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Research Article

Correlation of Atherogenic Index of Plasma and Atherogenic Coefficient with Cardiovascular Disease Risk Assessed by ASCVD Risk Estimator

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Abstract

Introduction**:** Cardiovascular disease (CVD) is the leading cause of approximately one-third of deaths worldwide. Absolute lipid parameters are inadequate in predicting CVD risk, and several lipid indices have been introduced, namely "Atherogenic index of plasma" (AIP) and "Atherogenic coefficient" (AC). Cardiovascular disease risk of a patient for the forthcoming 10 years can be calculated using the atherosclerotic cardiovascular disease (ASCVD) Risk estimator. Though this method is currently accepted, certain drawbacks have been reported. Therefore, this study aimed to investigate the correlation of AIP and AC with CVD risk estimation for the upcoming ten years calculated by ASCVD Risk estimator. Methods: A cross-sectional observational, retrospective study was conducted by recruiting hundred and fifty-three patients. Sociodemographic data were collected through an interviewer-based questionnaire developed in-house. Total cholesterol, High-Density Lipoprotein (HDL) cholesterol, Low-Density Lipoprotein (LDL) cholesterol, and triglyceride levels were obtained from the lipid profile test results of the study participants. AIP and AC were calculated using formulas while 10-year ASCVD risk was calculated by the ASCVD Risk estimator. Correlations were analyzed using Pearson's Correlation, and $p<0.05$ was considered significant. Results: There was no significant correlation between AIP and 10-year ASCVD risk ($p=0.880$), and AC and 10-year ASCVD risk ($p=0.576$). However, a significant correlation was observed between AIP and AC ($r=0.425$, $p=0.001$). Conclusions: AIP and AC were identified as potent CVD risk assessment tools. As the increase in 10-year ASCVD risk, AIP, and AC are associated with several CVD risk factors, CVD risk of patients should be assessed routinely, especially because the risk of most patients presenting with normal lipid profiles, may remain silent unless properly investigated using further laboratory investigations.

Keywords: Cardiovascular disease, Atherogenic index of plasma, Atherogenic coefficient, ASCVD Risk estimator

Introduction

Cardiovascular disease (CVD) includes a group of diseases affecting the heart and blood vessels, such as coronary artery disease (CAD), peripheral arterial disease, congenital heart disease, deep venous thrombosis, and pulmonary embolism. The first sign of underlying CVD is usually a heart attack or stroke [1]. Cardiovascular disease is

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responsible for almost half of non-communicable diseases (NCDs), and CVD remains the leading cause of global death, causing 17.3 million deaths per year, a number which will become 23.6 million by 2030 [2]. In 2017, almost 17.8 million deaths in the world occurred due to CVD [3].

Lipid profile is currently being used worldwide in CVD risk assessment, and existing prevention guidelines have recommended the use of standard lipid levels to assess the risk of CVD [4]. However, it has been reported that absolute lipid parameters are inadequate in predicting CVD risk, and several lipid indices have been brought forward to evade this deficiency [5,6].

One such index is the "Atherogenic index of plasma" (AIP), and it is based on triglycerides (TG) and high-density lipoprotein cholesterol (HDL cholesterol). AIP is a logarithmically transformed ratio of molar concentrations of triglycerides to HDL cholesterol, and its high predictive value is explained by the strong correlation of AIP with lipoprotein particle size [7]. It has been shown that AIP must be used as a regular monitoring index of CVD in routine practice, mainly in persons with other CVD risk factors, including physical activity, BMI, waist circumference, hypertension, fasting blood sugar, and lipid status. AIP was shown to be important as a predictor for atherosclerosis which could also be used as a highly sensitive index to assess CVD risk factors [8]. It has been proposed that AIP values of -0.3 to 0.1 represented a low risk, 0.1 to 0.24 indicated medium risk, and above 0. 24 indicated high cardiovascular risk [9].

"Atherogenic coefficient" (AC) is another index used in predicting the risk of CVD. It represents the total amount of cholesterol found in VLDL cholesterol, IDL cholesterol, and LDL cholesterol lipoprotein fractions as a ratio to HDL cholesterol fraction in the patient. Hence, it reflects the atherogenic tendency generated by the entire lipoprotein fractions [10].

In 2013, the American College of Cardiology/American Heart Association (ACC/AHA) included an atherosclerotic cardiovascular disease (ASCVD) Risk Estimator in the guideline on the treatment of blood cholesterol [11]. ASCVD Risk Estimator has been used as a non-invasive screening tool to determine the 10-year CVD risk. It has helped in risk stratification and treating low, medium, and high-risk patients who have not yet faced a cardiovascular event such as myocardial infarction or stroke [12]. The parameters used in the ASCVD Risk Estimator includes, age, sex, ethnicity, total cholesterol, HDL cholesterol, systolic blood pressure, presence or absence of diabetes, and smoking. This calculator has been used to estimate the 10-year risk for adults aged 40-79 years and their lifetime risk for CVD [13]. Therefore, the objective of the present study was to investigate the correlation of AIP and AC with cardiovascular disease risk assessed by the ASCVD Risk estimator. This was required as no studies were conducted in Sri Lanka to apply the outcome to the Sri Lankan population.

Methods

Study design

A cross-sectional observational, retrospective study was conducted on a defined population consisting of 153 individuals. The sample size was calculated using the equation derived by Pourhoseingholi *et al*. [14].

Study population and study setting

Ethical clearance was obtained from the Ethics Review Committee of the Faculty of Medicine, General Sir John Kotelawala Defence University, to conduct the study (ERC approval number – RP/S/2021/15). After obtaining ethics approval, patients who attended the medical clinic were selected based on the inclusion and exclusion criteria.

Individuals, both males, and females, within the age group of 40-79 years, who underwent serum lipid profile testing for CVD risk assessment, were included in the study, and only the already available lipid profiles which were less than three

months old by the time of data collection of our study were incorporated. Individuals who already had chest pain and those who were on natural cholesterol reducers such as fish oil and niacin, and synthetic cholesterol reducers such as statin and fibrates were excluded from the study. The above subjects were excluded since they were already clinically diagnosed as having heart-related disorders, and it would be meaningless to determine their risk of CVD for the upcoming ten years. All the patients fulfilling the inclusion criteria who attended the medical clinic of University Hospital KDU, Sri Lanka, from 1st November 2021 to 1st December 2021, were selected. The number of patients attending the medical clinic during sample collection (one month) was approximately 300.

