptoms. Hence, a larger systematic review is needed to get an accurate outcome.

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Table 4: Characteristic of Included Studies

Author /Year	Study Design	Participants Inclusion criteria Study Setting	Intervention	Outcome measures	Results
Delshad et al. (2019)	RCT	Participants N=87 Inclusion criteria 1) Working in the SBUMS as an employee. 2) working with a computer > 4 hours/day as a job. 3) Being satisfied to be studied. Study setting Two health networks affiliated with Shahid Beheshti University of Medical Sciences (SBUMS) in Tehran, Iran.	Intervention group (n=44) • 1st session (120 minutes): Educational program regarding the musculoskeletal system, right posture, occupational factor causes skeletal pain, complication, and benefit of SE (lecture, slide shows, role playing). • 2nd session (120 minutes): Discuss ways to reduce barriers and improve self-efficiency to do SE (60 minutes) and practice SE for different muscles (60 minutes). - Provide CD (contain whole educational program). - Installation of autoregressive software application in all participant's computers (as reminder). - Recommended to do SE for 10-30mins/day, 2-5 days/week, up to 10 weeks.	Musculoskeletal symptoms • Pain – Visual Analog Scale (VAS) • SE behaviors - Stretching Exercise Predicting Scale (SEPS) All participants were evaluated 3 times (baseline, 3- and 6-month follow-up).	Musculoskeletal symptoms • Pain severity significantly less in Intervention group compared to Control group at 6-month follow-up ($p<0.001$) SEPS score significantly improve in Intervention group compared to Control group at 3- and 6-month follow-up ($p<0.001$), indicating Intervention group had better SE behavior after the educational program

			(1-5 reps of neck, shoulder, and back SE). Control group (n=43) Not receive any educational program.		
Esmaeilzadeh et al. (2021)	RCT	Participants N=94 Inclusion criteria 1) Age between 18 – 60 years. 2) Full time working status (> 40 hours/week) 3) at least 1 year tenure in current position. 4) Minimum 3 hours/day of computer work or 15 hours/week. 5) Present of musculoskeletal symptoms in neck and upper extremity within past 12 months (VAS: 3). Study setting	Intervention group (n=47) • 1st session (90 minutes): Ergonomic training lesson theoretical and practical. • 2nd session: Receiving ergonomic training brochure regarding risk factor and prevention of WUEMSDs, workstation adjustment and workplace exercises. • 3rd session: Workstation evaluation by investigator based on OSHA and teaching on adjusting workstation. - Every month postintervention - Same investigator will visit to evaluate the workstation and give encouragement for participant to maintain the workstation adjustment. Control group (n=47)	Posture • Body posture and workstation layout - Ergonomic Questionnaire Musculoskeletal symptoms • Intensity of symptoms - Visual Analog Scale (VAS) • Duration of symptoms – Based on 5 categories: (a) < 1 day, (b) 1-7 days, (c) 8-30 days, (d) >30 days (not every day) and (e) > 30 days (every day).	Posture • Postural abnormalities and improper equipment location significantly reduced in Intervention group compared to Control group with ($p < 0.001$) and ($p = 0.002$), respectively. Musculoskeletal symptoms • Intensity of symptoms reduced significantly in Intervention group compared with Control group at 6-month follow-up ($p < 0.001$). • Duration of symptoms reduced significantly in Intervention group compared with Control group at 6-month follow-up ($p < 0.001$).

		Istanbul University Istanbul Faculty of Medicine.	• Not receive any ergonomic intervention.	• Frequency of symptoms – During last 3 months, based on 6 categories: (a) never, (b) one episode, (c) 2-4 episodes, (d) 5-10 episodes, (e) > 10 episodes and (f) always symptomatic. All participants were evaluated 2 times (baseline and 6-month follow up).	• Frequency of symptoms reduced significantly in Intervention group compared with Control group (p = 0.009).
Gerr et al. (2005)	RCT	Participants N=375 Inclusion criteria 1) Use single computer workstation for ≥15 hours/week. 2) Using a computer	Group A: Alternate Intervention group (n=126) • Provide with workstation adjustment (based on protective factor identified during preliminary analyses result from prospective study). Group B: Conventional Intervention group (n=130)	Musculoskeletal symptoms • Pain – Visual Analog Scale (VAS) All participants report musculoskeletal symptom	Musculoskeletal Symptoms • No significant difference in time to symptoms for neck/shoulder among the three groups. • No significant difference in time to symptoms for hand/arm

	workstation as many hours/weeks during previous job. 3) VAS < 6 in both neck/shoulder and hand/arm. 4) Not taking any analgesic for current musculoskeletal symptoms. Study setting Metropolitan Atlanta, Georgia (USA).	• Provide with workstation adjustment (based on recommendations from OSHA, NIOSH and private history). * Group A and B receive adjustment of workstation which include: - adjustment of location of keyboard (to achieve required distance between "J" key and edge of desk) - provide masking tape that contains intervention position of keyboard at work surface as visual reference. - replacement and adjustment of chair height (to achieve required angle of shoulder flexion and different between elbow height and "J" key height) - adjustment of chair armrest (to support arm) * Group A and B received educational component which include: - Instruction regarding desire posture verbally and written.	in weekly diary using VAS score for 6 months.	among the three groups.

		- Individual discussion regarding the importance of maintaining required posture. * 3rd and 7th day postintervention – researcher visited workplace to check and make sure participant maintains the desired posture.
	Group C: No Intervention group (n=119) • Not receive any ergonomic intervention.	

Note: RCT = Randomized Control Trial, SE = Stretching Exercise, VAS = Visual Analog Scale, SEPS = Stretching Exercise Predicting Scale, WUEMSDs = Work-related Upper Limb Musculoskeletal Disorders, OSHA = Occupational Safety and Health Administration, UEFS = Upper Extremity Function Scale, HRQoL = Health Related Quality of Life, WUEMSS = Work-related Upper Extremity Musculoskeletal Symptoms, Rt = Right, Lt = Left, NIOSH = National Institute for Occupational Safety and Health

HYDROTHERAPY AS A TREATMENT FOR NON-SPECIFIC LOW BACK PAIN: A SYSTEMATIC REVIEW

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ABSTRACT

Introduction: Properties of water like viscosity, buoyancy, and thermodynamics in hydrotherapy have been utilized to manage numerous musculoskeletal conditions, including non-specific low back pain (NSLBP). People with NSLBP experienced increased disability and depression. Vast of reviews regarding general management of low back pain in physical therapy was done. However, the review of the specific population of NSLBP and hydrotherapy is limited. Therefore, this study aims to systematically review randomized controlled trials on the effectiveness of hydrotherapy as management for NSLBP.

Methods: The data were searched using synonyms for "Hydrotherapy" and "NSLBP" within 2009 to 2019. The databases from the allied health science's field like Cinahl, Wiley Online Library, Taylor and Francis Online, Scopus, Science Direct, and Oxford Academic. The study selection was guided by inclusion criteria that had been justified.

Results From 214 articles, only eight articles were included. The articles were appraised and extracted by using the McMaster Critical Review Form for Quantitative Studies. The two poor methodological quality studies were excluded from the critical review due to insufficient information to assist the study. The methodological quality of the six included articles ranged from "fair" to "very good".

Conclusion There was a significant reduction in pre and post visual analog score (VAS) in the hydrotherapy group compared to no hydrotherapy group. However, the no hydrotherapy group reported a reduction of VAS but not significant. In conclusion, hydrotherapy offers a greater reduction of pain compared to no hydrotherapy group. Future research should include higher methodological quality studies to support the current finding.

Key words: hydrotherapy, back pain, disability, quality of life

INTRODUCTION

Low back pain (LBP) is a pain and discomfort between the costal margin and the inferior gluteal folds, with or without referred leg pain (Benzon et al., 2014). Some people will experience burning, throbbing, aching, sharp, or dull (Firestein, Gabriel, O'Dell, Budd, & McInnes, 2017). One will experience pain ranging from mild to severe LBP, and it can be sudden or gradual pain. LBP can be specific and nonspecific. The examples of specific LBP include Infection, tumor, cauda equina syndrome, fracture, inflammatory process, ankylosing spondylitis, radicular syndrome, or osteoporosis etc. Non-specific low back pain (NSLBP), it is defined as LBP not attributed to known specific pathology of LBP (Béatrice Duthey, 2013).

According to National Medical Care Statistics 2014 by Clinical Research Centre, Ministry of Health Malaysia, musculoskeletal symptom/complaints were the fifth most referral in primary care, while the back problem was among the top ten reasons most encounter in private clinics. This data indicates that back pain is quite a

common condition reported in Malaysia's primary care. Back muscle functions for optimal control of spinal and trunk movement. When there is pain or injury to the back muscle, it affects the structure and function of the muscle. Long term pain can cause structural and functional changes in the back muscles, such as atrophy, reduced endurance, or strength (Hodges & Danneels, 2019). It is believed that therapeutic exercise can activate back muscles and consequently reduce the pain intensity in LBP (Berry et al., 2019). One of the alternative therapeutic exercise treatment methods is hydrotherapy.

The effectiveness of hydrotherapy intervention is still debatable among researchers. Masumoto (2005) said there is a significant improvement in pain tolerance but not in muscle strength, while Gunsoo Han (2011) said there is a relevant improvement in both pain tolerance and muscle strength. This statement is also supported by Olson (2012); water has been highly considered for the rehabilitation of patients with back pain due to its seven main properties, such as buoyancy, density, and hydrostatic pressure that promising low-risk intervention in treating LBP. Regardless of various research studies, however, there is still no convincing evidence on the outcome of hydrotherapy in NSLBP. There was insufficient evidence to recommend hydrotherapy as an effective treatment for patients with LBP in physical rehabilitation management. Therefore, this research aims to systematically analyse all evidence available in the literature about the effectiveness of hydrotherapy in managing NSLBP.

NSLBP causes frustration and disability among sufferers. It is more burdening when there are recurrent episodes of LBP. It just does not affect physical wellbeing but it also affects the mental health too (Farrag, Nasar, Assaf, Ibrahim, & Al-Sheikh, 2019). This happens when NSLBP causes significant impairment in quality of life, because of which one frequently takes the medical leave, it may even be challenging to continue the studies, and even to socialize with friends. There are many causes of NSLBP; some are prolonged abnormal posture, reduced muscle strength, and endurance, muscle tightness, or even impairment in the inert structure of the spine like the posterior intervertebral disc dislocation.

Hydrotherapy may be an alternative solution to the NSLBP. Hydrotherapy uses the unique physical characteristics of water that offer pain-free exercise, natural resistance, and counterbalance gravity that can enhance the flexibility and strength of the abdominal and trunk muscles. Due to limited research previously, the current study is focussed on use of hydrotherapy in the NSLBP population. Parallel to this view, it is expected that this study can offer this population a better way to implement sufficient hydrotherapy as an alternative solution for NSLBP.

The aim of the current systematic review was to know the effects of hydrotherapy on the management of acute or chronic NSLBP. The aim of study was to systematically review the effect of hydrotherapy on pain intensity among patients with NSLBP.

Further, this study aims to promote people to participate in exercises actively and to keep up with a healthy lifestyle regardless of their underlying comorbidities.

The findings from this study will provide information regarding the outcome of hydrotherapy treatment on LBP. Besides, hydrotherapy can be alternative management for patients with NSLBP. Besides that, it also may add valuable information on the effectiveness of hydrotherapy on NSLBP and simultaneously provide an improvement to the quality of healthcare service especially in LBP. From this systematic review, the limitation of the study will be taken as an improvement in further research.

There are many alternatives to treating low back pain; some are laser, acupuncture, tai chi, yoga, and hydrotherapy. Each of these interventions has its benefits as well. Hydrotherapy offers benefits due to the unique properties of water, like the density and specific gravity, hydrostatic pressure, buoyancy, viscosity, and thermodynamics (Becker, 2009). People with LBP frequently complain of difficulty in doing exercises on land. Because of gravity and high impact on land there is elevated pain intensity accompanied by fear-avoidance behaviour or lack of motor control (Becker, 2009).

Buoyancy of water that causes the body to offload the immersed joints named buoyancy. It relaxes the muscles, and the limbs are more comfortable to move and offload the immersed joints (Lorrez-Ronda Alcazar, 2014). Therefore, due to buoyancy property, an individual will have less impact and simultaneously offer a more pain-free exercise.

The property of density water will exert higher force to the human body and caused the human body to float (Lorrez-Ronda & Alcazar, 2014).

When there is motion in the fluid, it faces the resistances, which are shape, wave, and friction resistance due to viscosity (Lorrez-Ronda & Alcazar, 2014). All this type of resistance acts as natural resistance to the body in water. Different temperature setting offers a different therapeutic effect. For example, 37.5- 41ºC gives relaxation effect to the participant since water transfer heat 25 times faster than air (Lorrez-Ronda & Alcazar, 2014).

Han et al. (2011) designed aquatic therapy in 19 elderly subjects with LBP and found that, aquatic exercise significantly reduced pain and improved muscle strength. The viscosity can provide natural resistance during exercise; therefore, there is a significant improvement in muscle power.

Baena-Beato et al. (2015) found that eight weeks of intensive hydrotherapy program of high-frequency (five times/week) decreases back pain intensity and disability, improves the quality of life and improves body composition and health-related fitness in sedentary adults with chronic LBP.

