

## Atherogenic risk pattern among Nigerian hypertensive and diabetic patients undergoing follow-up visit in a tertiary hospital

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### Abstract

**Objectives:** Cardiovascular risk can be predicted using lipid ratios such as the atherogenic index which is defined as the base 10 logarithm of the ratio of plasma triglyceride (TG) to high density lipoprotein cholesterol (HDL-C) – it is a useful prognostic parameter for guiding timely interventions and has also been employed as a predictor of cardiovascular risk. However, this is rarely used in the clinical practice in developing countries including Nigeria.

**Methods:** This study was a hospital-based cross-sectional study of 382 hypertensive and diabetic patients attending outpatient clinics of a tertiary hospital in Nigeria. Atherogenic risk profile, was categorized as low risk (<0.1), intermediate risk (0.1–0.24), and high risk (>0.24). Predictors were established using regression analysis. Level of significance was set at p-value of <0.05 and 95% confidence interval.

**Results:** The mean age of participants was 56±12 years, 31.4% of participants had high atherogenic risk. This was higher among female patients (60.0%). Participants with high TC, high LDL, uncontrolled blood pressure had odds of 1.64, 1.43 and 1.17 times of developing high atherogenic risk respectively.

**Conclusion:** A significant proportion of participants in this study population were at risk of developing atherosclerosis. Key identified populations at risk of CVD should be considered for routine atherogenic assessment.

**Keywords:** Atherogenic, indices, hypertension, diabetes

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## Profil de risque athérogénique chez les patients nigériens hypertendus et diabétiques subissant une visite de suivi dans un hôpital tertiaire

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### Resume

**Objectifs:** Le risque cardiovasculaire peut être prédit à l'aide des ratios lipidiques tels que l'indice athérogène, défini comme le logarithme en base 10 du ratio des triglycérides plasmatiques (TG) sur le cholestérol lié aux lipoprotéines de haute densité (HDL-C) - il s'agit d'un paramètre pronostique utile pour guidant des interventions opportunes et a également été utilisé comme facteur prédictif du risque cardiovasculaire. Cependant, cela est rarement utilisé dans la pratique clinique dans les pays en développement, y compris le Nigéria.

**Méthodes:** Cette étude était une étude transversale en milieu hospitalier de 382 patients hypertendus et diabétiques fréquentant des cliniques de consultation externe d'un hôpital tertiaire au Nigéria. Le profil de risque athérogène a été classé dans les catégories suivantes: risque faible (<0,1), risque intermédiaire (0,1–0,24) et risque élevé (> 0,24). Les prédicteurs ont été établis par analyse de régression. Le niveau de signification a été fixé à une valeur p de <0,05 et un intervalle de confiance à 95%.

**Résultats:** L'âge moyen des participants était de 56 ± 12 ans, 31,4% des participants avaient un risque athérogène élevé. Ce taux était plus élevé chez les patientes (60,0%). Les participants présentant une pression artérielle élevée, un cholestérol LDL élevé et une tension artérielle non contrôlée élevée avaient respectivement des chances de développer un risque élevé de risque athérogène de 1,64, 1,43 et 1,17.

**Conclusion:** Une proportion significative des participants de cette population étudiée présentait un risque de développer une athérosclérose. Les populations clés identifiées à risque de MCV doivent être considérées pour une évaluation athérogénique de routine.

**Mots-clés:** athérogène, indices, hypertension, diabète

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## INTRODUCTION

The atherogenic index of plasma (AIP), is defined as the base 10 logarithm of the ratio of plasma triglyceride (TG) to high density lipoprotein cholesterol (HDL-C), and has been shown to be significant predictors for metabolic disturbances including dyslipidemia, atherosclerosis, hypertension and cardiovascular diseases (CVD) (1,2). The term was proposed by Dobiasova and Frohlich to indicate that plasma atherogenicity was also a significant independent predictor of coronary heart disease (CHD) (3, 4). It has been established that an AIP value of less than 0.11 is associated with low risk of CHD; the values between 0.11 to 0.24 and greater than 0.24 are associated with intermediate and high risks, respectively (5, 6). Sensitivity of AIP has also been demonstrated in a cohort of patients undergoing coronary angiography, where it was found to be better than age, body mass index (BMI), waist circumference, type 2 diabetes mellitus (DM), blood pressure (BP), smoking, TG, total cholesterol (TC), low density lipoprotein (LDL-C), HDL-C, and TC/HDL-C, in predicting the possibility of positive findings (6,7).

