SERUM LIPID AND LIPOPROTEIN LEVELS IN GHANAIANS WITH DIABETES MELLITUS AND HYPERTENSION

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Both diabetes mellitus and hypertension alter lipid and lipoprotein metabolism and increase the risk of coronary artery disease. We have reported previously on lipid and lipoprotein levels in healthy Ghanaians, and this study deals with the levels of these biochemical parameters in Ghanaians with diabetes mellitus and hypertension. Fasting serum lipoproteins were determined on blood samples drawn from healthy male and female Ghanaians as well as age-matched individuals with either diabetes or hypertension. Cholesterol, high-density lipoprotein cholesterol (HDL-C), triglycerides, and fasting blood glucose were measured. Low-density lipoprotein cholesterol (LDL-C) and very low-density lipoprotein cholesterol (VLDL-C) were derived.

Total serum cholesterol levels were 4.43±0.22 mmol/L and 4.67±0.26 mmol/L for diabetic males and females, respectively. High-density lipoprotein was 1.55±0.09 mmol/L and 1.50±0.09 mmol/L for male and female diabetics, respectively. Lipid and lipoprotein levels in the hypertensive patients did not differ from the above values. The levels of cholesterol and lipoprotein obtained in Ghanaians with hypertension and diabetes mellitus were similar to those of their age-matched healthy controls. These results suggest a reduced risk of coronary artery disease from the atherogenic effects of cholesterol in Ghanaians with diabetes mellitus and hypertension. (*J Natl Med Assoc.* 1997;89:191-196.)

Key words: lipids ◆ lipoproteins ◆ diabetes mellitus ◆ hypertension ◆ Ghanaians

Diabetes and hypertension are becoming important metabolic disorders in Ghana.[1] The prevalence of the two disease states is on the increase in other parts of Africa as well.[2-4]

Abnormal lipid and lipoprotein values have been noted in diabetes and in hypertension.[5-8]

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In hypertension, abnormalities may be seen in glucose, insulin, and lipoprotein metabolism. These abnormalities have been found to be present in first-degree relatives of hypertensive patients.[9] Recently, Reaven et al[10] have proposed that insulin resistance and compensatory hyperinsulinemia are primary events with enhanced sympathetic activity and diminished adrenal medullary activity being important links between the defect in insulin action and the development of hypertension and the subsequent metabolic abnormalities.

There is evidence that the high blood triglyceride levels and low high-density lipoprotein cholesterol (HDL-C) seen in diabetes mellitus may be related to abnormal lipid metabolism induced by insulin resis-

Table 1. General Characteristics of the Subjects*

	Healthy		Diabetics		Hypertensives	
	Male (n=11)	Female (n=10)	Male (n=36)	Female (n=27)	Male (n=11)	Female (n=13)
Age (years)	50.36±1.36	48.70±2.02	51.17±1.50	52.26±1.75	51.55±2.52	47.85±3.68
Body mass index (kg/m^2)	23.64±0.89	25.91±1.29	21.74±0.52	27.49±0.97	26.28±1.22	28.59±2.37
Arm circumference (cm)	27.58±0.55	25.78±1.84	27.87±0.58	32.07±1.05	31.18±0.64	32.23±1.57
Skinfold (mm)	10.73±1.56	16.33±3.20	7.77±0.68	6.32±0.98	17.55±1.80	31.73±2.52
Alcohol (g/week)	46.36±21.1	12.50±6.93	Nil	Nil	Nil	Nil
Education (%)						
Primary	53.70	12.00	55.56	70.37	18.18	53.84
Secondary	14.80	52.00	33.33	22.22	45.45	23.08
Tertiary	31.50	36.00	11.11	7.41	36.36	23.08
Time since diagnosis (%)						
New	—	—	33.33	14.81	54.55	15.38
<5 years	—	—	41.67	40.74	9.10	23.08
>5 years	—	—	25.00	44.44	36.36	61.54

*Given as mean±standard error of the mean.

tance or inadequate insulin action. The major catabolic pathway for triglycerides is via lipoprotein lipase, an enzyme that is expressed on the endothelial surface of adipose tissues, skeletal muscle, and cardiac muscle. The enzyme is insulin dependent. In the setting of insulin deficiency or resistance, the enzyme activity is reduced, leading to the buildup of triglycerides.