Rakhi (2019) performed an experimental study comparing conventional physiotherapy and hydrotherapy-based exercise for chronic NSLBP. They found that there is a significant improvement of pain between the two groups; however, no significant difference in the range of motion, muscle power, and Modified Oswestry Low Back Pain Disability Index. Rakhi (2019) mentioned that exercise in water takes the weight off a painful joint while also providing resistance,

improved muscle strength, greater flexibility, and range of motion of the spine. Hydrotherapy based exercise able to reduced stress in the back pain and keeps the body in a neutral spine position during exercises.

Bello et al. (2010), in their experiment regarding the management of chronic LBP pain using land-based versus hydrotherapy, measure the spine mobility and pain score. They found that the pain and trunk extensor endurance has a significant improvement compared to the initial measurement. This result confirms hydrotherapy as a treatment of choice for exercise performance. The buoyancy effect reduces gravitational force acting on the musculoskeletal system, thereby granting a difficult-free movement and conservation of energy.

METHODOLOGY/ METHODS

This study used Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines as a method to assist in reporting the findings. The result of the systematic review on the effects of an intervention from the randomized controlled trials or other types of study was reported by PRISMA (Brooks & Mcneely, 2013).
The PRISMA flow chart has verified the number of studies identified, screened, eligible, and finally included (Brooks & Mcneely, 2013). Figure 1 shows the guideline of PRISMA (Moher et al., 2009).

INCLUSION CRITERIA

Before the data collection process commenced, a list of inclusion criteria was constructed. It was established to ensure the data collection process corresponded with the aim of the study. The inclusion criteria was defined using the PICOS (Population, Intervention, Comparison, Outcome, and Study Design) model as described in Table 1. Those studies that do not fit the inclusion criteria were excluded and recorded with reasons. The articles that were should be published in the English language and in full-text version to assist in assessing the methodological quality.

EXCLUSION CRITERIA

Conditions other than NSLBP, date of publication before 2009 and studies not published in English

Table 1: Component of PICOS and its Description

Component	Justification
P: Aged above 18-60 years old / Female / Male with NSLBP	To obtain heterogeneity across the studies.

I: Hydrotherapy / Aquatic Therapy / Aquatic Exercises	Focus on intervention provided in ordinary water without a mixture of any remedy like in balneotherapy and spa therapy.
C: Land exercises / Control / No intervention	A comparison should be with any no hydrotherapy group to achieve a robust comparison between hydrotherapy and no hydrotherapy treatment.
O: Any appropriate pain assessment tool	To measure the pain intensity in pre and post-treatment.
S: Randomised Controlled Trial (RCT)	RCT offers the best study design in evaluating treatment effectiveness (Hariton & Locascio, 2018).

IDENTIFICATION

There are two steps in identification that were used in this study, which seek articles through databases and additional through other sources. The health-based databases searching were the PubMed, IIUM Library database, PEDro (Physiotherapy Evidence Database), Medline (Bibliographic Medical Database), Cochrane Library, SPORTDiscus, and EMBASE, Cumulative Index to Nursing and Allied Health Science (CINAHL) database. The year for the study were ranging from 2009-2019. Besides the databases, another additional source like Google Scholar was used. The above-mentioned databases were used as they are health-based databases and published RCT studies.

The identification process used the following combination of terms; "non-specific low back pain", "non-specific lower back pain", "non-specific low backache", "non-specific lower backache", "recurrent non-specific low back pain", "mechanical low back pain", "postural low back pain" in combination with "hydrotherapy", "aquatic therapy", "aquatic exercise", "hydro exercises", "water exercises" and "water therapy". The boolean operator like "OR" and "AND" also were utilized in this process. The bibliographies from the previous systematic review and the selected articles hat related to the study were review to identify any additional studies.

SCREENING

All the collected studies were screened to sort out any duplicates. The remaining studies were screened by the title and abstract related to the research question and objectives. The study that is irrelevant, inappropriate, or does not meet the one or more inclusion criteria were excluded and recorded with reasons.

ELIGIBILITY

The full texts of the included studies were obtained, and further screening process was done according to the inclusion criteria. The eligibility of the screened studies was reviewed, as stated in the PICOS model mentioned above model. Those studies that do not fit the inclusion criteria were excluded and recorded with reasons. The articles

that fulfilled the inclusion criteria and the eligibility criteria were included in the study.

METHODOLOGICAL QUALITY ASSESSMENT

McMaster Critical Review Form for Quantitative Studies was used to assess the methodological quality of the included studies. The form was composed of 17 items. The study's purpose, study design, sample, outcome measure, intervention, results, and the conclusion are the components that were assessed to qualify the methodological quality of each study. This assessment is guided by The Guidelines for Critical Review Form for Quantitative Studies.

For the scoring system, each item is scored as "one" when it fulfilled the criteria and "zero" if it did not fulfil the criteria. The quality of methodology was categorized by the total score added from each item. The study that scored from "0 to 8" was categories as poor, "9 to 10" as fair, "11 to 12" as good, "13 to 14" as very good, and "15 to 16" as excellent methodological quality (Wells, Kolt, Marshall, Hill, & Bialocerkowski, 2014). As this review only selected RCT study design; therefore, item 3 is not applicable to be scored. Table 3.2 shows the item and description of the item used in assessing methodological quality.

Table 2: Item and Description in the McMaster Critical Review Form for Quantitative Studies

Item	Description
1. Purpose	Was the purpose stated clearly?
2. Literature review	Was relevant background literature reviewed?
3. Study Design	What is the study design?
4. Sample Size Justification	Was the sample justified?
5. Sample Size	Was the sample described in detail?
6. Reliability of Outcome Measure	Were the outcome measures reliable?
7. Validity of Outcome Measure	Were the outcome measures valid?
8. Intervention Described in Detail	Intervention was described in detail?
9. Contamination	Contamination was avoided?
10. Co-intervention	Co-intervention was avoided?
11. Statistically Significant	Results were reported in terms of statistical significance?

12. Statistical Analysis	Were the analysis method(s) appropriate?
13. Clinical Importance	Clinical importance was reported?
14. Drop-Outs	Drop-outs were reported?
15. Conclusion	Was the conclusion appropriate given study methods and results?
16. Clinical Implications	Were the implications of these results for practice reported?
17. Study Limitations	Were the main limitations or biases in the study reported?

RESULTS

The data was collected from seven databases which are Cinahl, Wiley Online Library, Taylor and Francis Online, Scopus, PeDro, Proquest, Oxford Academic, and Science Direct. In the identification process, a total of 207 articles were collected from the databases and seven articles from the additional sources. Articles from the additional sources were acquired from Google Scholar and the bibliography of other studies.

From the total number of articles, 188 duplicate articles were excluded in the screening process. Then the titles and abstracts from the collected articles were further inspected. 167 articles were excluded at the end of the screening process. The articles were excluded due to not published in the English language, not evaluating the effects of hydrotherapy, and not focusing in population with NSLBP.

In the eligibility process, the full-texts of the screened articles were obtained. Fifteen articles were excluded because not focusing on people with NSLBP and not comparing hydrotherapy group with non-hydrotherapy group like control group or land-based exercise group. In the final process, eight included articles were selected for the systematic review. Figure 2 presents the processes of identification, screening, eligibility and included by using PRISMA guideline.

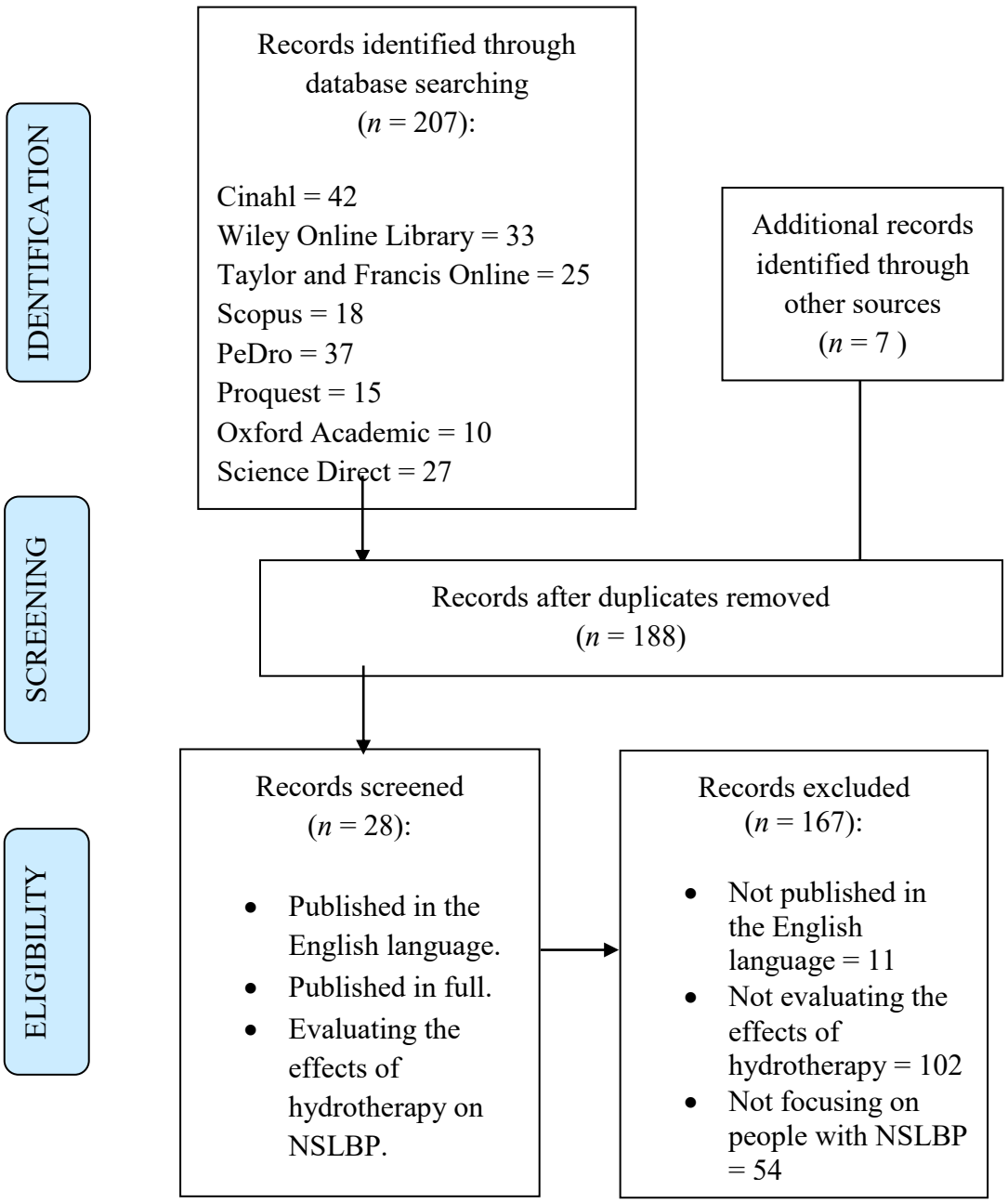


Figure 1. The Processes of Identification, Screening, Eligibility and Included by using PRISMA Guideline

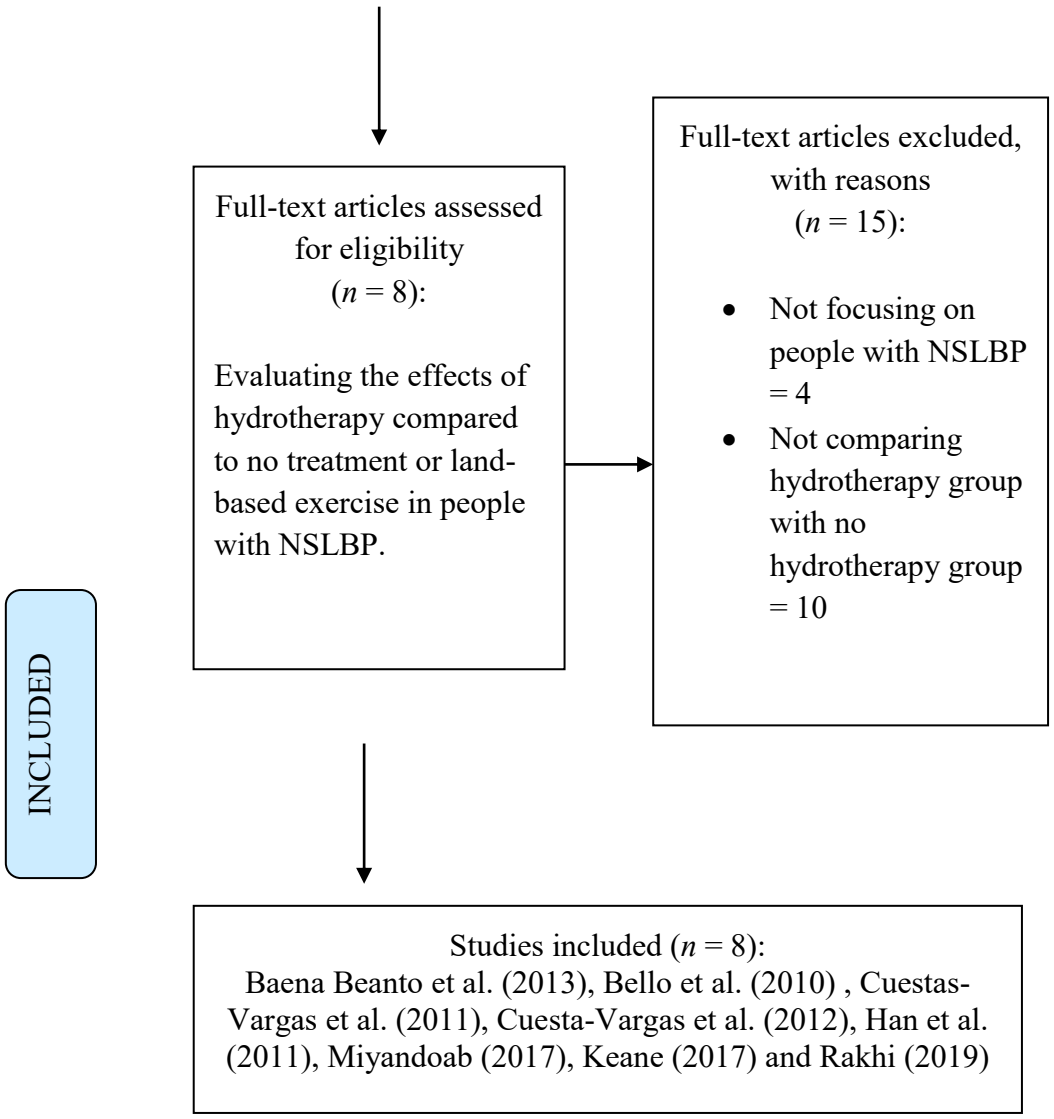


Figure 2. The Processes of Identification, Screening, Eligibility and Included by using PRISMA Guideline- Continued

METHODOLOGICAL QUALITY

A total of 17 items in this methodological quality assessment form were assessed. From the identification, screening, and eligibility processes, only eight studies were included to be assessed. The methodological quality was assessed by two reviews using the McMaster Critical Review Form for Quantitative Studies. The scoring

system for this assessment form was adapted from the McMaster Critical appraisal form for Quantities study, which has been used by a study from Wells, Kolt, Marshall, Hill, and Bialocerkowski (2014). Table 3 presents the methodological quality of the included studies using the McMaster Critical Review Form for Quantitative Studies.