In Western populations, dyslipidemia among patients with hypertension is a common finding. The prevalence of dyslipidemia coexisting with hypertension has been estimated at 15–24% (8,9). Over 40% of all newly diagnosed hypertensive patients have at least one lipid abnormality (10). There is limited data on the burden of dyslipidemia among patients with hypertension in sub-Sahara Africa (SSA) whereas; hypertension and dyslipidemia are both identified as independent modifiable risk factors for CVD. Some studies have suggested that dyslipidemia may play a role in the development of hypertension via endothelial damage (11) and the risk for CVD is higher in the presence of both hypertension and dyslipidemia than by the individual disease entities (12). In high income countries, strategies targeting the reduction of serum cholesterol levels provide the single most important benefit against CVD resulting from coronary heart disease (CHD) (13).

Presently, medical practice encourages risk stratification for all persons at risk of CHD including those with hypertension. This is advantageous for timely intervention in preventing CHD and its' sequelae. Cardiovascular risk assessment based solely on serum low density lipoprotein cholesterol (LDL-C) has been found to be inadequate (14, 15) and even in those on statin therapy with normal or

near normal LDL-C serum levels, there remains risk for future cardiovascular events. Hypertriglyceridemia has been identified as an independent cardiovascular risk factor (16,17). Hypertriglyceridemia is a proxy for atherogenic dyslipidemia (elevated triglyceride (TG) and low high-density lipoprotein cholesterol) (17, 18), a component of the metabolic syndrome and a known risk factor for CHD. Despite interaction with other lipids that might increase atherogenic risk and in-subject variation, elevated TG has been shown to be a good predictor of CHD in consideration of the HDL-C levels (18) and is used in clinical practice to predict atherosclerosis (18, 19) The lipid ratio  $\log [TG/HDL-C]$  (atherogenic index) provides an alternative simple option for risk stratification. The use of this ratio is to reflect the balance between risk and protective lipoprotein forces (16) as well as acting as a correlate with LDL-C particle size (20), LDL-phenotype B, and small HDL-C particles (4). This ratio has also been evaluated as a prognostic tool in predicting CHD (4) and its predictive value far outweighs that of absolute lipid parameters (21, 22) as well as the TC /HDL ratio (22) given its strong correlation with lipoprotein particle size.

Nigeria bears a significant burden of hypertension and like other SSA countries is not adequately equipped with the necessary resources, expertise, and technology to manage the CVD sequelae. A rural population in Uganda reflected the dominant dyslipidemia pattern to be that of low serum HDL-C levels and a good proportion with hypertriglyceridemia (23). Whereas there are well-recognized recommendations on the use of serum LDL-C and TC for cardiovascular risk assessment, there is limited progress in addressing concerns with low serum HDL-C which may lead to underestimation of CHD risk (24). Thus, assessment of atherogenic index provides a simple and reliable method for point of care risk assessment that can be done by healthcare providers even within hard-to-reach areas. The aim of this study was to assess the atherogenic risk profile using the atherogenic index among Hypertensive and Diabetic Patients in University of Ilorin Teaching Hospital.

## METHODS

### Study design and study setting

This was a hospital-based cross-sectional study among registered patients with hypertension and diabetes attending outpatient clinics (General Outpatient Department and the

Medical Outpatient Department) of the University of Ilorin Teaching Hospital (UIITH), Ilorin, Nigeria. The hospital serves as a tertiary health facility and receives referral from public and private hospitals from within and outside the state. Adult patients (of over 18 years of age) with hypertension, or having both hypertension and diabetes were recruited into the study. Desired sample size of 382 patients was recruited using systematic random allocation over 6 months in 2016.

