IS HIGH DENSITY LIPOPROTEIN CHOLESTEROL USEFUL IN DIAGNOSIS OF METABOLIC SYNDROME IN NATIVE AFRICANS WITH TYPE 2 DIABETES?

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Background: High-density lipoprotein (HDL) hypocholesterolemia predicts metabolic syndrome among Caucasians and is one of the World Health Organization (WHO) diagnostic criteria of the syndrome. Plasma lipid levels are, however, influenced by genetic and environmental factors.

Objective: To determine the relationship between HDL cholesterol and metabolic syndrome among native Africans with type 2 diabetes.

Methods: Indigenous Nigerians with type 2 diabetes (N=254) aged 35–80 years (mean: 52.0 ± 11.7 years) with male:female ratio of 1.5:1 were studied prospectively. Outcome measures included anthropometric indices, plasma lipid concentrations, uric acid, microalbuminuria, and predictive values.

Results: Of the 254 diabetic patients, 150 (54.3%) had metabolic syndrome. Dyslipidemia occurred in 184 (72.4%) patients. Of these, 54 (29.4%) had HDL hypocholesterolemia. Mean HDL cholesterol among patients with HDL hypocolesterolemia and those with normocholesterolemia were 32.4 ± 5.7 mg/dL and 51.3 ± 9.9 mg/dL, respectively. Prevalence of metabolic syndrome did not differ significantly between the two groups (56% vs 70.4%; P=.08). Linear regression analysis showed no association between HDL cholesterol and metabolic syndrome (r=0.01; P=.2), body mass index (r= 0.02; P=.4), waist circumference (r=0.07; P=.42) and microalbuminuria (r=0.03; P=.8). A positive correlation occurred between HDL cholesterol and triglyceride concentrations (r=0.6). The sensitivity, specificity, and positive and negative predictive values of HDL hypocholesterolemia in the diagnosis of metabolic syndrome were 25%, 84.6%, 70.4%, and 44%, respectively.

Conclusion: High-density lipoprotein cholesterol may not be a reliable diagnostic tool of metabolic syndrome among native Africans with type 2 diabetes. (*Ethn Dis.* 2005;15:6–10)

Key Words: Africans, HDL-Cholesterol, Metabolic Syndrome, Predictive Values

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INTRODUCTION

Dyslipidemia is a component of metabolic syndrome, a clustered multifaceted metabolic disorder that also includes systemic hypertension, obesity, microalbuminuria, and hyperuricemia.[1] Its prevalence rate ranges from 13% to 33% among the general Caucasian general population[2,3] but could be as high as 70%-80% among persons with type 2 diabetes.[4,5] Metabolic syndrome is emerging as a leading cause of morbidity and mortality among Caucasians.[5,6] Insulin resistance and compensatory hyperinsulinemia are the underlying pivotal etiopathogenic factors of the syndrome.[1]

Insulin resistance causes enhanced alpha-adrenergic activities and deficiency of lipoprotein lipase, an insulin sensitive enzyme.[7] These result in quantitative and qualitative lipid abnormalities including hyperlipidemia (elevated plasma levels of total cholesterol, triglyceride, and low density lipoprotein [LDL] cholesterol), high density lipoprotein (HDL) hypocholesterolemia, changes in LDL cholesterol composition, and increased susceptibility of LDL to oxidation.[8] Of these lipid abnormalities, low HDL cholesterol and hypertriglyceridemia predict metabolic syndrome among Caucasians[9] and constitute part of the current World Health Organization (WHO) diagnostic criteria of the syndrome, which is defined as type 2 diabetes and any two of the following: obesity, hypertension, microalbuminuria, and dyslipidemia defined as HDL cholesterol <40 mg/dL (female) or <50 mg/dL (male) and triglyceride >150 mg/dL.[2] Insulin resistance is required for individuals with normal glucose tolerance.

Plasma lipid levels among patients with diabetes and hypertension are dependent on genetically determined insulin resistance and environmental factors, including calorie and fat intake and degree of physical activity. Africans tend to have plasma lipids different from Caucasians in both health and disease.[10,11] This study aims to determine the relationship between HDL cholesterol and metabolic syndrome among Africans with type 2 diabetes. It provides insight into the usefulness of HDL cholesterol level in diagnosing the syndrome in this population.