Table 3. The Methodological Quality of the Included Studies using the McMaster Critical Review Form for Quantitative Studies

Individual Item	Study							
	Baena-Beanto et al. (2013)	Miyandoab (2017)	Bello et al. (2010)	Cuesta-Vargas et al. (2011)	Cuesta-Vargas et al. (2012)	Han et al. (2011)	Rakhi (2019)	Keane (2017)
1	1	1	1	1	1	1	1	1
2	1	1	1	1	1	1	1	1
3	NA	NA	NA	NA	NA	NA	NA	NA
4	0	0	0	0	0	0	0	0
5	0	0	1	1	1	0	1	1
6	1	0	0	0	1	0	0	0
7	0	0	1	0	0	0	1	1
8	1	0	1	1	1	0	0	1
9	1	0	1	1	1	0	0	0
10	1	0	1	1	1	0	0	1
11	1	1	1	1	1	1	1	1
12	1	1	1	1	1	1	1	1
13	1	1	1	1	1	0	0	0
14	1	0	1	1	1	1	1	1
15	1	1	1	1	1	1	1	1
16	1	1	1	1	1	1	1	1
17	1	1	1	1	1	1	0	1
Total (/16)	13	8	14	13	14	8	9	12
Qualitative Descriptor	Very Good	Poor	Very Good	Very Good	Very Good	Poor	Fair	Good

Two reviewers reviewed the eight selected studies. The agreement for the quality of assessment score was achieved from the discussion between both reviewers. The methodological quality of studies ranged from 6 to 14, representing "poor" to "very good" methodological quality. Baena-Beanto (2013), Bello (2010), Cuesta-Vargas (2011), and Cuesta-Vargas (2012) were the studies that were representing very good methodological quality. They were scored as very good quality because they described the sample size, justified the selected sample size, reported the reliability and validity of each outcome measures used, and described the procedure in detail that was able for replication in practice. Keane (2016) and Rakhi (2019) were categorized as good and fair.

However, two studies scored poor methodological qualities, Han et al. (2011) and Miyandoab (2017). They were categorized as a study with poor methodological quality due to lack of sample size description and justification, did not report the reliability and validity of the outcome measures used. These failed to describe intervention conducted in detailed and did not state any report on how they control the contamination, co-intervention, and managed drop-outs. The poor methodological quality studies were excluded from the assessed studies as they were unable to provide sufficient information for this review.

Therefore, the included studies were Beana-Beanto et al. (2013), Bello et al. (2010), Cuesta-Vargas et al. (2011), Cuesta-Vargas et al. (2012), Keane (2017), and Rakhi (2019). Keane (2017) and Rakhi (2019) were the two additional studies that have not been reviewed by the previous systematic review studies.

DESCRIPTION OF INCLUDED STUDIES

From the six included articles, the number of subjects who participated in the study ranged from 12 to 58. The ages were ranged from 18 to 60 years old. The statistical analysis reported the mean difference of post-intervention VAS between the groups, pre and post-intervention VAS between the groups, and pre and post-intervention VAS within the group. The significant level of all studies was set at $p < 0.05$. The population, intervention, comparison, and outcome measures for each included article were tabulated in Table 4.

Table 4. The Study, Methodological Quality, Score, Population, Intervention, Comparison, Outcome Measures and Results for each Included Articles

Study **[Methodological Quality, Score]**	**Population**	**Intervention and Comparison**	**Outcome Measures** **[Timing]**	**Result**
Baena-Beanto et al. (2013) **[Very Good, 13/16]**	49 self-reported nonspecific chronic LBP	Aquatic therapy (n = 24): In a 29 ± 1°C of pool water temperature, done 10 minutes of warm-up, 15–20 minutes of resistance exercise, 20–25 minutes of aerobic exercise, and 10 minutes of cool-down supervised session per week. Equipment used is noodle and cuff. No exercise (n = 25)	Visual Analog Score (VAS) [2 months, 40 sessions 5 days per week]	Significant reduction of the pre and post-treatment VAS in the aquatic therapy group compared to no exercise group ($p < 0.001$).

Table 4. The Study, Methodological Quality, Score, Population, Intervention, Comparison, Outcome Measures and Results for each Included Articles- Continued

Bello et al. (2010) **[Very Good, 14/16]**	12 mechanical chronic low back pain	Hydrotherapy (n = 6): In 32 to 34 °C pool water temperature, done warm-up and stretching phase, main exercise phase, and cool-down phase 45-60 minutes supervised session per week. Land-based (n = 6): Same as hydrotherapy but on land 45-60 minutes supervised session per week.	Visual Analog Score [6 weeks]	No significant reduction of the post-intervention VAS between hydrotherapy and land-based group (p = 0.532). Significant decrease of the post treatment VAS within each group. Hydrotherapy group reported p = 0.024 while the land-based group with p = 0.025.
Cuesta-Vargas et al. (2011) **[Very Good, 13/16]**	46 non-specific chronic low back pain	20 minutes deep water running (DWR) + Multimodal physical therapy program (MMPTP) (n = 25): Manual therapy, education and exercises 15 minutes of mobility exercises, 15 minutes of motor control activities, 30 minutes of resistance and muscle strengthening exercises supervised session per week. MMPTP (n = 24): Received the same manual therapy and education supervised session per week.	Visual Analog Score [15 weeks, 3 times per week]	No significant reduction of the post-intervention VAS between DWR and MMPTP with MMPTP alone ($p > 0.05$). Significant decrease of the post-treatment VAS within each group ($p < 0.05$).

Table 4. The Study, Methodological Quality, Score, Population, Intervention, Comparison, Outcome Measures and Results for each Included Articles- Continued

Cuesta-Vargas et al. (2012) **[Very Good, 14/16]**	58 nonspecific chronic low back pain	DWR and general practice (GP) (n = 25): 30 minutes of DWR equipped with flotation belts supervised session per week. General practice (GP) which participants were given consultation and educational booklet. GP (n = 24): Participants were given consultation and educational booklet.	Visual Analog Score [4 months, 3 times per week, 6 months, 12 months]	Significant reduction of the post-treatment VAS in the GP and DWR group compared to GP alone (p = 0.049).
Rakhi (2019) **[Fair, 9/16]**	30 nonspecific chronic low back pain	Hydrotherapy (n = 15): Stretching exercises for hip and lower back, 13 strengthening exercises for abdominals, glutei, trunk, lumbar and lower limb and walking forward and backward supervised session. Conventional therapy (n = 15): Hot packs for 15 min, supervised session of static back exercises, Stretching, strengthening exercises with ergonomic advice.	Visual Analog Score [NA]	Significant reduction of the post-treatment VAS in the hydrotherapy group compared to the conventional therapy group (p = 0.018). Significant decrease in the post-treatment VAS within each group (p < 0.05).
Keane (2017) **[Good, 12/16]**	29 nonspecific chronic low back pain	Aqua stretch (n = 10): In 30°C of pool water temperature, done 30-minute aqua stretch sessions with pool temperature of 30°C. Procedure of play, freeze, pressure and move. Stretch with wall hang procedure and one leg standing weighted procedure supervised session per week. Land-based (n = 10): Static and dynamic	Visual Analog Score [12 weeks, 2 times per week]	Significant reduction of the pre and post-treatment VAS within the aqua stretch group (p = 0.006). The land-based and control group reported a no significant reduction of the pre and post-treatment VAS within the group.

Table 4. The Study, Methodological Quality, Score, Population, Intervention, Comparison, Outcome Measures and Results for each Included Articles- Continued

	stretching for lumbo-pelvic-hip complex and upper body supervised session per week. Control (n = 9): maintained any pre-trial treatment and/or exercise program unsupervised session.	

SUBJECTS CHARACTERISTICS

A total of 224 subjects with non-specific chronic LBP, and mechanical chronic LBP were randomly assigned in the hydrotherapy and no hydrotherapy group. Table 4 listed more detailed patient characteristics of the included studies.

INTERVENTION

From the six included studies, four studies divided the subjects into the experimental and control groups. However, Keane (2017) randomly assigned the subjects into three groups which were the aqua stretch group, land stretch group, and control group.

The hydrotherapy group received water-based therapeutic exercises, aqua stretch, deep water running, multimodal physiotherapy intervention, and general practice. The non hydrotherapy group received the land-based therapeutic exercises, multimodal physiotherapy intervention, general practice, and no exercise. Beana-Beanto et al. (2013) and Keane (2017) are only studies that kept the control group from any exercises or general practice.

The water-based therapeutic exercises were the strengthening and stretching exercises. It included rectus abdominal, erector spinae, glutes, and hamstrings stretching and strengthening exercises. Some of the exercises were squatting, hip flexion, hip abduction, and lunges. The land-based therapeutic exercises were the same as the exercises mentioned above, but it was done on land.

The deepwater running is one of high-intensity aerobic exercise, it was conducted by running in the water for 20 to 30 minutes with flotation belts, which were provided to the participant. Multimodal physiotherapy programs included mobility exercises, motor control activities, manual therapy, resistance exercises, and patient education. Conventional therapy used hot packs, stretching and strengthening exercises, and ergonomic advice. Aqua stretch consisted of stretch with wall hang procedure and one-leg standing weighted procedure. For general practice, the subjects were given consultation and educational booklets. Table 4 listed the more specific intervention used in the included studies.

DURATION OF ASSESSMENT

The duration of intervention ranged from 30 to 60 minutes, two to five times per week. Rakhi (2019) conducted the least duration of the assessment, which was only one session only, Cuesta-Vargas et al. (2012) made up the highest follow-up which was up to 12 months while the other assessed ranged from six to eight weeks. Table 4 listed more details duration of the assessment conducted in the included studies.

Visual Analog Score was used by the six included studies to rate pain intensity. All studies used 10cm VAS except Cuesta-Vargas et al. (2011) and Cuesta-Vargas et al. (2012) that used 100mm for the pain score. Table 4 listed the more specific outcome measure used, baseline, and post-intervention mean (SD) VAS in the included studies.

From the data extracted, only Baena-Beanto et al. (2013) reported the mean difference of VAS in the pre- and post-intervention between the hydrotherapy and no exercise group. Bello et al. (2010), Cuesta-Vargas et al. (2011), Cuesta Vargas et al. (2012), and Rakhi (2019) reported a mean difference of VAS in the post-intervention between the hydrotherapy and no exercise group while Keane (2017) only reported the mean difference of VAS in the pre- and post-treatment within the group.

From the tabulated results, Bello et al. (2010) and Cuesta-Vargas et al. (2011) reported that there was no significant difference in the post-intervention VAS reduction between the hydrotherapy group and no hydrotherapy group. Nevertheless, the hydrotherapy group reported more pain reduction compared to no hydrotherapy group.

On the contrary, Cuesta-Vargas et al. (2012) and Rakhi (2019) recorded a significant difference in the post-intervention VAS in the hydrotherapy group compared to no hydrotherapy group. Keane (2017) also noted a significant VAS reduction in the pre- and post-intervention within the intervention group. This finding was parallel with Beana-Beanto et al. (2013), where they found that there was a significant decrease of VAS in pre and post hydrotherapy sessions compared to no exercise group. From the study, there was a significant reduction of the post-intervention VAS in the hydrotherapy group compared to no exercise group. Table 4 listed the detailed results in the included studies.

DISCUSSION

From the six studies, only four (Baena-Beanto et al., 2013; Bello et al., 2010; Cuesta-Vargas et al., 2011; & Cuesta-Vargas et al., 2012), reported as very good methodological studies and the remaining categorized as good (Keane, 2017) and fair (Rakhi, 2019). Out of four very good methodological quality studies, only two studies (Baena-Beanto et al., 2011 & Cuesta-Vargas et al., 2012), one good methodological quality study (Keane, 2017) and a fair methodological quality study (Rakhi, 2019) reported there was a significant reduction of VAS after the hydrotherapy session compared to no hydrotherapy session.

