Arterial Stiffness and its Association with Dyslipidemia

Razman MR[a], Jamaluddin AR[a], Ellyda MN[b], Seikh FA[a]

[a] *Department of Community Medicine, Kulliyyah of Medicine, International Islamic University Malaysia, Kuantan, Pahang, Malaysia*
[b] *Department of Radiology, Kulliyyah of Medicine, International Islamic University Malaysia, Kuantan, Pahang, Malaysia*

ABSTRACT

Introduction: Cardiovascular diseases (CVD) are the leading cause of mortality in Malaysia as well as in other countries. It is associated with many risk factors, such as increasing age, hypertension, diabetes, dyslipidemia, oxidative stress and autonomic dysfunction and arterial stiffness. The objectives of this study were to measure the prevalence of arterial stiffness and to assess its association with dyslipidemia. **Methods:** A cross sectional study was conducted in a rural community in Malaysia involving 146 subjects. Data were collected using an interviewer administered questionnaire which included three sections – sociodemographic characteristics, personal profile, and past medical history. In addition, Seca Body Meter (Seca 220) was used to measure height and weight. Sphygmomanometer (OMRON Automatic Blood Pressure Monitor HEM 907) and SphygmoCor-AtCor MM3 SERIAL/RS-232 were used for blood pressure and augmentation index (AIx) measurement. Data were analysed using the SPSS for Windows, Version 18.0. **Results:** The mean age of respondents was 49.5 years, SD±15.6. The prevalence of arterial stiffness was 23.3% (95% Confidence Interval (CI): 16.44 – 30.16). The prevalence of dyslipidemia was 82.9% (95% CI: 76.79 – 89.01). Multivariate logistic regression revealed that total cholesterol was significantly associated with arterial stiffness (OR=4.56, CI 1.10-18.90). **Conclusion:** The prevalence of dyslipidemia was high. Despite an insignificant association between dyslipidemia and AIx, there is a significant association between TC level and AIx.

KEYWORDS: Arterial stiffness, dyslipidemia, Augmentation Index, total cholesterol

INTRODUCTION

Over the last four decades, cardiovascular disease (CVD) has been the leading cause of death in Malaysia as well as in many countries.[1,2] Many factors can cause CVD and arterial stiffness is one of them.[2]

Arterial stiffness is a generic term for arterial compliance, distensibility and elasticity.[3] Increased arterial stiffness is proposed as a possible mechanism in the initiation and/or progression of atherosclerosis and hypertension. Dyslipidemia is associated with a number of cardiovascular risk factors, which was supported by a study done in 2006 by The National Cardiovascular Disease Database in which the prevalence of dyslipidemia among CVD patients was 55.9%.[4]The Malaysia National Health and Morbidity Survey III 2006 (NHMS, 2006) found that the prevalence of dyslipidemia was 20.7%. Dyslipidemia is defined as a condition whereby lipid values of a person fall outside the norm as according to Malaysia Clinical Practice Guidelines (CPG) on Management of Dyslipidemia (4th edition).

Several parameters can provide information on arterial stiffness. Among all these techniques are AIx, augmentation pressure (AP), pressure pulse waveforms (PPW), ejection duration and subendocardial viability ratio (SEVR).[5] In this study; the AIx was used as a parameter to measure arterial stiffness because previously, there was a study that showed a positive correlation between AIx and cholesterol levels.[6,7] Therefore, this study focused to measure the prevalence of arterial stiffness and its association with dyslipidemia. Table I briefly summarizes the various studies conducted on the association between arterial stiffness and lipid parameters.