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METHODS

Patients

We recruited 278 indigenous Nigerians with diabetes mellitus seen between January and August 2002 at the medical outpatient and inpatient units of Usmanu Danfodiyo University Teaching Hospital, Sokoto, a tertiary institution with a catchment population of about 8 million in Northwestern Nigeria. Of these, 254 (91.4%) with type 2 diabetes mellitus were studied. The remaining 24 patients had type 1 diabetes and were excluded from the study. Mean age of patients was 52.0 ± 11.7 years (range: 35–80 years). Male:female ratio was 1.5:1.

This study aims to determine the relationship between HDL cholesterol and metabolic syndrome among Africans with type 2 diabetes.

Sociodemographic and Clinical Data

Sociodemographic and clinical data, including occupation, educational status, ischemic heart disease (evidenced by history of angina pain, myocardial infarction, and coronary artery surgery), family history of diabetes and hypertension, diet, alcohol consumption, and cigarette smoking were obtained with a questionnaire. Drinking 20 or more units of alcohol weekly and smoking 10 or more cigarettes daily constituted significant alcohol consumption and cigarette smoking.

Diabetes mellitus was diagnosed using WHO diagnostic criteria.[12] A patient diagnosed diabetic with no record of ketosis and on oral hypoglycemic drugs, diabetic diet, or both was considered to have type 2 diabetes. Blood pressure was measured in triplicate using the patient's non-dominant arm and after 10 minutes of rest. Systolic blood pressure (phase 1) $\geq$140 mm Hg, diastolic blood pressure (phase 5) $\geq$90 mm Hg,[13] or use of antihypertensive medications was required to diagnose systemic hypertension. Anthropometric indices, including weight, height, and waist circumferences, were measured with patients lightly clothed and without shoes. Body mass index $\geq$30 kg/m^2 and waist circumference $\geq$88 cm (females) or $\geq$102 cm (males) constituted obesity.[14,15] All patients had routine 12-lead electrocardiography to detect myocardial infarction.

Biochemical Data

About 10 mL fasting serum was drawn into heparinized bottles of fluoride oxalate and centrifuged at 100 rpm for 5 minutes. The supernatant was separated into appropriate containers for analysis. Samples were analyzed within 24 hours of collection or stored at 4°C. Fasting blood glucose was measured by glucose oxidase test.[16] Total plasma cholesterol was determined by using ferric per chlorate methods.[17] High-density lipoprotein cholesterol was determined after precipitation of low-density lipoprotein cholesterol with phosphotungstate and magnesium.[18] Triglyceride was measured by using the colorimetric enzymatic method.[19] Low-density lipoprotein cholesterol was calculated from the formula:

LDL cholesterol=Total cholesterol-HDL cholesterol-(Triglyceride/5)[20]

Plasma uric acid level was determined. A prepared laboratory standard for lipid analysis was used to ensure quality of specimens. Early morning urine specimen was obtained to determine microalbuminuria by using micral R test (Boehringer-Mannheim, Germany).

Patients with secondary hypertension or lipid altering diseases including, nephrotic syndrome, hepato-biliary disease, and hypothyroidism, and those taking lipid-lowering drugs were excluded from the study.

A type 2 diabetes patient was considered to have metabolic syndrome if he had any two of the following: hypertension, dyslipidemia (triglyceride>150 mg/dL or HDL-cholesterol<40 mg/dL), obesity, and microalbuminuria.[2]

Statistical Analysis

Data entry and analysis were done using a statistical software package (SPSS). Means are presented as values $\pm$ standard deviation. Patients with metabolic syndrome and those without were compared with regards to prevalence of HDL hypocholesterolemia by using chi-square test, while body mass index, waist circumference, HDL cholesterol, and triglyceride levels among the two groups were compared by using independent *t* test (two-tailed). Independent *t* test (two-tailed) was also used to compare body mass index, waist circumference, plasma triglyceride, and uric acid levels among diabetes patients with HDL hypocholesterolemia and those with HDL normocholesterolemia. The frequency of microalbuminuria in the two groups was compared by using chi-square test. Linear regression analysis was used to test the association between HDL cholesterol and metabolic syndrome, body mass index, waist circumference, and plasma triglyceride. The predictive values of HDL hypocholesterolemia in the diagnosis of metabolic syndrome were determined. A *P*-value $<$.05 was considered statistically significant.