### Informed consent and Ethics

Informed consent was obtained from eligible patients after explaining research concept to the patients in the language they best understand. Ethical approval for this study was obtained from the UIITH Ethical Review Committee.

### Data collection and analysis

Data was collected using Clinical Report Form (CRF) and a standardised questionnaire. The CRF was used to collect data on patients' medical information and records of parameters such as; BP, BMI, biochemical profile, disease history, drug history, complication and comorbidity history and hospital follow-up history. An interviewer-administered questionnaire was used to collect information on socio-demography.

### Measurement

**Physical Measurement:** Blood pressure measurement, height and weight were measured as described by Riha et al (25). Participants found to have systolic blood pressure  $\geq 140$ mmHg and/or diastolic pressure  $\geq 90$ mmHg were referred to as having poorly controlled hypertension. Participant categorization using BMI was as follows: BMI  $< 18.5$ , "underweight," BMI 18.5–24.9, "normal weight," BMI 25–29.9, "overweight," and BMI  $\geq 30$ , "obese".

**Laboratory Measurement:** Participants underwent phlebotomy where blood samples for lipid profile (TC, TG, HDL-C, and LDL-C) were collected. Blood samples were transported on the same day of collection to a central laboratory for processing and testing. Lipid profile analysis was done using the enzymatic colorimetric assay by the Cobas Integra 400 Plus©. Cut-off values for the different lipid parameters representative of dyslipidemia were as follows: TC  $> 5.2$ mmol/L, TG  $> 2.3$ mmol/L, LDL-C  $> 3.4$ mmol/L and HDL-C  $< 1.04$ mmol/L for male, and  $< 1.3$ mmol/L for female. Atherogenic risk profile, was categorized

as low risk ( $< 0.1$ ), intermediate risk (0.1–0.24), and high risk ( $> 0.24$ ).

The data was analysed using IBM© SPSS version 22. A descriptive analysis of socio-demographic characteristics, biophysical, biochemical and clinical profile was done. Inferential statistics on determinants of atherogenic index risk was performed using t-test and F-tests. These formed the basis for regression analyses (simple and binary). The levels of significance were set at 95% confidence interval (95% CI) while p-value of  $< 0.05$  was set to be statistically significant.

### RESULTS

Table 1 shows the socio-demography and clinical profile of patients. The mean age of participants was  $56 \pm 12$  years. Patients within the age group 41-60 years constituted the majority (47.6%) of the study population while females predominate in all the age group except in those aged 40 years with slightly lower proportion (49.0%). Majority (74.6%) were married and largely engaged in small business (49.2%).

Biochemically, only 23.0% of the patients whose blood samples were analysed for TC had desirable (normal) TC ( $< 5.2$ mmol/l) while majority 75.9% had high TC. However, 69.4% had desirable triglyceride, 49.5% and 78.5% had normal HDL-c and LDL respectively (Table 1).

Biophysical characteristics revealed that 3.7% of the patients were underweight with BMI  $< 18.5$  while over a quarter (36.9%) were overweight. Higher proportions of female participants were found to be overweight and obese accounting for 67.4% and 87.7% respectively. Similarly, higher proportions of females (55.7%) had uncontrolled BP than the males (44.3%).

Atherogenic risk: More than a quarter of participants (31.4%) had high atherogenic risk ( $> 0.24$ ). Gender stratification shows that high atherogenicity was higher among female patients than males (60.0% and 40.0% respectively). Factors associated with atherogenic risk are as shown in table 2. Participants whose ages were 40 years and 61 years had higher proportions (40.8% and 33.6%) of high Atherogenic risk respectively, however, this association was not found to be statistically significant (p-value = 0.164). Furthermore, 28.6% of participants with high TC had intermediate Atherogenic risk, while 59.8% of those with high TG and 55.0% of abnormal HDL had high Atherogenic risk with varying statistical significance (p-values of

0.048,  $< 0.001$  and  $< 0.001$  respectively). However, obesity, uncontrolled BP and high serum glucose among the study subjects were found not to be statistically significant.