Collection of sociodemographic and medication related data

An in-house developed, interviewer-administered questionnaire was used to collect information on sociodemographic data, history of diabetes, and whether they consumed fish oil. Other information, including systolic and diastolic blood pressure (less than 120/80 mmHg), alcoholic consumption status, smoking status, physical activity level (whether physically active or not), whether taking antihypertensives or not, whether on anti-hypercholesteremic medication or not, and further details of medication history, including fibrates, niacin, and aspirin therapy, were obtained using the questionnaire and reports documented on each patient's clinical record.

Collection of biochemical analyses of data

The biochemical data required for the study were extracted from patients' clinical records, not older than three months. Serum total cholesterol, HDL cholesterol, and triglycerides values were obtained from lipid profile test results of the individuals as determined by Abbott ARCHITECT plus C4000 automated analyzer; estimation of total cholesterol was by cholesterol oxidase enzymatic colorimetric method with lipid clearing factor; HDL cholesterol was by accelerator selective detergent method; and triglycerides were by glycerol phosphate oxidase method. Serum LDL cholesterol values were obtained from the lipid profile test results of the individuals as calculated by Friedewald's formula [15].

Measuring systolic and diastolic blood pressure

Before measuring blood pressure, the patients were allowed to relax for 5 minutes, in a comfortable seated posture, with both feet resting on the ground. The patients were made to empty their bladder, and was asked to avoid caffeine, smoking, or exercise 30 minutes before taking the blood pressure measurement. The average of two measurements taken on two occasions was recorded from each patient for both systolic and diastolic blood pressure values. Those who were on medication for hypertension, and hypotension were excluded from the study. This was due to the medication interference, which adversely affected the ASCVD Risk measurement, and would result in an inaccurate representation of the actual risk.

Systolic and diastolic blood pressure were measured by the Philips IntelliVue MX-450 automatic blood pressure monitor on the same day of collecting patients' clinical history and medication history. Blood pressure measurement and venipuncture for lipid profile analysis were conducted on different days since readily available lipid profiles by the time of data collection were utilized in the study.

Collecting data on risk factors of the population

Although it was difficult to state clear definitions which thus leads to inherent limitations in these types of retrospective studies, the data on alcohol consumption, smoking status, and physical activity level (physically active/ physically non-active) of our study population were collected via our in-house developed, interviewer-administered questionnaire.

Calculation of Body Mass Index (BMI)

The parameters, including weight, and height were taken from the patients' clinical records, and the BMI was calculated manually using the following formula.

BMI = Weight (in kilograms)/ Height^2 (in meters)

Calculation of atherogenic index of plasma (AIP)

AIP was calculated according to the following formula and its risk categories are given in Table 1.

Atherogenic Index of Plasma (AIP) = log TG/HDLc [11]

Where,
TG - Triglycerides
HDLc - High-Density Lipoprotein cholesterol

Table 1: Atherogenic Index of Plasma risk categories [9]

AIP Range	Risk Category
-0.3 to 0.1	Low Risk
0.1 to 0.24	Intermediate Risk
above 0. 24	High Risk

Calculation of atherogenic coefficient (AC)

The calculation of AC was done according to the following formula its risk categories are given in Table 1.

Atherogenic Coefficient (AC) = (TC– HDLc)/HDLc [11]

Where,
TC - Total cholesterol
HDLc - High-Density Lipoprotein Cholesterol

It should be noted that an accepted cut-off value for the atherogenic coefficient (AC) is yet to be developed.

Calculation of CVD risk by ASCVD Risk estimator

The parameters; age, sex, ethnicity, total cholesterol, HDL cholesterol, systolic blood pressure, presence or absence of diabetes, and smoking or non-smoking were inserted into the ASCVD Risk Estimator to obtain the data regarding CVD risk [16]. The ASCVD risk categories are given in Table 2.

Table 2: ASCVD risk categories [16]

ASCVD score (percentage)	ASCVD risk Category
0.0-4.9	Low Risk
5.0-7.4	Borderline Risk
7.5-20.0	Intermediate Risk
>20	High Risk

ASCVD - atherosclerotic cardiovascular disease

Data analysis

All the statistical analyses were done using the standard statistical software, SPSS version 20.0, IBM, Chicago, USA. Sociodemographic data and results of laboratory investigations were analyzed using descriptive statistics. The correlations between continuous variables were analyzed by Pearson's correlation coefficient and the analysis between multiple variables was done by cross-tabulations. The level of significance considered was $p<0.05$ on all associations.

Results

Sociodemographic data

A total of 153 participants were recruited for the study. The mean age of the study population was 59.31±9.62 years. The ratio between female to male participants was 2:1. More than 96% of participants were married, and the number of unemployed subjects (n=85) was greater than that of employed (n= 68).

Table 3: The risk factors associated with CVD in the study population (N=153)

Parameter		**Results**
BMI category, **n (%)**	Underweight and healthy weight Overweight and obesity	74 (48.3%) 79 (51.6%)
History of diabetes mellitus, **n (%)**	Absent Present	51(33.3%) 102(66.7%)
History of hypertension, **n (%)**	Absent Present	54(35.2%) 99(64.7%)
Alcohol consumption, **n (%)**	No (non-alcoholics) Yes (alcoholics)	140(91.5%) 13(8.5%)
Smoking, **Mean ± SD**	No (non-smokers) Yes (smokers)	150(98.0%) 03(2.0%)
Physical activity **n (%)**	Physicallynon-active Physically active	127(83.0%) 26(17.0%)
Fasting blood sugar **n (%)**	Normoglycemia Hyperglycemia	44 (28.9%) 108(71.1%)
Systolic blood pressure (Hgmm), **Mean ± SD**		147.20±26.32
Diastolic blood pressure (Hgmm), **Mean ± SD**		87.80±14.52
Total cholesterol (mg/ dL), **Mean ± SD**		183.768±40.95
HDL cholesterol (mg/ dL), **Mean ± SD**		50.348±14.08
Triglycerides (mg/ dL), **Mean ± SD**		128.737±48.18
LDL cholesterol (mg/ dL), **Mean ± SD**		106.959±35.90
Gender **n (%)**	Female	104 (68%)
	Male	49 (32%)

CVD- Cardiovascular Disease, BMI – Body mass index, HDL- High-Density Lipoprotein, LDL- Low-density Lipoprotein, AIP – Atherogenic index of plasma, AC- Atherogenic coefficient, ASCVD- atherosclerotic cardiovascular disease

Risk factors associated with CVD in the study population

The factors associated with the CVD risk of the participants are given in Table 3. The number of subjects was almost equal when considering both the underweight and healthy weight groups, and the overweight and obese groups. The patients with a history of diabetes were twice as many as those with no history of diabetes. The ratio between the study participants with a history of hypertension and without was 2:1. The number of non-alcoholic subjects was nearly ten times higher than those who were alcoholic. The study population consisted of almost 100% non-smokers. The hyperglycemic to normoglycemic ratio of patients in our study population was almost 3:1.

