ORIGINAL ARTICLE

Comparison of plasma lipid profiles and atherogenic indices among hypertensives with or without type 2 diabetes

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ABSTRACT

Background: Several atherogenic indices derived from the lipid profiles are postulated to better detect dyslipidemias and predict the risk of having cardiovascular events even in the presence of insignificant changes in individual lipid parameters. **Objective:** To compare the lipid ratios and atherogenic index of plasma (AIP) to conventional atherogenic indices among hypertensive type 2 diabetics to hypertensive nondiabetes (HND) controls. **Materials and Methods:** A case–control study in which 210 participants with type 2 diabetes mellitus with hypertension (hypertensive-diabetic [HD]) compared with 150 (n = 155) hypertensive without diabetes (HND) with similar ages were enrolled. Blood samples for fasting lipid profile were collected and analyzed, and the following indices and ratios were calculated: (TC/high-density lipoprotein-cholesterol [HDL-C]), (low-density lipoprotein-cholesterol [LDL-C]/HDL-C), (HDL-C/LDL-C), and AIP. The indices were compared in both the participants and control group. **Results:** There was no significant difference in the clinical characteristics of HD compared to the HND except the systolic blood pressure, weight, and HDL-C which were lower in the HND group. The frequency of dyslipidemia was found to be significantly higher in the HD group except elevated LDL-C in males (25.8% vs. 17.4%, χ^2 = 0.055, respectively). Furthermore, all the lipid ratios, except (Castelli risk index II [CRI– II] were found to be significantly different among HD as compared to HND group (P = 0.002, P = 0.045, respectively). **Conclusions:** This study concludes that Nigerians with both type 2 diabetes and hypertension have worse dyslipidemia and abnormal lipid ratios compared to those with only hypertension.

Keywords: Atherogenic indices, cardiovascular risks, dyslipidemias, lipid ratios, type 2 diabetes

INTRODUCTION

Nigeria, as well as other developing countries, is faced with increasing prevalence of premature deaths due to noncommunicable diseases, with diabetes mellitus (DM) ranking third, only after cardiovascular diseases and cancers.[1] In patients with type 2 DM (T2DM), several important health indices are altered among which are fasting

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blood sugar, blood pressure, lipid profile, and immune response.[2-4]

In patients with type 2 DM, changes in plasma lipoproteins can be caused by the defects in insulin action and hyperglycemia. Lipid abnormalities (also termed dyslipidemia) are strongly associated with insulin resistance irrespective of adequate or inadequate glycemic control. Dyslipidemia is not common in T1DM but rampant among patients with impaired fasting glucose, impaired glucose tolerance, and T2DM.[5] Furthermore, trials have shown the benefits of tight glycemic control in preventing microvascular diabetic complications; however, these trials have not been able to show the beneficial effects of improved glycemic control on macrovascular diseases such as coronary arterial disease (CAD), stroke, and peripheral arterial disease.[6]

Dyslipidemias in type 2 diabetes and hypertension are both quantitative and qualitative.[7-9] Quantitative abnormalities include increased levels of Plasma total cholesterol (TC), triglyceride (TG), and decreased level of high-density lipoprotein cholesterol (HDL-C). Qualitative abnormalities include changes in the composition of low density lipoprotein-cholesterol (LDL-C) (small dense LDL-cholesterol, increased TG content, and increased electronegativity of LDL-cholesterol). These changes make LDL-cholesterol susceptible to oxidation and glycation, with consequential foam cell formation, endothelial dysfunction, and atherosclerosis.[7,9]

Evaluating lipid profiles have in times past been limited to the estimation of the conventional lipid profiles–TG, LDL-C, HDL-C, and total cholesterol (TC). It has however been reported that these alone are inadequate to characterize lipid abnormalities as they could be apparently normal in some patients and yet these patients are still at risk of developing cardiovascular diseases.[10] This brought about the requirement of a new approach and has birthed the estimation of cardiovascular risk using other methods such as Castelli's Risk index–I (CRI–I), Castelli's Risk Index–II (CRI–II), atherogenic co-efficient (AC), CHOL Index, and the atherogenic index of Plasma (AIP) which has all been shown to be useful and effective in otherwise conditions.[11-14]

Hence, this present study evaluated the extent of the alteration of lipid profiles in hypertensive-diabetics (HD) patients as compared to hypertensive nondiabetic (HND) participants. It also investigated the extent of the alteration of these new novel indices and ratios to determine the extent to which HD Nigerians are at risk of developing cardiovascular diseases compared to their HND counterparts.