While the other two very good methodological quality studies (Bello et al., 2010 & Cuesta-Vargas et al., 2011) stated that both groups reported a reduction of VAS. However, there was no significant difference between the groups reported. It can be concluded that there was a significant reduction of pain post hydrotherapy session on NSLBP. This result is consistent with a systematic review done by Shi et al. (2017). They found that hydrotherapy showed statistically significantly reduce pain among LBP. Besides that, the other systematic review (Olson, 2011) supported that the aquatic exercise group is more effective than no exercise group.

The study involved hydrotherapy in managing rheumatoid arthritis also reported a positive outcome in pain management (Al-Qubaeissy, Fatoye, Goodwin, & Yohannes, 2012). Besides that, Corvillo et al. (2019) also stated that a significant reduction of neck pain after the aquatic therapy sessions compared to no treatment or other treatment. It is in line with Neira, Marques, Pérez, Cervantes, and Costa (2017) that pain among subjects with fibromyalgia was significantly improved after the aquatic therapy sessions. A six-week aquatic therapy session on

persistent knee pain patients also reported a significant reduction of pain compared to usual medical care and adjunctive therapies. (Mcilroy, Sayliss, Browning, & Bearne, 2017)

However, no hydrotherapy group like land-based, MMPTP etc has proven to manage low back pain. It is proven that exercises in any medium can improve physical function. Beana-Beanto et al. (2013) reported the land-based therapeutic exercises had the same pain reduction as the hydrotherapy group. This finding was supported by (Moon et al., 2013) that strengthening exercise on land also provide significant reduction of VAS among chronic LBP participants. Olson (2011) compared aquatic exercise with land-based exercise and found that there were no significant differences in VAS between the two sessions.

Hydrotherapy can reduce pain among LBP sufferers by counterbalancing the effect of gravity. The counterbalancing gravity effect will reduce the impact on the joints; thus, it is beneficial for those with pain or overweight (Torres-Ronda & Alcázar, 2014). Keane (2017) was able to reduce the pain from 5.7 to 2.6 post-intervention compared to the land based stretching exercise. This is because the gravity limits stretching exercise on land while in water, joints can move freely in all directions.

Apart from that, the strengthening exercises done in the hydrotherapy group as reported by Beana Beanto et al. (2013), Bello et al. (2010), and Rakhi (2019) also resulted in a reduction of pain. Becker (2009) stated that the viscosity of water will provide resistance to the body. This will be used to get the benefits of strengthening exercises.

The DWR also significantly reduce pain as this exercise give valuable effects in improving the physical function as mobility, and muscle endurance. Nava, Tozim, Morcelli, and Navega (2018) mentioned that there is an association between low back pain and the reduction of trunk muscle endurance. Thus DWR will benefit patients with NSLBP.

Beana-Beanto et al. (2013), Cuesta-Vargas et al. (2012), Keane (2017), and Rakhi (2019) concluded the duration for each hydrotherapy session was 30 to 60 minutes. And those studies reported a significant reduction of pain in the hydrotherapy group compared to no hydrotherapy group. Thus, it justifies that 30 to 60 minute of the intervention was effective in treating pain.

Besides that, the studies, as mentioned earlier, also proved that short-term hydrotherapy sessions effectively manage NSLBP. The duration of assessment across the studies was ranging between six weeks to 15 weeks. Only Cuesta-Vargas et al. (2012) reported the duration of assessment up to 1 year of follow-up. More long-term studies are needed to support the effectiveness of hydrotherapy.

IMPLICATIONS AND CONCLUSION

It can be concluded that there was a significant reduction of pain post hydrotherapy session compared to no hydrotherapy session among NSLBP patients. This reflected that hydrotherapy was effective as the alternative approach in managing NSLBP compared to no hydrotherapy approach like land-based therapeutic therapy, multimodal physiotherapy program, and general practice.

Hydrotherapy could be the treatment of choice and proven to be effective than any other intervention. Regardless of their comorbidity, people can always stay active while receiving the indirect benefits of exercises in reducing their pain and simultaneously improving their quality of life. Water-based therapeutic exercises, aqua stretch, and DRW are the example of hydrotherapy intervention. The uniqueness of hydrotherapy that not limit their intervention in one approach only can give people a flexible choice to choose their preferred mode of exercise.

This finding can be as the added value in improving the quality of healthcare system. It fulfilled World Health Organization's goal in achieving high-quality system, which is customer-centered (WHO, 2015). By offering the effective treatment to the patient, it contributes patient satisfaction to the healthcare service provided.

However, no hydrotherapy approach like land-based therapeutic exercise and MMPTP also reported a decrease in VAS. It is upon one's preference whether he or she prefers to be in a traditional exercise way or trying something new that can help them with their current concern like NSLBP.

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ACADEMIC STRESS AND SLEEP QUALITY AS A PREDICTOR TOWARDS EATING BEHAVIOUR AMONG UNIVERSITY STUDENTS

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ABSTRACT

Introduction: Academic stress has been identified to be the main stressor, particularly among university students which cause negative effects on health as well as academic performance. University students also experience poor sleep quality. This study is conducted to identify the level of academic stress, sleep quality and eating behaviour, the relationship between academic stress, sleep quality and eating behaviour as well as to investigate the influence of academic stress and sleep quality towards eating behaviour among IIUM students. **Methods**: A cross – sectional study was conducted using convenience sampling, with a total sample of 410 students. Data were collected using the Educational Stress Scale for Adolescents (ESSA), Sleep Quality Scale (SQS) and Dutch Eating Behaviour Questionnaire (DEBQ). **Results**: The study reported that 46.3% of the students experienced low academic stress. Furthermore, there is a significant association between academic stress with restrained (r=0.245), emotional (r=0.224) and external eating behaviour (r=0.180). There were 75.6% of students reported having no sleep problem. There is a significant association between sleep quality with restrained (r= 0.162), emotional (r=0,260) and external eating behaviour (r=0.184). In addition, the result from regression analysis for academic stress and sleep quality towards restrained eating behaviour explained only 7.1% variance. Similarly the percentage of variance explained for emotional behaviour was 9.4% and external eating behaviour was just 5.3%. Thus, emotional eating behaviour is the most significant compared to other associations. **Conclusion:** This finding can be helpful in increasing the awareness of the students towards healthy lifestyle and provide a good intervention to manage academic stress as well sleep problem.

KEYWORDS: academic stress, sleep quality, eating behaviour, university students

INTRODUCTION

In several years, stress and its mental health allusion among university students has become a worldwide debate (Portoghese et al., 2019). Masih and Gulrez (2006) defined stress as a lifestyle crisis that impacts everyone, regardless of developmental level. This commonly happens among adolescents because this is a crucial time for social, biological, emotional, and psychological development (Ramadhani & Mahmudiono, 2021). Nonetheless, sleep problems among university students are frequently associated with mental health concerns as well (Schlarb, Anja & Classen, 2017). One of the crucial aspects under the area of nutritional habits is eating behaviour, defined as a series of behaviours creating humans' connection with food (Domínguez-Vásquez, 2008), which includes drinking habits, dietary preferences, culinary preparations, and quantity of food consumed.

However, when compared to other sources of stress, academic stress is the most significant. Kember and David (2004) identified several examples of academic-related pressures, such as insufficient instructional methods, limited teacher-student interactions, overwhelming academic workload, substandard physical classroom conditions, difficulty in managing school and leisure time, and disarray concerning academic assignments and schedules. Furthermore, sleep deprivation is becoming increasingly common among adolescents, especially university students. In fact, sleep deprivation among adolescents has been described as a quiet global epidemic. Quality of sleep time is critical for adults and children to maintain good health. According to Sivertsen et al. (2014), numerous research studies have been conducted to emphasize the detrimental physical, psychological, and social consequences of sleep loss on the health and well-being of teenagers.

In addition, sleep quality is likely to influence several elements of health. It is critical to investigate the elements that contribute to the onset of sleep problems. To support these statements, researchers have proposed numerous etiological and physio-pathological prototypes to comprehend

sleep difficulties. It is based on the 3P model which are predisposing, precipitating and perpetuating factors of sleep disorders including medical conditions (e.g., respiratory problem), psychiatric conditions (e.g., stress and anxiety), environmental conditions (e.g., sleep interruptions) and behavioural conditions that can affect sleep on these three different levels (Spielman et al., 1987). Hence, it is very important to conduct this study to measure the relationship of academic stress, sleep quality, and eating behavior among IIUM students.

METHODS

Subjects

Four hundred and ten students of IIUM from Gambang, Kuantan, Gombak, and Pagoh campuses from a variety of courses and level of studies were selected to be the participants of this research.

Study Design

This quantitative research was conducted using cross-sectional design involving all students of IIUM and a series of questionnaires was created by adopting and adapting previous studies with some modifications. Ethical approval was obtained from the Kulliyyah Postgraduate and Research Committee (KPGRC) and International Islamic University Malaysia Research Ethical Committee (IREC) before the study was conducted (KAHS 17/23). A set of questionnaires and informed consent were prepared and distributed to the selected respondents via Google Form.

Sampling Method

The sampling method that was used for this study is convenience sampling. The students that were included to be part of the sample should be those who are willing and interested and those who met the requirements of the inclusion and exclusion criteria that have been set to obtain reliable results from the reliable respondents in this research.

Instruments

A set of questionnaires comprised of four parts were distributed to the respondents through online. Firstly, sociodemographic factors such as gender, age, race, campuses, academic level, kulliyyah, year of study and current living. The second part was to assess the academic stress level using Educational Stress Scale for Adolescent (ESSA) consisting of 16 questions on a 5-point Likert scale with reliability index of 0.86 on Cronbach alpha. Scores of academic stress level were classified into high (score > 58), moderate (score 51-58), and low (score < 50). To identify the level of sleep quality, the Sleep Quality Scale (SQS) was used which consists of 28 items and 6 domains of sleep quality: daily symptoms, restorative after sleep, difficulties initiating and maintaining sleep, trouble waking, and sleep satisfaction. This self-reported questionnaire employs a 4-point Likert scale to reflect specific sleep habits (0 = "rarely," 1 = "sometimes," 2 = "often," and 3 = "almost always"). Total ratings range from 0 to 84, with higher values indicating more severe sleep issues. The reliability is 0.81 on Cronbach alpha. Lastly, the Dutch Eating Behaviour Questionnaire (DEBQ), which consists of 33 items were used to measure the eating behaviour among IIUM students. This assessment is used in students to evaluate three unique distinct eating behaviours in adults: emotional eating, external eating, and restrained eating. The DEBQ items used a 5-pointed Likert scale that scored from 1 (never) to 5 (very often), with higher scores indicating higher evidence of the eating behaviour. The reliability for DEBQ is 0.90 on Cronbach alpha.

Statistical Analysis

The data collected was analyzed by using SSPS version 29 software. The descriptive analysis was used to measure the percentage, mean and standard deviation (SD) of the socio- demographic data, meanwhile Pearson's correlation and multiple linear regression was used to analyze the relationship between academic stress, sleep quality and eating behaviour.

RESULTS

Socio-demographic factors

Descriptive analysis showed that 81% of the respondents were female. Most of the respondents were at the age of 20-21 years old (50.2%), followed by 22-23 years old (39.8%), 18-19 years old (6.3%), 24-25 years old (2.9%) and > 25 years old (0.8%). Malay was the dominating race among the respondents, shown by 100%. Most of the respondents (94.4%) were undergraduate students and 5.1% were foundation students while the remaining 0.5 % were postgraduate students that comprises 21.7% from year 1, 21.5% year 2, 40% year 3, 10.2% year 4 while the rest 1.5% were students of year 5 and above. In addition, students were from Kuantan (61%), Gombak (25.9%) and Pagoh (8%) while the least was from CFS Gambang (5.1%). There was also a huge difference between the living situation of the students in which many of them were already on-campus (97.6%, n = 4-00) while 1.7% (n = 7) and 0.7% (n= 3) were off - campus and stayed with family. Hence, the result of the respondents' socio-demographics factor was presented in Table 1.

Table 1: Sociodemographic factors of respondents

Sociodemographic Factors	Categories	Frequency (n)	Percentage (%)
Gender	Male	78	19
	Female	332	81
Age	18-19	26	6.3
	20-21	206	50.2
	22-23	163	39.8
	24-25	12	2.9
	25 and above	3	0.8
Race	Malay	410	100
Campus	CFS Gambang	21	5.1
	Kuantan	250	61
	Gombak	106	25.9
	Pagoh	33	8
Year of Study	CFS	21	5.1
	Year 1	89	21.7
	Year 2	88	21.5
	Year 3	164	40
	Year 4	42	10.2
	Year 5	6	1.5
Academic Level	Foundation	21	5.1

	Undergraduate	387	94.4
	Postgraduate	2	0.5
Living Campus	On Campus	400	97.6
	Off Campus	7	1.7
	Stay with Family	3	0.7
Kulliyyah	KAHS	195	47.6
	KAED	6	1.5
	KOD	4	1.0
	KENMS	18	4.4
	KOED	12	2.9
	KOE	8	2.0
	KICT	7	1.7
	KIRKHS	49	12.0
	KLM	19	4.5
	AIKOL	3	0.7
	KOM	13	3.2
	KON	18	4.4
	KOP	12	2.9
	KOS	46	11.2

Academic Stress Level

Descriptive analysis was done to identify the prevalence of academic stress among IIUM students. Based on the Table 2, it was reported that most of the students had low academic stress level with the prevalence of 46.3% followed by high 28.1% and moderate 25.6% of the students.