Lipid profile of the study population

The distribution of desirable, borderline high, and high total cholesterol levels was 75.2%, 14.4%, and 10.5%, respectively. The number of non-hypercholesteremic patients was almost seven times greater than that of hypercholesteremic patients. The distribution of HDL cholesterol for low, normal, and high levels in the study population was 26.1, 51.6, and 22.2% respectively. The participants with normal triglyceride levels were nine times greater than the hypertriglyceridemic patients. The number of study participants with normal LDL cholesterol levels was seven times greater than those with high LDL cholesterol levels.

Association between 10-year ASCVD risk and age

The correlation between 10-year ASCVD risk and the age of the subjects is depicted in Figure 1. Among the participants of age less than 40-60 years, only 3.3% were the high risk for ASCVD. In the study population above 60 years old, the number of patients under the high-risk category was almost 20 times greater than the low-risk category. There was a significant association, a strong positive correlation between ASCVD risk and age (r=0.760, p=0.001).

Association between 10-year ASCVD risk and employment status

Table 4 shows the distribution of ASCVD risk among the study population based on employment status. Among the unemployed study participants, the number for the high-risk category was the same as the low-risk category. Among the employed participants, the ratio between low and high ASCVD risk was 2:1. A significant association was observed between ASCVD risk and employment status (p=0.039).

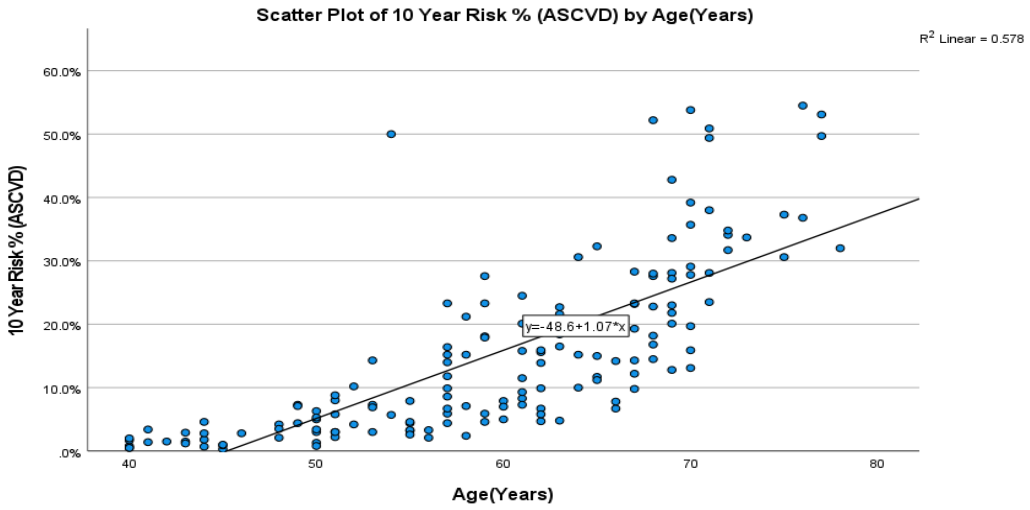

Figure 1: Correlation between 10-year ASCVD Risk and age of subjects

Table 4: Association, correlation and distribution of ASCVD risk categories *vs* risk factors

Risk Factor	p value	r value	Sub categories of the risk factor	The percentage from the total population in each ASCVD risk category			
				Low risk	Borderline risk	Intermediate risk	High risk
Employment status	0.039	-	Unemployed	12.50%	5.30%	17.10%	21.10%
			Employed	17.80%	5.90%	11.20%	9.20%
			Total	30.30%	11.20%	28.30%	30.30%
History of diabetes mellitus	0.02	-	History of Diabetes absent	15.10%	3.90%	8.60%	5.90%
			History of Diabetes present	15.10%	7.20%	19.70%	24.30%
			Total	30.30%	11.20%	28.30%	30.30%
Systolic blood pressure	<0.001	r=0.386	Low	13.07%	1.96%	4.57%	1.96%
			High	17.00%	9.15%	23.52%	28.10%
			Total	30.06%	11.11%	28.10%	30.06%

ASCVD- atherosclerotic cardiovascular disease

Association between 10-year ASCVD risk and the history of diabetes mellitus

Table 4 indicates the distribution of ASCVD risk among the study population with a history of diabetes mellitus. The number of study participants with a history of DM in the ASCVD high-risk category was almost three times greater than the borderline category. It was also noted that study participants between the above two groups were equally distributed in the low-risk category. ASCVD risk was significantly associated with the number of subjects with a history of diabetes mellitus (p=0.02).

Association between 10-year ASCVD risk and systolic blood pressure

Table 4 depicts the distribution of ASCVD risk among the study population based on systolic blood pressure. The ratio between study participants in the high and low ASCVD risk categories was 11:1. Ninety-six of the high-risk group had high systolic blood pressure. Furthermore, 10-year ASCVD risk showed a significant positive association with systolic blood pressure (p<0.001) and a moderate, positive correlation was observed between 10-year ASCVD risk and systolic blood pressure (Pearson's correlation r=0.386).

Ten-year ASCVD risk showed no significant association with other risk factors associated with CVD risk, such as gender (p=0.398), marital status (p=0.544), body mass index (BMI) (p=0.080), history of hypertension (p=0.060), smoking (p=0.195), alcohol consumption (p=0.780),

Table 5: Association, correlation and distribution of AIP Risk Categories based on different risk factors

Risk Factor	p value	r value	AIP Risk Category	Percentage from the total population in each risk factor		
				Low risk	Intermediate risk	High risk
HDL	p=0.001	r=-0.682	Low	0.00%	1.30%	24.83%
			Normal	0.00%	6.53%	45.09%
			High	7.18%	3.92%	11.11%
			Total	7.18%	11.76%	81.04%
Triglycerides	p=0.027	r=0.829	Optimal	7.18%	11.11%	53.59%
			Borderline	0.00%	0.65%	19.60%
			High	0.00%	0.00%	7.84%
			Total	7.18%	11.76%	81.04%

HDL- High-Density Lipoprotein, AIP – Atherogenic index of plasma

diastolic blood pressure (p=0.202), physical activity (p=0.560), total cholesterol (p=0.828), HDL cholesterol (p=0.336), triglycerides (p=0.721), LDL cholesterol (p=0.686), fasting blood sugar (p=0.348), AIP (p=0.880) and AC (p=0.576).

