PATTERN OF DYSLIPIDAEMIA AMONG NIGERIANS WITH TYPE 2 DIABETES MELLITUS

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ABSTRACT

Objective: To characterize the pattern of lipid profile abnormalities among Nigerians with type 2 diabetes mellitus attending the Diabetes clinic of a tertiary referral centre in Nigeria.

Method: A cross sectional analysis of 192 diabetic patients consecutively recruited from patients attending the Diabetes clinic and 52 volunteering non-diabetic and non-hypertensive controls was undertaken. The main outcome measures were lipid profile and anthropometric indices. Data analysis was done with SPSS version 10. Results were expressed as mean $\pm$ SD. Differences between groups were regarded as significant at $p < 0.05$. Comparisons of means, test of association were done using independent t-test, chi-square test and bivariate (Pearson's) correlation analysis.

Results: Eighty-nine percent of the patients had at least one abnormal lipid profile while 64.5% had combined dyslipidaemia. Reduced HDL-C and raised TG constituted the most (88.0%) and least (25.0%) prevalent abnormalities respectively. Significant difference in the mean values of HDL-C and LDL-C was observed between the patients and controls.

Conclusion: Dyslipidaemia is common among patients with type 2 diabetes mellitus in Nigeria with majority of the patients having a combined dyslipidaemia. There is therefore the need to pay great attention to the lipid parameters in Nigerians with type 2 diabetes mellitus.

Abbreviations: TG Triglycerides, TC total cholesterol, LDL-C Low Density Lipoprotein Cholesterol, HDL-C High Density Lipoprotein Cholesterol, WC Waist circumference, HC Hip circumference, BMI Body mass index, WHR Waist-hip ratio.

INTRODUCTION

Type 2 diabetes mellitus is commonly associated with a cluster of abnormal lipid profiles which are known to be atherogenic. Dyslipidaemia is a well recognized and modifiable risk factor for cardiovascular diseases which is currently a leading cause of morbidity and mortality world wide in both developed and developing regions including Africa.[1] Among other disorders, it is one of the defining factors or criteria for the metabolic syndrome [2] and it is associated with obesity most especially the visceral type; also a defining criterion for metabolic syndrome. Currently, environmental adaptations and changes in lifestyle are known to be responsible for the rise in the prevalence of obesity being witnessed in most parts of the world. These changes are related to increasing sedentary lifestyle and physical inactivity ('westernisation').Developing nations are currently witnessing rapid urbanisation, industrialisation as well as increased economic capabilities; which has the propensity of leading to abnormal weight gain and development of various complication of obesity. Obesity has been linked with lipid abnormalities in Africans.[3] In Nigeria, hypertension and diabetes mellitus were noted to occur in 10-15% and 2-4% of the population respectively.[4] Diabetes and hypertension however are known to frequently co-exist though they are independent risk factors for dyslipidaemia. The frequency of hypertension among diabetic patients in Nigeria is between 20 40%.[5]

Several combinations of abnormal lipid parameters have been noted [6,7,8], but the combination of raised triglycerides, low high-density lipoprotein, apo-B,

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small dense low density lipoprotein particles characterizes diabetic dyslipidaemia. Each of these abnormalities is however, independently atherogenic.[7] The very high risk of atherogenicity associated with the small dense LDL particles has resulted in emphasis on ensuring that LDL-C is within the therapeutic goal in management of dyslipidaemia in diabetic patients. In China, typical diabetic dyslipidaemia was reported by Ko GT et al.[9] Other patterns such as elevated TG and low HDL-C as well as significant proportion of quantitative dyslipidaemia especially with the Total--and LDL-cholesterols have been observed in Kuwait [7] and Nairobi [10] respectively.

In this report, we analysed the pattern of dyslipidaemia among adult diabetic patients attending the out-patient diabetes clinic of a tertiary hospital in Nigeria.

