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ORIGINAL ARTICLE Open Access

Factors affecting waiting time in Outpatient Pharmacy at Hospital Raja Perempuan Zainab II (HPRZII)

Fairul Ezwan Fahrurazi[1*], Nur Husna Ibrahim[1], Nurul Musfirah Mafauzy[1], Wan Nor Ain Wan Ismail[1] and Syauqin Syazwani Mohamed Rusli[1]

ABSTRACT

Introduction: World Health Organization (WHO) has identified that patient waiting time as one of the most important measurements of a responsive health system for healthcare services. Outpatient pharmacy is associated with patient waiting time as the indicator for satisfaction of the services. This study aimed to determine the factors affecting waiting time in Hospital Raja Perempuan Zainab II, Kelantan.

Method: A cross-sectional study was conducted by collecting prescription received in outpatient pharmacy from 1st October 2020 till 31st December 2020. All prescriptions prescribed manually were excluded. Multiple linear regression was performed to determine the factors affecting waiting time and the data were analysed using SPSS version 25.

Results: A total of 248 prescriptions were collected in outpatient pharmacy. The mean waiting time in outpatient pharmacy was 23.0 minutes (SD = 11.0). Waiting time was found to be associated with number of medications in the prescription, number of staff working on that day, prescriptions which required intervention and filling personnel.

Conclusion: The waiting time at the outpatient pharmacy of HRPZ II indicated the acceptable range of quality services which met the patient's satisfaction. Future studies are needed to confirm the satisfaction level of patients and further improve quality of the service.

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Introduction

Outpatient pharmacy refers to the pharmacy department in charge of dealing with patients that do not occupy the beds in hospitals or other inpatient settings (Hammouda & Hammouda, 2012). The outpatient pharmacy is often associated with the waiting time as the degree to which the patients are satisfied with the care received and strongly related to the quality of the waiting experience (Nosek Jr & Wilson, 2001). The aim and vision to improve healthcare quality has always been a great concern in healthcare services. Quality itself can be defined as conformance to specific requirements and standards given (Alodan et al., 2020). Therefore, pharmacy unit needs to improve the services quality as regulated according to the Ministry of Health.

Several studies used different techniques to overcome healthcare services problems and improve quality. A study utilized Six Sigma processes and able to reduce waiting time by 50% in an outpatient pharmacy in a local hospital specialized in cancer treatment in Pakistan (Arafeh, Barghash, Sallam, & AlSamhouri, 2014). Suss *et al.* (2017) implemented a patient flow project to improve efficiency spends in pharmacy queues to reduce waiting time. Every problem was given solutions and a framework was provided to evaluate pharmacy performance based on simulations (Suss, Bhuiyan, Demirli, & Batist, 2017).

World Health Organization (WHO) has identified that patient waiting time as one of the most important measurements of a responsive health system for healthcare services (Sun et al., 2017). Waiting time in outpatient pharmacy has been defined as the length of time from when the patient received the queue number at the counter to the time the patient being called to the counter (Afolabi & Erhun, 2003). Excessive waiting time shows the lack of efficiency of pharmacy services. Such delay leads to dissatisfaction, loss of patronage and poor patients' compliance (Kusumowardhani & Ilyas, 2019; Lin et al., 1999). Therefore, waiting time should be addressed as part of good management practice.

The waiting time in the outpatient pharmacy is usually attributable to the tedious process of packaging, labelling and prescription intervention (Ndukwe, Tayo, & Sariem, 2011). In addition, internal operational factors also contribute to the increase in time spent, for example, prescription requires extemporaneous preparation, low percentage of staff at work and long list of medication in one prescription (Ndukwe et al., 2011). The factors affecting the waiting time are somehow multifactorial and to date, studies determining factors affecting waiting time have been inadequate especially in local setting in Malaysia. Therefore, we aim to determine the mean waiting time as well as factor affecting waiting time in outpatient pharmacy in Hospital Raja Perempuan Zainab II (HRPZ II), Kelantan, Malaysia.

Methodology

Design and study population

A cross sectional study was conducted for 3 months from 1 October 2020 until 31 December 2020. The inclusion criterion was all electronic prescriptions received at the outpatient pharmacy during the study period whereby any manual prescription was excluded.

Data collection

The waiting time in HRPZ II's outpatient pharmacy was defined as the time taken from when the patient received the queue number at the counter to the time the patient was called at the counter using Queue Management System (QMS). The QMS was utilised to determine the length of time taken for each prescription being called at the counter. There are four main dispensing counters available. All prescriptions were given numbers based on the number of medications and the type of diseases in the prescription. Prescriptions with 3 medications or less with acute diseases were given queue number 2, 3 medications or less with chronic disease were given queue number 3, more than 3 medications were given queue number 4 and queue number 5 was given to prescriptions which requires extemporaneous preparation.

For each queue number, systematic random sampling was applied to pick the prescriptions for this study. The sampling interval was determined by dividing the average daily number of prescriptions with the number of samples required for each queue number. Then, random starting point was determined using random table and the sampling interval was repeated to choose subsequent prescription. A form which consists of all the necessary data and possible factors affecting waiting time was collected and attached with the copied prescription.

Sample size calculation was calculated for each objective. Single mean formula was used for determination of mean waiting time. The values of two-tailed $\alpha = 0.05$, $\sigma = 20$ and $d = 2.5$ were entered in the equation which yielded a minimum of 246 prescriptions (Ndukwe et al., 2011) .For the second objective, 200 was set as the minimum sample size based on the rule of thumb as suggested by Green for any regression analysis (Green, 1991). Thus, by comparing the samples required for both objectives, the minimum prescriptions needed was 246.

Statistical analyses

Data analyses were carried out by using SPSS version 25.0 (IBM Corp, 2017). The descriptive statistics were presented in categorical and numerical data. The categorical data were summarised in frequencies and percentages. Meanwhile, numerical data were presented with mean and standard deviation (SD). Multiple linear regression was utilised to determine the factors associated with waiting time. Statistical significance was set at 95% confidence level.

Ethical approval

This research has obtained ethical approval from the Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia (NMRR-20-2610-57076) while permission to conduct the study at the site was granted by the Director of HRPZ II.

Results

Sociodemographic characteristics

A total of 248 prescriptions were collected during the study duration. The mean age of the patients was 41.9 years (SD = 21.7) and more than half of them were female. Half of the prescriptions were obtained from queue number 2 and majority of them were collected on Wednesday. The average number of staff was around 23 people. The mean waiting time for outpatient pharmacy was 23.0 minutes (SD = 11.0).

Most of the prescriptions were chronic diseases, with ≤ 5 medications, contained standard medications, from outpatient clinics, only one clinic and arrived during peak hours. In addition, the majority of them were new prescriptions, did not require SPUB, contained no extemporaneous preparations, not required intervention, medication filled by others and counterchecked by pharmacists (Table 1).

Table 1: Sociodemographic characteristics of patients/prescriptions (n=248)

Characteristics	n	%
Age (year)	41.9*	21.6#
Gender		
Male	110	44.4
Female	138	55.6
Queue number		
2000 – 2999	124	50.0
3000 – 3999	38	15.3
4000 – 4999	65	26.2
5000 – 5999	21	8.5
Day of visit		
Sunday	27	10.9
Monday	42	16.9
Tuesday	59	23.8
Wednesday	79	31.9
Thursday	41	16.5
Number of medications	3.3*	2.4#
Types of medication		
Standard medications	218	87.9
Others (e.g. Special medications)	30	12.1
Number of staff	23.7*	1.2#
Types of patients		
Discharged	18	7.3
Outpatient	230	92.7
Sources of prescription		
One clinic	243	98.0
Multiple clinic	5	2.0
Patient's arrival time		
Peak hour (10am- 1pm)	132	53.2
Non-peak hour (8am- 10am, 1pm-5pm)	116	46.8
Types of prescription		
New	195	78.6
Refill	53	21.4
SPUB prescription		
Yes	18	7.3
No	230	92.7
Extemporaneous prescription		
Yes	22	8.9
No	226	91.1
Intervention prescription		
Yes	12	4.8
No	236	95.2
Filled by		
Pharmacist	102	41.1
Others	146	58.9
Counterchecked by		
Pharmacist	191	77.0
Others	57	23.0

*mean
#standard deviation (SD)

Factor associated with waiting time

In univariable analysis, there were no statistically significant differences in types of patients, sources of prescriptions, types of prescriptions, SPUB prescriptions and extemporaneous prescriptions towards waiting time in outpatient pharmacy (Table 2). The multivariable analysis was carried out for all significant variables to determine which factors associated with waiting time. Total number of medications, total number of staff, prescription requiring intervention and filling personnel were found to be significant factors which associated with waiting time. An increase of one medication in the prescription, will increase the waiting time by 1.4 minutes (95% CI = 0.90, 1.94). The waiting time will be reduced by 1.8 minutes (95% CI = -2.87, -0.65) if the number of staff is increased by one person. Prescriptions with intervention increased the waiting time by 10.0 minutes (95% CI = 4.09, 15.94). The waiting time is reduced by 3.1 minutes (95% CI = -5.68, -0.52) if the medication in the prescription is filled by pharmacist in comparison to other personnel such as PRP, pharmacy assistant and student.