The altered concentrations of blood plasma lipoproteins are a cause of serious morbidity and mortality. In the United States, 75% to 80% of adult diabetic patients die from coronary heart disease, cerebrovascular disease, or peripheral vascular disease. Such serious morbidity may not be evident in the African diabetic or hypertensive patient because of racial differences in lipid levels.

Some reports from Africa have commented on the levels of lipoprotein and lipids in hypertensive and diabetic Africans.[11,12] Oyelola et al[11] found in a similar study with additional measurements of serum apolipoproteins that Nigerians with diabetes and hypertension had significantly higher levels than controls of those lipids considered to be atherogenic.

A previous study conducted by us showed that healthy Ghanaians had levels of cholesterol that were much lower than levels noted for individuals living in industrialized nations.[13] Similar results have been obtained from other parts of Africa.[14,15] We believe that the lower incidence of coronary heart disease in Africa may be related to this favorable lipid profile.[12,16,17] We have carried these studies further and have examined lipid levels in Ghanaians with conditions known to adversely impact on serum lipid and lipoprotein levels.

METHODS

A total of 108 subjects (63 patients with diabetes mellitus, 24 patients with hypertension, and 21 age-matched controls) were randomly selected for this study. The patients with diabetes mellitus and hypertension were all attending outpatient clinics at the University of Ghana Medical School in Accra. The diagnosis of diabetes mellitus and hypertension was based on World Health Organization (WHO) criteria.[18,19] Subjects in the control group were recruited from the work force of the University of Ghana. Relevant demographic data were obtained by means of formal interview and by the use of questionnaires. A 12-lead electrocardiogram as well as systolic and diastolic blood pressures were recorded by a specially trained technician. Anthropometric data, body weight, height, triceps skinfold, and mid-arm circumference also were obtained.

Fasting serum lipid, lipoprotein, and glucose levels were determined on a 10-mL sample of blood obtained without venostasis. Total and free cholesterol levels were determined enzymatically.

Table 2. Clinical and Biochemical Characteristics of the Subjects*

	Healthy		Diabetics		Hypertensives	
	Male (n=11)	Female (n=10)	Male (n=36)	Female (n=27)	Male (n=11)	Female (n=13)
Blood pressure (mm Hg)						
Systolic	126.36±2.79	127.00±4.95	126.11±2.80	135.93±3.71	163.09±5.27	159.23±5.37
Diastolic	82.72±1.41	83.50±3.11	78.06±1.90	84.07±1.79	106.91±3.68	105.38±1.83
Fasting blood sugar (mmol/L)	5.53±0.20	4.73±0.26	8.95±0.82	11.77±1.12	5.17±0.24	4.83±0.20
Urea nitrogen (mmol/L)	1.73±0.15	1.78±0.12	1.71±0.11	1.69±0.14	1.77±0.19	2.17±0.30
Serum creatinine (μm)	100.15±2.58	85.30±3.33	103.68±4.52	84.97±3.24	145.81±7.53	142.04±12.94
Albumin (g/L)	42.32±1.17	39.71±1.74	40.71±0.80	39.76±0.74	46.00±0.85	45.20±0.88
Globulin (g/L)	27.61±1.61	27.36±1.68	31.66±0.81	33.28±0.91	29.00±1.80	30.37±1.06

*Given as mean±standard error of the mean.

Lipoproteins were fractionated using the combined centrifugal-precipitation method.[20]

The cholesterol content of the HDL fractions was determined enzymatically.[21] The triglyceride content of the sera was determined with triglyceride assay kits. Low-density lipoprotein cholesterol (LDL-C) and very low-density lipoprotein cholesterol (VLDL-C) levels were calculated from the data.