PATIENTS AND METHODS

A cross-sectional survey of 192 type 2 diabetic patients (83 males, 109 females) in attendance at the diabetic clinic of the Lagos University Teaching Hospital (LUTH) and 52 non-diabetic controls was undertaken. LUTH is one of the premier tertiary hospitals in Nigeria. It is located in lagos, Western Nigeria, the former capital of Nigeria and a well known commercial nerve centre in the country.

Consenting adult type 2 diabetic patients (diabetic patients who were being managed on oral hypoglycaemic agents or insulin as a result of secondary failure of oral hypoglycaemic agents) were consecutively recruited. Patients who failed to give informed consent or who were on lipid lowering drugs were excluded. Fifty-two non-diabetic and nonhypertensive controls were also recruited for the study.

Diagnosis of diabetes mellitus in new patients was based on the diagnostic guidelines according to American diabetes association (ADA) [11] while dyslipidaemia was defined using the National Cholesterol Education Programme (NCEP-ATP III) criteria as follows: TC > 5.2 mmol/l, LDL-C > 3.4 mmol/l, HDL-C < 1.03 mmol/l for males, < 1.3 mmol/l for females and TG > 2.3 mmol/l [12] . Hypertension was considered present if a patient had been a known hypertensive and / or is on antihypertensive medication(s) or have taken such medications in the past having been prescribed by a doctor.

Blood pressure readings were based on the JNC VI classification and guidelines.[13] Waist and hip circumferences were determined using a flexible tape with subjects putting on light clothing only and in the standing position.

Waist circumference was measured at the midpoint between the costal angles and the iliac crests while hip circumference was measured at the level of the greater trochanters.

Lipid profiles: Fasting venous blood sample drawn from the subjects after adequate disinfection of the skin over the venepuncture site, was separated to obtain plasma which was then stored frozen until analysed. Samples were analysed within forty-eight hours after collection. Total cholesterol was determined using the ferric perchlorate method [14] while HDL-C was determined after precipitation of LDL-C with phosphotungstate and magnesium.[15] LDL-C was calculated from Friedwald's formula: LDL-C = TC HDL-C (TG/5) [16]

TG was measured using the colourimetric enzymatic method [17]

Assessment of glycaemic and blood pressure control was based on average of the readings from consecutive visits which included last visit before recruitment, day of recruitment and the next visit after recruitment.

Statistical analysis;

Data analysis was done using SPSS v 10. Results were expressed as mean ± SD where necessary. Comparisons of means, test of association were done using independent t-test, and chi-square test. Bivariate correlation was performed using Pearson's correlation coefficient. $p < 0.05$ was regarded as statistically significant.

RESULTS

A total of 244 subjects (192 patients and 52 controls) were studied. Gender distribution were as follows: 83 male (41.2%) and 109 female (56.8%) patients and 25 male (48.1%) and 27 female (51.9%) controls. They were aged 55.4 ± 11.3 yrs and 46.3 ± 11.9 yrs respectively (p<0.001) with a range of 27 to 84 years. 99 patients (51.7%) had a co-existing hypertension. Mean duration of illness was 7.6 ± 6.9 years. Control of diabetes and / or hypertension was good in only 33.3% of the patients (37 out of 111 patients). 61.3% had both poor control and dyslipidaemia. Some clinical and biochemical characteristics (mean ± SD) of the patients and control groups are shown in table 1 Mean values of lipid profiles were higher in the patients than controls. LDL-C and HDL-C were significantly higher and lower respectively. No significant differences were observed for the others. The patients also had significantly higher BMI than the controls. Similar differences were also noted in both the WC and WHR though it is to be noted that gender-specific cut-off levels are recommended for use in identifying individuals with central obesity.