Corresponding author:

Dr Razman Mohd Rus
Department of Community Medicine,
Kulliyyah of Medicine,
International Islamic University Malaysia,
25200 Kuantan,
Pahang, Malaysia
Tel:+60169890228
Fax: +6095716798
Email: razman@iium.edu.my

Table I. Summary statement of various studies on the association between arterial stiffness and the various lipid parameters

Lipid parameter	Studies showed association		Disproving association	
	Study	Method	Study	Method
HDL	Miao, Ye *et al*. 2011	LV Diastolic Function Index (E/Em)	Wilkinson et al., 2002	AIx and Aortic PWV
	Sutton-Tyrrell, *et al.*, 2001	Aortic PWV		
LDL	Brinkley *et al.*, 2009	Aortic PWV	Miao, Ye et al. 2011	LV Diastolic Function Index (E/Em)
TG	Legedz, Bricca *et al*. 2006	Aortic PWV	Wilkinson et al., 2002	AIx, Aortic PWV
	Sutton-Tyrrell, *et al.*, 2001	Aortic PWV		
TC	Wilkinson *et al.*, 2002	AIx and Aortic PWV	Miao, Ye et al 2011	LV Diastolic Function Index (E/Em)
	Pirro *et al.*, 2004	Aortic PWV		

PWV: pulse wave velocity, Aix: Augmentation Index, LV: left ventricular.

METHODOLOGY

A cross-sectional study was carried out among adults in a rural community (Kampung Alor Batu in Kuantan, Pahang, Malaysia) from 17th February 2012 to 4th March 2012. Adults were defined as residents aged 18 years and above. There were 1260 inhabitants in 200 houses. Single proportion formula was used to determine the sample size. By using P as 0.207 based on the prevalence of dyslipidemia in NHMS III 2006 and detectable difference of 0.05, the minimum required sample is 252 samples. Another 20% was added considering the non-respondent, making the final required sample size of 300 samples. However, it was possible to obtain 146 samples within the stipulated time-frame as mentioned earlier.

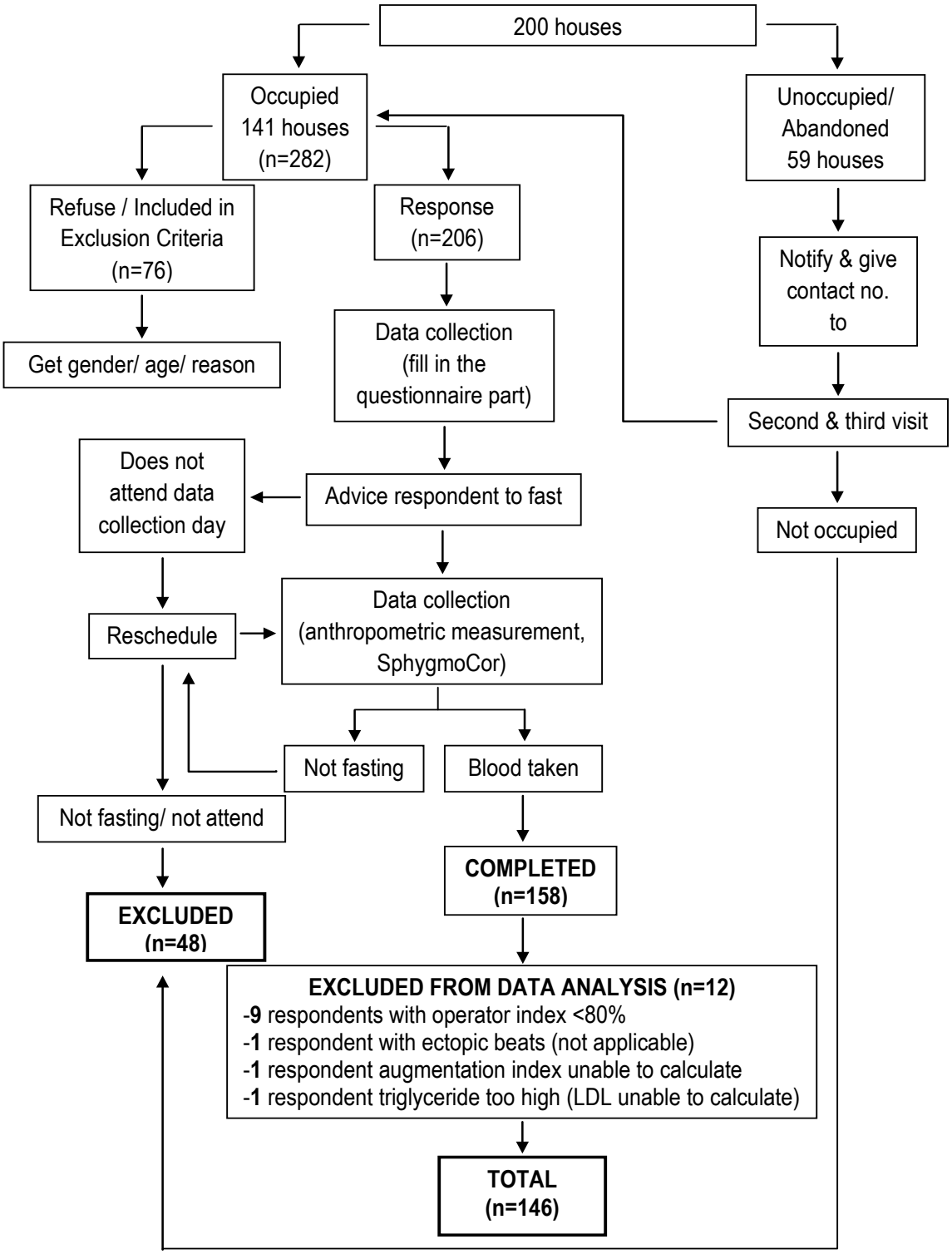
All adults fulfilled the criteria of being a Malaysian and current resident of the studied community. Interviewer -based questionnaire was conducted. Adults who refused to participate; not available at home after three visits; failed to present themselves during blood taking, SphygmoCor and anthropometric measurement day; and pregnant women were dropped from this study (refer Figure 1). Out of the 158 respondents, 12 of them were further excluded from the data analysis due to incomplete data in which there were nine respondents with operator index <80%, one respondent with ectopic beats (not applicable), one respondent with AIx that was unable to be calculated and one respondent with too high TG (LDL was not able to be calculated). Thus, final total sample of this study was 146.