MATERIALS AND METHODS

Study design

This was a hospital-based case–control study conducted at the outpatient clinic of the Endocrinology and Diabetes Unit of LAUTECH Teaching Hospital, Ogbomoso, Nigeria. Data were conducted over a 6-month period from March to July 2017.

Study setting

The study setting was LAUTECH teaching hospital, Ogbomoso, in Ogbomoso North Local Government Area, Oyo State. The hospital which was established as a tertiary hospital in 2011, runs both inpatient and outpatient services. In addition, the hospital also operates a diabetes clinic manned by endocrinologists on Tuesdays.

Study population

The study population consists of 210 HD patients who were recruited consecutively from the outpatient clinic of the Endocrinology and Diabetes Unit of LAUTECH Teaching Hospital, Ogbomoso, Nigeria. One hundred and fifty-five (n = 155) apparently healthy age-matched participants having no history of DM but with hypertension were consecutively recruited into the study from the general outpatient clinic of the hospital. Only patients who attended the hospital during the study period were included in the study. Both sample sizes for the cases and control were determined as a nonprobability convenience method. Patients with type 1 diabetes, those on cholesterol lowering drugs, and those with significant history of alcohol consumption were excluded from the study. Also excluded were individuals with chronic liver disease, heart failure, or on cancer diagnosis/treatment.

Data and blood sample collection

A questionnaire was administered to obtain basic sociodemographic and clinical information. Anthropometric information was obtained using a portable stadiometer for the measurement of height to the nearest 0.1 cm and a portable weighing scale was used to measure weight to the nearest 0.1 kg. Other clinical parameters such as blood pressure were also measured using the standard guidelines. A blood sample was taken from each patient after at least 8 h overnight fast for lipid profile analysis – total cholesterol (TC),

LDL-C, HDL-C, and TG. The fasting serum sample was analyzed using the Randox laboratories lipid profile kits (United Kingdom) at the chemical pathology department of LAUTECH Teaching Hospital, Ogbomoso.

Informed consent was obtained from all participants, and the study was approved by the Ethics and Research Committee of the institution. All the procedures have been carried out as per the guidelines given in Declaration of Helsinki 2013.

Lipids, atherogenic index, and lipid ratio evaluation

Lipid abnormality (dyslipidemia) was defined as abnormality in at least one of the following lipid profiles; raised TG level ≥1.7 mmol/L, LDL-C ≥2.6 mmol/L, reduced HDL-Cholesterol <1.03 mmol/L in males and <1.30 mmol/L in females and TC level ≥5.2 mmol/L (200 mg/dL).[15]

The following indices and lipid ratios were calculated using the following established formulas.[13,16]

1. $$AIP = \text{Log}\left(\frac{TG}{HDLc}\right)$$
2. $$\text{Castelli risk index} - \text{I}(\text{CRI} - \text{I}) = \frac{TC}{HDLc}$$
3. $$\text{Castelli risk index} - \text{II}(\text{CRI} - \text{II}) = \frac{LDLc}{HDLc}$$
4. $$\text{Atherogenic co-efficient}(AC) = \frac{TC - HDLc}{HDLc}$$
5. $$\text{CHOLIndex} = LDL_c - HDL_c \ (TG < 400)$$
$$= LDL_c - HDL_c + 1/5TG \quad (TG > 400)$$

The following are the abnormal values of AIP, lipid ratios, and CHOL Index for cardiovascular risk: AIP >0.1, CRI–I >3.5 in males and >3.0 in females, CRI–II >3.3, AC >3.0 and CHOLIndex >2.07.[12,13,17,18]

Statistical analysis

This was performed using the SPSS software version 20.0 (SPSS, Chicago, Illinois, USA). Data were analyzed as mean ± standard deviation or mean ± standard error of the mean and proportion (percentages) for the continuous and categorical variables, respectively. The comparison between the groups was done using the Student's *t*-test and Chi-square for continuous and categorical variables, respectively. A logistic regression was used to determine the predictors of abnormal lipid ratio among the participants. $P < 0.05$ was considered statistically significant. Clustered bar chats were also used to present the categorical variables.