Table 2: Factors associated with waiting time in outpatient pharmacy (n=248)

Variables	SLR[a]			MLR[b]		
	b[c]	95% CI	*P*-value	adj. b[d]	95% CI	*P*-value
Types of disease						
Acute						
Chronic	2.87	0.14, 5.60	0.040			
Number of medications	1.49	0.96, 2.03	< 0.001	1.42	0.90, 1.94	< 0.001
Types of medications						
Special medication						
Standard medication	-3.26	-7.45, 0.93	0.126			
Number of staff	-1.09	-2.27, -0.09	0.070	-1.76	-2.87, -0.65	0.002
Types of patients						
Discharged						
Outpatient	1.77	-3.53, 7.06	0.512			
Sources of prescriptions						
One clinic						
Multiple clinic	0.92	-8.85, 10.69	0.853			
Arrival time						
Non peak hour						
Peak hour	8.60	6.07, 11.13	< 0.001			
Types of prescriptions						
New						
Refill	-1.94	-5.28, 1.40	0.253			
SPUB prescriptions						
Yes						
No	-1.29	-6.57, 4.00	0.633			
Extemporaneous prescriptions						
Yes						
No	-2.03	-6.8, 2.79	0.408			
Intervention prescriptions						
No						
Yes	10.56	4.31, 16.82	0.001	10.01	4.09, 15.94	0.001
Filling by						
Others						
Pharmacist	-2.47	-6.26, -0.49	0.081	-3.10	-5.68, -0.52	0.019
Countercheck by						
Others						
Pharmacist	-4.74	-20.07, .10.60	0.544			

[a]Simple Linear Regression
[b]Multiple Linear Regression (R^2 = 0.182; The model reasonably fits well; Model assumptions are met; There are no interactions between independent variables and no Multicollinearity problem)
[c]Crude regression coefficients
[c]Adjusted regression coefficients

Discussion

This study reported the mean (SD) waiting time of 23.0 minutes (SD = 11.0) which is lower than waiting time reported in other studies in Malaysia. Yi et al. (2021) reported that the waiting time in Klinik Kesihatan Bandar Mentakab and Klinik Kesihatan Temerloh were 29.7 minutes and 28.4 minutes respectively (Yi et al., 2021). A study by Huang (1994) concluded that patients were satisfied if the waiting time is not more than 37 minutes (Huang, 1994) whereas a study by Afolabi & Erhun (2003) mentioned that the average waiting time should be between 10-30 minutes for patient's satisfaction (Afolabi & Erhun, 2003). Our findings were within the recommended range of waiting time, but we did not investigate the level of satisfaction in our population. Different population may have different perceptions on the length of time they need to wait to get their medication.

There were four factors which had significant effect on the waiting time in our study which were 1) number of medications in the prescription, 2) number of staff, 3) prescriptions required intervention and 4) filling process. The number of medications in the prescription influenced the waiting time by increasing the time by 1.4 minutes per item in the prescription. According to a study conducted by Loh et al. (2019), a reduction in average waiting time was shown when a fast-track dispensing window was introduced to dispense prescription with three medications or less (Loh et al., 2017). Another study by Yang et al. (2019), also suggested that prescriptions with less item reduced the chances of medication error and thus reduces the waiting time (Yang, Liao, Lin, & Wu, 2019). This is because number of errors tend to increase with more numbers of drug orders in each prescription. As a result, waiting time increased due to the medication errors, with some of the processes need to be repeated before medications being dispensed. Another study also proved that a fast-track counter containing items less than 3 medications showed a reduction in the waiting time from 20 to 23 minutes to an average of just 4 minutes (Sadi, Harb, El-Dahiyat, & Anwar, 2019).

In our study, it was found that the number of staff working reduced the waiting time by 1.8 minutes when the staff was increased by one person. Understaffing creates instability in the pharmacy operations leading to long queues and long prescription preparation times (Arafeh et al., 2014). This then causes longer waiting time. Another study has shown that a higher number of pharmacy technicians was associated with higher percentage of prescription served less than 30 minutes (Loh et al., 2017). This indicated that pharmacy technician plays an important role in medication dispensing activity, assisting in recording, packaging and labelling of medications (Loh et al., 2017). Another study suggested that lack of staffing is a known major contributor to lengthy waiting time in hospital outpatients and public health clinics (Ahmad, Khairatul, & Farnaza, 2017). Therefore, a recommendation was made to increase the number of registration staff to two members to cope with the tasks (Ahmad et al., 2017). A previous study revealed that waiting time was highly dependent on the number of pharmacists. It was suggested that employing 2 additional pharmacists, could lower the maximum patient waiting time from 58.2 minutes to 27.0 minutes (Tan, Chua, Yong, & Wu, 2009).

Third factor that affecting waiting time is when certain prescriptions required intervention. Based on our study, prescription that required intervention increased the waiting time by 10.0 minutes. Intervention of the prescription was the main contributing factors of increased waiting time because pharmacist needs to contact the prescriber to rectify any problem before it can proceed to the next steps. Kim and Schepers (2003) reported that majority of the error (76%) did not reach to the patients but had significant potential to cause morbidity and mortality (Kim & Schepers, 2003). In addition, another study revealed that high dose errors were the most common category of interventions which constitutes for 43.6% of interventions (Alderman & Farmer, 2001). This shows the importance of intervention to optimize patient therapy although it will lead to an increase in waiting time.

The filling process was also proven to affect the waiting time. The waiting time was reduced by 3.1 minutes if the item in the prescription was filled by pharmacist in comparison to other personnel such as PRPs, pharmacy assistants and students. Pharmacists are challenged with keeping up on the increasing number of new drugs and literature. Drug information and literature evaluation skills are crucial for building clinical knowledge and providing evidence-based recommendations. A study conducted in 2015 has shown that time taken to fill up the prescriptions were shorter when it was done by pharmacists because they are more familiar with the medications (Ghaibi, Ipema, & Gabay, 2015). Perhaps, similar exposure in term of Continuing Professional Development (CPD) should be given to other staff as well in order to ensure they are also familiar with the medication and thus can help in reducing waiting time.

The limitation of our studies include that we did not investigate the satisfaction level of patients with the current waiting time. Future studies may investigate this aspect to ensure healthcare services can be improved in term of efficiency, effectiveness and patient satisfaction. According to a study conducted by Fauzia et al., (2017), the patient's satisfaction with the outpatient hospital pharmacy was influenced by the dispensing process, consultation service by pharmacist, and general satisfaction aspect where the dispensing processes includes the time for filling prescription (Fauzia, Setiawati, & Surahman, 2017). Therefore, improving and making the filling process efficient and timely is an effective method to improve service quality and improve customer satisfaction. Our study did not find a significant association among other predictors like age, gender, queue number, day of visit, types of disease, medications and burden of prescriptions. Based on R2 value, R2 = 18.2% indicated there are still many factors which are not considered in this study but might influence waiting time in outpatient pharmacy. However, this study still might be useful in providing insights on current level of performance to improve to even better service for the public in future.

Conclusion

The waiting time at the outpatient pharmacy of HRPZ II indicated the acceptable range of quality services which met the patient's satisfaction. The factors contributed to waiting time included number of medications in the prescription, number of staff working on that day, prescriptions requiring intervention and filling personnel. Future studies are needed to confirm the satisfaction level of patients and further improve quality of the service.

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Conflict of Interest

The authors declare that they do not have any personal conflict of interest that may arise from the research publication.

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Prescribing practices of Antibiotics for acute diarrhea in children aged less than five years old in Pakistan

Durr-e-Shahwar Siddiqui[1*]

ABSTRACT

Introduction: Childhood diarrhea accounts for 16% of child deaths in Pakistan. Irrational prescribing of antibiotics, prescribing of antibiotics for viral infections, self-medication using antibiotics, prescription sharing, and refilling are very common practices in Pakistan. The aim of this study was to evaluate the prescribing practices of antibiotics for acute diarrhea in children less than five years of age at a Secondary Healthcare Hospital of Pakistan and to assess the compliance of prescribers with authentic clinical guidelines of treatment for childhood acute diarrhea.

Method: A cross-sectional study was conducted for a period of one year, from August 2020 to August 2021, at a Secondary Care Hospital of Karachi, Pakistan. It was based on the collection of outpatient clinic prescriptions of children aged less than five years and suffering from acute diarrhea. The regimens or suggested therapies by prescribers for acute diarrhea were assessed as per The National Institute of Care and Health Excellence and World Health Organization guidelines. A brief questionnaire was also distributed among prescribers, pharmacists, and caretakers of children to extract their opinions regarding antibiotic prescribing in acute diarrhea.

Results & Discussion: Antibiotics were inappropriately prescribed for acute diarrhea among children in Pakistan because p-value was less than 0.05 ($p<0.05$) as calculated by descriptive statistical tools using Z-test. More than 90% prescriptions of acute diarrhea in children less than five years of age failed to comply with the authentic treatment guidelines. Due to the limited knowledge of prescribers regarding treatment guidelines and compliance of parents with antibiotic prescribing for diseases in children, irrational prescribing of antibiotics for acute diarrhea in children less than five years of age is frequent in Pakistan. Healthcare professionals must be adequately trained to ensure the proper management of acute diarrhea by following authentic clinical guidelines.

Conclusion: Antibiotics are irrationally prescribed for acute diarrhea in children less than five years of age in Pakistan and prescriptions do not comply with authentic clinical guidelines.

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Introduction

Diarrhea is the frequent passage of three or more loose or watery stools per day which is more than normal for an individual. According to the World Health Organization (WHO), diarrhea is the second leading cause of death in children less than five years of age. Its causes may include infection by parasite, virus or bacteria, malnutrition, contaminated water, and unhygienic conditions (World Health Organization, 2017). When increased bowel movement terminates within three weeks, it is called acute diarrhea, but if it persists for more than three weeks it is called chronic diarrhea (Marsha & Anthony, 2012).

Symptoms of chronic diarrhea include uncontrollable bowel movements, nausea, abdominal pain, cramps, vomiting, shivering and fever. These symptoms can lead to severe dehydration and mal absorption (National Institute of Diabetes and Digestive and Kidney Diseases, 2017). Antibiotic-associated diarrhea is mild diarrhea that can occur in children and adults and does not cause decrease in weight or dehydration and terminates within one to two days of stopping the antibiotic (Fliesher & O'Ryan, 2017).

Childhood diarrhea under two years of age accounts for 72% deaths globally (Walker et al., 2013). It also leads to impairment in the growth of children as well as cognitive development (Checkley et al., 2008) (Lorntz et al., 2006). Diarrheal diseases in children below five years of age in low or middle-income countries need immediate treatment to reduce mortality rate (Ugboko et al., 2020).

In Pakistan, childhood diarrhea accounts for 16% of child deaths and it was suggested that a cost-effective, standardized, and accessible mode of treatment along with public education and awareness regarding childhood diarrhea must be established (Quadri et al., 2013). Diarrhea in children can be prevented up to major extent by vaccination against Escherichia coli, Shigella spp. and rotavirus, promoting health hygiene, consuming non-contaminated water and good sanitary conditions (Mokomane et al., 2018).

Acute diarrhea should not necessarily be treated by antibiotics in children because rehydration therapy is proven to be the mainstay treatment and usually the symptoms subside without requiring any specific therapy. In case of severe diarrhea, traveler's diarrhea, antibiotic-associated diarrhea, or chronic diarrhea, one may opt to antibiotics or antimicrobial therapy. Oral doses of co-trimoxazole or metronidazole or parenteral doses of ceftriaxone or ciprofloxacin can be a choice for empiric therapy in severe cases of diarrhea (Bruzesse et al., 2018).

