Atherogenic Index of Plasma and its Relationship with Cardiovascular Risk Factors Among Adult Patients Attending a Primary Care Clinic in South West Nigeria

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ABSTRACT

Background: Cardiovascular diseases have remained major causes of death globally. Early identification of individuals at risk of cardiovascular disease and appropriate intervention is needed in order to reduce the disease burden. The Atherogenic index of plasma (AIP) defined as logarithm of triglyceride (TG) and high-density lipoprotein cholesterol (HDL-C) is emerging as a strong marker in predicting the risk of cardiovascular disease. This study assessed the relationship between AIP and cardiovascular risk factors among adults attending a primary care clinic in South West Nigeria.

Methods: It was a descriptive cross-sectional hospital-based study among 286 respondents who were recruited by systematic random sampling over a period of three month. Venous blood samples were collected for lipid profiles and plasma glucose estimations, respondents blood pressure, anthropometric parameters and AIP were also measured. Data was analyzed using descriptive and inferential statistics.

Results: The age of the respondents ranged between 19 to 85 years with a mean age of 48.6 ± 15.8 years. Male to female ratio was 1:1.5. According to the AIP category: 68.5%, 12.4% and 19.1% respectively had low, moderate and high-risk AIP for cardiovascular disease. AIP was significantly associated with hypertension, diabetes-mellitus, smoking, alcohol intake, obesity and dyslipidaemia. Diabetes mellitus, Low-density Lipoprotein cholesterol, waist circumference and smoking emerged as independent predictors of higher risk AIP. (OR= 4.28, CI: 1.56 – 11.73; P< 0.05).

Conclusion: The study demonstrated a significant relationship between high-risk AIP and several cardiovascular risk factors. The use of AIP in stratifying cardiovascular risk is recommended.

Keywords: Atherogenic Index of Plasma (AIP), Cardiovascular risk factors, Primary care clinic, Nigeria.

INTRODUCTION

The burden of cardiovascular disease is enormous and at present escalating as an important component of non-communicable disease burden worldwide. It is a global health problem and the majority of those affected are in developing countries.[1] Cardiovascular diseases (CVDs) have been established as the leading cause of death globally and remain a major cause of morbidity and mortality including sudden death in most nations of the world.[2] A World Health Organisation (WHO) Global Status Report on non-communicable diseases (NCDs) estimated that CVD remains the leading cause of NCD deaths globally and the annual mortality has been projected to increase from 17.5 million deaths in 2012 to 22.2million deaths by 2030.[3] Sub-Saharan African countries are also currently experiencing a rapid increase in the incidence of cardiovascular diseases.[4] In Nigeria, CVDs are the fourth among the top 20 diseases responsible for mortality,[5] and have become a major public health problem, characterized by high rates of disability, case fatality and preventable deaths.[6] Recent studies in Nigeria have demonstrated an increase in the prevalence of CVDs in most parts of Nigeria.[6-8]

Major modifiable risk factors attributed to developing CVDsinclude hypertension, diabetes mellitus, obesity, low fruit and vegetable intake, high fat and salt intake, smoking, excessive alcohol intake, physical inactivity and dyslipidaemia.[9,10]

The atherogenic index of plasma (AIP) is an emerging index that fulfils the criteria to be used as a stand-alone index for cardiac risk stratification.[11] The AIP is a mathematical logarithm(log) relationship between total triglycerides (TG) and high-density lipoprotein cholesterol (HDL-C) expressed as log TG/HDL-C and has been successfully used as an additional index when assessing cardiovascular risk.[12]

Studies have shown that AIP can be used to identify hypertensive, dyslipidaemia and insulin-resistant patients who are likely to be at greatest risk for cardiovascular disease.[13,14] AIP has been noted to reflect the zones of atherogenic indices and is a useful indicator for assessing response to pharmacologic treatment of dyslipidaemia.[15] In determining CVD risk, the AIP is 40% more informative at predicting mortality, and more than twice as informative than the total cholesterol level.[16]

As part of strategies towards mitigating the burden of CVDs through screening and secondary prevention, studies have shown that AIP can be used as a rapid screening measure of cardiovascular risk. However, there is a paucity of data, especially in this part of the world, regarding the use of AIP and its relationship with cardiovascular risk factors. The primary care outpatient setting presents a veritable opportunity for early screening and assessment of cardiovascular risk profiles and the initiation of appropriate interventions.