Association between AIP and HDL cholesterol

The distribution of AIP risk among the study population based on HDL cholesterol concentration is shown in Table 5. The highest percentage of study subjects under the high-risk category had normal HDL levels. This number was almost twice as higher than subjects with low HDL levels and four times greater than those with high HDL levels within the same category. A significant association between AIP and HDL cholesterol was observed (p=0.001), and a strong, negative correlation was found between AIP and HDL cholesterol (Pearson's correlation r=-0.682).

Association between AIP and triglycerides

The distribution of AIP risk among the study population based on triglyceride concentration is shown in Table 5. The majority of participants within the high-risk category had optimal triglyceride levels. This value was almost three and seven times greater than borderline and low triglyceride levels. A significant association and a strong positive correlation were observed between AIP and triglycerides (p=0.027, Pearson's correlation r=0.829).

AIP did not show any significant association with other risk factors associated with CVD such as age (p=0.118), gender (p=0.239), marital status (p=0.748), employment status (p=0.086), BMI (p=0.917), history of diabetes mellitus (p=0.101), history of hypertension (p=0.649), smoking (p=0.434), alcohol consumption (p=0.453), physical activity (p=0.448), fasting blood sugar (p=0.375), systolic blood pressure (p=0.782), diastolic blood pressure (p=0.870), total cholesterol (p=0.508), and LDL cholesterol (p=0.305).

Association between AC and total cholesterol

The distribution of AC risk categories among the study population based on total cholesterol concentration is given in Table 6. The ratio between high and low-risk AC categories within the desirable group was 1:3. The least percentage of participants were in the high total cholesterol group. A significant moderate, positive correlation was observed between AC and total cholesterol level (r=0.425, p<0.001).

Thirty-three participants had low AC values in the high HDL cholesterol category. A significant negative correlation was observed between AC and HDL cholesterol (r=-0.509, p<0.001).

Association between AC and triglycerides

The distribution of AC risk categories among the study population based on triglyceride concentration is shown in Table 6. The majority of the study population belonged to the optimal

Table 6: Association, correlation and distribution of AC Risk Categories based on different risk factors

Risk Factor	p value	r value	AC Risk Category	Percentage from the total population in each risk factor		
				Desirable	Borderline High risk	High risk
Total Cholesterol	p=0.000	r=0.425	Low	52.94%	5.88%	6.53%
			High	22.22%	8.49%	1.53%
			Total	75.16%	14.37%	10.45%
HDL cholesterol	p=0.000	r=-0.509	Low	6.53%	31.37%	21.65%
			High	19.60%	20.26%	0.65%
			Total	26.14%	51.63%	22.22%
Triglycerides	p=0.000	r=0.336	Low	49.01%	9.80%	0.65%
			High	22.87%	10.45%	0.65%
			Total	71.89%	20.26%	7.18%
LDL cholesterol	p=0.000	r=0.461	Low	54.90%	3.92%	0.65%
			High	22.22%	7.18%	11.11%
			Total	77.12%	11.11%	11.76%

HDL- High-Density Lipoprotein, LDL- Low-density Lipoprotein, AC- Atherogenic coefficient

Association between AC and HDL cholesterol

The distribution of AC risk categories among the study population based on HDL cholesterol concentration is given in Table 6. Most participants were within the normal HDL cholesterol category and had low AC values.

triglyceride category. Within the optimal category, the ratio between low and high AC risk was 2:1. A significant moderate, positive correlation was observed between AC and triglyceride levels (r=0.336, p=0.000).

Association between AC and LDL cholesterol

Table 6 indicates the distribution of AC risk categories among the study population based on LDL cholesterol concentration. The highest percentage of study subjects was within the optimal LDL cholesterol category. Within the optimal category, most participants had low AC values. A significant moderate, positive correlation was observed between AC and LDL cholesterol (r=0.461, p=0.000).

Association between AC and AIP

Figure 2 depicts the Correlation between AC and AIP of the study population. The highest risk for CVD was observed in 60 patients with high AIP and AC values. Meanwhile, 11 patients belonged to the low-risk category. A strong significant, positive correlation was shown between AC and AIP in the study population (Pearson's correlation r=0.732, p=0.001).

AC did not show any significant association with other risk factors associated with CVD, including age (p= 0.150), gender (p= 0.313), marital status (p= 0.183), employment status (p= 0.854), BMI (p= 0.418), history of diabetes mellitus (p= 0.130), history of hypertension (p= 0.925), smoking (p= 0.764), alcohol consumption (p= 0.396), physical activity (p= 0.505), fasting blood sugar (p= 0.951), systolic blood pressure (p= 0.481), diastolic blood pressure (p= 0.167), and 10-year ASCVD risk (p=0.576).

Discussion

CVD remains a leading cause of mortality in the world. Ranawaka *et al*. [17] reported that the estimated community prevalence of coronary heart disease in Sri Lanka is around 9.3%. CVD risk estimation in Sri Lanka is extremely important to plan preventive and effective treatment strategies. The present retrospective study evaluated CVD risk using a 10-year ASCVD risk estimator, AIP, and AC. At the same time, their correlation with traditional CVD risk factors was also evaluated.

Out of 153 participants in the present study, 51.3% were overweight or obese, while 48.7% were underweight or healthy. Though obesity is considered one of the main factors contributing to the risk of CVD, we did not find any significant association between BMI and 10-year ASCVD risk. The absence of the above association could be because obesity is mediated through other CVD

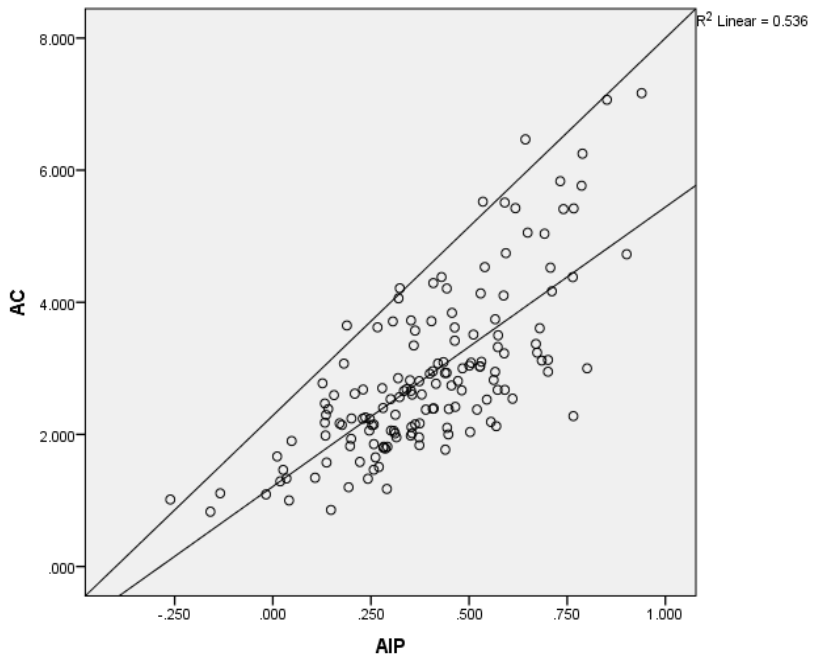

Figure 2: Correlation between 10-year ASCVD Risk and age of subjects

risk factors, including hypertension, diabetes, and hypercholesterolemia which are components of the risk score. Moreover, the study conducted by Tulloch-Reid *et al*. [18] depicted similar findings.