RESULTS

The demographic and clinical characteristics of the two study groups are presented in Table 1. The study comprised of 365 individuals aged between 18 and 88 years and of two groups (210 HD and 155 HND individuals). The HD group (cases) had 97 male and 113 female participants whereas the HND (control group) had 69 male and 86 female participants. There was no significant sex difference between the two groups ($P = 0.751$). However, there were significant differences in all the parameters between the two groups except for age and systolic blood pressure (SBP) where the differences were not significant for in males and females ($P = 0.491$ and $P = 0.971$, respectively).

Table 2 shows the prevalence of dyslipidemia between the two groups. The most common lipid abnormality was low HDL-C in both groups, its prevalence was significantly higher in females who are HND and this difference was also significant in males (65 vs. 73; $P \leq 0.001$, 35 vs. 37; $P = 0.018$) [Table 3]. Elevated LDL followed the same trend being the most prevalent lipid;

Table 1: The demographic and clinical characteristics of the population

Variable	Hypertensive Diabetic (Mean±SD)			Hypertensive Non–Diabetic (Mean±SD)			P†
	Male (*n*=97)	Female (*n*=113)	Total	Male (*n*=69)	Female (*n*=86)	Total	
Age (yrs)	60.44±13.93	58.13±14.29	59.20±14.14	59.48±16.24	56.99±16.42	58.10±16.33	0.491
SBP (mmHg)	137.72±28.03	142.33±30.08	140.21±29.18	144.45±31.42	137.01±25.75	140.32±28.56	0.971
DBP (mmHg)	83.64±13.58	82.42±13.96	82.98±13.77	81.19±16.26	78.81±12.91	79.87±14.50	0.038*
Weight (Kg)	71.03±15.60	66.69±16.37	68.69±16.13	59.93±12.43	56.70±10.56	58.14±11.50	<0.001*
WC (cm)	90.30±13.57	93.33±13.22	91.95±13.43	82.79±15.95	84.29±11.02	83.62±13.42	<0.001*
BMI (kg/m²)	25.74±5.62	26.66±6.45	26.23±6.08	23.47±7.93	23.44±5.98	23.45±6.89	<0.001*
TC (mmol/L)	3.79±1.37	3.96±1.39	3.88±1.38	3.15±1.08	3.12±0.95	3.13±1.01	<0.001*
HDL (mmol/L)	1.24±0.56	1.27±0.66	1.26±0.61	1.10±0.57	0.96±0.38	1.02±0.48	<0.001*
LDL (mmol/L)	2.07±1.06	2.29±1.21	2.19±1.14	1.93±1.45	1.84±1.02	1.88±1.23	0.013*
TG (mmol/L)	1.19±0.92	1.11±0.64	1.15±0.78	0.75±0.32	0.83±0.63	0.79±0.52	<0.001*

*†P – value for comparison between the total values for diabetic group and the control group BMI = Body Mass Index, WC = Waist circumference, SBP = Systolic Blood Pressure, DBP = Diastolic Blood Pressure, TC = Total Cholesterol, HDL-C = High density lipoprotein-Cholesterol, LDL-C = Low density lipoprotein-Cholesterol, TG = Triglycerides. *Statistical Significant*

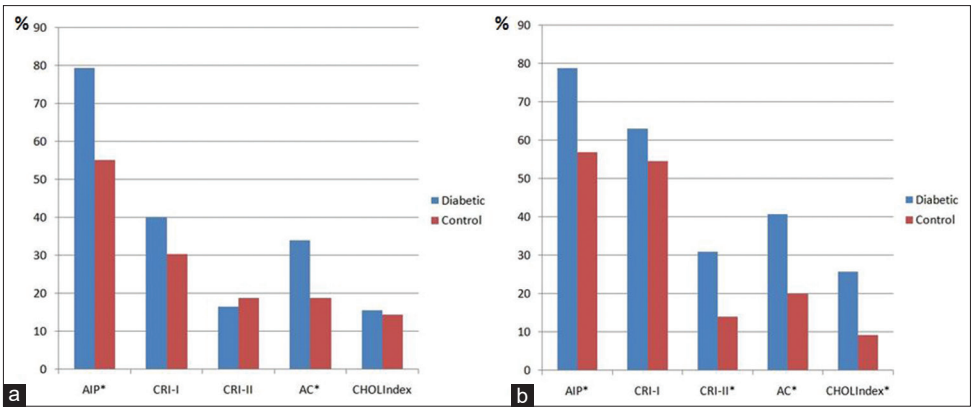

Figure 1: The prevalence and distribution of abnormal lipid indices and ratios in (a) males and (b) females