RESULTS

Two hundred fifty-four (254) type 2 diabetes patients aged 52.0 $\pm$ 11.7 years (range: 35–80 years) with male:female ratio of 1.5:1 were studied. The baseline sociodemographic, clinical, and biochemical characteristics of patents are shown in Table 1. Though all (100%) adhered to traditional fiber-rich food choices (rice, millet, corn, and beans) as staples, 112 (44.1%) also consumed dairy products, animal fats, beef, lamb, eggs, soft drinks, and sweetened tea. All patients had daily activities that were physically demanding, though only 32% reported engaging in regular formal exercise.

The frequencies of individual components of metabolic syndrome were as follows: dyslipidemia 72.4% (*N*=184), hypertension 54.3% (*N*=138), obesity 42.5% (*N*=112), microalbuminuria 44.9% (*N*=114) and hyperuricemia 32.3% (*N*=82). Ischemic heart disease (myocardial infarction) occurred in 6

Table 1. Baseline characteristics of an African population with type 2 diabetes

Characteristics	Values *N* (%)
Gender	
Males	154 (60.6)
Females	100 (38.4)
Tribes	
Hausa and Fulani	188 (74.9)
Ibo	18 (7.1)
Yoruba	22 (8.7)
Others	26 (10.2)
Socioeconomic status	
Upper	50 (19.3)
Middle	60 (23.6)
Lower	144 (56.7)
Family history	
None	162 (63.7)
Diabetes (DM)	32 (12.6)
Hypertension (HBP)	32 (12.6)
HBP + DM	28 (11.)
Cigarette smoking	72 (26.3)
Alcohol consumption	34 (13.4)
Concurrent HBP and DM	138 (54.3)
	Means ± SD
Age (years)	52.0 ± 11.7
Duration of diagnosis of HBP (years)	6.1 ± 6.7
Duration of diagnosis of DM (years)	4.1 ± 4.4
Systolic blood pressure (mm Hg)	135.0 ± 21.1
Diastolic blood pressure (mm Hg)	83.1 ± 11.8
Body mass index (kg/m^2)	25.8 ± 6.1
Waist circumference (cm)	95.5 ± 6.2
Fasting blood sugar (mmol/L)	10.5 ± 5.4
Total cholesterol (mg/dL)	178.4 ± 28.4
High-density lipoprotein cholesterol (mg/dL)	47.3 ± 12.2
Triglyceride (mg/dL)	155.7 ± 42.2
Serum uric acid (mg/dL)	6.9 ± 2.4

(2.4%) patients. Of the 254 patients with diabetes, 150 (59.1%) had metabolic syndrome according to the WHO definition. Full-blown metabolic syndrome (types 2 diabetes mellitus, hypertension, obesity, dyslipidemia, and microalbuminuria) occurred in 52 (20.5%) patients. High-density lipoprotein hypocholesterolemia occurred in 54 (21.2%) of all patients with type 2 diabetes and 54 (29.4%) type 2 diabetes patients with dyslipidemia.

Compared with diabetes patients without metabolic syndrome, those with the syndrome had significantly higher body mass index (28.4 ± 5.6 vs 22.4 ± 3.6 kg/m^2; t=6.9; P=.00), waist circumference (100.2 ± 13.3 vs 87.5 ± 8.7 cm; t=6.0; P=.00), plasma triglyceride (169.2 ± 38.1 vs 135.2 ± 39.5 mg/dL; t=4.8; P=.00), total cholesterol (187.6 ± 28.2 vs 166 ± 24.1 mg/dL; t=4.4; P=.00) and uric acid (7.6 ± 2.2 vs 5.9 ± 2.3 mg/dL; t=4.0; P=.00). Microalbuminuria was also significantly more prevalent among diabetes patients with metabolic syndrome than those without (58.7 vs 15.4%; P=.000; odds ratio (OR)=10.37; 95% confidence interval (CI)=5.30–20.51). Mean HDL cholesterol was not significantly higher among diabetes patients with metabolic syndrome than those without (48.5 ± 12.7 mg/dL vs 45.5 ± 11.2 mg/dL; t=1.3; P=.2).

