ORIGINAL ARTICLE

ATHEROGENIC INDEX OF PLASMA IN SCHOOL CHILDREN AGED 6-12 YEARS IN CALABAR, NIGER-DELTA REGION OF SOUTHERN NIGERIA

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ABSTRACT

Background:

Despite evidence that Atherogenic Index of Plasma (AIP) may be useful for prediction of cardiovascular disease (CVD) risk, there is paucity of research on the index among children in sub-Saharan Africa. We aimed at assessing pattern and factors associated with abnormal AIP among children in Nigeria.

Methods: Cross-sectional descriptive study was conducted among randomly selected school-age children in Calabar, Nigeria. Bio-data, anthropometry, blood pressure, random blood sugar and lipid profile were measured. The AIP was calculated as logarithm of ratio of triglyceride (TG) and high density lipoprotein (HDL), with values categorized as low (<0.11), moderate (0.11-0.21), and high (>0.21) risk. Data were analysed using SPSS version 21.0, with significant p-value set at 0.05.

Results: Three hundred and seventy four (374) subjects aged 6-12 years with male:female ratio of 1:0.75 were surveyed. Mean age was 9.48 ± 1.42 years. Overweight / obesity was found in 8.7% Abnormal systolic and diastolic blood pressures were found in 9.6% and 6.7%, respectively. Moderate and high risk level of AIP were found in 17.6% and 53.3%, respectively. There was significantly higher proportion of moderate or high AIP risk among overweight/obese compared with subjects with normal BMI (84.8% vs. 68.9%, p<0.05). Other anthropometric, biochemical and sociodemographic characteristics, were not significantly associated with AIP.

Conclusion: Prevalent high-risk levels of AIP found in this study, suggest need for regular school-based cardiometabolic screening. There is also need for nutritional health education and adequate physical exercise among children. Further studies in other settings are recommended.

KEY WORDS: Atherogenic index, Cardiovascular diseases, Cardio-metabolic diseases Dyslipidemia, obesity.

INTRODUCTION

In developing countries, inappropriate adoption of Western civilization through the decades, have contributed to dietary and lifestyle changes, which increased risk of several non-communicable diseases (NCDs) including cardiometabolic diseases even among children [1]. Proliferation and patronage of fast food centres especially in urban regions, increased consumption of sugary drinks and beverages, in addition to much physical inactivity due to frequent use of automobile transportation are among such potentially adverse forms of civilization [1-2]. Consequently, the burden of cardiovascular diseases (CVDs) has been on the rise, causing at least one in every three deaths globally [3]. Developing countries like Nigeria, due to weak primary health care systems and high burden of coexisting communicable diseases, are worse hit [4].

There is increasing burden of CVD risk factors, with innocuous onset in childhood when preventive measures should have been instituted. Risk factors such as childhood obesity, high blood pressure (BP), and dyslipidemia, are often associated with hereditary predisposition and physical inactivity[5]. Dyslipidemia as key biochemical parameter, is marked by high total cholesterol (TC), Low Density Lipoprotein-cholesterol (LDL-C), Very Low Density Lipoprotein--cholesterol (VLDL-C), triglyceride (TG), and low High Density Lipoprotein)-cholesterol (HDL-C)[6]. The balance in the degree of these harmful or protective lipoproteins is reflected in the Atherogenic Index of Plasma (AIP)[7]. AIP, calculated as the logarithmic ratio of TG and HDL-C, is an evidence-based predictor of high cardiovascular risk[7]. Low, intermediate, and high CVD risks are represented by AIP values less than 0.11, 0.11 to 0.21, and greater than 0.21, respectively [7].

Considering the limitations of use of body mass index (BMI) for predicting CVD risks in significant proportion of individuals, there is need to optimize existing evidence of blood lipid biomarkers, for improvement in risk prediction [8]. The potential therapeutic and preventive benefits of such index may improve morbidity and mortality associated with cardiometabolic diseases [9]. Such evidence-based predictive capacity of AIP, is a novel index that has been established among adults [9]. Studies [10-11] have also suggested AIP to be a useful predictor of cardiometabolic risk among children, as has been established for adults. In a cross-sectional study among school children in Mexico, high level of AIP was found to be associated with presence of pre-hypertension in both obese and non-obese subjects. In addition, a community based cross-sectional study among 208 school children in Chile, found 54% prevalence of high risk level of AIP [11]. Mean AIP was 0.25 ± 0.27, with no significant difference comparing males and females (0.25 vs. 0.26, $p=0.645$) [11]. Obese subjects had significantly higher mean AIP compared with those that were overweight and had normal BMI. However, in Africa, there is paucity of research on AIP in children [12].