Table 2: Academic stress level

Stress level	**n**	%
High (>58)	115	28.1
Moderate (51-57)	105	25.6
Low (<50)	190	46.3

Sleep Quality Level

Descriptive analysis was done to identify the prevalence of sleep quality among IIUM students. Table 3 showed that most of respondents have no sleep problem with a prevalence of 75.6 % and 24.4% of the students have sleep problems.

Table 3: Sleep quality level

Stress level	**n**	%
Yes (more than 84)	100	24.4
No (less than 84)	310	75.6

Correlation between academic stress, sleep quality and eating behaviours.

Pearson correlation test was done to investigate the relationship between academic stress and sleep quality towards eating behaviour. Table 4 indicated the results of correlation analysis between

academic stress, sleep quality and three types of eating behaviour that consist of restrained, emotional, and external eating behaviour among IIUM students. The results for correlation analysis between academic stress and restrained eating behaviour is (r = 0.245, p < 0.01), academic stress and emotional eating behaviour (r = 0.224, p < 0.01), lastly is academic stress and external eating behaviour (r = 0.180, p < 0.01). Next, there are also the results of correlation analysis between sleep quality and three types of eating behaviour among IIUM students that demonstrated the correlation between sleep quality and restrained eating behaviour (r = 0.162, p < 0.01), sleep quality and emotional eating behaviour (r = 0.260, p < 0.01) as well as sleep quality and external eating behaviour (r = 0.184, p < 0.01). Overall, all variables have a significant relationship with each other since p < 0.01 for all variables and are explained in Table 4.

Table 4: Correlation analysis for academic stress, sleep quality and eating behaviours.

Variables	1	2	3	4
1. Academic stress	-			
2. Sleep quality	.253**	-		
3. Restrained eating behaviour	.245**	.162**	-	
4. Emotional eating behaviour	.224**	.260**	.201**	-
5. External eating behaviour	.180**	.184**	-.013	.391**

*Correlation is significant at the 0.01 level (2-tailed)
Correlation is significant at the 0.05 level (2-tailed)

Regression between academic stress, sleep quality and restrained eating behaviour

Table 5 illustrated the result of the regression analysis that conducted to identify the predictive factor of academic stress and sleep quality towards restrained eating behaviour among IIUM students. According to the table above, R value = 0.266 and R^2 value = 0.071 showed only 7.1% variance between three variables. F value showed that there is a significant relationship between the variables that prove that academic stress and sleep quality can lead to restrained eating behaviour among IIUM students F (2, 407) = 15.464, p < 0.0001.

Table 5: Summary for regression analysis between academic stress, sleep quality and restrained eating behaviour.

R	R^2	Adjusted R^2	Standard error of the estimate	F (df = 2, 407)	Sig.
0.266	0.071	0.066	8.634	15.464	0.000

Based on Table 4.6, it is found that academic stress (b = 0.167, p < 0.0001) and sleep quality (b = 0.109, p < 0.0001) are significantly predictive towards restrained eating behaviour among IIUM students. However, only 7.1% of variance explained which is very low for academic stress and sleep quality to be a predictor towards restrained eating behaviour.

Table 6: Coefficient regression analysis between academic stress, sleep quality and restrained eating behaviour.

Model	Unstandardized coefficients		Standardized coefficients		
	B	Std. Error	Beta	t	Sig.
(Constant)	15.128	2.239		6.757	0.000
1. Academic stress	0.167	0.038	0.218	4.415	0.000
2. Sleep quality	0.109	0.050	0.106	2.154	0.032

Dependent variables: Restrained eating behaviour

Regression between academic stress, sleep quality and emotional eating behaviour

Table 7 illustrated the result of the regression that conducted to identify the relationship between academic stress and sleep quality towards emotional eating behaviour among IIUM students. According to the table above, R value = 0.307 and R^2 value = 0.094 that showed only 9.4% variance explained by the two variables. F value showed that there is a significant influence of academic stress and sleep quality towards emotional eating behaviour among IIUM students F (2, 407) = 21.206, p < 0.0001.

Table 7: Summary for regression analysis between academic stress, sleep quality and emotional eating behaviour.

R	R^2	Adjusted R^2	Standard error of the estimate	F (df = 2, 407)	Sig.
0.307	0.094	0.090	10.466	21.206	0.000

Based on Table 8, it is found that academic stress (b = 0.159, p < 0.0001) and sleep quality (b = 0.273, p < 0.0001) are significantly predictive towards emotional eating behaviour among IIUM students. However, the prevalence of academic stress and sleep quality to be a predictor towards emotional eating behaviour is 9.4% which the highest percentage among other types of eating behaviour.

Table 8: Coefficient regression analysis between academic stress, sleep quality and emotional eating behaviour.

Model	Unstandardized coefficients		Standardized coefficients		
	B	Std. Error	Beta	t	Sig.
(Constant)	18.916	2.714		6.971	0.000
1. Academic stress	0.159	0.046	0.169	3.463	0.001
2. Sleep quality	0.273	0.061	0.217	4.459	0.000

Dependent variables: Emotional eating behaviour

Regression between academic stress, sleep quality and external eating behaviour

Table 9 illustrated the result of the regression analysis that conducted to identify the predictive factor of academic stress and sleep quality towards external eating behaviour among IIUM students. According to the table above, R value = 0.230 and R^2 value = 0.053 that showed only 5.3% variance explained by the predictor variables. F value showed that there is a significant relationship between the variables proving that academic stress and sleep quality can lead to external eating behaviour among IIUM students F (2, 407) =11.364, $p < 0.0001$.

Table 9: Summary for regression analysis between academic stress, sleep quality and external eating behaviour.

R	R^2	Adjusted R^2	Standard error of the estimate	F (df = 2, 407)	Sig.
0.230	0.053	0.048	5.347	11.364	0.000

Based on Table 10, it is found that academic stress (b = 0.067, $p < 0.0001$) and sleep quality (b = 0.093, $p < 0.0001$) are significantly predictive towards external eating behaviour among IIUM students. However, the prevalence of academic stress and sleep quality to be a predictor towards external eating behavior is 5.3% which the lowest percentage among other types of eating behaviour.

Table 4.10: Coefficient regression analysis between academic stress, sleep quality and external eating behaviour.

Model	Unstandardized coefficients		Standardized coefficients		
	B	Std. Error	Beta	t	Sig.
(Constant)	21.474	1.387		15.487	0.000
1. Academic stress	0.067	0.023	0.142	2.854	0.005
2. Sleep quality	0.093	0.031	0.148	2.971	0.003

Dependent variables: External eating behaviour

DISCUSSIONS

Level of Academic Stress

The first objective of this study is to identify the academic stress level and sleep quality among IIUM students. According to the results, majority of IIUM students have been categorized as perceived low academic stress level. However, that was contradict with the previous study by Zamroni et al. (2018) that found out majority of the university students experienced with high level and moderate level of academic stress. Based on that study, 72 students enrolled in the Medicine and Pharmacy program at the Universitas Islam Negeri (UIN) Maulana Malik Ibrahim Malang, Indonesia were chosen to find out

how much academic stress they felt throughout their study journey. The degree of academic stress as perceived by the UIN students was later shown to be higher than the amount of academic stress as reported by the IIUM students. The difference in emphasis on the kinds of courses that the participants took may be the cause of the discrepancy between the current finding and the results of the prior study.

Another reason for the difference in prevalence between UIN students and IIUM students was that UIN study was conducted primarily among medical and pharmaceutical students, whereas the study that has been performed by IIUM students was in general for all courses. As a result, the prevalence of academic stress among the university students was varied in these two-research due to the diverse participant background study and criteria. As a result, it can be inferred that since participants in this study came from a variety of academic backgrounds rather than just students with the same background.

Level of Sleep Quality

When comparing the findings of earlier local studies conducted during COVID-19 pandemic, which varied from 45.2% to 57.3% that showed a reduced prevalence of poor sleep quality was discovered (Md Zuki et al., 2021). The fact that this survey was undertaken after Malaysia had been in lockdown for one and half years, starting in March 2020, may be a plausible explanation for the lower prevalence revealed in the current study. With increasing confinement or lockdown time, it is thought that the quality of sleep dropped. In conclusion, compared to the other two learning centres, the community health facility had the largest percentage of students who slept poorly (Ngu et al., 2017). This finding was supported by the previous study by Corrêa et al. (2017) that reported majority students from health sciences program had highest score that indicates having sleep problems.

However, the results from the current study were contradictory since IIUM students showed that the prevalence of sleep quality among them is good while they do not have any sleep problems. The inconsistency of the current finding with the previous study may be due to the different focus on the types of the courses taken by the participants since this study is looking into general courses whereas the previous study is performed specifically among community health centres and programs of health sciences.

The relationship between academic stress, sleep quality and eating behaviour among IIUM students.

Academic Stress and Eating Behaviour (Emotional, Restrained and External)

This study aims to investigate the relationship between academic stress and three types of eating behaviour among IIUM students. This research validated earlier findings about this link since eating behaviour is thought to be a coping mechanism to deal with stressful situations. In addition, the range of student responses on the scale for emotional eating was towards the middle and students tend to eat more when they are feeling sad. This is consistent with Caso et al. (2020) showing a higher food consumption was related with sadness, anger, and anxiety. Based on the result for this study, academic stress expectations were positively associated with sweet food consumption and snacking which can be categorized under restrained eating behaviour. Additionally, the association found between snacking and academic stress, it is possible that students who are under stress are consuming most of their unhealthy food through between-meal snacks.

The last association for academic stress is about the association between academic stress and external eating behaviour. According to Deborah et al. (2022), stress was observed to affect snack intake

in those with either a moderate or high level of external eating behaviours, which was found to be significantly associated with stress-eating patterns. In addition, the previous analysis also found inconsistent results regarding the moderating effect of external eating behaviour on both stress and food intake, with some studies suggesting higher external eating is linked to more daily snacks consumed when experiencing stress (O'Connor et al., 2008). It should be made clear that there is not enough evidence on the association between academic stress and external eating behaviour. As a result, it lacks a solid assertion to support this association.

Sleep Quality and Eating Behaviour (Restrained, Emotional, External)

According to Saleh-Ghadimi et al. (2019), the result from his study showed that there is a significant difference in emotional eating behaviour between the two groups of sleep problems and non-sleep problems among students. The observed result was supported by a substantial correlation between insufficient sleep and emotional eating. The association is confirmed by looking at the scoring which if the score is increasing, hence the score for emotional eating also will increase. This finding is consistent with a study by Dweck et al. (2014) that discovered a relationship between emotional and external eating and poor sleep quality. Therefore, a lack of sleep may make it difficult to control the regulation of emotions, which may make people want to eat more.

Based on the current research, there is a significant association between sleep quality with restrained eating behaviour among IIUM students. However, Blumfield et al. (2017) found no association between poor sleep quality and restrained eating behaviour, refuting the notion that those with sleep disorders or insufficient sleep are more likely to overeat. To support this matter, a lack of sleep has been shown to cause elevated ghrelin levels and lower leptin levels, which result in hunger and appetite (Filiatrault et al., 2014). Hence, this increases the likelihood of overeating, especially when being awake longer results in more opportunities to eat and weight gain. Therefore, it should be made apparent that there is lack of sufficient evidence and research to prove this association.

The influence of academic stress and sleep quality towards eating behaviour among IIUM students.

Another aims for this study also include the influence of academic stress and sleep quality towards eating behaviour among IIUM students. According to Chamberlin et al. (2018), there is significant association between academic stress and emotional eating behaviour. This is due to those who are got higher grade point average (GPA) may experience higher levels of stress about studies, which would increase the possibility that they would turn to emotional eating as a coping mechanism. Even restrained eating habits is not common among university students, but it still gives an impact to them. Restrained eating behaviour basically involves in restricting food intake goes against physiological controls like hunger and satiety with the purpose of controlling body weight (Polivy et al., 2020). On the other hand, it also has been found to be negatively related with the eating of low energy high nutrition foods (i.e., healthy foods), notably fruit and vegetables, with intake of these foods decreasing as stress levels rise.

Furthermore, sleep quality also can influence restrained eating behaviour. This can be proof by Filiatrault et al. (2014) study that showed relationship between restrained eating behaviour with sleep quality and duration seem to influence this relationship. However, this study demonstrated that characteristics of restrained eating behaviour are also associated with the success of weight loss. Susceptibility to hunger and its related subcores all diminished as a treatment effect. These adjustments help people lose weight since increased hunger susceptibility levels make it difficult to avoid consuming too much energy in the future and are positively correlated with obesity levels (Elfhag, 2005). To support this matter, lack of sleep has been demonstrated to result in increased ghrelin levels

and decreased leptin levels, which result in hunger and appetite (Paturel, 2022). As a result, there is a higher chance of overeating because staying awake longer gives one more opportunity to eat and puts on weight. Therefore, even though poor sleep quality and controlled eating habits are associated, this relationship cannot be proven because there is insufficient data for this study.

CONCLUSION

In summary, students also can be affected by the stress perceived. The biggest source of stress for this age group would consequently be academic-related issues as they spend most of their time at school or university. Even though the majority of IIUM students reported experiencing low of academic stress, the prevalence of students reporting moderate to high levels of academic stress was alarming because this situation can be worsened in the future if no intervention taken. Sleep quality also can affect eating behaviour among students especially those who are having sleep problems because it will link to unhealthy eating habits, thus can affect students' health condition.