A validated questionnaire was administered to the participants. The three sections of the questionnaire were sociodemographic history, personal history, and past medical history. Measurements taken for the study were anthropometry, blood pressure, BMI and AIx. AIx was measured using Sphygmocor-AtCor MM3 SERIAL/ RS-232 and was defined as the difference of the first systolic and second pressure peak, expressed as a percentage of the pulse pressure. The numerical values of AIx indicate estimation of arterial stiffness, correlating with the increase in aortic pressure. According to SphygmoCor interpretations, normal AIx is when the value is not within the upper 5% of the confidence interval (CI) while abnormal AIx is when the value is within the upper 5% of CI.[8] Only two team members became operators of the device, and an operator index of 80% was set as the lowest limit in order to obtain valid results.

Dyslipidemia was defined based on CPG, Management of Dyslipidemia 2011, (4th Edition) by analyzing the fasting blood lipid profile. Respondents were instructed to fast starting at least 6 hours prior to blood taking. Blood was withdrawn from the brachial vein at antecubital fossa and transferred to appropriate tube before being analyzed. Other measuring tools used were OMRON Automatic Blood Pressure Monitor HEM 907 for blood pressure measurement; and Seca Height and Weighting Scales (Seca model 220) respectively for height and weight measurement. Training was conducted among the researcher of this study to

standardize the measurement according to the Centre for Disease Control (CDC) National Health and Nutrition Examination Survey (NANES 2004) to reduced inter-operator and intra-operator variability. Days prior to data collection and under the supervision of a medical assistant, students were trained to appropriately use measuring tools, especially SphygmoCor, until constant and reliable values were achieved for each measurement. All measurements were taken during the five data collection sessions which took place throughout five days of three consecutive weekends.