Hypertension contributes to the elevation of CVD risk, 65.1% had a history of hypertension, and 34.9% did not. The participants' mean systolic and diastolic blood pressures were 147±20 mmHg and 87.80±14.52 mmHg, respectively. We further observed a moderate positive correlation between 10-year ASCVD risk and systolic blood pressure. Moreover, Wheltonn *et al.* [19] had similar observations, and it had been mentioned that, among individuals without traditional ASCVD risk factors, there was a gradual increase in both coronary artery calcium and ASCVD incidence with increasing systolic blood pressure levels.

The alcoholic or non–alcoholic status as well as smoking status were collected from clinical records of the patient. However, due to the nature of our study, we were unable to arrive at clear conclusions on particulars such as defining an individual as an alcoholic or a smoker. The prevalence of alcohol consumption and smoking among our study participants was very low. Non-alcoholic and non-smokers in our study population were 140(91.5%) and 150(98.0%), respectively. The nature of our study population explains the biases in favour of non-smokers and non-alcoholics in this study owing to the fact that majority of the participants were females, who are much less likely to smoke compared to males in our country.

Diabetes mellitus has been recognized as an important risk factor associated with CVD. Among the participants, only 66.7% had a clinical history of diabetes, and there were 71.1% hyperglycaemic, and 28.9% normoglycaemic participants. There was a significant association between having a history of diabetes mellitus and 10-year ASCVD risk. The study done by Faradonbeh *et al.* [20] observed that the mean ASCVD risk score is significantly high in patients with diabetes mellitus.

However, we found that elevated systolic blood pressure, hyperglycemia, and diabetes mellitus were the predominant CVD risk factors in our study population, with a prevalence of 77.7, 71.1, and 66.7%, respectively. This observation was supported by Esteghamati *et al*. [21]. According to that, diabetes and hypertension were the leading risk factors, which either directly or indirectly interferes with more serious complications of coronary heart disease. A study done by Gerstein *et al*. [22] suggested that an increase in systolic blood pressure is associated with increased cardiovascular events, where each 10 mmHg increase in systolic blood pressure increases the risk of myocardial infarction by 11%.

The present study found a strong, positive correlation between age and ASCVD risk. Compared to the age group less than 60 years old, the participants above 60 years were at a higher risk for CVD. Our finding was supported by the studies by Faradonbeh *et al*. [20] and Ejim *et al*. [23].

Employment status showed a statistically significant association with ASCVD 10-year risk in the study population. The unemployed individuals were at a higher risk compared to employed individuals. Similar findings were observed by Ko *et al*. [24]. According to Carson *et al*. [25] and Commodore-Mensah *et al.* [26], employed women had a lower CVD and stroke risk than housewives. However, the contradicting result observed by Sánchez-Chaparro *et al*. [27] reveals that the prevalence of cardiovascular risk factors in the working population is higher, predominantly among males. Interestingly, Steptoe *et al*. [28] reported that long-term stress, including social isolation and chronic work-related stress, is associated with a 40–50% increase in the occurrence of CHD.

Our findings did not show a significant association between gender and 10-year ASCVD risk. A study by Tulloch-Reid *et al*. [18] too showed similar observations. In comparing the calculated mean ASCVD 10-year risk for males and females in our

study, males showed a trend of higher risk than females, though it was not statistically significant. A possible reason for this outcome would be the higher prevalence of certain risk factors, such as smoking and alcohol consumption in males. The study conducted by Commodore-Mensah *et al*. [26] found that the 10-year CVD risk of men was higher than that of females.

Further, Borhanuddin *et al*. [29] showed similar findings where males had a higher 10-year CVD risk overall than females. The authors suggested that these observations are due to the higher prevalence of smokers, elevated systolic blood pressure, lower HDL level, and higher diabetes comorbidity in the male participants in the study [28]. Contradicting the above findings, Gheisari *et al*. [30] and Dosi *et al*. [31] observed that although the incidence of CVD was comparatively lower in premenopausal women than in men of the same age, its incidence had increased drastically in women older than 50 years. This dramatic increase is attributed to the lack of estrogen and its indirect cardio-protective benefits. This biological defense caused more than ten years of delay in presenting coronary artery disease in females compared to males. The study by Yamamoto *et al*. [32] showed that the prevalence of coronary artery disease increased in women with age. Another study reported that unique sex-specific risk factors are associated with women. One possible explanation is increased long-term CVD risk due to hypertensive disorders in pregnancy [32]. Moreover, Ko *et al*. [24] also showed that women have a higher CVD risk than men due to psychological stress during peri- and post-menopause, which seems to increase with age.

Investigations on lipid profiles are an integral component of CVD risk assessment. According to the findings of the present study, the total cholesterol, HDL cholesterol, LDL cholesterol, and triglyceride levels were within the normal ranges, and none showed associations with 10-year ASCVD risk. However, significant associations were observed with AIP and AC with lipid parameters. The study by Assmann and Schulte [33] reported that the combination of deranged lipid profile variables indicates a higher magnitude of risk than elevated LDL cholesterol alone. Hokanson [34] states that triglycerides are an independent CVD risk factor.

On the contrary, Orakzai *et al*. [5] reported that triglycerides are a risk factor associated with low HDL levels. Bhardwaj *et al*. [35] and Azeez [36] reported that using absolute lipid parameters is unsatisfactory when predicting CVD risk and further mentioned that utilization of lipid indices could help evade this. According to the studies done by Nwagha *et al*. [37] and Luz *et al*. [38], AIP was a diagnostic alternative for coronary disease where plasma triglyceride levels are normal, and individual lipid variables seem less useful. Since we obtained similar findings in our study, using traditional lipid profile parameters alone in CVD risk prediction is less reliable than their logarithmic ratios. The presence of lipid variables within the normal ranges could be misleading in CVD risk assessment because the CVD risk would not be evident under such instances, especially when the traditional CVD risk factors are absent.