Tables 3 and 4 demonstrate regression analyses. Simple linear regression revealed that TG, HDL and LDL had linear relationship with high atherogenic risk as an independent entity with significance at  $< 0.001$ . For every unit increase of atherogenic index; there was a corresponding increase in the serum level of TG by 0.540 mmol/L, and 0.062mmol/L increase for LDL. Conversely, for every decrease in a unit of atherogenic index, there was a corresponding decrease in the serum level of (abnormal) HDL by -0.775mmol/l.

Predictors of high atherogenic risk on binary regression were TC, LDL, abnormal BMI (overweight and obese), uncontrolled BP and high serum glucose. Participants with high TC were 1.64 times of having high atherogenic risk, while those with high LDL, overweight, obese, uncontrolled BP and high serum glucose were 1.43, 1.48, 1.34, 1.17 and 1.23 times of developing high atherogenic risk respectively.

## DISCUSSION

This study revealed that over three-quarter of the patients being followed-up at UITH Ilorin, had hypercholesterolaemia (TC) while half of them had dyslipidaemia (low serum HDL) which was more pronounced among female patients. This implied increased risk of developing CHD and worsened medical outcome (4). Similarly, large proportion of the study participants were obese and had uncontrolled BP despite being on treatment. These indicated inadequate treatment which could be multifactorial and corroborated findings from other studies that reported medical follow-up for hypertension in Nigeria. The study has established that both weight and uncontrolled BP are independent risks for CVD and CHD (4).

About a third (31.4%) of the participants had high atherogenic risk, of which females constituted majority (60%). This finding is higher compared to a similar study in Uganda where only a quarter had high atherogenic risk (4). Conversely, females were more at risk in our study than that of Ugandan study where males had higher risk. Almost half (49.5%) of the participants had uncontrolled BP with females being majority (55.7%) and the most likely explanation could be that females constituted the majority of the study population.

Factors that showed significant

association with high atherogenic risk in this study were abnormal TC, high TG and low serum level of HDL. A high serum level of TG and low serum HDL are integral of what constitute dyslipidaemia. This finding is in conformity with a population-based survey done in Iran and using the atherogenic index found a similar high estimate of atherogenic risk (27). Similarly, study involving 52 countries spread across all continents (INTERHEART study), found that persons with history of myocardial infarction had three times the odds of having atherogenic dyslipidemia compared to persons without history of myocardial infarction (28). Furthermore, an observational study done in Brazil found that persons with coronary disease had two times the odds of having an abnormal TG/HDL-C ratio (29). Although not found to be statistically significant in this study, high serum glucose level was also associated with high atherogenic risk. Diabetes affects the integrity of the vasculature and is also associated with other conditions that predispose to CHD, such as hypertension and dyslipidemia that may explain the increased risk (4).

Regression analyses revealed that the determinants of atherogenic risk were serum TG, HDL and serum LDL with significance at  $< 0.001$ . Participants with high TC were 1.64 times of having high atherogenic risk, while those with high LDL, overweight, obese, uncontrolled BP and high serum glucose were 1.43, 1.48, 1.34, 1.17 and 1.23 times of developing high atherogenic risk respectively. Previous epidemiological studies have shown that cholesterol, uncontrolled BP and serum glucose were predictors of CHD and LDL-C was associated with future risk (30); this is in tandem with our findings in this study. Similar to the Framingham and the INTERHEART studies (28, 30) obesity and overweight were associated with high atherogenic risk in this study population.

## CONCLUSION

A significant proportion of participants in this study population are at risk of developing atherosclerosis. Persons with uncontrolled hypertension, dyslipidaemia and uncontrolled glycaemia, appear to be more at risk and may be considered as target groups for intervention programs. Follow-up studies are needed to further assess the risk among younger age group. Assessment of atherogenic index for all patients at risk of developing metabolic syndrome should be given due consideration by healthcare providers since it has been established to provide

a simple and reliable method for point of care risk assessment even within hard-to-reach areas.