Other biochemical analysis performed included the determinations of serum concentrations of total proteins, albumin, and globulin. Serum proteins, blood urea nitrogen, and serum creatinine were measured using routine procedures. All determinations were done in duplicate.

Statistical Analysis

Results are presented as mean±standard error of the mean (SEM) where appropriate. Analysis of variance (ANOVA) and Spearman rank order analysis were performed to determine group differences and correlations in the various parameters measured. Statistical significance was set at the 5% level.

RESULTS

General Characteristics

Table 1 shows the general characteristics of the study subjects. The diabetic and hypertensive patients did not use alcohol. The male patients with diabetes were significantly leaner than their female counterparts ($P<.05$). Although the body mass index (BMI) for hypertensive males and females were similar, the skinfold thickness of the female hypertensives was significantly greater than the males.

Clinical and Biochemical Characteristics

The mean systolic and diastolic blood pressure of the diabetic subjects and controls were within normal range. Table 2 shows the biochemical data. Significant differences between the groups in terms of fasting blood glucose levels and creatinine were noted. Compared with the diabetics and age-matched controls, serum creatinine was significantly elevated in the hypertensive subjects ($P<.05$).

Abnormalities were detected in the electrocardiograms (EKG) of 10 (16%) diabetics and in 8 (33%) patients with hypertension. The electrocardiographic abnormalities included evidence of coronary ischemia–Q-waves, nonspecific ST segment and T wave abnormalities, left ventricular hypertrophy, and right bundle branch block.

Lipid and Lipoprotein Levels

The data in Table 3 show the total cholesterol, HDL-C, and LDL-C levels, as well as triglyceride levels in sera for the study subjects. No statistically significant differences were noted between the values for female and male diabetics and hypertensives. Low-density lipoprotein cholesterol levels were highest for the age-matched female controls and lowest in male diabetics. Conversely, the ratio of HDL-C/LDL-C and % HDL-C were highest in male diabetics. Compared with the age-matched

Table 3. Serum Lipids and Lipoproteins of the Subjects*

	Healthy		Diabetics		Hypertensives	
	Male (n=11)	Female (n=10)	Male (n=36)	Female (n=27)	Male (n=11)	Female (n=13)
Triglycerides (mmol/L)	1.11±0.15	1.10±0.09	1.54±0.12	1.63±0.17	1.55±0.26	1.29±0.17
Total cholesterol (mmol/L)	4.6760.17	5.0760.39	4.4360.22	4.6760.26	4.9660.37	5.1560.27
Free cholesterol (mmol/L)	1.25±0.08	1.47±0.13	1.24±0.04	1.27±0.06	1.45±0.10	1.37±0.06
HDL-C (mmol/L)	1.41±0.08	1.56±0.20	1.55±0.09	1.50±0.09	1.55±0.20	1.71±0.15
LDL-C (mmol/L)	2.68±0.25	2.98±0.37	2.16±0.02	2.53±0.22	2.69±0.36	2.83±0.29
VLDL-C (mmol/L)	0.58±0.15	0.51±0.03	0.72±0.06	0.74±0.08	0.73±0.12	0.61±0.08
HDL-C/LDL-C	0.53±0.14	0.52±0.12	0.72±0.06	0.59±0.20	0.58±0.29	0.60±0.23
% HDL-C	30.19±01.5	30.78±3.68	34.98±2.00	32.12±2.00	31.25±5.00	33.20±4.00

Abbreviations: HDL-C=high-density lipoprotein cholesterol, LDL-C=low-density lipoprotein cholesterol, and VLDL-C=very low-density liprotein cholesterol.
*Given as mean±standard error of the mean.

controls, triglyceride levels were qualitatively higher among the diabetic and hypertensive patients. Statistical analysis did not reveal any associations between concentrations of lipids and lipoproteins and EKG abnormalities($P>.05$).

Medications

A majority of the patients with diabetes mellitus (69% male and 85% female) were on oral hypoglycemic agents (ie, tolbutamide and glibenclamide). Twelve (19%) male and 7 (11%) female diabetic patients were on insulin. Seven male and 3 female patients were on no drug treatment. Statistical analysis did not show any correlations between either the type of treatment, time since diagnosis, fasting blood glucose level, and lipid and lipoprotein distributions.