AIP is suggested to assess CVD risk due to its high correlation with traditional CVD factors and certain CVD risk estimators. Our study showed that there was a significant positive correlation between AIP and serum triglycerides and a significant negative correlation between AIP and serum HDL cholesterol levels. Meanwhile, serum triglycerides and serum HDL cholesterol levels are not deranged within our study population, we expected that AIP value to be within the normal range, but the AIP value we obtained was above 0.24 (0.38 for females and 0.41 for males), indicating high CVD risk. Our findings suggest that even in lipid parameters within normal ranges, the actual CVD risk might be masked, and AIP could be used as a strong CVD diagnostic alternative. Similar findings were reflected in the studies conducted by Wu *et al*. [39] and Bo *et al*. [40]. In addition to serum triglycerides and serum

HDL cholesterol, their studies showed significant associations and correlations between AIP and other lipid parameters. AIP is independent of smoking habits, history of diabetes mellitus, and hypertension and was proposed as a better marker for increased CAD risk in contrast to total cholesterol, LDL cholesterol, and HDL cholesterol. On the contrary, Wu *et al*. [39] reported that AIP is a mathematical derivative of HDL cholesterol and triglycerides, which is directly linked with the risk of CVD mortality. This was assumed to explain the strong association between AIP and the 10-year CVD risk they found in their study population.

AIP did not show a statistically significant correlation with 10-year ASCVD risk in our study. Several possibilities for this outcome included a smaller population and a patient population solely based on a hospital setting. Using a larger population size and random samples could be solutions. Findings similar to our study were reported in the study conducted by Nansseu *et al.* [41] based on a Cameroonian population of postmenopausal women where they did not find a significant relationship between AIP and risk of CVD, which was assessed via the Framingham risk score. The reasons for their observation were the limited sample size, using a population from a hospital setting which may have overestimated their CVD risk, and using the Framingham risk score in risk estimation. Findings of the case-cohort study done by Rabizadeh *et al*. [42] using type 2 diabetes mellitus patients also showed that AIP did not predict the CHD risk, independent of the ASCVD risk score. Noumegni *et al*. [43], conducted a study on the HIV-infected black African population and found a significant association between AIP and the 10-year CVD risk. It has been mentioned that this association is due to AIP being significantly associated with certain CVD risk factors.

AC reflects the atherogenicity of entire lipoprotein fractions. The findings of our study showed a positive correlation between AC and total cholesterol, serum LDL cholesterol, and serum triglycerides, and a significant negative correlation with serum HDL cholesterol. These findings were evident since AC is the logarithmic ratio between non-HDL and HDL cholesterol. AC uses non-HDL cholesterol, a lipid parameter demonstrated to be a superior predictor of atherosclerosis compared to other conventional lipid values, as reported by Orakzai *et al.* [5]. The same study reported an association between AC and 10-year CVD risk score, but we did not observe any significant correlation between AC and 10-year ASCVD risk. The mean AC value calculated for males and females in our study were 2.94±1.24 and 2.85 ±1.25, respectively. However, since an accepted cut-off value has not yet been defined for AC, we could not interpret this finding. Meanwhile, several other studies had reported mean values as 3.25±1.36 (Brazil), 2.04±0.65 (India), 2.76±0.10 and 1.18±0.19 (Nigeria), 2.49±2.04, 3.4±0.91 and 1.27±1.54 (Turkey) [43]. In addition to that, the study carried out on fasting lipid profile and atherogenic indices in women diagnosed with pre-eclampsia and in women with normal pregnancy reported that the mean value of AC in the case group (4.614±0.6782) was higher than the control group (3.7908±0.7824). It was found to be statistically significant ($p<0.001$) [44].

Hermans *et al*. [45] and Nimmanapalli *et al.* [46] observed that non-HDL cholesterol is similar to Apo-B in assessing atherogenic cholesterol and lipoprotein burden. Non-HDL cholesterol is highly correlated with apolipoprotein B levels which is highly atherogenic and reflects lipoprotein burden. Moreover, Apo-B assessment is not always available in routine clinical settings. Therefore, AC could prove value in identifying increasing CVD risk and act as a potential biometrical equivalent to Apo-B.

Our study found a positive significant correlation between AIP and AC even though neither showed any correlation with the 10-year ASCVD risk. Since both AIP and AC are solely calculated using lipid profile variables alone, they have not shown a correlation to the multivariable-based 10-year

ASCVD risk estimate. The reason could be hypothesized as the effects of lipid profile variables being mediated by other CVD risk factors included in the 10-year risk estimator, hence leading to the absence of its correlation with either AIP or AC. On the other hand, it further suggests the possible neglect of CVD risk alone because the lipid profile variables are within the normal range. Abid *et al*. [44] reported that in instances such as intermediate risk when there are one or more risk factors such as elevated plasma lipids, high plasma glucose levels, hypertension, and overweight that surpass desirable levels or a positive family history, lipid profile variables and are less effective in predicting CVD risk. This has led to the development of novel biomarkers and more accurate indices. This research was conducted as a hospital-based rather than a community-based study, which could be identified as a limitation of this study.

Conclusion

The study did not show any significant correlation between AIP and 10-year ASCVD risk and AC and 10-year ASCVD risk. However, it was clear that CVD risk increased with age and systolic blood pressure. We also found that an increase in 10-year ASCVD risk, AIP, and AC was associated with several CVD risk factors, thereby any change in these risk factors affects the 10-year ASCVD risk, AIP, and AC accordingly. Furthermore, AIP and AC were more potent in CVD risk estimation than the traditional lipid parameters. This was evident by the correlation between AIP and AC and their correlation with several CVD risk factors, even though the lipid parameters within our study population were not deranged. Hence, the obvious CVD risk could be masked or underestimated, especially when the lipid parameters are not deranged and, in the presence, or absence of other traditional risk factors. Therefore, these indices proved more beneficial and appropriate in CVD risk assessment, which must be incorporated into routine clinical investigations.