**Conflict of Interest:** None to declare

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**Table 1: Sociodemographic, clinical, physical, and biochemical characteristics of Patients by gender.**

Variables	All participants (%)	Gender		$\chi^2$	P
		Male (%)	Female (%)		
<b>Demographic</b>					
<b>*Age Group</b>					
= 40	66 (17.3)	34 (51.0)	32 (49.0)	7.875	<b>0.019</b>
41 – 60	182 (47.6)	55 (30.2)	127 (69.8)		
= 61	134 (35.1)	52 (38.8)	82 (61.2)		
<b>Level of Education</b>					
Primary	69 (18.1)	29 (40.6)	41 (59.4)	71.263	<b>&lt; 0.001</b>
Secondary	73 (19.1)	36 (49.3)	37 (50.7)		
Quranic	9 (2.4)	2 (22.2)	7 (77.8)		
Tertiary	104 (27.2)	57 (54.8)	47 (45.2)		
Vocational training	9 (2.4)	5 (55.6)	4 (44.4)		
No formal education	118 (30.9)	7 (5.9)	111 (94.1)		
<b>Marital Status</b>					
Married	285 (74.6)	121 (42.5)	164 (57.5)	40.660	<b>&lt; 0.001</b>
Single	5 (1.3)	4 (80.0)	1 (20.0)		
Divorced	8 (2.1)	4 (50.0)	4 (50.0)		
Widowed	84 (22.0)	6 (7.1)	78 (92.9)		
<b>Occupation</b>					
Small business	188 (49.2)	44 (23.4)	144 (76.6)	28.031	<b>&lt; 0.001</b>
Large business	22 (5.8)	8 (36.4)	14 (63.6)		
Civil servant	116 (30.4)	51 (44.0)	65 (56.0)		
Unemployed	55 (14.4)	32 (58.2)	23 (41.8)		
<b>Biochemical characteristics</b>					
<b>Total cholesterol</b>					
Desirable (=5.2mmol/l)	88 (23.0)	32 (36.4)	56 (63.6)	0.042	0.838
High (>5.2mmol/l)	290 (75.9)	102 (35.2)	188 (64.8)		
<b>Triglyceride</b>					
Desirable (=2.3mmol/L)	265 (69.4)	93 (35.1)	172 (64.9)	0.023	0.880
High (>2.3mmol/L)	117 (30.6)	42 (35.9)	75 (64.1)		
<b>HDL-C</b>					
Abnormal (<1.04-m, 1.3-f), low	191(50.0)	76 (39.8)	115 (60.2)	3.874	<b>0.049</b>
Normal (=1.04-m, 1.3-f)	189 (49.5)	57 (30.2)	132 (69.8)		
<b>LDL-C</b>					
Normal (=3.4mmol/L)	300 (78.5)	110 (36.7)	190 (63.3)	1.076	0.300
High (>3.4mmol/L)	82 (21.5)	25 (30.5)	57 (69.5)		
<b>Serum glucose</b>					
Normal (< 11mmol/L)	340 (89.0)	119 (35.0)	221 (65.0)	0.215	0.643
High(= 11mmol/L)	36 (9.4)	14 (38.9)	22 (61.1)		
<b>Biophysical characteristic</b>					
<b>BMI</b>					
Underweight (<18.5)	14 (3.7)	7 (50.0)	7 (50.0)	50.361	<b>&lt; 0.001</b>
Normal (18.5–24.9)	118 (30.9)	67 (56.8)	51 (43.2)		
Overweight (=25)	141(36.9)	46 (32.6)	95 (67.4)		
Obese	106 (27.7)	13 (12.3)	93 (87.7)		
<b>Clinical characteristics</b>					
<b>Blood Pressure</b>					
Controlled (<140/90 mmHg)	233 (61.0)	69 (29.6)	164 (70.4)	8.573	<b>0.003</b>
Uncontrolled (=140/90 mmHg)	189 (49.5)	66 (44.3)	83 (55.7)		
<b>Atherogenic risk</b>					
Low (<0.1)	262 (68.6)	87 (33.2)	175 (66.8)	1.662	0.197
High (>0.24)	120 (31.4)	48 (40.0)	72 (60.0)		