Assessment of AIP may yield more objective prediction of children at risk of developing CVD in their early or later adulthood [13]. Thus, enabling provision of more focused care to at-risk individuals, as means of cost-effective utilization of scarce healthcare resources in developing countries. This study was therefore aimed at assessing pattern and prevalence of abnormal AIP, and its association with other predictive anthropometric parameters, among primary school-age children in Calabar, Southern Nigeria.

METHODS

This study was carried out between February to July, 2017 among primary school children aged 6 to 12 years, in Calabar. Calabar, as described by Ineji et al [14] is the Cross River State capital. Ethical approval for this study was obtained from the ethics committee of the University of Calabar Teaching Hospital, Calabar and Cross River State ethical committee. Questionnaires detailing the bio-data of each participant including parental educational levels and occupation were used and written consent obtained from parents/guardians. Socioeconomic status was done according to the method used by Oyedeyi in Nigeria [15].

Weight and height of each participant were measured, and body mass index (BMI), (weight in Kg/ Height in m^2) was calculated [16]. A body mass index of 85th to 94th percentile was taken as overweight, BMI of equal to or greater than the 95th percentile was considered as obesity, based on the International Obesity Task Force (IOTF)[17] BP was taken using the first and fifth Korotkoff sounds as recommended by the 4th report on the diagnosis, evaluation and treatment of high BP in children and adolescents [18].Three readings were taken per subject at 5 minutes intervals after a good rest and the averages recorded. Diastolic BP (DBP)/Systolic BP(SBP) between 90th to $< 95^{th}$ percentile is said to be elevated while, DBP/SBP $\geq 95^{th}$ percentile is defined as hypertension [18]. Waist circumference (WC) was measured at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest as described by the Nat Cen Protocol [16]. A WC of greater than the 90th percentile was taken as abnormally high based on the guidelines of the International Diabetic Federation (IDF) [19].

Blood samples were obtained aseptically between 9.0am to 10.0am (Samples were taken from the children irrespective of whether they had eaten or not before coming to school) and analysed for random blood sugar, TC, TG and HDL–C using kits from ACON Laboratory while LDL-C was calculated from the Friedwald's formula [20]. The Atherogenic Index of Plasma (AIP) was calculated from $\log_{10}$ (TG/HDL-C).

Data were entered and analysed using SPSS version 21.0. Socio-demographic characteristics of subjects were presented using frequency tables. Subjects were categorized based on their AIP values as low risk (<0.11), moderate risk (0.11-0.21), and high risk (>0.21).[7] Comparison of BMI and other relevant variables were done between the AIP groups using chi-square, independent t-test, and Analysis of Variance (ANOVA) as inferential statistics. Relationship between AIP and other relevant continuous variables was assessed using Pearson correlation coefficient with display of corresponding scatter graphs. Significant p-value was set at < 0.05.

RESULTS

Three hundred and seventy-four (374) subjects aged 6-12 years with male: female ratio of 1:0.75 were surveyed, with mean age of 9.48 ± 1.42 years. Approximately half of subjects (51.3%) were within lower social class. Overweight or obesity was found in 8.7% (table 1). Mean SBP and DBP were 95.9 ± 8.9 mmHg (65-120 mmHg), and 59.6 ± 5.5 mmHg (40-76 mmHg), respectively. Abnormal SBP and DBP were found in 9.6% and 6.7%, respectively. Normal levels of TC, TG, HDL-C, and WC were found in 93.3%, 77.0%, 67.6% and 92.2%, respectively. There was normal frequency distribution of AIP, with mean of 0.25 ± 0.09 ranging from -0.31 to 1.07. Most subjects (70.9%) had moderate (17.6%) or high (53.3%) risk level of AIP (table 1).

Socio-demographic characteristics including age groups, gender, and social class, were not significantly associated with AIP category (p>0.05, table 2). There was significantly higher proportion of moderate or high AIP risk among overweight/obese compared with subjects with normal BMI (84.8% vs. 68.9%, p<0.05). Status of WC, TC, SBP and DBP were not significantly associated with AIP category (p>0.05, table 2).