Table 2: Comparison of lipid parameters of diabetic patients and healthy control subjects according to genders

Variable	Male			Female		
	HD (*n*=97)	HND (*n*=69)	*P*	HD (*n*=113)	HND (*n*=86)	*P*
Elevated TC *n*(%)	14 (14.4)	3 (4.3)	0.028*	23 (20.4)	5 (5.8)	0.002*
Low HDL *n*(%)	35 (36.1)	37 (53.6)	0.018*	65 (57.5)	73 (84.9)	<0.001*
Elevated LDL *n*(%)	25 (25.8)	12 (17.4)	0.138	42 (37.2)	13 (15.1)	<0.001*
Elevated TG *n*(%)	20 (20.6)	0 (0)	<0.001*	19 (16.8)	6 (7.0)	0.029*

HD = Hypertensive Diabetic, HND = Hypertensive Non-Diabetic, TC = Total Cholesterol, HDL-C = High density lipoprotein-Cholesterol, LDL-C = Low density lipoprotein-Cholesterol, TG = Triglycerides. *Statistical Significant

Table 3: Comparison of different lipid ratios and atherogenic index of plasma (AIP) between diabetic and non-diabetic patients according to gender

Variable	Male (mean±SEM)			Female (mean±SEM)		
	HD	HND	*P*	HD	HND	*P*
AIP	0.35±0.03	0.12±0.03	<0.001*	0.39±0.03	0.15±0.03	<0.001*
CRI – I	3.78±0.22	3.44±0.26	0.003*	4.48±0.26	3.41±0.19	0.003*
CRI – II	2.24±0.19	2.38±0.28	0.093	2.90±0.22	2.10±0.19	0.093
AC	2.78±0.22	2.44±0.26	0.003*	3.48±0.26	2.41±0.19	0.003*
CHOLIndex	0.84±0.13	0.72±0.19	0.007*	1.15±0.13	0.54±0.11	0.007*

*HD = Hypertensive Diabetic, HND = Hypertensive Non-Diabetic, AIP = Atherogenic Index of Plasma, CRI - I = Castelli's Risk Index I, CRI - II = Castelli's Risk Index II, AC = Atherogenic coefficient. *Statistical Significant*

elevated TC and TG were significantly higher in the HD individuals than in the HND individuals.

All the lipid ratios except CRI-II were significantly higher in the HD than in the HND individuals, ($P \leq 0.001$). The frequency of abnormal AIP, CRI–I, and CHOLIndex is as shown in Figure 1. There was weak positive correlation between waist circumference and all plasma lipids; between body mass index (BMI) and all plasma lipids except HDL-C; and between diastolic blood pressure (DBP) and LDL-C, respectively. Furthermore, there was weak positive correlation between waist circumference and all the atherogenic indices as well as between BMI and AIP, but weak negative correlation between age and CRI-II [Table 4].

A logistic regression analysis of age, sex, systolic and DBP, waist circumference, and BMI with each of the serum lipid measure as the dependent variable returned diabetes as an independent predictor of abnormal concentrations of all the plasma lipids except HDL-C. Other independent predictors of abnormal plasma lipids included older age, higher BMI and waist circumference, higher SBP, and DBP. The male sex independently predicted lower HDL-C.

With multivariate logistic regression analysis, diabetes independently predicted abnormalities of all the atherogenic indices except CRI-I which had male sex as its only independent predictor. Other identified independent predictors of atherogenic indices include waist circumference, age, and DBP [Table 5].