Figure 1. Flowchart



Statistical Analysis

The data were analyzed by using SPSS software (PASW 18.0) for Windows. The descriptive statistics were described as mean and standard deviation (SD) or median and inter quartile range (IQR) for numerical variables. Numbers and percentage (%) were used for categorical variables. Chi-square analysis and independent sample t test were used to measure that association between arterial stiffness, and its risk factors namely age, gender, education level, BMI group, smoking, hypertension, diabetes mellitus and dyslipidemia. Logistic regression was performed to compute odds ratio (OR) and 95% CI for relationships between arterial stiffness, and its risk factors specifically dyslipidemia. All associations were first analyzed without adjustments and then with adjustment for potential confounder, which comprise of age, gender, smoking, BMI group, hypertension, and diabetes mellitus. The adjusted OR was estimated with 95% CI.

RESULTS

Table II shows the socio demographic characteristics and potential risk factors of arterial stiffness. The study population consisted of 146 respondents with mean age of 49.6 (15.60) years; 64.4% (94) were females; 32.2% (47) completed secondary level; 29.5% (43) were overweight and 39.7% (58) were obese. Meanwhile, 25.3% (37) were smokers; 25.3% (37) were hypertensives, 11.0% (16) were diabetics and 82.9% (121) (95% CI 76.92, 89.08) were dyslipidemia respondents.

Table II. Sociodemographic characteristics, status of arterial stiffness with potential risk factor

	Total Respondents (N=146)	Arterial Stiffness[a]		P value[b]
		Yes (N=34)	No (N=112)	
Age (year)	49.60 (15.60)[c]	37.03 (13.21)[c]	53.42 (14.25)[c]	<0.001
Monthly Household Income (RM)	895 (1125)[d]	1016.67 (1313)[d]	807.50 (1000)[d]	0.15
Gender (%)				
Male	52 (35.6)	10 (19.2)	42 (80.8)	0.39
Female	94 (64.4)	24 (25.5)	70 (74.5)	
Education (%)				
No Formal Education	16 (11.0)	3 (18.8)	13. (81.3)	0.03
Not Completed Primary	30 (20.5)	2 (6.7)	28 (93.3)	
Completed Primary	47 (32.2)	10 (21.3)	37 (78.7)	
Completed Secondary	47 (32.2)	17 (36.2)	30 (63.8)	
Completed Tertiary	6 (4.1)	2 (33.3)	4 (66.7)	
Smoking (%)				
Yes	37 (25.3)	6 (16.2)	31 (83.8)	0.24
No	109 (74.7)	28 (25.7)	81(74.3)	
BMI (%)				
Underweight	14 (9.6)	4 (28.6)	10 (71.4)	0.33
Normal	31(21.2)	4 (12.9)	27 (87.1)	
Overweight	43 (29.5)	13 (30.2)	30 (69.8)	
Obese	58(39.7)	13 (22.4)	45 (77.6)	
Hypertension (%)				
Yes	37 (25.3)	3 (8.1)	34 (91.9)	0.01
No	109 (74.7)	31 (28.4)	78 (71.6)	
Diabetes Mellitus (%)				
Yes	16 (11.0)	1 (6.3)	15 (93.8)	0.12
No	130 (89.0)	33 (25.4)	97 (74.6)	
Dyslipidemia (%)				
Yes	121 (82.9)	26 (21.5)	95 (78.5)	0.26
No	25 (17.1)	8 (32.0)	17 (68.0)	

[a] Arterial stiffness is defined as Augmentation Index (AIx) of upper 5% of reference range as determined by SphygmoCor;

[b] All P values are determined by X^2 test except for age and income (independent sample t test)

[c] Mean (SD), [d] Median (IQR).

The prevalence of arterial stiffness was 23.3% (34) (95% CI 16.14, 29.86) in this study population. Among the arterial stiffness group, the mean age was of 37(13.21) years; 70.5% (24) were females; 50% (17) completed secondary level; 38.3% (13) were overweight and obese; 17.6% (6) were smokers; 8.8% (3) were hypertensives and 2.9% (1) were diabetics.