This study aimed to assess cardiovascular disease risk using AIP among adult out-patient attendees of a primary care clinic and determine its relationship with specific cardiovascular risk factors.

METHODS

Study setting and subjects

This hospital-based descriptive cross-sectional study was carried out in the Family Medicine Out-patient Clinic, Obafemi Awolowo University Teaching Hospital Complex (OAUTHC), Ile-Ife, Osun state, South-west Nigeria. Nigeria is located in West Africa and is divided into six geopolitical zones namely: South-south, South-east, South-west, North-east, North-central and North-west. Nigeria has three main ethnic groups namely: Hausa, Igbo and Yoruba. Osun State is a city located in southwest, Nigeria and its people are mainly of Yoruba ethnic groups Ile-Ife is a semi-urban town within Osun State. The OAUTHC is a tertiary hospital that provides primary, secondary and tertiary care to all people within its environs and neighbouring states. The Family Medicine Out-patient Clinic is a primary care clinic within the OAUTHC, Ile-Ife and provides care for people aged 16 years and above. An average of 100 adult patients are seen daily in the Family Medicine Outpatient Clinic from Mondays to Fridays.

The study population comprised adult patients who attended the clinic during the three months of the study. All consenting eligible individuals, who were 18 years and above and could communicate in English or Yoruba (the predominant local language) were included in the study. The following were however excluded: acutely ill patients who required emergency treatment or admission, patients with severe cognitive impairments who may not follow instructions appropriately, those who were unable to assume appropriate positions for anthropometric assessment and patients on lipid-lowering agents.

Sample Size Determination

The sample size of 286 was based on the following parameters and assumptions; 95% confidence level, 5% margin of error, a prevalence of elevated TG of 23% from a previous study,[17] adjustments for a source population below 10,000 and a potential 10% non-response. A systematic random sampling method was used to select the respondents. Based on the clinic records, the average number of adult patients seen over three months was 6000. Thus, a sampling interval K = 20 was used (i.e. 6000 / 286 20). Clients who were not eligible were substituted by the very next eligible and consenting respondent. This process was continued daily until the sample size was completed. The respondents had their hospital record cards tagged to prevent re-enrolment during the subsequent visit(s).

Ethical approval and considerations: Ethical approval, (ERC/2017/05/07) was obtained from the Ethics and Research Committee of OAUTHC. Each of the selected respondent had the details of the study explained to them, their questions were clarified and they were assured of strict confidentiality. Their right to opt out from the study at any point in time without any prejudice or penalty was also affirmed. An informed, written consent was thereafter obtained.

Instruments and Data collection

Data collection was done using a pretested semi-structured interviewer-administered questionnaire adopted from the World Health Organization STEP-wise approach.[18] It was translated into Yoruba language and back translation into English left the version unchanged. The questionnaire was pretested in a similar study population with adjustments made.

Measurement of blood pressure: Each respondent's blood pressure (BP) was measured with an Accosson(R) Mercury Sphygmomanometer with the appropriate cuff within the same time frame each day. The blood pressure reading was taken in a sitting position after the respondents had rested for about five minutes, two readings were taken five minutes apart, and the average of the two readings was recorded as the final BP measurement. A respondent was classified as hypertensive based on a history of hypertension or current treatment with antihypertensive drugs or systolic blood pressure (SBP) ≥ 140mmHg and/or diastolic blood pressure (DBP) ≥ 90mmHg.[19]

Anthropometric measurements: A ZT-160 height and weight scale was used to measure the height (in centimetres) and weight (in kilogrammes) of each respondent. The stadiometer calibrated in centimetres was used to measure the height of each respondent to the nearest 0.1cm, while the weighing scale calibrated in kilograms was used to measure the weight of each respondent to the nearest 0.1kg. Each respondent had their weight and height measured and recorded. The weight was measured with the respondents in light clothing to the nearest 0.1kg with all accessories such as shoes, coats, cardigans, headgear, caps, purses, cell phones, keys and pocket diaries removed before weighing. The height was measured with the respondents standing erect against the scale, without shoes or hats and looking straight ahead to the nearest 0.1 centimetres at a horizontal level. The body mass index (BMI) – defined as the weight in kilogram divided by the square of the height in meters (kg/m^2) was calculated from the measured weight and height. BMI was categorised into normal (18.5 -24.9 kg/m^2), overweight (25.0 – 29.9 kg/m^2) and Obesity (≥ 30kg/m^2).[20]