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ANXIETY AND SOCIAL MEDIA ADDICTION ON EATING BEHAVIOUR AMONG UNIVERSITY STUDENTS

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ABSTRACT

Introduction: University students may encounter a variety of stressful scenarios that may have an impact on their health and well-being as they negotiate the academic and social demands of a better education. Eating disorders are one such difficulty that may have a negative impact on both mental and physical fitness. This is due to the numerous difficulties faced by university students, which have a negative impact on how they eat. There are three types of eating behaviours can be distinguished: restrained, emotional, and external. Anxiety and addiction to social media are two elements that influence unhealthy eating behaviour. Therefore, this study is conducted to identify the relationship among anxiety, social media addiction and eating behaviour among IIUM students. **Methods:** This study used cross sectional design, in which samples were obtained using convenience sampling, with a total sample of 410 students. Data were collected using the General Anxiety Disorder-7 (GAD-7), Social Media Addiction Scale (SMAS) and Dutch Eating Behaviour Questionnaire (DEBQ). **Results:** The

study reported that 53.1% experienced mild anxiety of the students. Furthermore, there is a significant association between anxiety and restrained (r= 0.165, p < 0.05), and emotional (r= 0.113, p < 0.05). However, there is no significant association between anxiety and external eating behaviour. Other than that, 64.9% of students reported that they developed a little addiction to social media. Thus, there is a significant association between social media addiction towards emotional eating behaviour (r= 0.231, p < 0.05) and external eating behaviour (r= 0.201, p < 0.05), meanwhile there is no significant association between social media addiction and restrained eating. **Conclusion:** Emotional eating behaviour has a weak correlation with anxiety and social media addiction.

Keywords: Anxiety, Social Media Addiction, Eating Behaviour, Students

INTRODUCTION

Eating behaviour is a complex and multifaceted phenomenon that includes social, cultural, and environmental elements in addition to physiological needs (Mohammedi et al., 2017). The physiological side of eating involves the body's physiological signals for hunger, satiety, and nutrient deficiency as well as how to deal with these sensations. These cues are controlled by hormones that tell the brain when to eat or stop eating, such as ghrelin and leptin (Gómez-Apo et al., 2021). However, eating habits are not just influenced by physiological needs; psychological considerations also come into consideration. A person's food choices and intake can be influenced by psychological elements such as stress, emotions, mood, and dietary preferences (Medina-Vera et al., 2019). Environmental elements including food accessibility and availability, marketing and social media influences, and economic position can all affect on how people eat.

Anxiety is one of the elements that can influence eating behaviour. Anxiety is a widespread mental health problem that impacts many people worldwide. Fear, concern, and nervousness are typical symptoms of the psychological disorder known as anxiety (Dunki & Vuleti, 2021; Medina-Vera et al., 2019). Anxious individuals may modify how they behave when they are eating. These alterations may appear in various ways, including increased or decreased appetite, binge eating and/or restricting food intake. The fight-or-flight reaction is triggered when a person feels anxious, which raises their cortisol and adrenaline levels. Depending on how a person reacts to anxiety, these hormones can both enhance and reduce appetite (Ans et al., 2018). Since fear suppresses hunger hormones in some people, this can result in decreased appetite (Rising et al., 2021). Over time, this may result in malnutrition and weight loss (Raikou, 2015).

Besides that, social media addiction also affects eating behaviour (Thakur & Varmani, 2015; Lahiry, 2022). First of all, social media can have a beneficial impact on eating behaviour by allowing users to find and share healthy recipes, connect with others who share their commitment to healthy eating, and get support and motivation in their quest to make better food choices (Chung et al., 2021). However, social media addiction can also lead to watching videos and images of unhealthy meals on social media which can make people crave them impulsively (Mason et al., 2020; Virmond et al., 2020). Furthermore, social media can promote disordered eating habits such as preoccupation with appearance and weight, obsession with healthy eating or bad diets, and comparison to the exaggerated body images presented on the internet (Shaw et al., 2018).

To sum up, social media and anxiety greatly influence on eating behaviour. There are negative impacts that might result in disordered eating habits. The results of the study will help to understand better how social media addiction and anxiety influence IIUM students and how they are related to unhealthy eating behaviours. The results can identify the level of anxiety and social media addiction, enabling the development of specific treatments. Students' health has suffered as a result of the concern that comes with being a young adult, particularly in terms of their eating habits and the quality of the food they consume. They must maintain good health by careful dietary choices to prevent long-term health effects and chronic diseases (Sprake et al., 2018).

MATERIALS AND METHOD

Subjects

This study involved 410 students of IIUM from Gambang, Kuantan, Gombak and Pagoh campuses from various courses and level of studies were selected to be the participants of this research.

Study Design

This quantitative research was conducted using cross sectional design involving all students of IIUM and a series of questionnaires was created by adopting and adapting previous studies with some modifications. Ethical approval was obtained from the Kulliyyah Postgraduate and Research Committee (KPGRC) and International Islamic University Malaysia Research Ethical Committee (IREC) before the study was conducted (KAHS 7/23). A set of questionnaires was prepared and distributed to the selected respondents via Google Form. Informed consent was also was included and filled in by the participants before they answered the questions.

Sampling method

A convenient sampling method was used to select the study respondents. After the respondents agree to the terms of the agreement, participants have the right to withdraw if they change their minds and do not want to participate.

Instruments

A set of questionnaires comprises of three part were distributed to the respondents through online platform. The first part of the questionnaire involve information regarding the sociodemographic background of the respondents such as gender, age group, race, campus of study, Kulliyyah, year of study and living status (eg: on campus, off campus, living with family). The second part was to assess the anxiety level using General Anxiety Disorder-7 (GAD-7) scale consisting of 7 questions on a 5-point Likert scale with a reliability index of 0.917 on Cronbach alpha. The scores of anxiety levels were classified into minimal, mild, moderate and severe. Next, the third part assessed the social media addiction level using The Social Media Addiction Scale (SMAS) that consists of 29 questions on a 5-point Likert scale with a realibility index of 0.918 on Cronbach alpha. The scores of social media addiction levels were classified into not addicted, little addicted, medium addicted and highly addicted. Lastly, Dutch Eating Behaviour Questionnaire (DEBQ) consisting of 33 questions on a 5-point Likert scale was used to assess the eating behaviour status of the students. It is a multidimensional questionnaire which consists of restrained eating (items 1-10), emotional eating (items 11-23) and external eating (items 24-33). The realibility index for retrained eating, emotional eating and external eating were 0.194, 0.927, 0.844 on Cronbach's alpha respectively.

Statistical Analysis

The data collected was analyzed using the SPSS version 29 software. The percentage, mean, and standard deviation (SD) of the sociodemographic data, level of anxiety and social media addiction level were measured by descriptive analysis. Pearson correlation was used to analyze the relationship between anxiety, social media addiction and eating behaviour (restrained, emotional and external) among IIUM students.

RESULTS AND DISCUSSIONS

Demographic Data

Descriptive analysis showed that 81% of the respondents were female. Most of the respondents were at the age group of 20-21 years old (50.2 %), followed by 22-23 (39.8 %), 18-19 years old (6.3%), 24-25 year old (2.9 %) and > 25 years old (0.8 %). Malay race was dominating among the respondents shown by 100%. The respondents included the students of foundation (5.1%), postgraduate (0.5%) and undergraduate (94.4 %) which comprises 21.7% from year 1, 21.5% year 2, 40% year 3,10.2% were year 4 and 1.5% were year 5. In addition, students from Kuantan (61%) and Gombak (25.9%) were the main contributors of the response, followed by the students from Pagoh campus (8%) and Gambang campus

(5.1%). Majority of the students were from Kulliyyah of Allied Health Sciences which contributes 47.6% from the respondents. There was also a huge difference between the living situation of the students in which the majority of them were already on-campus (97.6%) while 2.4% were off-campus. Details of the socio-economic characteristics of the respondents was summarized in the Table 1.

Table 1 Socio-economic characteristic of the respondents

Demographic Factor	Categories	Frequency (n)	Percentage (%)
Gender	Male	78	19
	Female	332	81
Age	18-19	26	6.3
	20-21	206	50.2
	22-23	163	39.8
	24-25	12	2.9
	25 above	3	0.8
Race	Malay	410	100
Campus	CFS Gambang	21	5.1
	Kuantan	250	61
	Gombak	106	25.9
	Pagoh	33	8.0
Year of study	CFS	21	5.1
	Year 1	89	21.7
	Year 2	88	21.5
	Year 3	164	40
	Year 4	42	10.2
	Year 5	6	1.5
Academic level	Foundation	21	5.1
	Undergraduate	387	94.4
	Postgraduate	2	0.5
Living Campus	On Campus	400	97.6
	Off Campus	7	1.7
	Stay with Family	3	0.7
Kulliyyah	KAHS	195	47.6
	KAED	6	1.5
	KOD	4	1.0
	KENMS	18	4.4
	KOED	12	2.9
	KOE	8	2.0
	KICT	7	1.7
	KIRKHS	49	12.0
	KLM	19	4.5
	AIKOL	3	0.7
	KOM	13	3.2
	KON	18	4.4
	KOP	12	2.9
	KOS	46	11.2

Anxiety level

A descriptive analysis was done to identify the prevalence of anxiety among IIUM students. Based on the Table 2, it was reported that most of the students were on mild level of anxiety with a prevalence of 53.1%, followed by minimal level (25.4%), moderate level (21.2%) and severe anxiety level (0.3%).

Table 2 Anxiety level

Anxiety level	Frequency (n)	Percentage (%)
Minimal	104	25.4
Mild	218	53.1
Moderate	87	21.2
Severe	1	0.3

The majority of students in the study have low levels of anxiety, according to score information on anxiety among IIUM students. Similar results are reported in Simegn et al. (2021) study of generalised anxiety disorder in Ethiopian university students, which reveals that 70% of the students experience only mild anxiety. Moreover, Islam et al. (2020) conducted a study on depression and anxiety in Bangladeshi first-year university students and discovered that the majority of the students had moderate anxiety. The study also revealed that 13% of the students had severe anxiety. The study by Islam et al. (2022) differs from the present study in its emphasis on first-year university students, while the present study primarily focused on IIUM students. The majority of IIUM students do not exhibit any signs of anxiety, and those who do can still manage their feelings and symptoms. This leads us to the conclusion that IIUM students have low anxiety levels.

Social Media Addiction Level

A descriptive analysis was done to identify the prevalence of social media addiction among IIUM students. Based on the Table 3, it was reported that most of the students were little addicted to social media with a prevalence of 64.9%, followed by medium addicted (19.3%), not addicted (14.9%) and highly addicted (0.9%).

Table 3 Social Media Addiction Level

Social Media Addiction level	Frequency (n)	Percentage (%)
Not Addicted	61	14.9
Little Addicted	266	64.9
Medium Addicted	79	19.3
Highly Addicted	4	0.90

Most IIUM students, according to the results, experience moderate social media addiction. Similarly, Iranian medical students, reported a moderate rate of social media addiction (Azizi et al., 2019). The prevalence of social networking addiction among students was also found to be 29.5% and 36.9%, respectively, in Singapore and India (Ramesh et al., 2018; Catherine So-kum Tang & Woen, 2017). The authors contend that students who don't learn to limit their time on social media will suffer serious personal and societal consequences. According to a 2016 study by Yamikani Ndasauka et al. people who spend too much time on social media experience a decline in their social life. Furthermore, lower levels of self-esteem are linked to higher levels of social media addiction as reported in a research by Hawi and Samaha (2016). As a conclusion, most IIUM students develop moderate addiction towards social media as social networks are a necessity for many students due to the abundance of academic and professional opportunities they offer.

Correlation between anxiety, social media addiction and eating behaviour (Restrained, Emotional and External)

Pearson correlation test was done to investigate the relationship between the independent variable (anxiety, social media addiction) and eating behaviour among IIUM students. Based on the results anxiety have a significant relationship between restrained (r = 0.165, $p < 0.01$), and emotional eating ($r = 0.113$, $p < 0.01$), meanwhile anxiety does not have a significant relationship with external eating behaviour ($r = 0.083$, $p > 0.05$) since p > 0.05. Next, based on the results social media addiction have a significant relationship with emotional ($r = 0.231$, p < 0.05) and external ($r = 0.201$, $p < 0 .01$), meanwhile social media addiction does not have a significant relationship with restrained eating behaviour ($r = 0.092$, $p > 0.05$). The results was shown on Table 4.

Table 4 Correlation among variables

Variables	Restrained eating	Emotional eating	External eating
Anxiety	0.165**	0.113**	0.083
SocialMedia Addiction	0.092	0.231**	0.201**

**Correlation is significant at the level 0.01 level (2-tailed)

We can infer from the findings of the present study that social media addiction and anxiety are connected to eating behaviours. Some eating behaviours, however, do not correlate with the variables. First, based on the findings, we can deduce that anxiety and emotional and restrained eating are significantly related. According to Aucoin et al. (2021), students with anxiety issues are more likely to limit their dietary intake. In order to feel more in control of their physical appearance, students who are experiencing anxiety and stress related to their studies and their daily lives may turn to dieting. The relationship between anxiety and external eating behaviour is, however, insignificant, these results were contrary to research from Ergun et al. (2013). This is because numerous studies have demonstrated a close relationship between anxiety and external eating behaviours.

Secondly, one of the elements influencing eating behaviours among IIUM students is social media addiction. The present study shows a significant connection between social media addiction towards emotional and external eating behaviour. This is because social media addiction is connected to more obvious eating patterns that can lead to emotional eating behaviour as claimed by Gao et al. (2020). Similarly, research found that individuals with higher propensities for social media addiction also had higher likelihoods of engaging in external eating behaviour. However, addiction to social media does not significantly correlate with restricted eating behaviour. These results were contradicted with other research as the author's claim that social media has been shown to affect people's perceptions of their appearance and lead to restrictive eating behaviour (Perloff, 2014; Handford et al., 2018).