Table 1. **Clinical and biochemical characteristics (mean ± SD) of the Subjects**

Characteristics	Patients (n = 192)			Controls (n = 52)	p value*
	Total (n=192)	Diabetes only (n = 93)	Diabetes and hypertension (n= 99)		
Age (yrs)	55.4±11.3	51.0±11.1	59.5± 9.9	46.3 ± 11.9	<0.001
Height (m)	1.64±0.09	1.65±0.09	1.64 ± 0.09	1.68 ± 0.09	< 0.05
Weight (kg)	77.6±14.6	77.0±15.0	78.1 ± 14.3	77.0 ± 13.0	>0.05
BMI (kg/m2)	28.7 ± 5.2	28.3 ± 5.3	29.1 ± 5.1	27.2 ± 3.8	< 0.05
Waist circumference (cm)	97.6±12.5	95.4±12.4	99.6 ± 12.2	91.8 ± 13.0	< 0.01
Hip circumference (cm)	105.2±11.1	105.2±11.4	105.3 ± 10.9	103.7±13.7	>0.05
WHR	0.91 ±0.13	0.89 ± 0.11	0.93 ± 0.14	0.86 ± 0.17	< 0.05
Total cholesterol (mmol/l)	5.57 ± 1.57	5.42 ± 1.27	5.70 ± 1.80	5.23±0.95	>0.05
LDL-C (mmol/l)	3.88 ± 1.45	3.83 ± 1.22	3.92 ± 1.64	3.48±0.94	< 0.05
HDL-C (mmol/l)	1.11 ± 0.47	1.12 ± 0.54	1.09 ± 0.39	1.25 ± 0.38	< 0.05
TG (mmol/l)	1.38 ± 0.77	1.37 ± 0.79	1.40 ± 0.75	1.27±0.46	>0.05

* - p value between patients and control subjects

Out of the 207 subjects with dyslipidaemia (i.e at least one abnormal lipid profile), 171 (82.6%) were patients while 36 (17.4%) were controls ($\chi^2 = 12.5$, df = 1, p < 0.001). The prevalence of dyslipidaemia among the patients was 89.1%. The mean values of the lipid profiles were significantly higher among the patients who had dyslipidaemia except for TG which was within the recommended value.

Figure. 1. **Distribution of lipid profile among the patients**
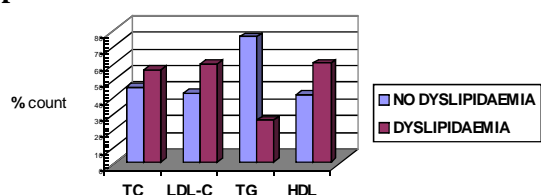
Dyslipidaemia was noted with each of the TC, LDL-C, HDL-C and TG as shown in figure 1. Reduced HDL-C constituted the highest single abnormality (59.4%) followed by elevated LDL-C (58.9%), TC (55.2%) and TG (25.0%).

Abnormalities in the lipid profile ranged from single to multiple abnormalities (fig 2). The two patients who had abnormalities in all the lipid profiles were both females. Obesity was common among the patients with dyslipidaemia. 88.3% of the patients with dyslipidaemia were obese

Table 2. **Mean Lipid Profiles Of Patients With And Without Dyslipidaemia (mean ± Sd) In Mmol/.**

Lipid Profile (Mmol/l)	No Dyslipidaemia (n=21)	Dyslipidaemia (n=171)	p value
TC	4.24±0.76	5.73±1.58	<0.001
HDL-C	1.41±0.53	1.07±0.445	0.01
LDL-C	2.49±0.54	4.05±1.44	<0.001
TG	1.25±0.48	1.40±0.80	>0.05