The waist circumference (WC) and hip circumference (HC) were measured using a flexible, non-stretchable measuring tape. Each respondent was made to stand upright with their abdominal muscles relaxed, the tape was placed mid-way between the lower border of the last palpable rib and the iliac crest and wrapped around the waistline starting from 0cm, (the tape was not too tight and not too loose). The WC was classified as normal if < 88cm in women and < 102cm in men and as abnormal (abdominal obesity) if ≥88cm and ≥102cm in women and men respectively. The hip circumference was taken at the widest diameter of the hip (buttock). The Waist-Hip Ratio (WHR) was then calculated. WHR value of > 0.9 in men and > 0.85 in women was classified as abnormal.[21]

Classification of lifestyle variables

Smoking: Cigarette smoking was assessed as never smoked and ever smoked.

Alcohol: Was categorised into never drank alcohol and currently drinking alcohol (within the previous six months). "Currently drinking" was referred to as those who drank a unit or more of alcohol daily or occasionally in one sitting. A unit of alcohol is equivalent to 10g of alcohol or one standard drink.

Physical activity: Was categorised as active or inactive. Respondents engaged in at least 30 minutes of daily moderate-intensity activity (brisk walking, gardening, dancing, sports activities etc.) for at least five days a week were categorised as "physically active" while respondents with levels of activities below this were categorised as "physically inactive".[18]

Low intake of fruits and vegetables was defined as the consumption of less than "five servings" of fruits and vegetables per day. The recommended servings of fruits and vegetables are a minimum of "five servings" per day. A serving of fruits is equivalent to a tennis ball or one hand, while a serving of vegetables is equivalent to a fist or cupped hand.[18]

Procedure for Sample Collection: About 5mls of venous samples were obtained from the antecubital vein for fasting plasma glucose (FPG) and fasting lipid profiles (FLP) following 10-12 hours overnight fast, which were transported immediately to the chemical pathology laboratory of the hospital for analysis.

Laboratory analysis: All the forms and sample bottles were pre-labelled with the respondent's special code numbers. The samples and results were processed by a Chemical Pathologist. The plasma glucose was measured using the enzymatic glucose oxidase method with a kit manufactured by Randox Laboratories Ltd, 55 Diamond Road, County Antrim, BT 294 QY, United Kingdom. A respondent was defined as having diabetes mellitus (DM) if the fasting plasma glucose level (FPG) was ≥ 7.0 mmol/l[22] and or a positive history of DM and or use of anti-diabetic agents.

The plasma levels of the respondent's total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG) were measured spectrophotometrically using a commercially manufactured assay kit by Randox Laboratories Ltd. The value of low-density lipoprotein cholesterol (LDL-C) was calculated mathematically using the Friedewald formula: LDL = TC – (HDL+TG/2.2) mmol/l.[23] The Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (NCEP ATP III) defined dyslipidaemia (abnormal lipid profile) as follows: Elevated TC defined as having TC levels of > 5.2 mmol/l

(>200mg/dl), Elevated TG as levels > 1.69 mmol/l (>150mg/dl), Elevated LDL-C as levels >3.38mmol/l (>130mg/dl) and low HDL-C as levels < 1.03mmol/l (<40mg/dl) for males and < 1.30mmol/l for females (<50mg/dl).[24] Presence of one or more abnormal lipid values was regarded as dyslipidaemia.

The Atherogenic Index of Plasma was calculated as logarithm (TG/+HDL-C) and categorised into low, moderate and high risk. AIP values of < 0.11 represented a low risk, while values of 0.11 – 0.21 signified a moderate risk and values > 0.21 were classified as a high risk for cardiovascular disease.[25]

Data Analysis: The data collected was encoded and analysed using the IBM SPSS (version 21). Descriptive statistics was used to summarize the data. Appropriate inferential statistics were carried out with AIP as the dependent variable. The independent variables include socio-demographic variables, lifestyle factors, blood pressure, BMI, WC, WHR, FPG and FLP. At the bivariate level, the Pearson Chi-square test was used to determine the significance of the association between AIP categories and the independent variables. The factors that were significant at the bivariate level were included in a multivariable analysis using an ordered logistic regression model to determine the independent predictors of high-risk AIP. Statistical significance was set at a $P < 0.05$.