DISCUSSION

The results revealed a generally higher lipid abnormality in the HD as compared to HND group, although females

in both groups had more dyslipidemia than their male counterpart. Using the conventional lipid profiles, low HDL-C was the most common lipid profile abnormality in our study, and this has been reported to be the most important lipid in cardio-protection which should be kept as high as possible, especially in women.[19,20] Furthermore, evidences are emerging suggesting that all the lipid profile components are independently atherogenic.[21]

Table 4: Correlation between Plasma lipids, atherogenic indices and potential correlates

???	???	Age	SBP	DBP	WC	BMI
Total Cholesterol	*r*	0.062	-0.005	0.023	0.223**	0.204**
	p	0.238	0.917	0.666	0.000	0.000
LDL-Cholesterol	*r*	0.050	0.044	0.160**	0.110*	0.154**
	p	0.338	0.401	0.002	0.040	0.003
HDL-Cholesterol	*r*	-0.050	-0.027	-0.026	0.129*	0.078
	p	0.344	0.610	0.620	0.016	0.138
Triglycerides	*r*	0.023	0.001	0.046	0.192**	0.185**
	p	0.664	0.989	0.383	0.000	0.000
AIP	*r*	-0.024	0.013	0.017	0.253**	0.175**
	p	0.655	0.801	0.749	0.000	0.001
CRI – I	*r*	-0.094	-0.006	-0.053	0.144**	0.079
	p	0.074	0.910	0.312	0.007	0.133
CRI – II	*r*	-0.133*	-0.009	-0.045	0.107*	0.046
	p	0.011	0.865	0.391	0.046	0.381
AC	*r*	-0.094	-0.006	-0.053	0.144**	0.079
	p	0.074	0.910	0.312	0.007	0.133
CHOLIndex	*r*	-0.098	-0.020	-0.040	0.117*	0.042
	p	0.062	0.699	0.448	0.029	0.429

TC=Total Cholesterol, HDL-C=High density lipoprotein-Cholesterol, LDL-C=Low density lipoprotein-Cholesterol, TG=Triglycerides AIP=Atherogenic Index of Plasma, CRI – I=Castelli's Risk Index I, CRI – II=Castelli's Risk Index II, AC=Atherogenic coefficient. *Significant at 95% Confidence level. **Significant at 99% Confidence level

The present study showed that the difference in most of the lipid profiles and lipid ratios of the HD and HND were statistically significant. These findings are consistent with previous studies which suggest that lipid abnormalities are higher in diabetics than nondiabetic participants.[22,23] The results also showed gender differences in lipid profiles concentration among the two groups with the lipid values higher in the females as compared to the males. In this study, the mean TC concentrations were 3.38 mmol/L and 3.18 mmol/L among HD females and males, respectively. These values are lower than those reported by Onyemelukwe and Stafford[24] in persons with type 2 diabetes and those reported by Khandekar *et al*.[25] Compared with HNDs, HDs had higher levels of lipid types considered as atherogenic (TC and LDL-C) and reduction of those considered as anti-atherogenic (HDL-C). These may be related to addictive effect in some of the parameters in the HDs, resulting in substantial increase in the total and other lipid values. Epidemiological studies have shown that hypertension and diabetes are the independent risk factors for the development of CAD and that the risk of CAD is increased in participants with both diabetes and hypertension.[26,27] Therefore, the occurrence of diabetes and hypertension may confer a worse outcome among these groups of Nigerians.

On the assessment of the lipid ratios, the findings in this study showed that AIP was significantly higher among

Table 5: Logistic regression of the predictors of Plasma lipids and atherogenic indices

Outcome Variable	Independent variable	Odds ratio	95% CI	*P*
Total Cholesterol	Age	1.033	1.006 - 1.062	0.018
	Diabetes	0.353	0.150-0.831	0.017
	Waist circumference	1.035	1.005 - 1.065	0.021
	Body mass index	1.064	1.013 - 1.118	0.013
HDL-Cholesterol	Male sex	0.299	0.187-0.479	<0.001
	Diabetes	2.356	1.435 - 3.869	0.001
LDL-Cholesterol	Age	0.979	0.962 - .997	0.025
	Systolic blood pressure	1.035	1.003 - 1.029	0.013
	Diastolic blood pressure	0.968	0.943-0.994	0.016
	Diabetes	0.392	0.223-0.691	0.001
Triglycerides	Diabetes	0.194	0.075-0.501	0.001
	Body mass index	1.066	1.012-1.123	0.016
AIP	Diabetes	0.408	0.246-0.676	<0.001
	Waist circumference	1.035	1.009 - 1.062	0.009
CRI – I	Male sex	0.366	0.233-0.575	<0.001
CRI – II	Age	0.967	0.948-0.986	0.001
	Diabetes	0.535	0.297-0.984	0.037
	Diastolic blood pressure	0.972	0.945 - 1.000	0.052
AC	Age	0.980	0.964-0.997	0.023
	Diabetes	0.980	0.964-0.997	0.001
CHOLIndex	Diabetes	0.508	0.267 - 967	0.039