Table 3 and figure 1 present relationship between continuous variables and AIP. Age (r=0.12), BMI (r=0.17), and WC (r=0.18), were significantly positively correlated with AIP (p<0.05). TC was indirectly correlated with AIP, though this was not statistically significant (r=-0.09, p=0.07). Blood pressure, BMI percentile, WC percentile, random blood sugar, and TC were not significantly correlated with AIP (p>0.05). BMI and WC were significantly correlated with TG, HDL-C and AIP (p<0.05, table 4). There was similarity in degree of significance of correlation with BMI comparing TG and AIP. There was also similarity in degree of significance of correlation with WC comparing HDL-C and AIP.

DISCUSSION

Childhood is a critical period for onset of atherosclerosis, whose clinical manifestations may present later in adulthood. In this study most subjects had normal BMI, WC, BP, and lipid profile. However, mean AIP was 0.25 ± 0.09 and 53.3% of subjects were within high risk level. This is similar to findings from similar cross-sectional study among 208 school-age children in Chile, which found 54.3% prevalence of high-risk level of AIP [21]. Similar mean AIP of 0.25 ± 0.27 was also obtained. High prevalence of high-risk levels of AIP, may be attributable to consumption of diets rich in carbohydrate [22], but lacking fish oils [23] as well as inadequate physical activities among school children in these settings [11].

The prevalence of high-risk level of AIP was found to be much higher than prevalence of abnormal levels of dyslipidemia (53.3% vs. 93.3%, 77.0% and 67.6% for total cholesterol, triglyceride, HDL-C, respectively). Similar study by Zhu et al [24] found better correlation between AIP and obesity compared with TG, HDL-C, and other lipoproteins (r=0.372 vs. ≤ 0.283, respectively). This may suggest AIP as potentially more sensitive measure of CVD risk compared with each of the blood lipoproteins.

Obesity was found to be significantly associated with higher AIP. This finding is in concert with established relationship between abnormal serum lipoproteins and obesity. It is thought that sedentary lifestyle and regular consumption of high caloric and fat diet potentially impairs serum lipoproteins, which contributes to obesity as well as higher AIP levels. Similar cross-sectional study among 414 sedentary young adult males in Enugu, South East Nigeria, found significant direct correlation between AIP and BMI and WC [25].

In this study, association was found to be statistically significant only for absolute BMI and its categories and not for BMI percentile (tables 2 and 3). This suggest that categorization of BMI into normal, overweight, and obese, may be more clinically relevant for prediction of CVD risk compared to absolute BMI percentile values.

In this study, there was no association between AIP and BP. This finding agrees with the study [26] among 283 children in Italy, which found no significant difference in systolic and diastolic blood pressures comparing those with normal and abnormal AIP. However, in adults a longitudinal study among middle-aged adults in Turkey, found high levels of AIP to significantly increase risk of coronary heart disease, diabetes, and hypertension [27].

There was no association between gender and AIP in this study. Like BP, the role of gender on CVD risk may not be clinically discernible until later on in adulthood. Potential similarities in level of physical activities and dietary habits between boys and girls, may be responsible for gender similarity in AIP found. However, other non-modifiable risk factors such as age, was found to significantly correlate directly with AIP. This suggests that older children compared with younger children may benefit more from use of AIP as screening tool for assessment of CVD risk. Older children are usually more independent in their choice of foods. They are therefore more likely to consume unhealthy diet that may impair their levels of blood lipoproteins yielding abnormal AIP [28].

There are many potential applications of AIP in tropical clinical paediatrics. Diabetic children may also benefit from use of AIP, as part of screening tool for monitoring of their renal and metabolic function. A retrospective study [29] among 645 diabetic patients in Turkey, found high risk level of AIP to be significantly associated with higher levels of serum creatinine, uric acid, HbA1c, and albuminuria. Care givers may therefore have higher index of suspicion of CVD risk, when AIP is high amidst concomitant abnormal levels of these glycemic biochemical parameters. Significantly higher levels of AIP have also been found among obese children that are glucose intolerant or insulin resistant. This suggest the potential use of AIP as part of regular screening of children with familial and other predictors of diabetes mellitus. It may also be useful for monitoring of effects of dietary, physical activity and other interventions for risk reduction or prevention of chronic metabolic diseases in children [30].

Dyslipidemia which is represented by suboptimal AIP, has been found to be associated with the presence and severity of several chronic diseases including Non Alcoholic Fatty Liver Disease (NAFLD), which is common in obese children [31]. Among obese subjects, a 5.37-fold risk of NAFLD was found among those with high compared with low AIP, suggesting potential use of AIP for predicting and monitoring of such chronic liver disease especially in resource-poor settings [32].