According to The National Institute for Care and Health Excellence (NICE) guidelines of 2009, acute diarrhea must be treated primarily by oral rehydration salt as 50ml/kg over 4 hours, diarrhea usually subsides within 2 weeks and if this duration is crossed then healthcare professional must be consulted (The National Institute for Care and Health Excellence, 2009). Oral Rehydration Salt (ORS) is the primary element of care in children with acute gastroenteritis and acute diarrhea because it has been reported that the efficacy of oral rehydration is comparable to the IV rehydration in severe dehydration while severe dehydration may require IV rehydration therapy (Guarino et al., 2014).

According to WHO, patients must obtain medicines as per their clinical necessity in appropriate doses and frequency for adequate duration of therapy with the lowest possible expense to promote rational use of medications. Prescribing of medicines without authentic clinical guidelines, polypharmacy, preference of injections when oral dosage form of same drug could be used, irrational use of antibiotics, self-medication and non-compliance with prescribed regimen are some of the examples coming under irrational use of medications.

This worldwide concern can be resolved mainly by ensuring that the medications are prescribed according to clinical guidelines, public awareness about medications, enforcement of policies and regulations by multidisciplinary national body for rational use of medicines, essential drugs list, pharmacy and therapeutic committee in healthcare areas, problem-based training of pharmacotherapy, supervision, and audits (World Health Organization, 2002).

A diarrhea control plan was launched by World Health Organization (WHO) and United Nations International Children's Emergency Fund (UNIICEF) in 2009 and Global Action Plan for Pneumonia and Diarrhea (GAPPD) in 2013 realizing the increased prevalence of these diseases in children (World Health Organization & UNICEF, 2013). National Essential Medicines List (NEML) of Pakistan includes low osmolarity ORS, 250mg and 500mg oral amoxicillin trihydrate and 20mg zinc sulphate as recommended by UNICEF and WHO for pneumonia and diarrhea (Drug Regulatory Authority of Pakistan, 2016).

Government of Pakistan has provided this list at primary as well as secondary healthcare settings in the country. A study conducted in Pakistan revealed that healthcare education to communities, health interventions for children and intensive supervision or healthcare audits can improve mortality rate in children less than 5 years of age suffering from diarrhea and pneumonia. It also suggested promoting rational use of medicines, activities of healthcare workers in community, training of healthcare workers, surveillance, and improvement in socio-economic conditions of people to reduce the risks and deaths caused by diarrhea and pneumonia (Hansen et al., 2020).

Irrational prescribing of antibiotics, prescribing of antibiotics for viral infections, self-medication using antibiotics, prescription sharing, and refilling are very common practices in Pakistan (Hameed et al., 2016). Inappropriate prescribing of antibiotics in low and middle-income countries is highly prevalent (8% to 100%) at primary healthcare settings which needs strategies for proper prescribing practices and implementation of national prescribing guidelines or recommendations of treatment by

WHO (Sulis et al., 2020).

Healthcare professionals must be trained periodically upon the proper management of diarrhea along with prescribing or indication of antibiotics for children under five years of age (Udoh & Meremikwu, 2017). The aim of this study was to evaluate the prescribing practices of antibiotics for acute diarrhea in children less than five years of age at a Secondary Healthcare Hospital of Pakistan and to assess the compliance of prescribers with authentic clinical guidelines of treatment for childhood acute diarrhea.

Methodology

This study was conducted for a period of one year at a Secondary Care Hospital of Karachi, Pakistan. It was a cross-sectional study based on the collection of outpatient clinic prescriptions at pharmacy from August 2020 to August 2021. The prescriptions were collected based on the inclusion and exclusion criteria such as pediatric prescriptions of acute diarrhea for both gender of children aged less than five years were included in the study while all such prescriptions of children greater than five years of age were excluded.

Total of 500 prescriptions were collected along-with the verbal consent and demography of children from their caretakers or attendants. The age, weight, duration of diarrhea, concomitant diseases, therapies given by caretakers at home for diarrhea and medications prescribed by prescribers were also noted. The compliance of prescribers with authentic clinical guidelines while prescribing treatment of acute diarrhea in children less than five years of age was evaluated.

The appropriateness and anti-microbial spectrum of prescribed antibiotics as per age of children, episodes of diarrhea and duration of diarrhea were noted. Regimens or suggested therapies by prescribers for acute diarrhea were also assessed as per NICE guidelines. Moreover, the opinions of prescribers, pharmacists, and caretakers of the children for prescribing antibiotics in children less than five years of age were also recorded through questionnaire.

The questionnaire contained some open-ended questions such as satisfaction with the prescribed regimen for acute diarrhea, episodes of diarrhea, nature of diarrhea, duration of diarrhea, knowledge about guidelines for childhood diarrhea and antibiotics, brief demography of case and concomitant diseases. The questionnaire contained scoring from 1 to 5 for each question. Descriptive statistics was used to describe the variables of the study. P values were calculated through Z-test using SPSS software and p-values less than 0.05 were considered as statistically significant.

Results

Table 1 shows the antibiotics prescribed for children less than 5 years of age for acute diarrhea. The prescribed antibiotics did not comply with NICE guidelines when assessed on the basis of nature, duration and episodes of acute diarrhea. Although the prescribing practices of injectable preparations in acute diarrhea was less than that of oral dosage forms but 480 prescriptions out of total 500 prescriptions contained un-necessarily prescribed antibiotics that can lead to antibiotic resistance in pediatric population. The combination of diloxanide furoate and metronidazole as syrup dosage form was the most frequently prescribed antibiotic for childhood acute diarrhea because prescribers considered that the anti-microbial coverage of this combination would be more effective than other single generic formulae of antibiotics.

Table 1: Prescribed medications for acute diarrhea in children less than 5 years of age

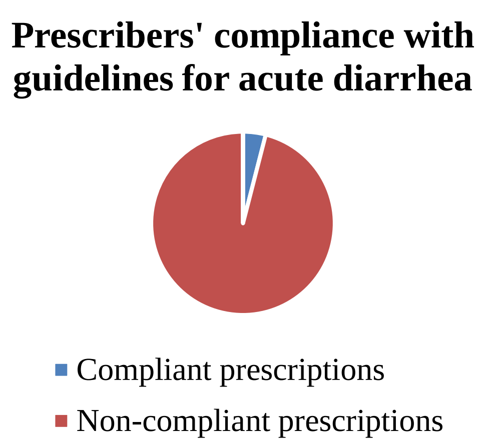
Medications	Number of Prescriptions (n=500)	Percentage of prescriptions
Oral Diloxanide furoate + Metronidazole combination	187	37.4%
Oral Ciprofloxacin	75	15%
Cefixime suspension	125	25%
Oral Metronidazole	65	13%
Metronidazole infusion	5	1%
Ceftriaxone infusion	3	0.6%
Nitazoxanide suspension	15	3%
Ciprofloxacin infusion	5	1%

In Table 2, it is evident that the probability of inappropriate prescribing of antibiotics in childhood diarrhea was higher because p-value was less than 0.05 as calculated by descriptive statistical tools. P-value was highly significant as determined by Z-test using SPSS software. The main concomitant symptoms were dehydration; vomiting and abdominal pain but these symptoms did not need antibiotic prescribing. Most of the children suffering from acute diarrhea had normal body weight and the duration of diarrheal episodes was than 3 days. The prescriptions of general practitioners for childhood acute diarrhea deviated more from NICE guidelines than that of pediatricians.

Only 4% prescribers had compliance with clinical guidelines for acute diarrhea in children less than 5 years of age while 96% prescribers irrationally prescribed antibiotics as shown in Figure 1. A brief questionnaire distributed among prescribers, pharmacists and caretakers of children revealed their opinions for the rationale of prescribing antibiotics in children less than 5 years of age for acute diarrhea.

The rationale put forward by most of the prescribers for antibiotic prescribing in such cases was to prevent further risks and chances of chronic diarrhea while some of them documented that antibiotic prescribing was for the satisfaction of caretakers as 90% of the parents complied with antibiotic prescribing in acute diarrhea and considered it effective for treatment. Only 3% prescribers accepted it being due to limited knowledge of authentic and updated clinical guidelines. Some of the pharmacists considered these practices as blindly following the past practices of other prescribers while most of them had opinions that it is due to the information provided by medical representatives to the prescribers about the benefits of the prescribed medicine (Figure 2).

Figure 1: Prescribers' compliance with guidance for childhood acute diarrhea



Discussion

The frequent passage of three or more loose or watery stools per day is referred to as diarrhea and when this increased bowel movement ends within three weeks, it is called acute diarrhea. As per the authentic treatment guidelines for acute diarrhea in children under five years of age, oral rehydration therapy is the mainstay of treatment. Irrespective of etiology, treatment with diosmectite and probiotic powders or solutions must continue along with rehydration therapy. Clinical conditions of child and host-related aspects must be considered while prescribing treatment for acute diarrhea.

Antibiotic therapy must not be started when clear indications for the need of antibiotic therapy are absent because symptoms of acute diarrhea usually subside with oral rehydration therapy and probiotics. Antibiotics can be considered for treatment if diarrhea becomes chronic, child is at risk or is severely ill but microbiological investigations are necessary. World Health Organization does not recommend the use of antibiotics in children for acute diarrhea except for those with severe clinically identified cases. Antibiotics can be considered for acute diarrhea with bloody stool, severe traveler's diarrhea, diarrhea with some other super-imposed infection for which antibiotic is essential, diarrhea with high grade fever and for immuno-compromised children. Oral zinc in the form of zinc sulphate suspension can also be prescribed as zinc is severely lost from the body during diarrheal condition.

Childhood diarrhea accounts for 16% of child deaths in Pakistan. The prescribing practices of injectable preparations in acute diarrhea is although less than that of oral dosage forms in Secondary Healthcare setting of Pakistan but irrational prescribing of antibiotics for diarrhea in pediatric population is common. This study revealed that the combination of diloxanide furoate and metronidazole was the most frequently prescribed antibiotic for childhood acute diarrhea.