CONCLUSION

In conclusion, social media and anxiety have a weak relationship with eating behaviour among IIUM students. According to the findings, majority of students have mild anxiety and little addiction to social media since they are still able to manage their symptoms. However, social media use and anxiety both have a negative effect on people's commitment to practising healthy eating habits. This study also shows the necessity for intervention programmes that target anxiety and addiction management, techniques and encourage healthy eating habits among university students. Universities need to take proactive measures to address these issues and provide a supportive and safe environment for its students.

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EXPLORING AN ADVERSE EFFECT OF SOCIAL MEDIA ON ADOLESCENT'S MENTAL HEALTH

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ABSTRACT

Background: Previous studies have reported that adolescent use of social media can have a negative impact on their mental health. In 2021, the National Institutes of Health Malaysia emphasized the urgent need to address digital-related mental health issues, which pose a significant gap in our understanding. Nevertheless, there has been a lack of research on the effects of social media addiction on the mental well-being of local adolescents. This study aims to examine the effect of social media use on mental health issues among adolescents in Kelantan, Malaysia. **Methods:** A total of 384 respondents voluntarily participated in this cross-sectional study involving ten districts in Kelantan using the snowball sampling method. **Results:** Analysed data finds social media addiction correlates significantly with depression ($r = .390$, $p < .01$), suicide ideation ($r = .188$, $p < .01$) and self-esteem ($r = .156$, $p < .01$). Multiple regression analysis indicated that suicide ideation was predicted by social media addiction ($\beta = -.01$, $p < .05$) and depression (β - .12, $p < .01$) but not self-esteem ($\beta = -.002$, $p > .05$). Furthermore, social media moderates the relationship between depression and suicidal ideation ($\beta = .0016$, $p < .05$). **Conclusion:** Controlling social media use may prevent addiction and promote greater mental health among adolescents.

KEYWORDS: social media addiction, depression, self-esteem, suicidal ideation, adolescent, Malaysia

INTRODUCTION

Social media is now a fundamental part of modern life, offering a platform for social connections, promoting products and services, and providing quick and easy access to information. Its growing role in the lives of Malaysian adolescents necessitates an investigation into its potential impact on their mental well-being. Excessive social media usage can lead to issues such as addiction and exposure to negative content, both directly and indirectly. Extensive research has indicated that this overuse can have detrimental effects on both physical and mental health, as demonstrated by studies like those conducted by David et al. in 2021 and Memon et al. in 2018. Recent research, including work by Twenge et al. (2018) and Rosen et al. (2013), has associated excessive social media use with various mental health challenges, including sadness, anxiety, and low self-esteem.

Researchers in Malaysia have specifically identified a strong connection between social media addiction and stress, anxiety, and depression among undergraduate nursing students in Kuantan, proposing that this negative impact includes a secondary layer of stress and despair (Cho et al., 2021). Furthermore, factors like cyberbullying (Abaido, 2020), statutory rape, unsafe sex (Bazlin & Noor Azlan, 2011), teenage pregnancy, and exposure to pornography (Kimemia & Mugambi, 2016) are hypothesized to contribute to the depression, anxiety, and stress experienced by adolescents. Additional findings indicate that adolescents may encounter adverse experiences on social media, including anxiety stemming from the need for approval and exposure to distressing content, which can further contribute to declining mental health (Samantha & Zhooriyati, 2022).

While the influence of social media on the mental health of Malaysian adolescents has gained attention, a significant research gap exists concerning its impact in rural areas. Existing studies have primarily concentrated on urban adolescents, neglecting the distinct experiences and challenges faced by their rural counterparts in the context of social media and mental health (NIHM 2021 & Shamsuddin et al. 2013).

Addressing this gap is essential for developing more effective interventions and strategies tailored to the specific needs of rural Malaysian adolescents, potentially enhancing their mental health outcomes. This study aims to investigate the consequences of social media addiction, focusing on suicidal ideation, depressive symptoms, and self-esteem among adolescents in Kelantan. The results will offer valuable insights into how social media affects the mental health of Malaysian adolescents, informing the development of interventions and policies designed to promote healthier social media usage within this demographic.

METHODOLOGY

In a cross-sectional survey spanning ten districts in Kelantan, we sourced adolescent population data from the Department of Statistics Malaysia (DOSM) website. The data was categorized by ethnicity (Malay, Chinese, Indian, Bumiputras), gender (male and female), and age groups (10-14 years, 15-19 years, and 20-24 years). To accommodate our research needs, we adjusted the starting age from 12 to 10 years old, ensuring that the 10-14 years age range included 12-year-olds during data sorting. The total adolescent population encompassed all ethnicities, genders, and age groups, amounting to N = 59,878,000. To determine the sample size, we utilized an online calculator at https://www.calculator.net/sample-size-calculator.html. Our study employed a 95% confidence level, a 5% margin of error, a population proportion of 50%, and a population size of N = 59,878,000. This calculation yielded a required sample size of n = 385.

This study employed a simple random sampling method to gather 385 samples, ensuring an unbiased selection process and equal opportunity for all adolescents in Kelantan. Eligibility criteria were established for participants. Inclusion criteria: i) Malaysian nationality, ii) age between 12-24 years, iii) current internet and social media use, iv) proficiency in Malay and/or English, and v) willingness to complete the survey. Exclusion criteria: i) non-Malaysian citizenship, ii) age below 12 or above 24, iii) no internet access or social media usage, iv) inability to comprehend Malay and/or English, v) lack of willingness to participate in the survey, and vi) a diagnosis of mental illness.

This study utilized the Google Form platform for our survey, and it was distributed via WhatsApp, Telegram, Facebook, Instagram, and Twitter. The form incorporated an information sheet explaining the study, a consent form, and four standardized questionnaires. These questionnaires assessed depression (using the Patient Health Questionnaire-9; PHQ-9), suicidal ideation (a component of the PHQ-9), self-esteem (utilizing the Rosenberg Self Esteem Scale; RSES), and social media addiction (assessed through the Social Media Addiction Questionnaire; SMAQ). To promote participation and minimize response bias, all questionnaire items were available in both English and Malay languages. To ensure complete responses, each item was configured as 'required' within the Google Form settings.

All potential respondents received an information sheet, consent form, and questionnaire through the provided link. Individuals under 18 years of age were required to obtain parental or legal guardian consent before completing the questionnaire. Data collection took place from September 3, 2022, to November 7, 2022. The completed questionnaires were collected and recorded in a Google Sheet, resulting in 384 responses, which were cleaned and prepared for analysis.

The data analysis utilized the Statistical Package for Social Sciences (SPSS) version 27.0. We employed both descriptive and inferential statistics, including frequency and percentage analysis for demographic items. Additionally, we utilized Pearson's correlation, multiple regression, and the Baron and Kenny (1986) method for moderation analysis to examine the relationships, predictions, and moderation between social media addiction and depression, self-esteem, and suicidal ideation. Multiple regression was also employed to control for confounding variables such as age and sex.

Instrumentation

Depression

The Patient Health Questionnaire-9 (PHQ-9) was used to assess depression. This scale was created by Kroenke et al. (2001) and it complies with the Diagnostic and Statistical Manual, Fourth Edition (DSM-IV)'s (diagnostic criteria for clinical depression). With an 88% sensitivity and specificity, this measure can detect depression. The response options for the question, which asks about depression symptoms that appeared within two weeks, range from 0 (hardly ever) to 3 (almost daily). Scores under 5 were seen as not indicative of a depressive disorder, however scores of 10 and more are indicative of one. The mean score for patients with major depressive disorder was 17 (SD = 6.1), while the mean score for individuals with other types of depressive disorders was 10.4 (SD = 5.4). PHQ-9 had exceptional reliability characteristics, with internal reliability measuring at Cronbach's alpha =.89. While the mean score between the first test and the retest was recorded at 5.08 and 5.03, the test retest, which was also done between 48 hours, produced reliability, r = 0.84 (Kroenke et al. 2001). The Malay version of the PHQ-9, which was translated and validated by Sherina, Arroll, and Goodyear-Smith (2012), was used for this investigation. The Malay version of the PHQ-9 has convergent validity with the General Health Questionnaire (GHQ-12) at r = 0.61, p 0.001, strong internal reliability, and sensitivity and specificity of 87% and 82%, respectively.

Suicidal ideation

A single PHQ-9 item used to assess suicidal ideation was used. If the respondent "Thought that you would be better off dead or of hurting yourself in some way," they must answer the item. The PHQ-9 questionnaire lists this item as item no. 9 (Kroenke et al 2001).

Self-esteem

The 10-item Rosenberg Self Esteem Scale (RSE) was used to assess general self-esteem. On a four-point Likert scale, from 1 ("strongly disagree") to 4 ("strongly agree"), participants gave answers like "On the whole, I am satisfied with myself" a rating. The reliability of the RSE has been proved by Cronbach's alpha scores, which range from.72 to.90. Li et al. reported in 2019 that the Cronbach's alpha values for factor 1 and factor 2 for upper secondary school pupils in Malaysia were, respectively,.78 and.60. The Rosenberg Self-Esteem Scale-Malay, which Li et al. (2019) translated and validated, is the RSE's translated Malay version. It was used in this study. Strong internal consistency has been demonstrated by this version, with alpha values starting at $\alpha = 0.624$ to 0.776 (Li et al. 2019).

Social media addiction

The Social Media Addiction Questionnaire (SMAQ), created by Hawi and Samaha in 2016, is a modification of the Facebook Intrusion Questionnaire (FIQ) in which "Facebook" has been replaced with "social media." The FIQ was an 8-item Facebook addiction assessment tool that was based on The Mobile Phone Involvement Questionnaire and Brown's 10 Behavioural Addiction Components. The SMAQ questionnaire's instructions state at the outset, "The following questions are about your relationship with and use of online social media." Eight comments about social media addiction are included in it, including "I frequently think about social media when I am not using it." These items are rated by respondents on a 7-point Likert scale, with 1 representing "strongly disagree" and 7 representing "strongly agree." Total scores can vary from 8 to 50; higher values suggest more serious addiction. SMAQ's internal consistency is strong, as seen by its Cronbach's alpha of .87. The typical score on the SMAQ is 24.5 (SD: 9.4). In general, female participants do better than male participants, with a mean score of 26.2 (SD=9.4) versus 22.8 (SD=9.4) for the latter. For the purposes of this study, the SMAQ was back translated by two translators from English to Malay. With a of 0.809, the Malay version of the SMAQ shows good internal consistency. Additionally, there was a positive but small correlation (r = 0.384, p 0.001) between the predictive validity of the Malay-SMAQ and the PHQ-9.

RESULTS

About 400 Google form links were distributed and only 384 responded. There is no incomplete data since the form were set to require all respondent responses on all items asked. This translates to 96% response rate. Normality test was executed prior other parametric test to avoid the violation of assumption. The normality was assess using histogram and Normal Q-Q plot of SMAQ. The histogram visualized as having normal distribution with mean of 27.12 and standard deviation of 9.398. Meanwhile in the Normal Q-Q plot, we observed that the data plot was mostly on the straight line. There are two data was seen as outliers in the boxplot namely data 375 and 364. However, we remain this data as their SMAQ score are on the acceptable range. Other than that, the data has no multicollinearity and shown homogeneity.

Among 384 respondents, 31% were male and the rest were female. The majority of the respondents' ages ranged from 18 to 24 years old (81.5%). Malay races and Islam affiliation dominates the sample which contributed 99.2% and 99.5% respectively. About 41.4% of respondents holds higher education certificates ranging from STPM to Diploma. Most respondents reside in Kota Bharu district (36.7%) and majority (85.4%) lived with their parents. the highest education for respondents' both father and mother were mostly SPM. More detailed socio-demographic profiles are shown in Table 1.

Table 1 Demographic profiles.

Profiles	Frequency (n)	Percent (%)
Gender		
Male	119	31
Female	265	69
Age		
12 -18 years	71	18.5
18 -24 years	313	81.5
Race		
Malay	381	99.2
Chinese	1	.3
Indian	1	.3
Others	1	.3
Religion		
Islam	382	99.5
Buddha	2	.5
Education		
PMR	31	8.1

SPM	59	15.4
Diploma/STPM/STAM/Matriculation	159	41.4
Bachelor Degree	132	34.4
Master	2	.5
PhD	1	.3
District		
Kota Bharu	141	36.7
Pasir Mas	94	24.5
Machang	43	11.2
Tanah Merah	17	4.4
Jeli	6	1.6
Pasir Puteh	18	4.7
Bachok	25	6.5
Kuala Krai	11	2.9
Gua Musang	8	2.1
Tumpat	21	5.5
Stay with		
Parent	328	85.4
Mother Only	40	10.4
Father Only	4	1.0
Grandparent	8	2.1
Adopt Family	4	1.0
Father education level		
PMR	51	13.3
SPM	146	38.0
Diploma/STPM/STAM/ Matriculation	60	15.6
Bachelor Degree	99	25.8
Master	20	5.2
PhD	8	2.1
Mother education level		
PMR	47	12.2
SPM	144	37.5
Diploma/STPM/STAM/Matriculation	63	16.4
Bachelor Degree	110	28.6
Master	14	3.6
PhD	6	1.6

Notes: PMR = Penilaian Menengah Rendah; SPM = Sijil Pelajaran Malaysia; STPM = Sijil Tinggi Pelajaran Malaysia; STAM = Sijil Tinggi Agama Malaysia, PhD = Philosophy Doctor.