Certain limitations must be considered in the interpretation of findings from this study. First, causal inference cannot be deduced from this study due to use of cross-sectional study design. A more robust longitudinal or experimental design may be required to establish causal relationship between AIP, BMI and other CVD risk predictors among children. Also, dietary habits and level of physical activity, as potential predictors of the presence and severity of dyslipidemia were not assessed. In this study the use of random samples for assessment of blood lipid values, may have overestimated the AIP calculated for each subject.

CONCLUSION

This study found high levels of AIP among school-age children in a developing country setting. This finding has significant implications for future burden of CVD especially in developing countries where there is little or no significant effort at CVD prevention in early childhood. Therefore, identification of children at higher risk of cardio-metabolic comorbidities using AIP should be followed by short and long-term therapeutic and preventive measures. These interventions may include making school-based sporting activities more fun and compulsory for pupils, and incorporating more practical nutritional health education in the learning curriculum. High prevalence of moderate and high-risk levels of AIP found in this study, deserves further research, especially towards its more precise estimation and assessment of causal relationship in developing countries.

CONFLICT OF INTEREST

There is no conflict of interest to declare.

FUNDING

No funding was received for this work.

AUTHORS CONTRIBUTION

Egorp Ineji – conceptualized the work, collected data, and wrote the manuscript
Chimereze Amajor --collected data, read and corrected the manuscript
Chigozie Uzomba – collected data, read and corrected the manuscript
Ekaette Nsa – collected data, read and corrected the manuscript
Maxwell Anah - designed the work read and corrected the manuscript
Imaobong Etuk – designed the work read and corrected the manuscript

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APPENDICES

Table 1: Sociodemographic, anthropometric, and biochemical characteristics **(N=374)**		
Variable	**Frequency**	**Percentage**
Age groups (years)		
<10	184	49.2
≤10	190	50.8
Gender		
Male	160	42.8
Female	214	57.2
Social class		
Upper	112	29.9
Middle	70	18.8
Lower	192	51.3
BMI percentile		
Normal	328	87.7
Overweight	31	8.3
Obese	15	4.0
Systolic Blood Pressure		
Normal	338	90.4
Elevated	27	7.2
Systolic hypertension	9	2.4
Diastolic Blood Pressure		
Normal	349	93.3
Elevated	24	6.4
Systolic hypertension	1	0.3
Total cholesterol		
Normal	349	93.3
High	25	6.7
Triglyceride		
Normal	288	77.0
High	86	23.0
High Density Lipoprotein		
Normal	253	67.6
Low	121	32.4
Waist Circumference		
Normal	345	92.2
High	29	7.8
Atherogenic Index of Plasma		
Low risk	109	29.1
Moderate risk	66	17.6
High risk	199	53.3

Table 2: Assessment of association between variables and AIP Category (N=374)				
Variable	**AIP Low Risk** n (%)	**AIP Mod/High Risk** n (%)	**AIP Total** n (100%)	**Chi-square (p-value)**
Age groups (years)				
<10	57 (31.0)	127 (69.0)	184 (100)	0.59
≥10	52 (27.4)	138 (72.6)	190 (100)	(0.44)
Gender				
Male	53 (33.1)	107 (66.9)	160 (100)	2.15
Female	56 (26.2)	158 (73.8)	214 (100)	(0.14)
Social class				
Upper	34 (30.4)	78 (69.6)	112 (100)	0.94
Middle	23 (32.9)	47 (67.1)	70 (100)	(0.62)
Lower	52 (27.1)	140 (72.9)	192 (100)	
BMI percentile				
Normal	102 (31.1)	226 (68.9)	328 (100)	4.93
Overweight/obese	7 (15.2)	39 (84.8)	46 (100)	(0.03)
Systolic Blood Pressure				
Normal	102 (30.2)	236 (69.8)	338 (100)	1.82
At least elevated	7 (19.4)	29 (80.6)	36 (100)	(0.18)
Diastolic Blood Pressure				
Normal	102 (29.2)	247 (70.8)	349 (100)	0.02
At least elevated	7 (28.0)	18 (72.0)	24 (100)	(0.90)
Total cholesterol				
Normal	104 (29.8)	245 (70.2)	349 (100)	1.09
High	5 (20.0)	20 (80.0)	25 (100)	(0.30)
Triglyceride				
Normal	108 (37.5)	180 (62.5)	288 (100)	42.3
High	1 (1.2)	85 (98.8)	86 (100)	(0.00)
High Density Lipoprotein				
Normal	106 (41.9)	147 (58.1)	253 (100)	61.6
Low	3 (2.5)	118 (97.5)	121 (100)	(0.00)
Waist Circumference				
Normal	103 (29.9)	242 (70.1)	345 (100)	1.09
High	6 (20.7)	23 (79.3)	29 (100)	(0.30)