Mean HDL cholesterol levels among diabetes patients with HDL hypocholesterolemia and those with normal HDL cholesterol were 32.4 ± 5.7 mg/dL and 51.3 ± 9.9 mg/dL, respectively (t=9.5; P=.000). Diabetes patients with HDL hypocholesterolemia and those with normal HDL levels (Table 2) did not differ significantly in body mass index (26.5 ± 6.0 vs 25.8 ± 6.0 kg/m^2; t=0.5; P=.6), waist circumference (96.4 ± 14.1 vs 94.7 ± 13.0 cm; t=0.5; P=.6), uric acid (7.1 ± 2.4 vs 6.3 ± 2.1 mg/dL; t=1.5; P=.1), and prevalence of microalbuminuria (44.0% vs 48.2%; χ^2=0.03; P=.87) and metabolic syndrome (56% versus 70.4%; χ^2=3.06; P=.08). Compared to diabetes patients with HDL hypocholesterolemia, those with normal HDL had significantly higher plasma triglyceride (164.8 ± 38.2 vs 119.8 ± 32.2; t=5.5; P=.000) and total cholesterol (182.6 ± 28.0 vs 162.5 ± 24.5; t=3.4; P=.001). Linear regression analysis confirmed lack of association between HDL cholesterol and metabolic syndrome (r=0.01; F=1.8; P=.2), body mass index (r=0.02; F=0.9; P=.4), waist circumference (r=0.07; F=0.64; P=.42), and prevalence of microalbuminuria (r=0.03; F=0.09; P=.8). Positive correlations occurred between HDL cholesterol and triglyceride (r=0.6; F=14,04; P=.00).

This study shows that HDL cholesterol is generally high and unrelated to metabolic syndrome or its components among Nigerians with type 2 diabetes.

Of the 150 diabetes patients with metabolic syndrome, 38 were correctly identified using HDL hypocholesterolemia, giving a sensitivity of 25.3%. Of the 104 without metabolic syndrome, 88 had normal HDL and were correctly identified as not having the syndrome, giving a specificity of 84.4%. The positive and negative predictive values of HDL hypocholesterolemia were 70.4% and 44% respectively.

DISCUSSION

This study shows that HDL cholesterol is generally high and unrelated to metabolic syndrome or its components among Nigerians with type 2 diabetes. Though HDL hypocholesterolemia was reasonably specific in predicting metabolic syndrome, its sensitivity and negative predictive values were low. Ischemic heart disease is also a relative rarity in this population.

These findings vary from those found in Caucasians[2–5] but are consistent with previous reports on Africans with diabetes mellitus and systemic hypertension. A multicenter study established higher HDL cholesterol and lower levels of other plasma lipids among Africans than Caucasians in both health

Table 2. Comparison of type 2 diabetes patients with HDL hypocholesterolemia and normal HDL