References

1. World Health Organization (2021) Cardiovascular Diseases (CVDs). Available at: https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds) / (Accessed 20 August 2021).
2. Laslett, L.J., Alagona, P., Clark, B.A., Drozda, J.P., Saldivar, F., Wilson, S.R., Poe, C. and Hart, M. The worldwide environment of cardiovascular disease: prevalence, diagnosis, therapy, and policy issues: a report from the American College of Cardiology. *Journal of the American College of Cardiology*. 2012;60(25):1-49.
3. Mensah, G.A., Roth, G.A. and Fuster, V. The global burden of cardiovascular diseases and risk factors: 2020 and beyond. *Journal of the American College of Cardiology*. 2019; 74(20):2529-2532.
4. Mora, S., Otvos, J.D., Rifai, N., Rosenson, R.S., Buring, JE and Ridker, P.M. Lipoprotein particle profiles by nuclear magnetic resonance compared with standard lipids and apolipoproteins in predicting incident cardiovascular disease in women. *Circulation*.2009; 119(7): 931-939.
5. Orakzai, S.H., Nasir, K., Blaha, M., Blumenthal, R.S. and Raggi, P. Non-HDL cholesterol is strongly associated with coronary artery calcification in asymptomatic individuals. *Atherosclerosis*, 2009;202(1):289-295.
6. Hermans, M.P., Sacks, FM, Ahn, SA and Rousseau, M.F., Non-HDL-cholesterol as valid surrogate to apolipoprotein B100 measurement in diabetes: Discriminant Ratio and unbiased equivalence. *Cardiovascular Diabetology*. 2011:10(1):1-7.
7. Dobiasova, M. AIP-atherogenic index of plasma as a significant predictor of cardiovascular risk: from research to practice. *Vnitrnilekarstvi*.2006;52(1):64-71.
8. Niroumand, S., Khajedaluee, M., Khadem-Rezaiyan, M., Abrishami, M., Juya, M.,

Khodaee, G. and Dadgarmoghaddam, M. Atherogenic index of plasma (AIP): A marker of cardiovascular disease. *Medical Journal of the Islamic Republic of Iran*. 2015;29:240.

9. Nimmanapalli, H.D., Kasi, A.D., Devapatla, P. and Nuttakki, V. Lipid ratios, atherogenic coefficient and atherogenic index of plasma as parameters in assessing cardiovascular risk in type 2 diabetes mellitus. *International Journal of Research in Medical Sciences*. 2016: 4(7):2863-2869.
10. Kamoru, A.A., Japhet, O.M., Adetunji, A.D., Musa, M.A., Hammed, O.O., Akinlawon, A.A., Abdufatah, O.A., Taofik, A.A., Kabiru, A.A. and Roji, S.M. Castelli risk index, atherogenic index of plasma, and atherogenic coefficient: emerging risk predictors of cardiovascular disease in HIV-treated patients. *Saudi Journal of Medical and Pharmaceutical Sciences*. 2017:1101-1110.
11. Pokharel, Y., Steinberg, L., Chan, W., Akeroyd, J.M., Jones, P.H., Nambi, V., Nasir, K., Petersen, L., Ballantyne, C.M. and Virani, S.S. Case-based educational intervention to assess change in providers' knowledge and attitudes towards the 2013 American College of Cardiology/American Heart Association Cholesterol Management Guideline. *Atherosclerosis*. 2016;246:115-120.
12. Robinson, S. Development and evaluation of a nurse practitioner-directed cardiovascular risk screening protocol for primary prevention in an outpatient cardiovascular practice. 2020. Wilmington University. Delaware.
13. Khambhati, J., Allard-Ratick, M., Dhindsa, D., Lee, S., Chen, J., Sandesara, P.B., O'Neal, W., Quyyumi, A.A., Wong, N.D., Blumenthal, R.S. and Sperling, L.S. The art of cardiovascular risk assessment. *Clinical cardiology*. 2018;41(5):677-684.
14. Pourhoseingholi, M.A., Vahedi, M., Rahimzadeh, M. Sample size calculation in medical studies. *Gastroenterol Hepatol Bed Bench.* 2013: 6(1):14-17).
15. Friedewald, W.T., Levy, R.I., and Frederickson, D.S. 1972. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clinical Chemistry 18: 499-502.
16. Clinical Calculator (2023) ASCVD Risk Calculator. Available at:https://clincalc.com/Cardiology/ASCVD/PooledCohort.aspx?example / (Accessed 25 August 2021).
17. Ranawaka, U.K., Wijekoon, C.N., Pathmeswaran, A., Kasturiratne, A., Gunasekara, D., Chackrewarthy, S., Kato, N. and Wickremasinghe, A.R., 2016. Risk estimates of cardiovascular diseases in a Sri Lankan community.*Ceylon Medical Journal*.2016; 61: 11-17.
18. Tulloch-Reid, M.K., Younger, N.O., Ferguson, T.S., Francis, D.K., Abdulkadri, A.O., Gordon-Strachan, G.M., McFarlane, S.R., Cunningham-Myrie, C.A., Wilks, R.J. and Anderson, S.G. Excess cardiovascular risk burden in Jamaican women does not influence predicted 10-year CVD risk profiles of Jamaica adults: an analysis of the 2007/08 Jamaica health and lifestyle survey. *PloSOne*. 2013;8(6).
19. Whelton, S.P., McEvoy, J.W., Shaw,L., Psaty, B.M., Lima,J.A.C., Budoff, M., Nasir, K., Szklo,M., Blumenthal, R.S., Blaha, M.J.Association of normal systolic blood pressure level with cardiovascular disease in the absence of risk factors. *JAMA Cardiology*. 2020;5(9):1011-1018.
20. Faradonbeh, N.A., Nikaeen, F., Akbari, M., Almasi, N. and Vakhshoori, M. Cardiovascular disease risk prediction among Iranian patients with diabetes mellitus in Isfahan Province, Iran, in 2014, by using Framingham risk score, atherosclerotic cardiovascular disease risk score, and high-sensitive C-reactive protein. *ARYA atherosclerosis*, 2018;14(4):163-168.
21. Esteghamati, A., Abbasi, M., Nakhjavani, M., Yousefizadeh, A., Basa, A.P. and Afshar, H.

Prevalence of diabetes and other cardiovascular risk factors in an Iranian population with acute coronary syndrome. *Cardiovascular Diabetology*, 2006;5(1):1-6.