Figure 2. **Proportion of Single And Combined Dyslipidaemia**
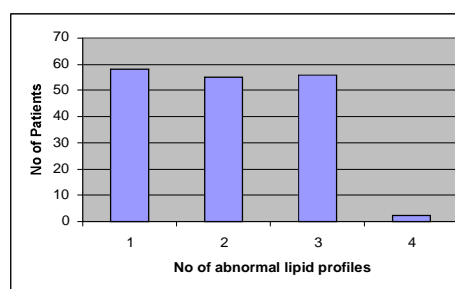
or overweight (using all the anthropometric indices which include: WC, WHR and BMI). There was no significant association between obesity and dyslipidaemia (χ^2 [with Yate's correction] = 0.349, df =1, p = 0.56). Out of 171 patients who were obese,

104 (60.8%) were females, while 67 (39.2%) were males. There was a significant association between obesity and gender ($\chi^2 = 10.4$, df = 1, p = 0.001)

The proportion of patients identified as being either overweight or obese is as shown in table 3.

Table 3. **Proportion of Patients Identified As Obese or Overweight Using The Anthropometric Indices of Obesity**

	WC(cm)	WHR	BMI(kg/m²)
Males	41.0%	48.2%	27.7%
Females	80.0%	83.5%	42.2%

All the measures of obesity identified greater number of female patients as being obese (table 3). Among both gender, waist to hip ratio (WHR) identified the highest (males = 48.2%; females = 83.5%) while body mass index (BMI) identified the least (males = 27.7%; females = 42.2%) proportions of obese patients.

The strengths and directions of association between the various lipid profiles, and / or anthropometric indices, which ranged from weak to strong, are shown in the correlation matrix (table 4). Generally, correlations were strong, positive, and significant between variables that measured similar attributes. For instance, LDL-C was strongly positive, and significantly correlated with TC while it was very weakly correlated with WC and WHR whereas the value of correlation coefficient between BMI and WC was also high and in the positive direction.

DISCUSSION

Dyslipidaemia was found to be highly prevalent (82.6%) among the subjects who participated in this study. This was relatively higher (89.1%) among the patients. This is similar to the observation that was made in South Africa where a prevalence of 90.3% was reported. [8] Our result appeared relatively higher than 60.4% earlier reported in Nigeria by Agbola-Abu et al [6]; a study that was done among subjects of high socioeconomic class. Though we did not classify our subjects based on socioeconomic class, our study suggests an increasing prevalence of dyslipidaemia considering the mixed nature of patients who attend the tertiary health care facilities in Nigeria. This difference also may be attributed to the underlying disease process in our patients i.e diabetes and hypertension. Diabetes mellitus has been associated with abnormal lipid profiles [7,9,10] and the presence of diabetes either alone or in co-existence with hypertension as in this study was significantly associated with dyslipidaemia. This may not be unrelated to insulin resistance which has been closely associated with diabetes dyslipidaemia, and hypertension.[18] Increasing urbanization is another factor that may explain the very high prevalence of dyslipidaemia in this study

Table 4. **Pearson's correlation coefficient (r) between the various anthropometric and biochemical variables**

	TC	LDL	HDL	TG	WC	HC	BMI
LDL	0.832**						
HDL	0.145*	-0.026					
TG	0.323**	0.120	0.123				
WC	0.035	0.010	0.074	0.172*			
HC	0.024	-0.003	0.029	0.090	0.757**		
BMI	-0.016	-0.040	0.075	0.065	0.713**	0.761**	
WHR	0.054	0.046	0.049	0.130	0.323**	-0.018	0.144*

* p < 0.05; ** p < 0.01

Increasing urbanization has been observed to be associated with modernization of lifestyle which is largely characterised by physical inactivity, change in dietary pattern and consequently, development of obesity. [19] In the past few years, most of our urban cities have witnessed an increase in the number of fast food outlets as well as information technology revolution; both of which have greatly influenced our way of life. Several studies have previously documented the lipid pattern in adult Nigerians living in different urban centres. These generally showed low lipid values compared to Caucasian values. Mean total cholesterol as observed among the apparently healthy controls in our study (5.23 ± 0.95 mmol/L) was higher than that observed in earlier studies in healthy Nigerians reported in Lagos (3.54 ± 0.14 mmol/L) [20], Benin (4.82 ± 1.03mmol/L), [21] and Port Harcourt (4.76 ± 1.06 mmol/L). [22] There is paucity of studies on insulin resistance among healthy Nigerians; therefore whether insulin resistance which is associated with dyslipidaemia played any role in these subjects is