Results

Socio-demographic characteristics

Table I: Socio-demographic characteristics of the respondents

variables	Frequency (n= 283)	Percentage (%)
Age group (Years)		
<45 (Young Adult)	123	43.5
45-64 (Middle Age)	109	38.5
≥ 65 (Elderly)	51	18.0
Sex		
Male	113	39.9
Female	170	60.1
Religion		
Islam	58	20.5
Christianity	225	79.5
Marital Status		
Currently Married	200	70.7
Not currently Married+	83	29.3
Ethnicity		
Yoruba	258	91.2
Hausa	4	1.4
Igbo	21	7.4
Level of Education		
No formal education	30	10.6
Primary	49	17.3
Secondary	65	23.0
Tertiary	139	49.1
Occupation		
Professional*	86	30.4
Artisan	41	14.5
Farming	19	6.7
Unemployed	47	16.6
Trading	90	31.8

KEY: *+Not currently married include; Single, Separated, Divorced and widowed. *Professionals include; bankers, civil servants, business men and managers.*

A total of 283 out of 286 respondents completed the study, three respondents had incomplete data collection giving a response rate of 98.9%. Data collection was over 12 weeks between November 2017 and January 2018. The respondent's ages ranged between 19 years and 85 years with a mean age of 48.61 ± 15.8 years. About 60% of the respondents were females with a male-to-female ratio of 1:1.5. Most of the respondents (70.7%) were married, 43.5% were young adults, 79.1% were Christians and 49.1% had tertiary education. (Table1)

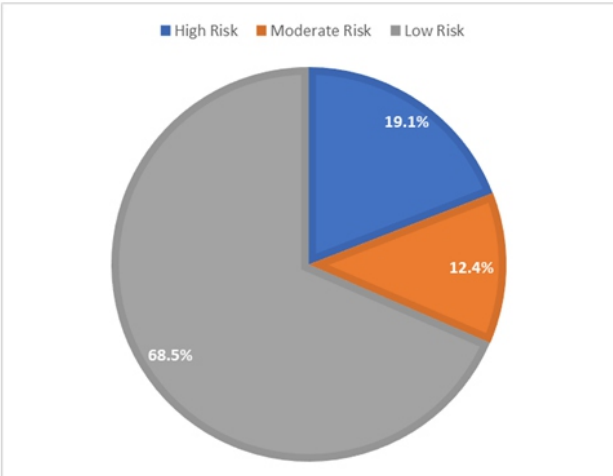

Figure 1: Pattern of Atherogenic Index of Plasma

The pattern of Atherogenic Index of Plasma: Most of the respondents (68.5%) had a low-risk category on assessment of AIP for cardiovascular disease, while 19.1% had a high-risk category. (Figure 1)

Table II: Relationship between AIP and Sociodemographic / Cardiovascular Risk Factors