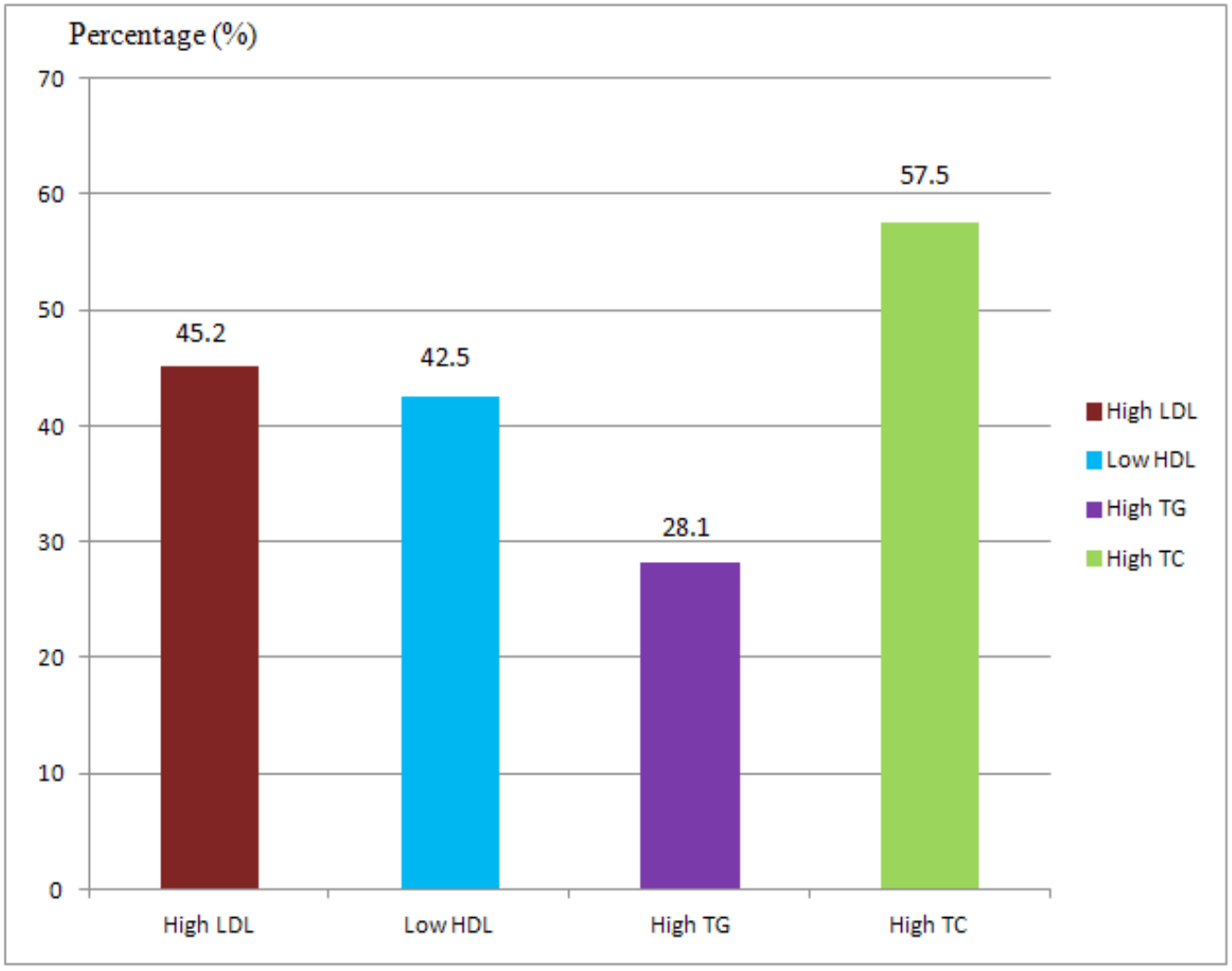


Figure 2. Distribution of different types of dyslipidemia

Figure 2 summarizes the distribution of different types of dyslipidemia. Among 146 respondents, it was found that 45.2% (66) had high LDL, 42.5% (62) had low HDL, 28.1% (41) had high TG and 57.5% (84) had high TC. Table III shows the association of arterial stiffness with age, gender, smoking habit, BMI group, diabetes mellitus, hypertension and dyslipidemia. In a simple model unadjusted for arterial stiffness risk factor, the OR for arterial stiffness of increasing age was 0.92 (95% CI 0.89, 0.95); male was 0.69 (95% CI 0.30, 1.59); smoker was 0.56 (95% CI 0.21, 1.48); diabetes was 0.20 (95% CI 0.03, 1.54); hypertension was 0.22 (95% CI 0.06, 0.78); and dyslipidemia was 1.72 (95% CI 0.67, 4.43). In bivariate analysis and adjusted for arterial stiffness risk factors, only increasing age which had OR of 0.92 (95% CI 0.88, 0.96) was associated with a decreased risk of arterial stiffness. The OR for both unadjusted and adjusted indicated that the elderly groups of respondents have a lower risk of getting arterial stiffness than younger respondents.

Table III. Association of arterial stiffness with age, gender, smoking habit, BMI group, diabetes mellitus, hypertension and dyslipidemia

	Unadjusted		Adjusted[a]	
	OR	95% CI	OR	95% CI
Increasing Age (per year)	0.92	0.89-0.95	0.92	0.88-0.96
Gender				
Male	0.69	0.30-1.59	0.51	0.14-1.88
Female	1.00		1.00	
Smoking				
Yes	0.56	0.21-1.48	2.28	0.46-11.19
No	1.00		1.00	
BMI Group				
Normal	1.00		1.00	
Underweight	2.70	0.57-12.91	1.93	0.30-12.46