Parameters	Patients with HDL Hypocholesterolemia (*N* = 54)	Patients with Normal HDL (*N* = 200)	*P* Value
	Mean ± SD	Mean ± SD*	
Age (years)	50.2 ± 12.2	52.5 ± 11.5	.36
Duration of diagnosis of diabetes mellitus (DM) (years)	4.0 ± 4.6	4.1 ± 4.4	.93
Systolic blood pressure (BP) (mm Hg)	130.4 ± 17.8	136.2 ± 22.0	.20
Diastolic BP (mm Hg)	80.4 ± 9.2	83.8 ± 12.3	.20
Body mass index (kg/m^2)	26.5 ± 6.0	25.8 ± 5.7	.60
Waist circumference (cm)	94.7 ± 13.0	96.4 ± 14.1	.60
Fasting blood sugar (mmol/L)	8.7 ± 4.0	10.9 ± 5.7	.05
Total cholesterol (TC) (mg%)	162.5 ± 24.5	182.6 ± 28.0	.00
HDL cholesterol (mg%)	32.4 ± 5.7	51.3 ± 9.9	.00
LDL cholesterol (mg%)	95.5 ± 19.4	108.7 ± 21.2	.00
Triglyceride (mg%)	119.8 ± 32.2	164.8 ± 8.3	.00
Uric acid (mg%)	6.3 ± 2.1	7.1 ± 2.4	.13
	No (%)	No (%)	
Male : female ratio	1.3	1.9	.93
Cigarette smoking	14 (25.9)	58 (29.0)	.80
Alcohol consumption	12 (22.2)	22 (11.0)	.03
Obesity	28 (51.9)	84 (42.0)	.30
Concomitant hypertension	24 (44.4)	114 (57.0)	.10
Microalbuminuria	26 (48.2)	88 (44.0)	.87
Metabolic syndrome	38 (70.4)	112 (56.0)	.08

and disease.[10] Reports from Nigeria and Central Africa consistently demonstrated higher HDL cholesterol level among diabetes patients than controls.[11,21–23] Similarly, HDL cholesterol level does not differ among Nigerian hypertensive and normotensive populations.[24–26] A recent comparative analysis of lipid profiles among Nigerians with diabetes, hypertension, and those with both showed that HDL cholesterol levels were not significantly different among any of the three groups compared to controls or between diabetic hypertensives compared to those with either of the two conditions occurring in isolation.[27] A direct relationship between HDL cholesterol and body mass index was recently demonstrated among East Africans.[28]

In our study HDL cholesterol level did not differ significantly among patients with metabolic syndrome and those without. Different plasma lipid profiles in different populations with diabetes are multifactorial in etiology. High-density lipoprotein hypocholesterolemia in type 2 diabetes patients is mainly due to insulin resistance-linked lipoprotein lipase deficiency, and reduction in HDL_2 sub-fraction is secondary to increased HDL cholesterol catabolism.[8] With respect to insulin resistance, different spectrums of type 2 diabetes probably exist in Africans. One report described a group with insulin resistance and increased susceptibility to cardiovascular mortality and morbidity and another group that is insulin sensitive with no increased risk of cardiovascular disease.[29] High-density lipoprotein cholesterol level is perhaps unaltered in insulin-sensitive African type 2 diabetes patients.

Differences in lifestyles are the strongest and most consistent factors explaining population differences in plasma lipid levels, including HDL cholesterol. Compared to Caucasians, Africans consume more vegetable fiber and less fat. In Rhodesia, for example, the ratios of carbohydrate:fat diet intake were 4:1 and 1.1:1 among Africans and Caucasians, respectively.[30] Fiber lowers plasma lipid level by reducing total fat intake, reducing fat and cholesterol absorption, and increasing bile secretion and insulin sensitivity.[31] Whether HDL cholesterol catabolism is inhibited by high fiber or racially determined biological factors is not known. High degree of physical activity also contributes to the high HDL cholesterol level among Africans.

The high degree of physical activity, low prevalence of cigarette smoking and alcohol consumption, and high plasma HDL cholesterol level would probably explain the low prevalence of ischemic heart disease among our patients, in spite of a high prevalence of metabolic cardiovascular risk factors. Low prevalence of alcohol consumption and cigarette smoking has previously been reported among Nigerians.[32]

In summary, HDL cholesterol is comparatively high among Nigerians with type 2 diabetes. It correlates poorly with metabolic syndrome and its markers. Its extremely low sensitivity and negative predictive value may make it a poor diagnostic criterion of metabolic syndrome in this population.

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AUTHOR CONTRIBUTIONS

Design and concept of study: Isezuo
Acquisition of data: Isezuo
Data analysis and interpretation: Isezuo
Manuscript draft: Isezuo
Statistical expertise: Isezuo
Acquisition of funding: Isezuo
Administrative, technical, or material assistance: Isezuo

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