Table 3: Correlation between variables and atherogenic index of plasma **(N=374)**		
Variable	**Correlation coefficient with AIP (r)**	**p-value**
Age	0.124	0.02
BMI	0.168	0.01
BMI Percentile	0.066	0.20
Systolic Blood Pressure	0.064	0.22
Systolic Blood Pressure Percentile	0.041	0.43
Diastolic Blood Pressure	0.023	0.65
Diastolic Blood Pressure Percentile	0.063	0.22
Total cholesterol	-0.092	0.07
Triglyceride	0.774	0.00
HDL-Cholesterol	-0.706	0.00
Waist circumference	0.183	0.00
Waist circumference Percentile	0.071	0.17
Random blood sugar	0.041	0.43

Table 4: Comparison of correlation of AIP and other blood lipids with anthropometry **(N=374)**				
Variable	**Total Chol.**	**Triglyceride**	**HDL-Chol.**	**AIP**
BMI				
Correlation coefficient	0.71	0.18	-0.11	0.17
p-value	0.17	0.00	0.03	0.00
Waist circumference				
Correlation coefficient	0.07	0.12	-0.18	0.18
p-value	0.21	0.02	0.00	0.00

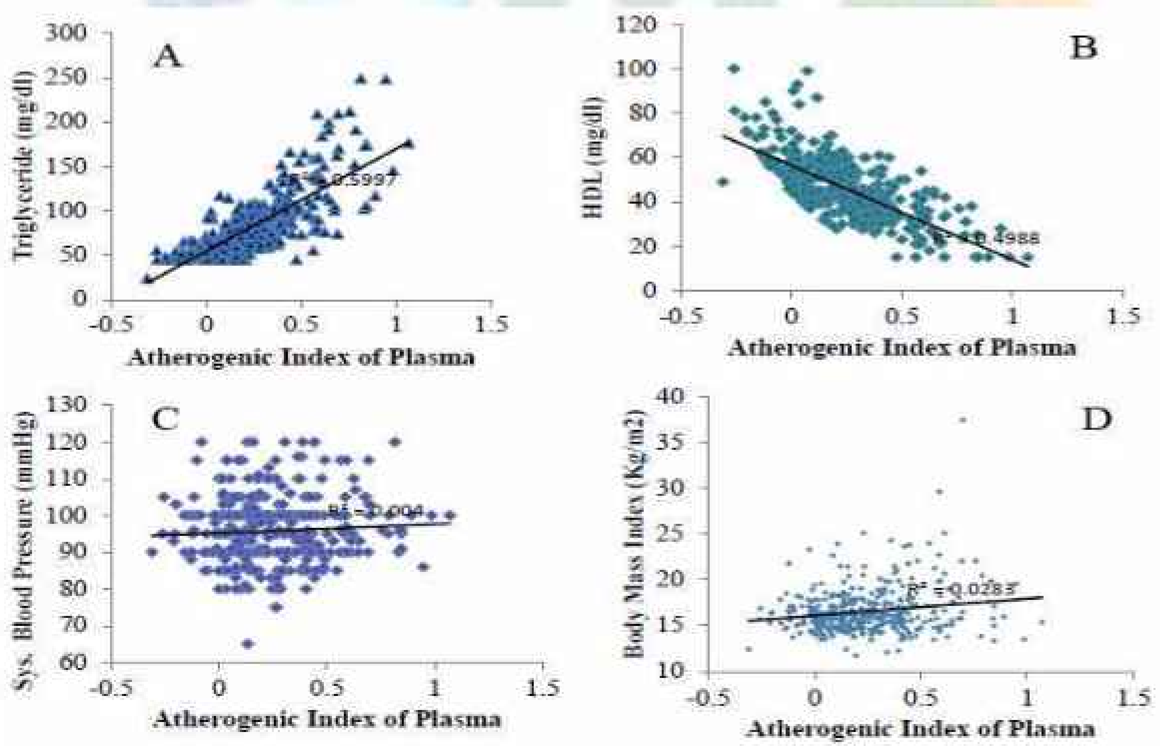

Figure 1: Scatterplot showing relationship between AIP and TG, HDL-C, SBP, BMI (N=374)