Table 2 shows the correlation between social media addiction, depression, self-esteem and suicidal ideation. Social media addiction was found significantly associated with depression ($r = .39$, $p < .001$) as well as self-esteem ($r = .16$, $p < .001$) and suicidal ideation ($r = .19$, $p < .01$). Meanwhile, depression significantly correlated with self-esteem ($r = .26$, $p < .001$) and suicidal ideation ($r = .68$, $p < 0.001$). A weak significant relationship was found between self-esteem and suicidal ideation ($r = .16$, $p < .001$).

Table 2 Inter variable correlation coefficient

	1	2	3	4
1 Social Media Addiction	1	.390**	.156**	.188**
2 Depression		1	.256**	.681**
3 Self-Esteem			1	.155**
4 Suicidal Ideation				1

**. Correlation is significant at the 0.01 level (2-tailed).

Table 3 shows the standard multiple regression used to assess depression, social media addiction and self-esteem to predict suicidal ideation after controlling the influence of gender, age, race, religion, level of education, socio-economic status and districts. Preliminary analyses were conducted to ensure no violation of the assumptions of normality, linearity, multicollinearity, and homoscedasticity. The total variance explained by the model as a whole was 47.1%, F (3, 380) = 112.86, p < .001. In the final model as shown in Table 4, only depression and social media addiction were statistically significant, with depression recording a higher beta value (β = .12, p < .001) than the social media addiction (β = - .01, p < .05), which means only depression and social media addiction predicts suicidal ideation. Meanwhile, poor self-esteem did not predict suicidal ideation among adolescents in Kelantan (β = -.002, p > .05).

Table 3 Model summary of predictors on suicidal ideation

Model Summary

Model	R	R^2	Std. Error of the Estimate	Change Statistic				
				R^2 Change	F Change	df1	df2	Sig. F Change
1	.686[a]	0.471	.72540	.471	112.864	3	380	0.000

a. Predictors: (Constant), Depression, Social Media Addiction, Self esteem

e. Dependent Variable: Suicidal Ideation

Table 4 Multiple regression on suicidal ideation

Model		Unstandardized Coefficients		Standardized Coefficients	t	*P*-value	95.0% CI of β	
		β	SE	Beta			Lower	Upper
1	Constant	-.396[a]	.159		-2.484	.013	-.710	-.083
	Depression	.120	.007	.720	17.366	.000	.106	.133
	Social Media Addiction	-.010	.004	-.090	-2.219	.027	-.018	-.001
	Self esteem	-.002	.005	-.016	-.415	.679	.013	.008

a. Dependent Variable: Suicidal Ideation

Note: SE = standard error, CI = confidence interval

In the table 5 the model contributes 48.0% of the variance changes in suicidal ideation, $R^2 = .4800$, $p < 0.001$. The analysis also shown a significant interaction effect where the effect of depression on suicidal ideation was moderated by social media addiction, $\beta = .0016$, 95% CI (.004, .0027), $t = 2.5768$, $p < 0.05$. The simple slope graph below (Figure 1) shows that all the β value effect of social media addiction is positive, which means social media addiction increased in proportion with the depression on suicidal ideation.

Table 5 Regression coefficient of moderation analysis

Model		Unstandardized Coefficient		t	*P*-value	95.0% CI of β	
		β	SE			Lower	Upper
1	Constant	.0731	.2309	.3165	.7518	-.3809	.5271
	Depression (X)	.0757	.0181	4.1863	.0000	.0401	.1113
	Social Media Addiction (W)	-.0294	.0088	-3.3536	.0009	-.0466	-.0122
	Interaction (XW)	.0016	.0006	2.5768	.0103	.0004	.0027

a. Dependent Variable: Suicidal Ideation
Note. $R^2 = 0.4800$
Note: CI = confidence interval; SE = standard error

As shown in the Table 6, at the lowest point of social media addiction, there is a significant positive relationship between depression and suicidal ideation, $\beta = .1022$, 95% CI (.0838, .1205), $t = 10.9336$, $p < 0.001$ and it can also be seen at the highest point of social media addiction, there is also a significant positive relationship between depression and suicidal ideation, $\beta = 0.1333$, 95% CI (.1162, .1503), $t = 15.3741$, $k < 0.001$. In other words, depression could affect on suicidal ideation are depend on how addicted the individuals are to social media. On the other hand, social media addiction could serve as a triple risk factor as depressed people nowadays rely on social media to cope with stress, killing time during self-isolation or being a victim from social media.

Table 6 Regression coefficient of depression on suicidal ideation according to the level of social media addiction

SMA	Effect (β)	t	*P*-value	LLCI	ULCI
17 (Low)	.1022	10.9336	0.000	.0838	.1205
26 (Mean)	.1162	17.1779	0.000	.1029	.1295
37 (High)	.1333	15.3741	0.000	.1162	.1503

Note: SMA= Social Media Addiction; LLCI = lower limit confidence interval; ULCI = upper limit confidence interval

The simple slope graph was plotted to visualize the moderation interaction of the social media addiction on the relationship between depression and suicidal ideation as shown in Figure 1.

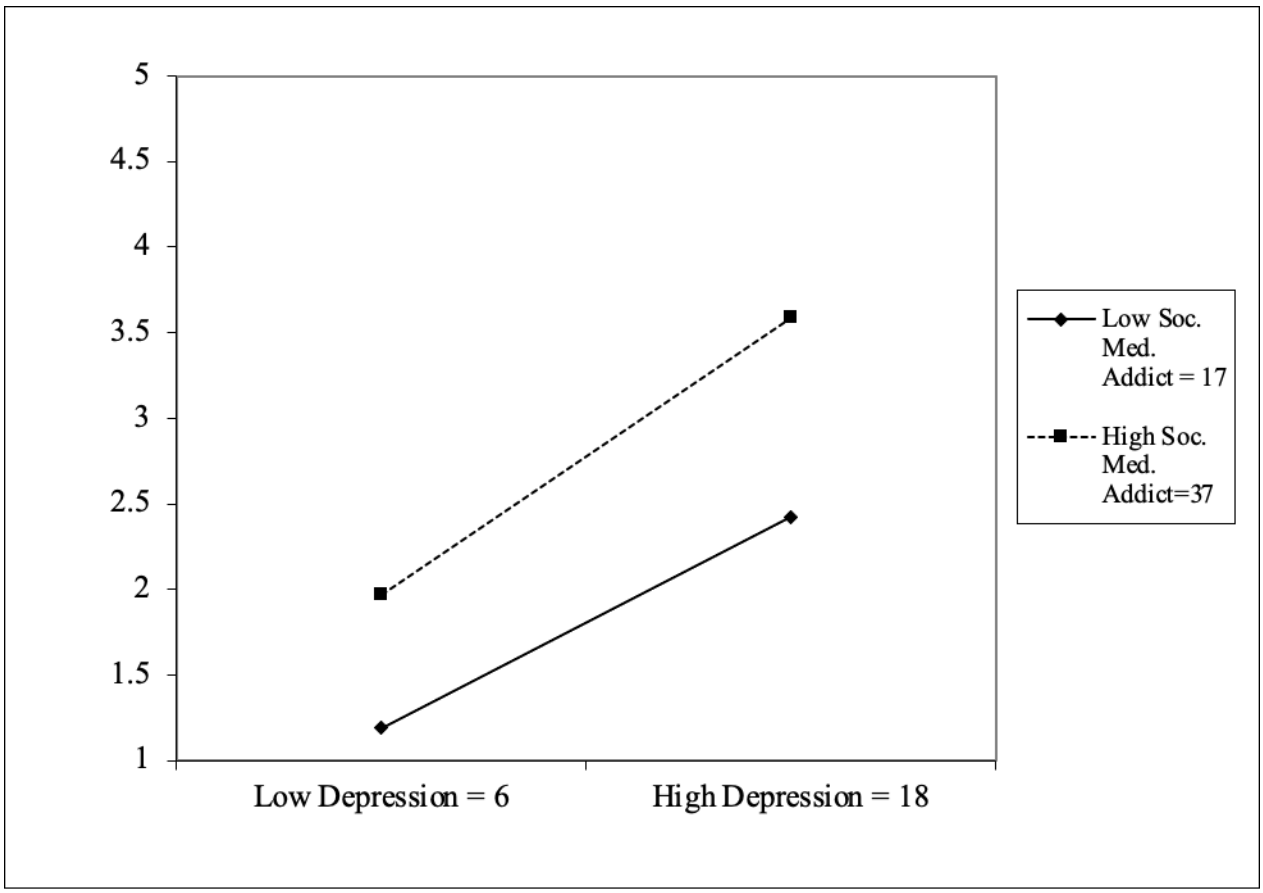


Figure 1. Simple slope interaction effect of social media addiction as moderator

DISCUSSION

Our research indicates that teenage social media addiction is highly associated with depression and suicidal ideation, and further investigation implies that depression and social media use may even be able to predict suicidal thoughts. This finding was further reinforced by research by Brunborg and Andreas (2019), who discovered a connection between adolescent depression symptoms and social media usage. Brunborg and Andreas (2019) clarified that the connection is merely fleeting. A systematic review reported that time spent, activity, investment and addiction on social media influences depression, anxiety, and psychological distress in adolescents (Keles et al. 2020). In addition, Keles et al. (2020) claim that specific attitudes or behaviours, such as social comparison, active or passive use of social media, and reasons for using social media, likely have a greater impact on mental health issues than how frequently someone uses social media or how many friends they have there. Our results, however, run counter to Keles et al. (2020) assertion that self-esteem did not predict suicidal ideation. Instead, the current study found a strong link between depression and suicide. In this regard, we concur with Ivie et al. (2020) that additional research is required to establish the link between social media use and depression. The link may be moderated or mediated by other factors.

It was believed that there were many types of additional factors. like murderous cyberbullying. According to Hinduja & Patchin (2015), "cyberbullicide" is a term used to describe suicide that has a link to cyberbullying. According to a study, social media users, particularly teenagers, are more likely to experience cyberbullying, which makes the victim feel unhappy and, in the worst cases, suicidal (Hinduja & Patchin 2019). Hinduja and Patchin (2015) explained that the victims of cyberbullying are two times likely to attempt suicide by amplifying the feeling of isolation, instability, and hopelessness especially those with pre-existing mental health issues. There is growing concern that social media may be a significant risk factor for suicide and urgently calls for attention as scrolling through social media has become a coping mechanism for depressed adolescents' social withdrawal.

Furthermore, pro-suicide influence groups, information on lethal means and forums discussing suicide methods are easily accessible at any time (Dunlop, More & Romer, 2011, Johnstone, 2011, Rajagopal, 2009, Rajagopal 2004; Brown & Barraclough 1997). Biddle (2008) examined 240 websites and

found that half of them were pro-suicide websites while Recupero et al. (2008) found 11% of 373 websites to be pro-suicide websites. Online chatrooms and forums provide a platform for suicidal ideators to connect and share common thoughts and feelings. Additionally, by participating in such group discussions, suicide ideators push others to commit suicide by providing them with instructions on where, what, and how to do it (Dunlop, More & Romer, 2011, Johnstone, 2011, Rajagopal, 2009, Rajagopal 2004; Brown & Barraclough 1997). When this happens, scholars refer to it as a suicide pact (Rajagopal 2004; Brown & Barraclough 1997). In other cases, suicide ideators may cooperate and agree with other suicide ideators to commit suicide at specific times and frequently using the same lethal means. with the past, people who knew one other well—such as family members, partners, or friends—would make suicide pacts. However, with cybersuicide pacts, most suicides are carried out by strangers (Rajagopal 2004; Brown & Barraclough 1997). Such occurrences have sadly occurred multiple times and have been reported in the media or propagated on social media among Malaysian teenagers and young adults (The Guardian, 2019). Nearby, residents also worry that suicide news may spread quickly. Users of social media and the internet, particularly young people, can pick up dangerous suicide techniques by imitating other suiciders, especially when the suicide was carried out by a well-known person (Williams 2011). Insist that proactive prevention measures must be taken immediately and at a higher level. Social media technology is advancing quickly, and as more people utilise social media, it should already be possible to create advanced artificial intelligence that can assist those who suffer from mental illness. Such technologies will aid those who are considering suicide by preventing them from seeing websites with information on suicide, directing them to helplines instead, and preventing them from conducting additional searches on suicide or self-harm. Utilising current technology, search engines now offer helplines when users enter the keywords "suicide" or "self-harm." That implementation, though, is passive. In the future, we envision artificial intelligence recognising patterns and behaviours that are associated with suicidal or self-harm activity and actively alerting loved ones or emergency personnel to the situation.

CONCLUSION

Modern technology makes it simple for kids to access and learn new information via the internet, which causes parents great worry and concern. Teenagers who rely on social media for social interaction are more likely to engage in cyberbullying, have a propensity for comparison, may discover explicit information, and engage in other high-risk behaviours. Teenagers who are depressed frequently post about how they are feeling on social media rather than discussing their difficulties. Some teens post pictures of their wounds on their arms as a way to communicate their tremendous sorrow, and other teenagers later discover that slashing their hands would help them feel better mentally.

Thus, this study argues the use of social media as a coping skill among adolescents during their depressive episode. Some parents may see their adolescent spending their free time by scrolling on social media is just a common thing and risk-free. It is suggested that behaviour activation strategies as a part of the therapy given to adolescents with depression to avoid them relying too much on social media when they have free time.

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