22. Gerstein HC, Malmberg K, Capes S, Yusuf S: Cardiovascular disease. Evidence-based diabetes care. Edited by: Gerstein HC, Haynes RB. 2001, London. BC Decker Inc, Hamilton, 498-500.
23. Ejim, E.C., Okafor, C.I., Emehel, A., Mbah, A.U., Onyia, U., Egwuonwu, T., Akabueze, J. and Onwubere, B.J. Prevalence of cardiovascular risk factors in the middle-aged and elderly population of a Nigerian rural community. *Journal of tropical medicine*. 2011;2011:DOI:10.1155/2011/308687.
24. Ko, H.Y., Lee, J.K., Shin, J.Y. and Jo, E. Health-related quality of life and cardiovascular disease risk in Korean adults. *Korean journal of family medicine*, 2015;36(6):349-356.
25. Carson, A.P., Rose, K.M., Catellier, D.J., Diez-Roux, A.V., Muntaner, C. and Wyatt, S.B. Employment status, coronary heart disease, and stroke among women. *Annals of epidemiology*. 2009;19(9):630-636.
26. Commodore-Mensah, Y., Hill, M., Allen, J., Cooper, L.A., Blumenthal, R., Agyemang, C. and Himmelfarb, C.D. Sex differences in cardiovascular disease risk of Ghanaian-and Nigerian-born west African immigrants in the United States: the Afro-Cardiac study. *Journal of the American Heart Association*, 2016;5(2): p.e002385.
27. Sánchez-Chaparro, M.A., Román-García, J., Calvo-Bonacho, E., Gómez-Larios, T., Fernández-Meseguer, A., Sáinz-Gutiérrez, J.C., Cabrera-Sierra, M., García-García, Á., Rueda-Vicente, J., Gálvez-Moraleda, A. and González-Quintela, A. Prevalence of cardiovascular risk factors in the Spanish working population. *Revista Española de Cardiología*.59(5);2006:421-430.
28. Steptoe, A., Feldman, P.J., Kunz, S., Owen, N., Willemsen, G. and Marmot, M. Stress responsivity and socioeconomic status. A mechanism for increased cardiovascular disease risk?. *European heart journal*, 2002;23(22):1757-1763.
29. Borhanuddin, B., MohdNawi, A., Shah, S.A., Abdullah, N., Syed Zakaria, S.Z., Kamaruddin, M.A., Velu, C.S., Ismail, N., Abdullah, M.S., Ahmad Kamat, S. and Awang, A. 10-Year cardiovascular disease risk estimation based on lipid profile-based and BMI-based framingham risk scores across multiple sociodemographic characteristics: the Malaysian cohort project. *The Scientific World Journal*. 2018.DOI:10.1155/2018/2979206.
30. Gheisari, F., Emami, M., RaeisiShahraki, H., Samipour, S. and Nematollahi, P.Therole of gender in the importance of risk factors for coronary artery disease. *Cardiology Research and Practice*, 2020.DOI:10.1155/2020/6527820.
31. Dosi, R., Bhatt, N., Shah, P. and Patell, R. Cardiovascular disease and menopause. *Journal of Clinical and Diagnostic Research*.2014;8(2):62-64.
32. Yamamoto, A., Horibe, H., Mabuchi, H., Kita, T., Matsuzawa, Y., Saito, Y., Nakaya, N., Fujioka, T., Tenba, H., Kawaguchi, A. and Nakamura, H. Analysis of serum lipid levels in Japanese men and women according to body mass index. Increase in risk of atherosclerosis in postmenopausal women. *Atherosclerosis*. 1999;143(1):55-73.
33. Assmann, G. and Schulte, H. Relation of high-density lipoprotein cholesterol and triglycerides to incidence of atherosclerotic coronary artery disease. *The American journal of cardiology*, 1992;70(7):733-737.
34. Hokanson, J.E. Hypertriglyceridemia as a cardiovascular risk factor. *The American Journal of Cardiology*, 1998; 81(4), pp.7B-12B.
35. Bhardwaj, S., Bhattacharjee, J., Bhatnagar, M.K., Tyagi, S. and Delhi, N. Atherogenic

index of plasma, castelli risk index and atherogenic coefficient-new parameters in assessing cardiovascular risk. *International Journal of Pharmacy and Biological Science*. 2013;3(3):359-364.

36. Azeez, TA Association between lipid indices and 10-year cardiovascular risk of a cohort of black Africans living with type 2 diabetes mellitus. *Journal of Advances in Internal Medicine*, 2021;10(1):38-42.
37. Nwagha, U.I., Ikekpeazu, E.J., Ejezie, F.E., Neboh, E.E. and Maduka, I. Atherogenic index of plasma as useful predictor of cardiovascular risk among postmenopausal women in Enugu, Nigeria. *African Health Sciences*, 2010;10(3):248-252.
38. Luz, P.L.D., Favarato, D., Faria-Neto Junior, J.R., Lemos, P. and Chagas, ACP High ratio of triglycerides to HDL-cholesterol predicts extensive coronary disease. *Clinics*. 2008; 63:427-432.
39. Wu, T.T., Gao, Y., Zheng, Y.Y., Ma, YT and Xie, X. Atherogenic index of plasma (AIP): a novel predictive indicator for the coronary artery disease in postmenopausal women. *Lipids in health and disease*. 2018;17(1):1-7.
40. Bo, M.S., Cheah, W.L., Lwin, S., Moe Nwe, T., Win, T.T. and Aung, M. Understanding the relationship between atherogenic index of plasma and cardiovascular disease risk factors among staff of an University in Malaysia. *Journal of Nutrition and Metabolism*, 2018. DOI:10.1155/2018/7027624.
41. Nansseu, J.R.N., Moor, V.J.A., Murielle Elsa D. Nouaga, M.E.D., Zing-Awona, B., Tchanana, G., Ketcha, A. Atherogenic index of plasma and risk of cardiovascular disease among Cameroonian postmenopausal women.*Lipids in Health and Disease*. 2016; 15: 49.
42. Rabizadeh, S., Rajab, A., Mechanick, J.I., Moosaie, F., Rahimi, Y., Nakhjavani, M. and Esteghamati, A. LDL/apo B ratio predict coronary heart disease in Type 2 diabetes independent of ASCVD risk score: A case-cohort study. *Nutrition, Metabolism and Cardiovascular Diseases*. 2021;31(5):1477-1485.
43. Noumegni, S.R., Nansseu, J.R., Bigna, J.J., Ama Moor, V.J., KembeAssah, F., Dehayem, M.Y., Kengne, A.P. and Sobngwi, E. Atherogenic index of plasma and 10-year risk of cardiovascular disease in adult Africans living with HIV infection: A cross-sectional study from Yaoundé, Cameroon. *Journal of the Royal Society of Medicine* Cardiovascular Disease.2017; 6:1-7.
44. Abid, H., Abid, Z. and Abid, S. Atherogenic indices in clinical practice and biomedical research: A short review: Atherogenic indices and cardiovascular diseases. *Baghdad Journal of Biochemistry and Applied Biological Sciences*. 2021:*2*(02):59-69.
45. Hermans, M.P., Sacks, FM, Ahn, SA and Rousseau, M.F., Non-HDL-cholesterol as valid surrogate to apolipoprotein B100 measurement in diabetes: Discriminant Ratio and unbiased equivalence. *Cardiovascular Diabetology*. 2011:10(1):1-7.
46. Nimmanapalli, H.D., Kasi, A.D., Devapatla, P. and Nuttakki, V. Lipid ratios, atherogenic coefficient and atherogenic index of plasma as parameters in assessing cardiovascular risk in type 2 diabetes mellitus. *International Journal of Research in Medical Sciences*. 2016: 4(7):2863-2869.