The two major reasons told by most of the prescribers for prescribing antibiotics were to prevent the transformation of acute diarrhea to chronic diarrhea and the compliance of parents with antibiotics for resolution of diarrheal condition. Pharmacists considered that the prescribing of antibiotics in acute diarrhea to children less than five years of age was due to the limited knowledge of prescribers for clinical guidelines, following the past practices of other prescribers or due to the information provided by the medical representatives from different pharmaceutical industries for their products.

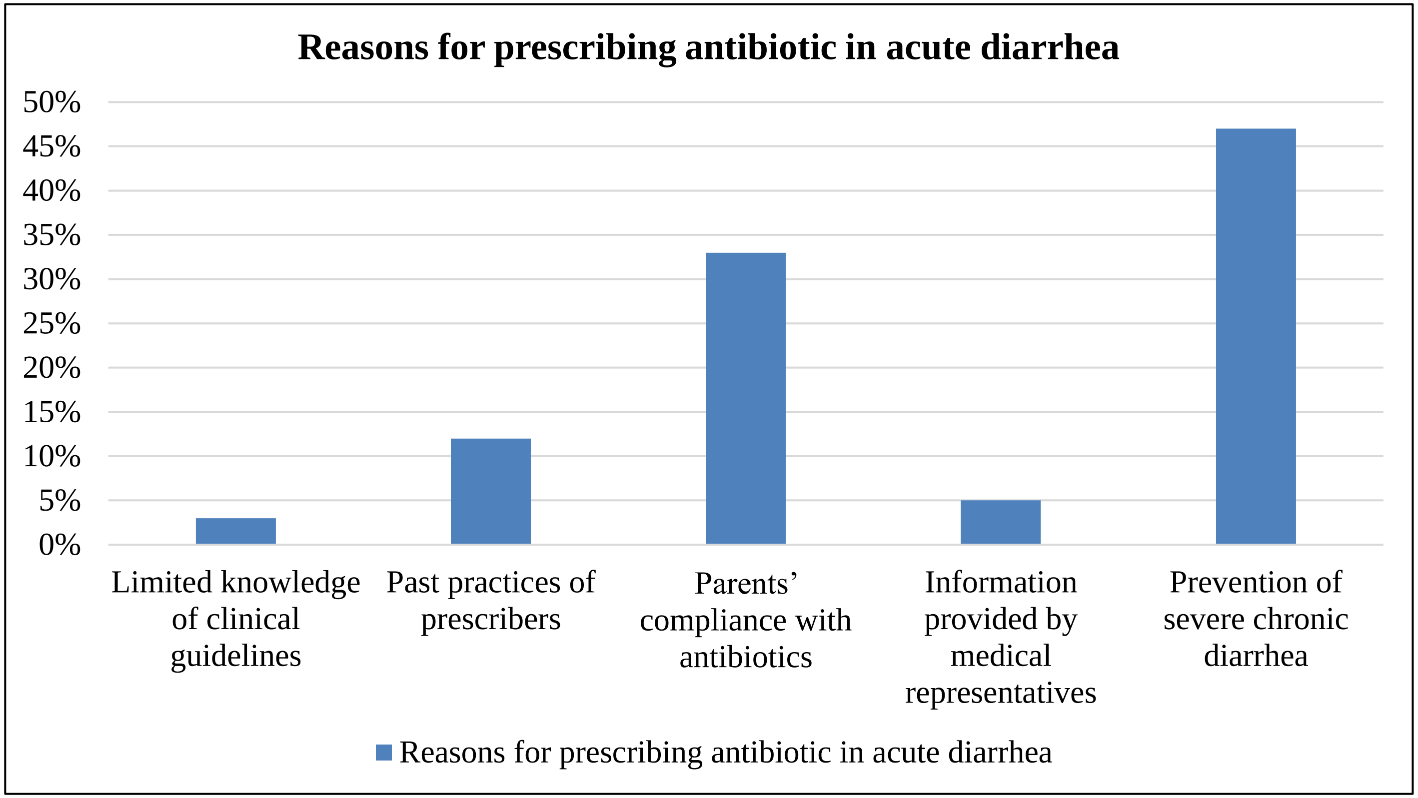
More than 90% prescriptions of acute diarrhea in children less than five years of age failed to comply with the authentic treatment guidelines. Healthcare professionals must be adequately trained to ensure the proper management of acute diarrhea by following authentic clinical guidelines, such as guidelines by WHO or NICE. Healthcare education and awareness programs, health interventions and healthcare audits are necessary to promote rational use of medications in childhood acute diarrhea.

Vaccinations of children against Escherichia coli, Shigella spp. and rotavirus must be regarded mandatory by the government. Presence of NEML must be assured at all the healthcare settings and all the medications mentioned in it for diarrhea must be available at every healthcare area of Pakistan. The therapy for acute diarrhea in children less than five years of age must be according to the severity of clinical condition and oral rehydration therapy must be ensured. Parents or caretakers of children must be convinced by healthcare professionals to discourage the irrational use or prescribing of antibiotics for acute diarrhea in children less than five years of age in Pakistan.

Table 2: Demography, concomitant symptoms, and prescribers’ qualification

Characteristics	Number of prescriptions	Inappropriate prescriptions	Percentage of inappropriate prescriptions	p value
Diarrhea	500			p<0.05
Age (months)				
1-12	130	125	96%	
13-24	142	140	98%	
25-36	107	106	99%	
37-46	52	49	94%	
47-60	69	60	86%	
Fever	60			
Dehydration	456			
Vomiting	391			
Abdominal pain	442			
Weight				
Under-weight	113			
Normal weight	387			
Overweight	0			
Duration of diarrhea				
Less than 3 days	289			
3-7 days	200			
8-14 days	11			
Prescirbers’ qualifications				p<0.05
General practitioners	215	208	96%	
Pediatricians	285	272	95%	

Figure 2: Reasons for prescribing antibiotics for acute diarrhea in children aged less than 5 years



Conclusion

Antibiotics are irrationally prescribed for acute diarrhea in children less than five years of age at Secondary Healthcare Hospital of Pakistan and prescriptions do not comply with the authentic clinical guidelines due to the limited knowledge of prescribers regarding treatment guidelines and compliance of parents with antibiotic prescribing for diseases in children.

Conflict of Interest

The author has no conflicts of interest to report.

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Journal of Pharmacy

REVIEW ARTICLE

Open Access

A systematic review of the hospitals' antimicrobial stewardship programs implemented to improve antibiotics' utilization, cost and resistance patterns

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ABSTRACT

Introduction: The high reliance of the physicians and surgeons on the antibiotics since their discovery has led to an irrational antibiotic utilization which not only has raised the incidence of antimicrobial resistance (AMR) but also increased the cost of treatment with antibiotics as high use of antibiotics has been found related to the occurrence of certain nosocomial infections which need extra antibiotic courses to be cured. In order to overcome these antibiotic utilization related problems an antimicrobial stewardship (AMS) program being the set of various persuasive, restrictive and structural interventions is considered an effective tool to rationalize the in-patient antimicrobial utilization worldwide.

Method: The focus of this review is on the interventions that are being implemented during the in-patient AMS programs and have been described effective in controlling the antibiotic utilization, their cost of treatment and an overall infection control. The literature containing the information about various AMS interventions effecting the utilization and cost patterns along with the impact on AMR was searched in various databases such as PubMed, Google Scholar, Science Direct, Ovid (Medline) and Scopus. The categorical sorting of the published data is based on various AMS interventions such as the guideline development, formulary restriction (pre-authorization), educative interventions, clinical pathway development and prospective (post prescription) audit. Considering the objectives of the study such as the goal to curb overutilization of antibiotics, control of their cost of treatment for in-patients and infection control the sorted literature is presented in three different tables describing the AMS impact on the said outcomes.

Results: The post AMS changes in utilization patterns are described as fall of antibiotics defined daily doses (DDD) and days of therapy (DOT) which resulted in the reduction of the cost of treatment with antibiotics. The reduction of the cost of treatment with antibiotics also resulted due to the AMS impact on the control of various nosocomial and multi-drug resistant (MDR) infections.

Conclusion: It has been concluded that the AMS program if implemented under the supervision of an expert AMS team mainly comprising of an infectious disease (ID) physician, clinical pharmacists and microbiologists with considerable support by the hospital authorities could be a highly efficient tool of the pharmacovigilance for rationalizing the in-patient antimicrobial practice.

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Introduction

The antibiotics after their discovery have become an important shield against the deadly infections but a rapid development of the antimicrobial resistance (AMR) or a decreased susceptibility of bacteria to the antibiotics has invited the researchers to address this serious healthcare problem (Suwantarat & Carroll, 2016). The most common bacteria resistant to the broad spectrum antibiotics such as third generation cephalosporins and fluoroquinolones are Escherichia coli and Klebsiella pneumoniae (Phoon et al., 2018). Staphylococcus aureus are the important bacteria that are resistant to the Methicillin and are known as Methicillin resistant Staphylococcus aureus (MRSA) (Mendem et al., 2016). Over the past decades Streptococcus pneumoniae have exhibited marked reduction in their susceptibility against various penicillins and this fact is elaborated in the published reports of World Health Organization (WHO) (Cottagnoud et al., 2013). Vancomycin resistant Enterococci (VRE), carbapenem resistant Enterobacteriaceae (CRE) and Pseudomonas aeruginosa contain an effective gene modification capacity and plasmid equipped resistance that enabled them to challenge the efficacy of certain broad spectrum antibiotics namely vancomycin, carbapenems, ceftazidime and gentamicin etc. (O'Driscoll & Crank, 2015).

The contemporary literature reveals that the overutilization of the antibiotics within the hospital wards is one of the major causes of increased AMR. There have been published studies that positively correlate the high consumption of antibiotics to that of the increased AMR (Miliani et al., 2011). The high incidence of AMR further increases the antibiotic consumption as the multi-drug resistant (MDR) microbes are the basic cause of the healthcare associated infections (HAI) or the nosocomial infections that not only renders the patients to the toxicological impact of the antibiotics but also elevates the overall cost of treatment (Khan et al., 2017). The statistics of the antimicrobial consumption within the hospital wards worldwide highlight the trend that 30% to 50% antibiotic prescriptions do not match with antimicrobial spectrum of the antibiotics (Livermore et al., 2013). The overuse of antibiotics within the hospital wards increase the total cost of treatment which is a matter of concern for both the patients and the healthcare providers (Chandy et al., 2014). In order to overcome the overutilization of the antibiotics and to minimize the cost of antimicrobial treatment for the in-patients various hospitals worldwide have adopted a strategy which is the set of interventions commonly known as antimicrobial stewardship (AMS) program (Knox & Wiemiller, 2017).