Variables n = 283	Atherogenic Index of Plasma: Low risk- n (%)	Moderate risk – n (%)	High risk- n (%)	Statistical Test: X^2	Df	P value
Age group (years)						
<45 (Young Adult)	94(76.4)	12(9.8)	17(13.8)	11.32⁺⁺	4	0.02*
45-64 (Middle Age)	65(59.5)	20(18.5)	24(22.0)			
≥ 65 (Elderly)	35(68.6)	3 (5.9)	13(25.5)			
Sex						
Male	68(60.2)	18 (15.9)	27 (23.9)	6.14	2	0.04*
Female	126 (74.12)	17 (10.00)	27 (15.88)			
Marital Status						
Currently Married	134 (67.0)	23(11.5)	43 (21.5)			
Not currently Married	60(72.3)	12 (14.5)	11(13.3)	2.75	2	0.25
Level of Education						
None	18(60.0)	4 (13.3)	8 (26.7)			
Primary	34 (69.4)	7 (14.3)	8 (16.3)	2.32⁺⁺	6	0.88
Secondary	43 (66.2)	8 (12.3)	14(21.5)			
Tertiary	99 (71.2)	16 (11.5)	24(17.3)			
Hypertension						
No	104 (76.5)	12 (8.8)	20 (14.7)	7.68	2	0.02*
Yes	90 (61.2)	23 (15.6)	34 (23.1)			
Diabetes mellitus						
No	185 (71.2)	31(11.9)	44 (16.9)	10.06⁺⁺	2	0.01*
Yes	9(39.1)	4(17.4)	10(43.5)			
Lipid Profile						
LDL-C Normal	148(73.6)	28 (13.9)	25 (12.4)	20.03	2	0.01*
Abnormal	46(56.1)	7(8.5)	29(35.4)			
TC Normal	141 (71.2)	29 (14.7)	28 (14.1)	11.88	2	0.01*
Abnormal	53(62.4)	6(7.1)	26(30.6)			
Body Mass Index (BMI)						
Normal	100 (78.1)	16(12.5)	12(9.4)	14.67	2	0.01*
Abnormal	94(60.6)	19 (12.3)	42(27.1)			
Waist Circumference						
Normal	121 (75.6)	19 (11.9)	20 (12.5)	11.12	2	0.01*
Abnormal	73 (59.4)	16 (13.0)	34 (27.6)			
Waist Hip Ratio (WHR)						
Normal	74 (74.0)	16 (16.0)	10 (10.0)	9.00	2	0.01*
Abnormal	120(65.6)	19 (10.4)	44 (24.0)			
Physical Activity						
Physically Active	79 (72.5)	13 (11.9)	17 (15.6)	1.56	2	0.46
Physically Inactive	115 (66.1)	22 (12.6)	37 (21.3)			
Cigarette Smoking						
Never smoked	184 (71.6)	30 (11.7)	43 (16.7)	11.59⁺⁺	2	0.03*
Ever Smoked	10 (38.5)	5 (19.2)	11 (42.3)			
Alcohol History						
Alcohol consumption	50(58.1)	12 (13.9)	24 (27.9)	7.25	2	0.02*
No Alcohol consumption	144(73.1)	23 (11.7)	30 (15.2)			
Diet Fruits/Vegetables						
Adequate Intake	17(62.9)	5 (18.5)	5(18.5)	1.05	2	0.59
Inadequate Intake	177(69.1)	30 (11.7)	49 (19.1)			

KEY: *X^2 = Pearson's chi-square, Df = Degree of freedom, * = Statistically significant, ++ =Likelihood ratio used due to a large number of expected counts less than 5 in the cells.*

Relationship between AIP and cardiovascular risk factors: As shown in Table 2, 25.5% of the elderly had a high risk for CVD when compared to the young adults (13.8%) and this was statistically significant. Likewise, a higher risk AIP was significantly associated with increasing age (25.5%) and the male gender (23.9%). The prevalence of the high-risk category of AIP was significantly higher among those who were hypertensive (23.1%) and diabetic (43.5%). With regards to lipid profile, the respondents with elevated LDL-cholesterol (35.4%) and elevated total cholesterol (30.6%) had higher risk AIP when compared with the respondents with normal LDL-cholesterol (12.4%) and normal total cholesterol (14.1%). Similarly, overweight and obesity i.e., BMI ≥ 25, abnormal WC (27.6%) and abnormal WHR (24.0%) were each significantly associated with high-risk AIP. Furthermore, cigarette smoking and the consumption of alcohol had a significant association with high-risk AIP. Among the respondents who ever smoked, 42.3% had high-risk AIP which was significantly higher than the 16.7% who never smoked. However, even though a higher proportion of physically inactive respondents (21.6%) had high-risk AIP compared to those who were active (15.6%), this did not reach the level of statistical significance.

Table III: Ordered logistic Regression Model for Predictors of AIP

Independent Variables	Dependent Variables: AIP, low Risk = 1, Moderate Risk = 2, High Risk = 3. Odd ratio	95% CI for Odds ratio	Significance P Value
Hypertension (Ref = No)			
Yes	1.5	0.82 – 2.54	0.20
Diabetes mellitus (Ref =No)			
Yes	3.4	1.48 – 8.15	0.04*
Cigarette Smoking (Ref = Never Smoked)			
Ever Smoked	2.6	1.08 – 6.29	0.04*
Alcohol (Ref = No Alcohol consumption)			
Alcohol consumption	1.7	0.94 – 3.18	0.08
Total Cholesterol (Ref = Normal)			
Abnormal	1.5	0.87 – 2.74	0.13
LDL-C (Ref = Normal)			
Abnormal	4.3	1.56 – 11.73	0.01*
Body mass index (Ref =Normal)			
Abnormal	1.8	0.42 – 1.70	0.63
Waist Circumference (Ref = Normal)			
Abnormal	2.3	1.14 – 4.62	0.02*
Waist Hip Ratio (Ref = Normal)			
Abnormal	1.3	0.74 – 2.39	0.35

*Significant value at p<0.05, C I = Confidence Interval.