unknown. Abnormalities of weight gain due to excess fat (overweight / obesity) may explain the rise in total cholesterol and other abnormalities. Our patient and control subjects had high values of mean BMI (28.7 vs 27.2 kg/m^2 respectively); both in keeping with overweight. This is similar to 28.76 ± 5.91 kg/m^2 observed by Akpa et al in Port Harcourt among healthy adults. [22]

Age may also have accounted for some of the differences observed in these studies. Though our subjects had mean age that was within the middle age group, they were older and younger than those studied in Port Harcourt [22] and Benin [21] respectively. Ageing can lead to increased sedentary living, excessive food intake, and consequently obesity. It is also associated with reduced cholesterol metabolism and thus increased accumulation of lipids in the body.

The commonest abnormality noted was low HDL-C (59.4%) with TG being the least (25%). While a lower prevalence of hypertriglyceridaemia was equally reported among urban African Americans [23], these seemed to vary with the pattern of raised TG which is one of the abnormalities that most commonly characterizes diabetic dyslipidaemia. [24] The predominance of combined dyslipidaemia noted in this study is comparable to other studies. [6,7,8] It is an indication of its metabolic basis and will affect its management as different classes of drugs can be used in its treatment depending on the predominant abnormalities.Obesity is a known determinant of abnormal lipid profile. High prevalence of obesity has been associated with dyslipidaemia. [3,7,25]. Other determinants include female gender, urban dwelling or socioeconomic class, glycaemic control and ethnicity. [7] The high prevalence of overweight / obesity in this study showed that abnormalities of weight are not only common among diabetic patients but also among healthy Nigerians. [22] This could add to the other driving forces responsible for the increasing prevalence of cardiovascular risk factors. Central obesity has been shown to be the most pathogenically important in the aetiology of metabolic disorders. Measures of central obesity (WHR and WC) identified greater proportion of individuals with obesity compared to BMI which is a measure of generalized obesity. This finding is similar to the observation made by Bakari et al [26] among type 2 diabetic Hausa-Fulani Nigerians in which BMI suggested that obesity is not common in Nigerian diabetic patients when compared to waist to hip ratio. There is the need to determine the cut-off values of these indices of obesity in Nigerians in conformity with prevailing ethnic and racial differences that have been observed and highlighted

in the 2005 definition of the metabolic syndrome by the International Diabetes Federation (IDF). [27] The control of diabetes and hypertension was poor in our study (61.3%). This is similar to the findings of Eid et al. [28] in which poor control of both morbidities was present in over 70% of their study population. Possible reasons for this include: poor health seeking behaviours, low level of literacy, poverty, poor compliance and adherence with follow up visits and medications. Chronic disorders are also sometimes viewed more from a spiritual point of view in Africa; hence, the common practice of the use of alternative medicines such as roots and herbs. This may adversely affect interventional outcomes due to unproven efficacy of these agents and their effect on compliance with standard medications. Treatment of patients should be individualized in other to enhance compliance and adherence. Lifestyle modifications which can be preventive and use of appropriate pharmacological agents will yield better results. [29,30]

In conclusion, this study has shown that the prevalence of dyslipidaemia is high among type 2 diabetic patients in Nigeria and that it is associated with high prevalence of obesity and combined dyslipidaemia. These factors will no doubt predispose them to increased cardiovascular morbidity and mortality especially in the presence of small dense LDL particles. Intensive effort at lowering abnormal lipid profiles therefore should be focused on; employing both non-pharmacological and pharmacological means. A review of the current status of non-communicable diseases in Nigeria is therefore necessary.

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