The improvement of the prescribing patterns of the antibiotics is one of the most important goals of the AMS program so as to ensure a rational use of antibiotics (Chen et al., 2014). The AMS interventions being implemented during an in-patient AMS program are classified as persuasive, restrictive and structural interventions (Teixeira Rodrigues et al., 2019). The persuasive AMS interventions are comprised of education of the prescribers, development of the AMS guidelines along with the modification of the clinical pathways (Neo et al., 2020). The formulary restriction (pre-authorization) of the prescriptions mainly from an infectious disease (ID) physician, microbiologist or clinical pharmacist, stop order (de-escalation) practice for some highly consumed antibiotics along with the practice of antibiotic cycling or switch over between various antibiotic groups are some of the restrictive interventions being implemented as part of the hospitals' AMS programs (Dutcher et al., 2020). The structural interventions for the AMS are mainly the prospective (post-prescription) audit and the introduction of the computerized decision support system (CDSS) that automatically guides the prescribers regarding the AMS guidelines for a particular antibiotic (Huh et al., 2016). Introduction of the computerized prescribing and recording of the patient data within the electronic software of a hospital for traceability is an important structural intervention practiced worldwide so as to implement the AMS efficiently (Kauppinen et al., 2017).

The effective and successful implementation of an AMS program requires a team of multi-disciplinary healthcare professionals holding the responsibility to ensure a prudent antimicrobial practice within the hospital wards dealing with the antibiotics (Apisarnthanarak et al., 2018). The Infectious Diseases Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA) in the policy guidelines pertaining to the AMS describe the structure of the AMS team and the responsibilities of its members regarding the enforcement and implementation of the AMS policy (Barlam et al., 2016). According to the AMS policy guidelines an AMS team should contain an ID physician and a clinical pharmacist (with a specialised training regarding the infectious diseases) being the core members (Waters, 2015). Additionally, the inclusion of a clinical microbiologist, an information technology (IT) technician and a hospital epidemiologist is highly recommended for the efficient performance of the AMS team (Murri et al., 2018). Additional to the above-mentioned members of the AMS team in the healthcare settings of England a physician expert for acute care, a surgeon, a member from the pharmacy department team of management, a paediatrician, a senior nurse and an anaesthetist is also included as core members of the AMS team (Ashiru-Oredope et al., 2016). Considering the assessment of the AMS impact on the targeted outcomes various study designs are followed that categorically describe and evaluate the impact of the AMS interventions on the study population. The most commonly implied study designs for the said purpose are controlled before after (CBA), randomized controlled trial (RCT), controlled clinical trial (CCT) and interrupted time series (ITS).

Methodology

In order to collect the data pertaining to the impact of AMS programs within the in-patient settings worldwide the databases such as PubMed, Google Scholar, Science Direct, Ovid (Medline) and Scopus were searched systematically. The searching terms used for data exploration were antimicrobial stewardship programs, impact of antimicrobial stewardship program on antibiotic utilization, cost and resistance for in-patients etc. The studies published in English and covering the scope of the hospitals' AMS programs for the in-patients describing at least one AMS intervention with the resultant impact on the reduction of the antibiotic utilization, cost of treatment along with the control of healthcare associated infections (HAI) and AMR were included.

The studies which were focused on the AMS programs of the primary care settings and pediatric care wards and did not clearly described the AMS interventions and their impact on the antibiotic utilization, cost and resistance patterns for the in-patients were excluded for this review.

Results

The primary search of the relevant articles for this review from the said databases consisted of 2767 articles from 2014 - 2021 out of which 130 articles were short listed. Finally, 49 studies were included in this review and evaluation of these articles was performed to describe the impact of the AMS interventions on antibiotic utilization, cost and resistance patterns of the antibiotics used for the hospitalized patients. 24 of the sorted studies (Table 1) primarily reported the AMS impact on antibiotic utilization whereas 12 studies (Table 2) focused on the economic impact of the AMS. 13 studies elaborating the AMS impact on the infection control and the control of the AMR are presented in Table 3. Out of 49 studies included for this review 20 studies used CBA study design to assess the impact of hospitals' AMS programs, 7 studies followed the RCT study design, 6 studies used the CCT study design whereas 16 studies used ITS study design to assess the impact of the AMS interventions on antibiotics utilization, cost and resistance patterns for the in-patients.

Studies describing the AMS impact on antibiotic utilization patterns

The Table 1. describes the impact of AMS on the antibiotic utilization patterns. Most of the studies reported the defined daily doses (DDD) and days of therapy (DOT) of the antibiotics in order to describe the impact of the AMS interventions on utilization patterns. 4 studies described the educative interventions that were implied by the AMS team, ID physicians or by the clinical pharmacists to enhance the awareness of the prescribers and antibiotic handlers. 11 studies described that the prospective audit of the antibiotic prescription orders by the AMS team and ID specialists as an intervention to control the over utilization of certain antibiotics within the hospitalized patients. 2 studies described that the over utilization of the AMS included antibiotics was controlled by improving the clinical pathways. 5 studies mentioned that the formulary restrictive (pre-authorization) interventions were implemented to control the irrational use of antibiotics within the in-patient settings. 2 included studies elaborated the guideline development and the steps taken by the AMS team to ensure the adherence to such AMS guidelines as an AMS intervention to ensure a judicious use of antibiotics.

Studies describing the AMS impact on cost patterns

The Table 2. describes the impact of AMS on the antibiotics cost patterns. 4 studies described the educative interventions being implemented to elucidate the prescribers about the importance of AMS to control the overall cost of treatment with the antibiotics. 3 studies described the prospective audit done by the AMS team, ID physician or the clinical pharmacists as an intervention to improve the cost patterns of the antimicrobial treatment. 1 study performed in the hospital of USA described that to control the cost of treatment with antibiotics the improvement of the clinical pathways was done as an AMS intervention. A study performed in a German hospital mentioned the formulary restrictive intervention as a tool to control the high cost of treatment with 3rd generation cephalosporins. 1 study conducted in the in-patient setting of Spain elaborated that adherence to the AMS guidelines resulted in the control of the cost of treatment with meropenem. A study of a Malawian hospital claimed that the CDSS based AMS interventions were found an effective tool to control the antibiotics cost of treatment for the in-patients.

Studies describing the AMS impact on resistance patterns

The Table 3. describes the impact of AMS on the infection control and AMR patterns. 6 studies described the formulary restrictive interventions that were implemented within the hospital wards helped to control the AMR. The improvement of the clinical pathway during the AMS program of a Taiwanese hospital helped in infection control for the in-patients. 3 studies described that a decline of the incidence of the AMR and certain nosocomial infections namely Clostridium difficile infection (CDI) was observed as a result of continuous medical education (CME) of the hospital staff.