Independent Predictors of Atherogenic Index of Plasma: An ordered logistic regression model was performed to identify the independent predictors of AIP. All the cardiovascular risk factors that had a significant bivariate association with AIP were included in the multivariable regression model (Table 3). The predictors of AIP among the respondents were diabetes mellitus, smoking, abnormal LDL-C, and abnormal waist circumference. Those who had elevated LDL-C were over four times more likely to have higher risk AIP for CVDs (OR= 4.28, 95% CI: 1.56 – 11.73; P< 0.05) than respondents who had normal LDL-C. Respondents with diabetes mellitus, ever smoked and abnormal WC were over two times more likely to have higher risk AIP for CVDs than their respective counterparts.

DISCUSSION

The pattern of AIP and its relationship with cardiovascular risk factors in a primary care setting was explored in this study. It was observed that most of the respondents were in the younger age group accounting for the high prevalence of low-risk AIP (68.5%) among the respondents. However, increasing age was significantly related to higher risk AIP for CVDs. Furthermore, the study demonstrated a significant relationship between AIP and CVD risk factors aside from physical activity and diets, as respondents with hypertension, diabetes mellitus, abnormal BMI, WC and WHR, cigarette smoking and alcohol consumption had higher risk AIP for cardiovascular disease and this was in concordance with a similar study done in South-south Nigeria among health care workers.[26]

Regarding the relationship between AIP and cardiovascular risk factors, this study in consonance with the preponderance of previous studies demonstrated a significant relationship between AIP and the WC, WHR, BMI, blood pressure, blood glucose and LDL.[25-28] A study carried out in Enugu state, Nigeria reported that AIP is significantly related to BMI, waist circumference and waist-hip ratio in a study among a sample of sedentary males, which was similar to the findings of this study.[27] Previous studies in different geographical regions have reported higher AIP values in chronic medical conditions, with a significant relationship between AIP and FBG, TC, LDL-C and TG.[28,29] In a study among the Iranian population, Niroumand et al[25] reported a significant relationship between AIP and hypertension, diabetes mellitus and total cholesterol, which is also consistent with the findings of this study.

These findings across different populations and settings, corroborated by this study underscore the role of AIP as a significant indicator of the degree of cardiovascular disease risk. A hospital-based study conducted among the Chinese population with coronary heart disease reported AIP as an independent risk factor for coronary heart disease.[30]

The level of physical activity and intake of fruits and vegetables were not significantly associated with high-risk AIP among the respondents, even though respondents with physical inactivity had a greater prevalence of high AIP when compared with those who were physically active (21.3% vs 15.6%), and this did not reach the level of statistical significance. However, this is at variance with the findings by Niroumand et al,[25] Similarly, another study among middle-aged Chinese men reported a statistically significant relationship between high-risk AIP and physical inactivity.[31] The self-reporting nature of these lifestyle factors and the difficulty often associated with their accurate measurement and recall by individuals may explain the lack of significance demonstrated among the respondents in this study.

Results from a logistic regression analysis model showed that diabetes mellitus, smoking, waist circumference and LDL-C were independent predictors of AIP among the study subjects. This is in contrast to the findings of Ezeukwu et al, who reported BMI as the only significant independent predictor of AIP.[27] On the other hand, Noumegni et al[28] reported LDL-C as an independent predictor of AIP which is in line with this study.

The findings from this study add to emerging data on the usefulness of AIP as a simple, yet effective index for assessing the risk of cardiovascular disease. Most primary care clinics in the tertiary, general and mission hospitals have laboratory facilities for evaluating lipid profiles, however, those in the remote communities may be limited from prompt assessment of the fasting lipid profile. It must also be kept in mind that, being a hospital-based study potentially limits the generalisability of the findings to the general population.

Conclusion

There was a significant relationship between AIP and cardiovascular disease risk factors. The Atherogenic Index of Plasma as a marker for stratifying cardiovascular disease risk may be adopted at the primary care clinic as a rapid screening measure for early identification of patients at risk of cardiovascular disease. Based on the findings of this study, it is recommended that community-based studies with larger populations be conducted to establish the role of AIP in predicting the long-term risk of the development of cardiovascular disease.

Conflict of Interest

The authors declared that there is no conflict of interest.

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