\* Mean  $\pm$ SD =56 $\pm$ 12 yrs

**Table 2: factors associated with Atherogenic risk among patients**

Variables	Atherogenic		$\chi^2$	P
	Low (%)	High (%)		
<b>Demographic</b>				
<b>Age Group</b>				
= 40	29 (59.2)	20 (40.8)		
41 – 60	144 (72.4)	55 (27.6)		
= 61	89 (66.4)	45 (33.6)	3.620	0.164
<b>Gender</b>				
Male	87 (64.4)	48 (35.6)		
Female	175 (70.9)	72 (29.2)	1.662	0.197
<b>Biochemical characteristics</b>				
<b>Total cholesterol</b>				
Normal	53 (60.2)	35 (39.8)		
Abnormal	207 (71.4)	83 (28.6)	3.910	<b>0.048</b>
<b>Triglyceride</b>				
Normal	215 (81.1)	50 (18.9)		
Abnormal	47 (40.2)	70 (59.8)	63.206	<b>&lt; 0.001</b>
<b>HDL-C</b>				
Abnormal	86 (45.0)	105 (55.0)		
Normal	174 (92.1)	15 (7.9)	97.277	<b>&lt; 0.001</b>
<b>LDL-C</b>				
Normal	201 (67.0)	99 (33.0)		
Abnormal	61 (74.4)	21 (25.6)	1.632	0.201
<b>Serum glucose</b>				
Normal	233 (68.5)	107 (31.5)		
High	23 (63.9)	13 (36.1)	0.323	0.570
<b>BMI</b>				
Underweight	10 (71.4)	4 (28.6)		
Normal	77 (65.3)	41 (34.7)		
Overweight	95 (67.4)	46 (32.6)		
Obese	78 (73.6)	28 (26.4)	1.986	0.575
<b>Blood Pressure</b>				
Controlled (<140/90 mmHg)	163 (70.0)	70 (30.0)		
Uncontrolled (=140/90 mmHg)	99 (66.4)	50 (33.6)	0.521	0.470

**Table 3: Simple Linear Regression of predictors of atherogenic risk**

Variables	Standardized Coefficients		Sig.	95.0% Confidence Interval for B	
	Beta ( $\beta$ )	t		Lower Bound	Upper Bound
Total Cholesterol (TC)	-0.072	-1.395	0.164	-0.026	0.004
Triglyceride (TG)	0.540	12.514	<b>&lt;0.001</b>	0.150	0.206
HDL (abnormal)	-0.775	-23.919	<b>&lt;0.001</b>	-0.309	-0.262
LDL	0.062	3.612	<b>&lt;0.001</b>	0.006	0.019
Serum Glucose	-0.003	-0.571	0.568	-0.008	0.004
BMI	-0.004	-0.280	0.780	0.000	0.000
Average Systolic Dominant	0.036	0.708	0.480	-0.001	0.001
Average Diastolic Dominant	0.049	0.962	0.337	-0.001	0.002
Age	-0.024	-1.647	0.100	-0.001	0.000

**Table 4: Binary regression analysis of high atherogenic risk of patients**

Variables	B	P	Odd Ratio	95% C.I	
				Lower	Upper
<b>Age</b>					
> 60 (RC)		.168			
= 40	-0.599	0.073	0.549	0.285	1.059
41 – 60	-0.310	0.366	0.733	0.374	1.437
<b>Cholesterol</b>					
Total cholesterol (high)	0.499	0.049	<b>1.647</b>	1.002	2.707
Triglyceride (high)	-1.857	< 0.001	0.156	0.097	0.253
HDL (abnormal)	-2.651	< 0.001	0.071	0.039	0.129
LDL (high)	0.358	0.203	<b>1.431</b>	0.824	2.483
<b>BMI</b>					
Underweight (RC)					
Normal	0.108	0.864	1.114	0.323	3.840
Overweight	0.394	0.179	<b>1.483</b>	0.835	2.635
Obese	0.299	0.292	<b>1.349</b>	0.773	2.355
<b>Blood pressure</b>					
Controlled (RC)					
Uncontrolled	0.162	0.471	<b>1.176</b>	0.757	1.827
<b>Serum glucose</b>					
Serum glucose (high)	0.208	0.571	<b>1.231</b>	0.601	2.522