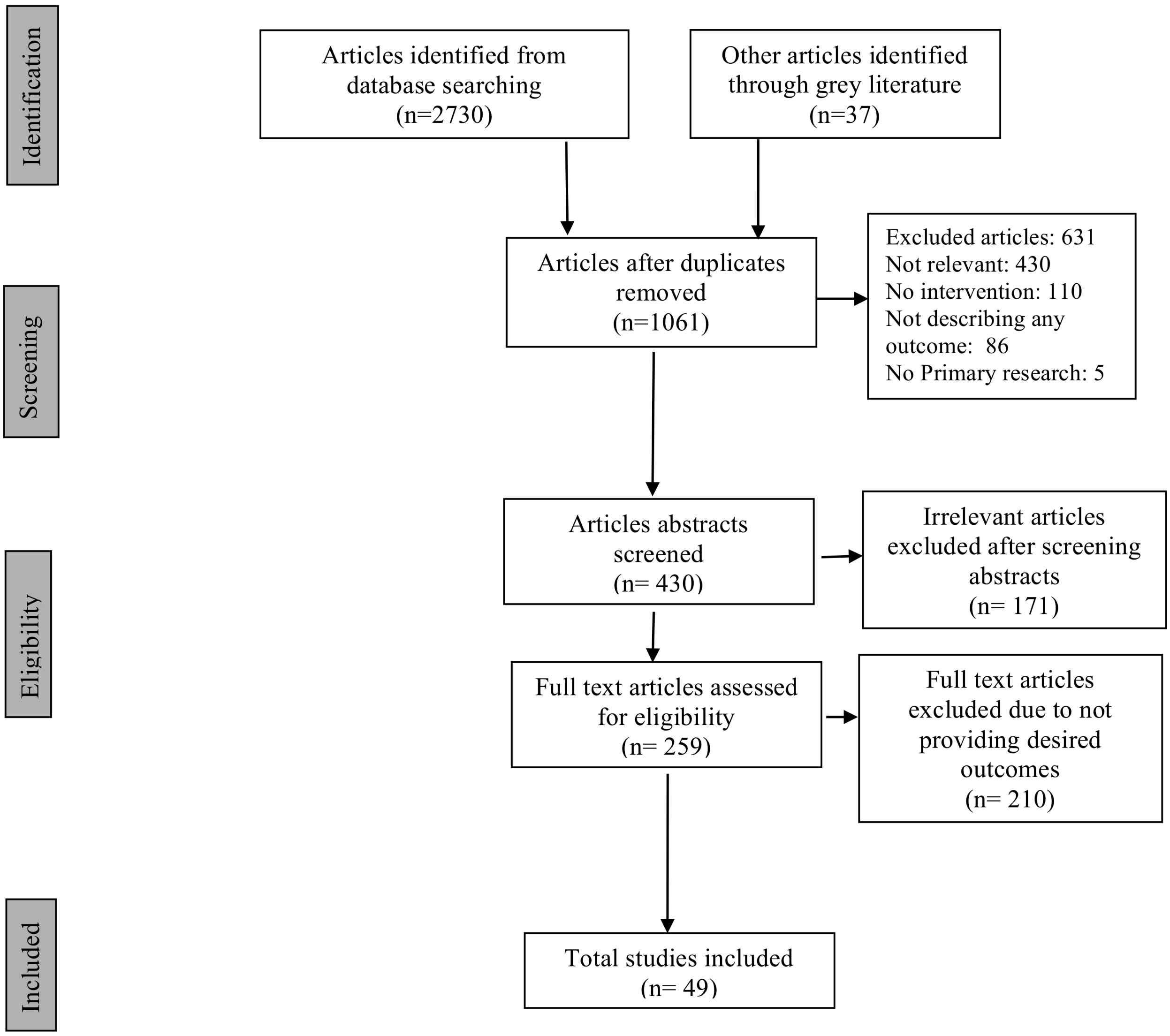

Figure 1: Study selection flowchart according to PRISMA checklist

Table 1: Studies describing the outcomes AMS impact on utilization

Author/Country/ Reference	Study Design	Intervention/Activity	AMS Intervention category	Results
(Garcell et al., 2017), Qatar	RCT	Education of the prescribers for judicious prescribing of antibiotics after appendectomies.	Educative	Post-AMS fall of the antibiotics defined daily dosses (DDD) by 18.9%
(Okumura et al., 2015), Brazil	CCT	Pharmacist led bundled AMS program	Educative	Post-AMS fall of antibiotic use by 140.2 DDD/1000 bed days (BD)
(Murri et al., 2018), Italy	CCT	Enhanced involvement of microbiologists to onset definitive therapy quickly	Clinical pathway development	Significant ($P<0.002$) fall of the number of days of therapy (DOT)
(Ruiz et al., 2018), Spain	RCT	Regular review of the prescriptions by AMS team and relevant feedback for prescribers	Prospective audit	Significant ($P<0.015$) fall of the number of DDD/100 stays
(Pitiriga et al., 2018), Greece	CCT	Mandatory order form introduced for broad-spectrum antibiotics prescribing	Formulary restriction	Significant ($P<0.05$) fall of the number of DDD
(Tang et al., 2018), United States of America (USA)	CBA	Continuous medical education of ward staff by clinical pharmacist by twice weekly ward rounds	Educative	Significant ($P=0.01$) fall of the number of DOT
(Palmay et al., 2014), Canada	RCT	Audit & feedback-based review of the prescriptions in ICU by the AMS staff.	Prospective audit	Significant ($P=0.004$) post-AMS fall of the number of DDD by 21%
(Didiodato et al., 2016), Canada	ITS	Prescription review by AMS staff for the patients with community acquired pneumonia (CAP)	Prospective audit	Post-AMS decline of the DOT by 29%.
(Khdour et al., 2018), Palestine	CBA	Regular prescription review by the AMS team for the intensive care unit (ICU) patients	Prospective audit	Significant ($P<0.001$) post-AMS fall of the use by 21.2 DDD/100 BD
(Lesprit et al., 2015), France	RCT	Regular post prescription review by the infectious disease (ID) physician	Prospective audit	Significant ($p=0.003$) post-AMS fall of DOT by 3 days
(Nilholm et al., 2015), Sweden	CBA	ID specialist led twice weekly audit of antibiotic prescriptions	Prospective audit	Significant ($p<0.001$) post-AMS fall of the number of DOT
(Boyles et al., 2017), South Africa	CBA	Review of antibiotic prescriptions during ward rounds by AMS team and feedback	Prospective audit	Post-AMS fall of antibiotic use by 178 DDD/1000 BD
(Trupka et al., 2017), USA	CCT	De-escalation of antibiotics for non-responsive ventilator patients	Formulary restriction	Fall of the number of DDD (non-significant)
(Seah et al., 2017), Singapore	CCT	Dose optimization of carbapenems after prescription review by AMS team	Formulary restriction	Significant ($p<0.001$) post-AMS fall of the number of DDD/1000 BD of carbapenems
(Tartof et al., 2020), USA	CBA	Targeted de-escalation of AMS included antibiotics implemented by the AMS team	Formulary restriction	Post-AMS fall of DDD by 6.1% & DOT by 4.3%
(García-Rodríguez et al., 2021), Spain	CBA	Post prescription audit of carbapenem prescriptions	Prospective audit	Significant ($P<0.05$) fall of the number of DDD of carbapenems

Table 1 (cont.): Studies describing the outcomes AMS impact on utilization

Author/Country/ Reference	Study Design	Intervention/Activity	AMS Intervention category	Results
(Dutcher et al., 2020), USA	CBA	Pharmacist led education for prescribers to encourage implementation of AMS prescribing guidelines for antibiotics	Educative	Significant ($P<0.001$) fall of the number of DDD of co-trimoxazole
(Surat et al., 2021), Germany	CBA	Introduction of AMS guidelines for postoperative treatment with antibiotics	Guideline development	Significant ($P<0.035$) fall of the number of DDD/100 BD
(Paulson et al., 2020), USA	CBA	Introduction of time out alerts for antibiotics used for 72 hours for the ICU patients	Formulary restriction	Significant ($P<0.014$) decline of the number of DOT
(Shively et al., 2020), USA	ITS	Post prescription review of antibiotic prescriptions by ID physician	Prospective audit	Significant ($P<0.001$) fall of DOT by 24.4%
(Du et al., 2020), China	ITS	Pharmacist led antibiotics prescription audit	Prospective audit	Significant ($P<0.01$) decline of DDD
(Pineda et al., 2020), USA	ITS	MRSA screening AMS introduction for rapid onset of definitive therapy	Clinical pathway development	Decline of use by 2.1 DOT/1000 BD
(Faraone et al., 2020), Italy	ITS	Adherence to the multimodal AMS guidelines for carbapenem use	Guideline development	Fall of carbapenem use by 3.6 DDD/100 BD
(Knight et al., 2020), USA	CBA	Post prescription review of broad-spectrum antibiotics by ID physician	Prospective audit	Post-AMS fall of the DOT/1000 BD by 4.6%

Table 2: Studies describing the AMS impact on cost of treatment with antibiotics

Author/Country/ Reference	Study Design	Intervention/Activity	AMS Intervention category	Results
(Lee et al., 2014), Canada	CBA	Introduction of electronic check list for antibiotics to perform twice weekly audit	Prospective audit	Fall of cost of treatment with antibiotics by $69424
(Box et al., 2015), USA	ITS	Rapid diagnosis of Gram +ve bacteremia	Clinical pathway development	Fall of cost of treatment with antibiotics by $7240
(Cisneros et al., 2014), Spain	RCT	Counselling sessions for prescribers by AMS team	Educative	Fall of post-AMS antibiotics treatment cost by 42%
(So et al., 2018), Canada	CCT	Academic detailing to treat leukemia patients in oncology unit	Educative	Significant (P=0.03) decline of cost of treatment with antibiotics
(Chandrasekhar & PokkaVayalil, 2019), India	CBA	Continuous medical education (CME) courses by AMS personnel	Educative	Significant (P<0.05) fall of cost of treatment with antibiotics by 19.5%
(Libertin et al., 2017), USA	CBA	Counselling sessions for prescribers by AMS team as part of continuous medical education (CME)	Educative	Decline of antibiotics treatment cost by 50% with savings of $280000/year
(García-Rodríguez et al., 2019), Spain	CBA	Formal guidelines issued to meropenem prescribing physicians by the ID physician	Guideline development	Significant (P<0.05) reduction of post-AMS cost of treatment with meropenem
(Seah et al., 2014), Singapore	ITS	Post prescription review by AMS team	Prospective audit	Significant (P=0.01) post-AMS fall of antibiotics treatment cost by $149/patient
(Cisneros et al., 2014), Spain	RCT	Counselling sessions for prescribers by AMS team	Educative	Post-AMS fall of antibiotics cost by 42%
(Borde et al., 2014), Germany	ITS	Replacement of 3rd generation cephalosporins with penicillins and fluoroquinolones	Formulary restriction	Significant (P<0.05) reduction of treatment cost with 3rd generation cephalosporins
(Day et al., 2015), USA	RCT	Hiring of an ID physician to check accurate susceptibility of microbes with the prescribed antibiotics	Prospective audit	Fall of cost of treatment with antibiotics by 42%
(Lester et al., 2020), Malawi	CBA	Introduction of software for the selection of empiric therapy of antibiotics to reduce high 3rd generation cephalosporin consumption	CDSS	Post-AMS savings by $15000 for antibiotics treatment cost

Table 3: Impact of the AMS on resistance patterns

Author/Country/ Reference	Study Design	Intervention/Activity	AMS Intervention category	Results
(Wenisch et al., 2014), Austria	CBA	Preauthorization declared compulsory for moxifloxacin supply to patients	Formulary restriction	Significant (P<0.005) decline of the incidence of *Clostridium difficile* infection (CDI) by 46%
(Wang et al., 2014), Taiwan	ITS	Rapid onset of blood culture guided definitive therapy	Clinical pathway development	Gradual post-AMS decline of infections
(Libertin et al., 2017), USA	CBA	CME for prescribers by AMS team	Educative	Decline of the occurrence of CDI from 3.35 to 1.35 cases/1000 BD
(Percival et al., 2015), USA	CBA	CME done for prescribers dealing with the urinary tract infections (UTI)	Educative	Significant (P<0.05) decline of the occurrence of AMR by 5% after AMS
(Hecker et al., 2019), USA	ITS	Syndrome specific use for fluoroquinolones	Formulary restriction	Significant (P<0.05) control of *Pseudomonas aeruginosa* infection
(Tedeschi et al., 2017), Italy	ITS	Protocol revision for prophylactic therapy with antibiotics	Formulary restriction	Significant (P<0.001) fall of *Pseudomonas aeruginosa* infections
(Horikoshi et al., 2017), Japan	ITS	Investigation of gram-negative bacteria (GNB) resistance against carbapenems	Prospective audit	Significant (P<0.01) fall of *Pseudomonas aeruginosa* resistance for carbapenems
(Lawes et al., 2015), United Kingdom	ITS	Health screening termed mandatory for the penicillin, cephalosporins and fluoroquinolone use	Formulary restriction	Significant (P=0.006) fall of the occurrence of methicillin resistant *Staphylococcus aureus* (MRSA) by 50%
(Peragine et al., 2020), Canada	ITS	Regular ward rounds by AMS team for audit and feedback of antibiotic prescriptions	Prospective audit	Post-AMS decline of antibiotic resistant organisms by 9%
(Yusef et al., 2021), Jordan	CBA	Preauthorization policy introduced for carbapenems	Formulary restriction	Significant (P<0.024) fall of carbapenem resistant *Acinetobacter baumannii* infections
(Mardani et al., 2020), Iran	ITS	Regular audit and feedback of antibiotic prescriptions by AMS team	Prospective audit	Significant (P<0.05) reduction of the incidence of CDI
(Strazzulla et al., 2020), France	CBA	Training of prescribers and nurses by AMS team in urological ward	Educative	Significant (P<0.004) post-AMS fall of ofloxacin resistance by 16%
(Al-Omari et al., 2020), Saudi Arabia	ITS	Restrictive antibiotic usage policy for carbapenems and fluoroquinolones	Formulary restriction	Significant (P<0.024) fall of CDI & significant (P=0.001) fall of ventilator associated pneumonia (VAP)

Discussion

This review mainly focused on the impact of the AMS programs implemented within the hospital wards that resulted in the control of the overuse of antibiotics, the reduction of the antimicrobial cost of treatment and the control of the AMR.