TC = Total Cholesterol, HDL-C = High density lipoprotein-Cholesterol, LDL-C = Low density lipoprotein-Cholesterol, TG = Triglycerides
AIP = Atherogenic Index of Plasma, CRI – I = Castelli's Risk Index I, CRI – II = Castelli's Risk Index II, AC = Atherogenic coefficient
CI = confidence interval

HDs compared with HNDs ($P < 0.001$). Studies have shown that the ratio of TG to HDL-C, which is an inverse relationship, is a strong predictor of acute myocardial infarction,[28] and AIP value above 0.24 is associated with high cardiovascular risk.[17] This finding was similar to elevated AIP value obtained among angiograhically confirmed patients with CAD among Indian population as compared to non-CAD individuals.[9] Studies have shown that in situations where other atherogenic parameters such as TG and HDL-C appears apparently normal, AIP may be used as diagnostic alternative[29] and also used to predict cardiovascular risk and monitoring of therapy of effectiveness.[30]

Castelli's risk ratio (CR1), (also called cardiac risk ratio, or atherogenic ratio) and Castelli's risk ratio-II (CRI-II) were both found to be higher in HDs as compared to HNDs, although CRI-II was not statistically significantly higher. We observed CRI-I in our HD females was >4 which is consistent with other studies,[23] but <4 among hypertensive males; Onyemelukwe and Stafford[24] reported an atherogenic ratio of 4.4 in type 2 diabetics in Nigeria. This CRI-I calculated as TC/HDL-C ratio is associated with coronary plaques formation.[31] However in our study, CRI-II was found to be below the upper limit for normal range of <3 as observed in other studies.[32,33]

The CHOLIndex, which is a relatively new index has been adjudged to be the most sensitive in CV risk assessment, as it better predict cardiovascular disease occurrence,[13] is found to be relatively higher in the HD group compared to participants with hypertension but without diabetes. This CHOLIndex together with AIP, CRI–I, and AC was significantly different among the diabetics as compared to those without diabetes but had hypertension.

On performing regression analyses, we found diabetes as an independent predictor of abnormal concentration of lipids, further supporting the fact that diabetes is a disease with increased risk of cardiovascular disease and worsens cardiovascular risks among hypertensives.

Limitation

This is a cross-sectional study highlighting the fact that the lipid profile and other atherogenic indices are significantly elevated among type 2 diabetics with hypertension as compared to those with only hypertension but no diabetes. However, this study did not go further to relate the elevated indices to worse cardiovascular outcomes which can only be shown in a longitudinal/prospective study. In addition, it was a hospital-based study so might not provide the true reflection of the magnitude of this comparison in the immediate community.

CONCLUSIONS

This study concludes that Nigerians with both type 2 diabetes and hypertension have worse dyslipidemia and abnormal lipid ratios compared to those with only hypertension. This is due to the fact that both hypertension and type 2 diabetes are independently associated with elevated atherogenic lipids and reduction of anti-atherogenic lipid. Hence, HDs may be at particularly high risk of CAD and other atherosclerosis-associated morbidity and mortality because of their addictive effects. Therefore, such patients need to be closely evaluated, monitored and clinically scrutinised as a means of primary preventive measure against lipid-related morbidity and mortality. Furthermore, lipid ratios such as AIP, CRI, and AC could be used for identifying individuals at increased risk of CV disease in the clinical setting among the Nigerian population especially when individual lipid profile component seem apparently normal.

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Conflicts of interest

There are no conflicts of interest.

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