Overweight	2.93	0.85-10.06	3.21	0.75-13.76
Obese	1.95	0.58-6.60	1.58	0.38-6.53
Diabetes Mellitus				
Yes	0.20	0.03-1.54	0.67	0.07-6.12
No	1.00		1.00	
Hypertension				
Yes	0.22	0.06-0.78	0.72	0.17-3.06
No	1.00		1.00	
Dyslipidemia				
Yes	1.72	0.67-4.43	0.84	0.25-2.83
No	1.00		1.00	

[a] Adjusted for age, gender, smoking, BMI group, diabetes mellitus, hypertension and dyslipidemia

We had found in this study that arterial stiffness was not significantly associated with dyslipidemia with adjusted OR of 0.84 (95% CI 0.25, 2.83). However, when we further analyzed the result, we found that only high TC was significantly associated with arterial stiffness with adjusted OR of 4.56 (95% CI 1.10, 18.90) as in Table IV.

Table IV. Association of arterial stiffness with status of lipoproteins

	Unadjusted		Adjusted[a]	
	OR	95% CI	OR	95% CI
Low Density Lipoprotein				
High	0.69	0.31 – 1.51	1.87	0.49 – 7.22
Normal	1.00		1.00	
High Density Lipoprotein				
Low	0.93	0.43 – 2.03	0.85	0.31 – 2.37
Normal	1.00		1.00	
Triglycerides				
High	0.47	0.18 – 1.24	0.38	0.10 – 1.45
Normal	1.00		1.00	
Total Cholesterol				
High	1.07	0.49 – 2.33	4.56	1.10 – 18.90
Normal	1.00		1.00	

[a] Adjusted for age, gender, smoking, BMI group, diabetes mellitus and hypertension

DISCUSSION

In this study, prevalence of dyslipidemia was 82.9% (95% CI 77.4, 88.4). This was very much different from NHMS 2006, which stated that the prevalence of dyslipidemia in Malaysia was 20.6% (95% CI 20.1, 21.3). However, the difference in the prevalence of dyslipidemia found was probably due to the difference in definition used by NHMS 2006, in which only TC was taken into account.