Impact of AMS programs on antibiotic use

The AMS programs that primarily aimed to rationalize the antimicrobial use indirectly contribute to minimize various healthcare associated infections (HAI) (Deptuła et al., 2015). The occurrence of nosocomial infections within the in-patient populations contribute to the extra usage of broad-spectrum antibiotics which not only impart the adverse effects on patients' health but also increase the cost of treatment (So et al., 2018). The reviewed studies describing an AMS impact on the antibiotic utilization showed that DDD and DOT were the main matrices that were recorded to determine the AMS impact on antibiotic utilization. Impact of AMS on DDD was estimated in 14 studies while 10 studies described the AMS impact of DOT of the antibiotics. The implementation of prospective audit intervention to reduce the antibiotic utilization was the major AMS intervention being implemented during the AMS programs. Formulary restrictive and educative interventions were the other AMS interventions mainly used to curb the unjustified antibiotic utilization. It is suggested that an estimation of the impact of AMS on prescribed daily doses (PDD) other than DDD and DOT could outline the prescribing frequency of the antibiotics. But it is a common trend that most of the studies that focus on antibiotic utilization mainly use DDD and DOT as the PDD is a more efficient matrix to evaluate the drug (antibiotic) utilization for a particular clinical condition or infection (Gagliotti, et al., 2014). Among the antibiotic groups carbapenems were the antibiotics that were targeted by the AMS interventions in order to minimize their unjustified utilization within the hospital wards. Since carbapenems are the broad-spectrum antibiotics and must be protected by the AMS interventions as they have the ability to cure various deadly infections. Due to this reason most of the AMS programs have aimed to minimize carbapenem use for empiric therapy.

Impact of AMS programs on antibiotic cost

The high antimicrobial treatment cost is the matter of concern both for the patients and the healthcare providers (Chandrasekhar & PokkaVayalil, 2019). Due to such concerns the health governing bodies of USA such as the CDC and SHEA since 2014, have recommended a mandatory AMS program for every in-patient setting that deals with the antibiotics and infectious diseases (Lee et al., 2014). Out of the 12 studies in which the post-AMS reduction of the cost of treatment with antibiotics was observed 5 studies were found to report a significant ($P<0.05$) fall of the cost of treatment. The educative interventions being implemented during the AMS programs were found highly effective to minimize the antimicrobial cost of treatment. Similar to the educative interventions the prospective audit proved an efficient intervention in controlling the cost of treatment with the antibiotics where the post-prescription audit by the ID specialist and the AMS team effectively improved the un-justified inclusion of the antibiotics which indirectly minimized the antimicrobial treatment cost. It is suggested that the implementation of antibiotic rotation or antibiotic cycling (replacement of broad-spectrum expensive antibiotics with cost-effective antibiotics) interventions in the hospitals could be highly lucrative pertaining to the reduction of the in-patients' cost of treatment with antibiotics (Bruno-Murthaet al.,2005).

Impact of AMS programs on antimicrobial resistance

The AMS interventions performed for the in-patients targeting the control of various nosocomial infections mainly depicted a fall in the incidence rate of Clostridium difficile, Pseudomonas aeruginosa, Acinetobacter baumannii, Enterobacteriaceae and MRSA infections which due to their multi-drug resistant capacity contribute to high utilization of the broad-spectrum antibiotics and sequentially a higher cost of antimicrobial treatment (Thampi et al., 2019). Out of the 13 studies describing the AMS interventions on the control of the AMR, 10 studies described a significant ($P<0.05$) fall of the AMR and certain nosocomial infections. Formulary restriction was found the most common intervention being implemented during the AMS programs that retarded the incidence of AMR and the nosocomial infections. The control of CDI was the main outcome being observed in majority of the AMS programs designed to control the AMR and nosocomial infection outbreaks. It is suggested that the hospitals that primarily deal with the infectious diseases and wide range of antimicrobials must hire an ID specialist physician to monitor the AMS activities targeting the infection control. As in developing countries the financial constraints hinder the availability of infectious disease physicians thus, to overcome such constraints the training of the physicians and pharmacists in the perspective of infection control could be a highly effective AMS intervention aimed to minimize AMR and nosocomial infections' outbreaks. Such moves would not only help the developing countries but also globally minimize the spread of AMR along with the preservation of the existing antibiotics' efficacies against various infections as the spread of antibiotic resistant microbes from one part of the world to other is much easier nowadays due to high tourism and efficient transportation (Dancer, 2013).

An AMS program is the set of interventions that requires a coordinated support from the health governing bodies to enforce the AMS guidelines and sequentially, the adherence of the prescribers (physicians and surgeons) to such policy guidelines is of utmost importance for the success of the AMS (Barlam et al., 2016). The ID physicians, clinical pharmacists and microbiologists are the leading healthcare personnel responsible to implement the AMS interventions and to monitor the degree of adherence of the antibiotic prescribers to the hospital's AMS policy (Waters, 2015). Most of the studies are performed over a limited period of time with brief follow up pertaining to the impact of AMS programs. The successful implementation of the AMS programs is highly dependent on the coordination of the various services and units of the hospital under the supervision of an AMS team led by the ID specialist (Garcell et al., 2017). The availability of the AMS experts and the monetary support ensured by the hospital directors is of prime importance as it has been observed that in low- and middle-income countries (LMIC) as compared to the developed countries the commitment of hospital management in terms of fund allocation for the AMS is much lower (Boyles et al., 2017). Therefore, a more systematic formative evaluation of the hospital's antibiotic related problems is of prime importance before finalizing the hospital's AMS policy as the intensity of the infection and antibiotic related problems vary country wise and region wise (Knight et al., 2020). Such formative evaluation prior to the onset of an AMS program must include the identification of the infections related problem, designing of a suitable intervention for the identified problem needing the AMS, successful implementation of the AMS intervention by ID specialists and finally the evaluation the outcomes of the AMS program is considered highly important (Adhikari et al., 2018). The coordination of pharmacy department, medical wards, medical record department, information technology department (ITD), microbiology department under the supervision of the ID specialists being the members of the hospital's AMS team is mandatory for a successful AMS program (Tartof et al., 2020). The AMS related data of the individual hospitals could be compiled into national database which enables the health policy makers to evaluate the AMS progress in national perspective (Aldeyab et al., 2012). Ultimately, a data sharing among various countries could contribute to the achievement of the United Nation's goal number 3 being designed for the global healthcare that also addresses the common threat of the onset of a post antibiotic era worldwide (Sadiq et al., 2018).

Conclusion

The AMS programs outlined in this review mainly implemented the prospective audit, formulary restrictive, educative, clinical pathway development and guideline development related interventions that controlled the misuse of antibiotics with the aim of the reduction of the antibiotic use related resistance and ultimately the higher cost of treatment. Most of the included studies focused the in-patient settings in relation to the AMS impact on antibiotic utilization, cost and infection control which invites the researchers to further explore the regionwide AMS related data so as to adopt a common global AMS policy that will also guide the LMIC lacking the strategy and resources for the AMS implementation. The findings of this study elucidate the effectiveness of AMS programs in controlling the irrational use of antibiotics within the in-patient clinical settings that is considered the first step towards the infection control and to minimize the cost of treatment with antibiotics.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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ORIGINAL ARTICLE Open Access

Validity of claims database compared with the electronic medical record of private health clinics in Malaysia: A pilot study

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ABSTRACT

Introduction: The validity of health insurance claims data in private health sectors has been widely reported in many developed countries to monitor details of private healthcare utilisation. Little is known regarding the data validity of private health care services and insurance claims in Malaysia. This pilot study aimed to validate the claims data from a private health insurance database, using electronic medical records (EMR) at the private clinics as the gold standard.

Method: Patients' data were retrieved from the PMCare health insurance database from 2016-2019 recorded for International Islamic University Malaysia employees. Patients were sampled from the PMCare database and manually compared with data from EMR of selected private panel clinics. Data were analysed for descriptive statistics using Microsoft Excel 2013.

Results: A total of four panel clinics consented to the study, and data were available for 2016, 2017 and 2019. The number of observations obtained from 118 patients (male = 63, female = 55) was 386, with the most common diagnosis reported in the PMCare database was acute upper respiratory tract infection (63.6%). Total accuracy between PMCare and EMR data was 91.5%, with an 8.5% difference or inaccuracy. Percentage accuracy was varied between different clinics (A= 92.6%, B=84.7%, C=98.6%, D=82.6%).

Conclusion: Data submitted to PMCare claims by private health clinics had high accuracy (>90%) and is acceptable for research and other applications. Future studies should investigate the differences in clinic-based practice for documenting the identified types of discrepancies to improve the accuracy of private health insurance databases.

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Introduction

The healthcare system in Malaysia has been primarily divided into private and public sectors. High concentrations of private practices utilised by the community are covered by private health insurance companies (Thomas et al., 2011). Many private practices have also been affiliated as panel health clinics to government and private organisations which subsidise certain medical insurance coverage as health benefits for their employees with variable premiums charges (Chua &Cheah, 2012). Private health insurance companies record the data on patients' claims such as diagnosis, prescribed medications and cost submitted by the panel health clinics from their medical records. The format for the claims database could be different between companies, but it generally collects information on prescriptions, procedures and administrative costs of inpatients and outpatients.