One of the main objectives of this study was to find the association of dyslipidemia and arterial stiffness. We found that dyslipidemia after adjusting for all other confounders to be not significantly associated with arterial stiffness (adjusted OR 0.84, 95% CI 0.25, 2.83). After analyzing the different types of dyslipidemia, even after adjusting for other confounders, we found that TC was significantly associated with arterial stiffness as the odds ratio was 4.56 (95% CI 1.10, 18.90). This result was also demonstrated in another research perform in the United Kingdom.[7] We found that high LDL, low HDL and high TG levels were not associated with arterial stiffness as it was statistically not significant. This result was in line with a study in China, which stated that LDL and HDL were not associated with arterial stiffness and another research in France, which said that there was a negative relationship between HDL and arterial stiffness.[9,10]

The prevalence of arterial stiffness in this study was 23.3% (95% CI 17.1, 29.5). From that, we found that the majority of respondents with arterial stiffness were females; which is 70.6% (95% CI 63.9, 77.3). After adjusting for other confounders, the association of gender with arterial stiffness in this study was found to be statistically not significant (adjusted OR 0.51, 95% CI 0.14, 1.88). This finding was not in line with another study, which stated that more adult males would develop stiffer large vessels. [11] Another study in Florida also showed that males were more likely to get arterial stiffness.[12]

In terms of age, this study showed an inverse relation between increasing age and arterial stiffness. In fact, after adjusting for other confounders it was statistically significant (adjusted OR 0.92, 95% CI 0.88, 0.96). A different study done stated that arterial stiffness could be as a result of ageing, which differ from this study.[13] However, there was a study which found that non invasive measurement of arterial stiffness such as SphygmoCor was unreliable for healthy young adults, which may have caused some of the over estimation of arterial stiffness in young individuals.[14]

In an Irish study, current and ex-smokers had significantly higher pulse wave velocity and AIx compared with non-smokers.[15] As for this study, even after adjusting for other risk factors, current and ex-smokers have statistically no significant association to arterial stiffness (adjusted OR 2.28, 95% CI 0.46, 11.19). Although statistically not significant, the odds ratio of diabetes mellitus (adjusted OR 0.67, 95% CI 0.07, 6.12) and hypertension (adjusted 0.72, 95% CI 0.17, 3.06) were found to be much lower as compared to non diabetic patients and non hypertensive patients respectively. These results did not go with other studies, which stated that diabetes mellitus and hypertension were positively associated with increased arterial stiffness.[16,17]

This study also did not show any association between obesity and arterial stiffness as it was statistically not significant even after adjusting for other confounders (adjusted OR 1.58, 95% CI 0.38, 6.53). Nonetheless, this finding was different to a study done in France, which revealed that obese subjects were more likely to have arterial stiffness.[18]

In terms of limitations, debates on the reliability of SphygmoCor have long been ongoing. A study by Hope et al., reported that there was no correlation between measured AIx and that estimated from a transfer function (TF) and thus of no additional clinical benefit.[19] The main disadvantage of using the radial pulse is that the use of TF might inevitably result in some errors in estimating the true AIx.[20] This is due to pressure contour changes appreciably as it travels from the aorta to more peripheral sites.[21] The categorization of AIx into two major group namely normal or stiff arterial group decreased the power of the data. The AIx normal range is based on a research conducted in Cardiff UK. However, there has been no local research done to analyze the compatibility of this range in this region.

The findings from this study urged us to take serious actions. High prevalence of dyslipidemia and obese people indicate lack of health awareness among the population. Even more surprisingly, dyslipidemia is not only common among the elderly, but also a common scenario among the younger age group as supported by a study done in Mumbai. This study revealed a high prevalence of dyslipidemia among young males which increase their risk of developing Coronary Artery Disease (CAD) that may lead to premature cardiovascular infarction.[22] Thus, screening of dyslipidemia should be encouraged at an earlier age. Health promotion programmes such as dietary modification, smoking-cessation programme and physical exercise should be conducted in a fresher and creative approach.

CONCLUSION

The researchers attempted to find the association between dyslipidemia and arterial stiffness as there is known correlation between these two. Using a cross-sectional study with 146 samples, the researchers found a high prevalence of dyslipidemia; however, the researchers did not find any significant association between dyslipidemia and AIx. Despite an insignificant association between dyslipidemia and AIx, there is a significant association between TC level and AIx. We however, found a statistically significant inverse relation between increasing age and arterial stiffness.

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