Claims data are useful to monitor details regarding healthcare utilisation, including disease and prescription patterns. However, it requires high accuracy with good validity and reliability components to be tested so that the characteristics and limitations of the dataset are well understood (Iwamoto et al., 2015; Du et al., 2006). Validity studies are crucial owing to increased reliance on health insurance claims, and thus the credibility of such data should be confirmed (Koram et al., 2019). There have been limited validation studies reported in the Asia Pacific region, including Australia, South Korea, New Zealand, Thailand, Singapore and Japan (Koram et al., 2019). To our knowledge, there have been no studies available reporting the validity of the claims database in Malaysia. Little is known whether prescription patterns, medication utilisation, and cost can be accurately obtained from private insurance databases. It is important to test the accuracy of insurance database documentation to ensure the credibility of research utilising databases. Validity of database of private insurance companies will facilitate research towards sustainable reimbursement policy, optimal utilisation of medications and patient outcomes.

A review has highlighted that the gold standard for database validity research was obtained from medical records, registry data, self-reported questionnaires and other data sources (Koram et al., 2019). Validated outcomes included variables such as medical conditions (Takeda et al., 2016), risk monitoring (Tomlin, Reith & Woods, 2017) and disease-specific comorbidities (Yamana et al., 2017). The present study aimed to investigate the accuracy of the claims data of a private health insurance company, PMCare, compared with electronic medical records (EMR) of private panel clinics that are covered by PMCare.

Methodology

This study was approved by the International Islamic University Malaysia Ethical Committee (IREC-2019-212). It was conducted from February to July 2020 at panel private health clinics in two states of Pahang and Selangor, Malaysia. The results were reported in an aggregated manner using de-identified data. Informed consent was not required as this study did not involve direct patient interaction.

This retrospective pilot study collected data for 2016-2019 provided by the private health insurance company PMCare for outpatient settings. The PMCare insurance was subsidised by International Islamic University Malaysia (IIUM) for its employees. Based on the policy, the claim limit was set at Ringgit Malaysia (RM) 45 per visit per patient. The panel private health clinics (PHC) were identified to collect the original data from EMR. The inclusion criteria were clinics with a high frequency of attendance by IIUM employees, used EMR and consented to the study. The exclusion criteria were those with low frequency of patients, used manual medical records and did not consent to the study. A total of four panel clinics were included, and data were collected from EMR.

Patient selection

The selection of patients was conducted using systematic sampling. Three patients per month were selected at the beginning, middle and end of each month from the PMCare database. The inclusion criteria were patients who had three or more medications. The search was conducted using a unique claim code that extracted the correct data regardless of the date recorded for database claim, patient's visit or delayed submission of claims to PMCare. Data collection included information on claim code, date of prescription, name of the patient, patient identification, diagnosis, name of medications, number of medications per prescription, the number of drugs supplied, consultation fee, the total cost of medications and amount paid by the patient. Validated outcomes included diagnosis, medication name, number of medications per prescription, the quantity of medication, and the amount claimed to the health insurance. Majority of previous studies (83%) have reported similar data collection methods where cases were most frequently validated against diagnoses in medical records (Widdifield et al., 2013).

Accuracy measurement

The accuracy was obtained by comparing the PMCare dataset with the original data from EMR by dividing the number of observations found to be the same by the total number of data elements of the PMCare database then multiplying that total by 100. The agreement exceeding 90% was considered as a good benchmark when data elements from the two sources were found not to be the same, noting the reasons (for example, unclear data definitions) as reported in previous studies (Iwamoto et al., 2015; Miller et al., 2009). The discrepancy was determined when the inaccuracies of observations recorded in the EMR and PMCare database were identified. The discrepancies were calculated by dividing the number of observations found to be different with the total observations from selected PMCare data then multiplying by 100.

Results

A total of 118 patients (age: mean ±SD, 33.2 ± 12.7) were selected based on the availability of data from EMR (Table 1). Although there were three patients selected per month from 2016-to 2019, many patients had to be excluded due to changes in the recording system used at the clinics, crash of the software and incomplete record of EMR. We found that several observations from EMR recorded extra medications (415 observations) compared to the PMCare database, which was 386 observations. Electronic medical records contained original data entered from patients' prescriptions. The number of observations recorded in the EMR was higher than the PMCare database because the EMR captured the total number of medications prescribed to each patient.

In contrast, only a few medications were recorded for insurance claims to PMCare for the coverage limit of RM45. Therefore, after removing extra observations from EMR for accuracy measurement, the total number of observations for both EMR and PMcare database was 386. As presented in Table 2, the number of patients included in the present pilot study was sufficient as reported by a similar study that measured accuracy and validity of a hospital database (Cook et al., 2002).

The advantage of using EMR was that additional information was available and comprehensively recorded for each visit. We found that consultation fees were varied between clinics and between clients depending on the number of medications prescribed and adjustment to the insurance eligibility. Data from EMR provided the amount of out-of-pocket money paid by the patients if the total charges for consultation and medications exceeded the insurance coverage of RM 45, including the detailed price for each medication with a specific quantity. On the contrary, the PMCare database did not have this information. Discrepancies were found due to differences in recording the name and quantity of medications, diagnosis, the number of medications and the missing information in either EMR or PMCare database for the variables investigated. The most common diagnosis reported in the PMCare database was acute upper respiratory tract infection (URTI) (63.6%), followed by acute gastroenteritis and colitis (13.5%).

Table 1: Demographics of patients from four private medical clinics.

Characteristics	N = 118	Frequency (%)
Gender:		
a. Male	63	53.4
b. Female	55	46.6
Age (years):		
Mean (SD)	33.2 (12.7)	
Median (range)	35 (4 – 61)	
Diagnosis:		
a. Acute Upper Respiratory Infection, unspecified	75	63.6
b. Infectious Gastroenteritis and Colitis, Unspecified	16	13.5
c. Unspecified Abdominal Pain	3	2.54
d. Anemia, Unspecified		
e. Others (Urticaria, Low back pain, Acute Tonsillitis, Viral Infection Unspecified, Dermatitis and Eczema, Conjunctivitis, Gout, Hemorrhoids, Hordeolum (Externum) (Internum) of Eyelid, Gastritis, Myalgia, Mycosis)	3 21	2.54 17.8

Discussion

The accuracy of the PMCare database has never been validated to determine its credibility to be used for database research in Malaysia. The present study reported that the PMCare claims database had overall 91.5% accuracy and 8.5% discrepancies compared with EMR data as a gold standard for four different panel clinics for the segregated patient samples collected in 2016, 2017 and 2019. This outcome indicated an ideal accuracy value that was set as above 90% to be considered valid (Miller et al., 2009). Our finding was lower than that reported by a study in Japan, that demonstrated 99% accuracy in estimating opioid consumption among cancer patients (Iwamoto et al., 2015).

Another study validated claims algorithm and clinical operative reports with 97% accuracy (Miller, Saigal & Warren, 2009). However, a different study has indicated a lower range of good accuracy with 80% and above for a pilot study reporting database validity (Cook et al., 2002). The analysis for an individual clinic showed that accuracy could achieve above 98% with a systematic and appropriate recording of claims data according to EMR (Table 2).

Table 2: Discrepancies of data from EMR of respective clinics in comparison to PMCare Database

Variables	Clinic A	Clinic B	Clinic C	Clinic D	Total
No. of patients	30	15	50	23	118
Year of observations	2016	2016	2016-2017	2019	
No. of Observations from EMR	94	59	147	86	386
No. of Observations from PMCare claims database	94	59	147	86	386
No. of observations with discrepancies	7	9	2	15	33
Types of discrepancies	Name and quantity of medication.	Name and quantity of medication, diagnosis.	Name of medication.	Name and quantity of medication, diagnosis.	
Percentage of discrepancies (%)	7.4	15.3	1.4	17.4	8.5
Percentage of accuracy (%)	92.6	84.7	98.6	82.6	91.5

Investigation of data discrepancy showed that types of discrepancy tend to vary between clinics. This could be due to the nature of PMCare claims data, where data were created and submitted later from the date of the patient's visit, whereas the EMR data showed the actual medications dispensed daily. Although the differences in characteristics exist, both data were prone to human error in entering the details into the online system, which resulted in discrepancies (Iwamoto et al., 2015). It is also important to note that claims databases could only cater for specific data covered by the insurance company for certain medications and diseases. A review of previous studies has also highlighted the critical measures of diagnostic accuracy (sensitivity, specificity, and positive and negative predictive values) and disease prevalence in reporting validity of administrative database algorithms (Widdifield et al., 2013).

Our study identified the discrepancies by including the missing names of medication or different medications recorded when compared between EMR and PMCare database. The diagnosis error was included when the diagnosis submitted to the PMCare database was different or unspecified compared to EMR. The limitation of this study was that we did not have specific details regarding the options given for each data category in the claim database system, such as general option (e.g. unspecified abdominal pain) or specific option for accurate diagnosis (e.g. dyspepsia, gastritis). We did not consider that specific, or general diagnosis of similar nature or location was different unless the difference was obvious such as abdominal pain (EMR) versus URTI (PMCare). From the perspective of the claims database and EMR, we propose that details listed in the claims database should be the same as those recorded in EMR. It was expected that the number of observations in EMR would be greater than those in the claim database since the insurance company covers only certain medications. The consistency in recording the data will improve the accuracy and validity of the data from both sources.

The major limitation of our pilot study was that the sample size was relatively small compared to previous studies (Iwamoto et al., 2015; Takeda et al., 2016) but was sufficient to report validity for a pilot study (Cook et al., 2002). Our study was multi-centred, with a standardised data format from the PMCare database, which allowed the comparison of varying practices between settings. Future studies may identify interventions for corrective actions to ensure high accuracy of the claims database. The results suggest that PMCare database is valid and accurate as a valuable resource to be used for research purposes but with careful analysis and interpretation considering the data characteristics. The identified discrepancies were common for certain variables in database validity studies as previously reported in other studies (Cook et al., 2002; Gabriel et al., 2005). However, improved documentation practice is required at the specific settings to improve the accuracy of the claims database.

Conclusion

Data from the health insurance claims database was valid and applicable for research purposes with careful analysis and interpretation. The overall high accuracy of the health insurance claims database in this study indicated its validity. However, variation in accuracy level was found between different clinics attributable to varying practices in recording the data. Future studies are required to identify effective interventions to improve the accuracy of claims databases with gold standards.

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Data Availability Statement

Request to access the datasets should be directed to International Islamic University Malaysia Research Ethical Committee. The de-identified data could be shared with interested researchers after obtaining approval from the above ethical committee. The restriction on public data deposition is due to the privacy and confidentiality of patients' health data.

Conflict of Interest

The authors have no conflict of interest to declare. The funder had no role in study design, data collection and analysis, decision to publish or prepare the manuscript.

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