Most of the hypertensive patients were on furosemide and either alpha-methyldopa or propranolol. No correlations were observed between lipid and lipoprotein levels and blood pressure control, age, type of drug treatment, and time since diagnosis.

DISCUSSION

In a previous study, we reported on serum lipid levels in healthy Ghanaians and found that, consistent with population and regional variations in serum lipid values, the % HDL-C cholesterol of total cholesterol for healthy male South Africans and Ghanaians were 37±2.74% and 33±2.04%, respectively, compared with 22% and 26% for Kenyans and African Americans.[13,22]

High-density lipoprotein cholesterol remains the most powerful cholesterol fraction in predicting coronary artery disease risk. In African patients with diabetes mellitus and hypertension, the incidence of coronary artery disease is low.[17] The extent of hyperlipidemia and hence the rate of development of atherosclerosis bears a direct relationship to mortality from coronary artery disease. The mean % HDL-C of Ghanaian male diabetics was 37±2%. This value was higher but not significantly different from that obtained for controls and the other groups in the study. It is also interesting to note that the ratio of HDL-C/LDL-C was high in all the groups. Our data do not support the results of previous work documenting a decrease in HDL-C in association with hypertriglyceridemia in diabetics.[11,23]

Studies elsewhere also indicate that triglyceride, LDL-C, and total cholesterol levels are highest in overweight obese diabetic patients while HDL-C concentrations are highest in the lower weight division.[24] The results of this study did not demonstrate any correlation between cholesterol or lipoprotein levels and the weight of the subjects. The male diabetics had relatively lower albeit statistically nonsignificant LDL-C, consistent with the comparable BMI and arm circumference observed for the diabetic and age-matched healthy control group. The skinfold measurements suggested that the diabetics were relatively leaner.

Propranolol, a nonselective beta-adrenergic antagonist with no intrinsic sympathetic activity is widely used in Ghana for treating hypertension. Some of the hypertensive patients were on propranolol during this study. Propranolol has been shown to increase the risk of noninsulin-dependent-diabetes mellitus. Glucose uptake in peripheral tissues has been shown to decrease by 32% in propranolol-treated patients,[25] and in the same study, propranolol use was associated with a 25% increase in plasma triglyceride levels.[25] This increase in plasma triglyceride concentration is thought to be due to a decrease in activity of lipoprotein lipase in skeletal muscle.[25] Drug treatment did not produce any significant deleterious effect on lipoproteins in the Ghanaian hypertensives who were on propranolol. It should be interesting to study this group to see if glucose disposal has been affected by propranolol use. Racial differences that exist in the pharmacokinetics and beta-adrenergic receptor effects of propranolol also should be noted.[26] Venter and Joubert[27] have reported that black subjects in South Africa are less sensitive to intravenous propranolol than white subjects. These differences also may be present at the level of beta-adrenergic receptor function involving lipid metabolism and merits further investigation.

Glycated hemoglobin (HgA1) levels were not measured in this study. It would have been preferable to relate diabetes control using HgA1 to levels of serum cholesterol and LDL-C. We did not find any significant correlation between the degree of hyperglycemia and serum cholesterol and LDL-C. Previous studies have reported a relationship between poor metabolic control of diabetes and high levels of cholesterol and LDL-C.[28,29] In another study, hemoglobin A1 was positively correlated with the levels of total cholesterol, total triglycerides, and LDL-C in whites and black men but this relationship was absent in black women.[30] In the white diabetics in that study, a reduction in hemoglobin A1 of one percentage point was statistically associated with a decrease of 0.16 to 0.17 mmol/L in total plasma cholesterol and a decrease of 0.10 to 0.13 mmol/L in LDL-C. A reduction in triglycerides also was noted. This study by Semenkovich et al[30] provides evidence for a racial factor in the distribution of plasma lipids and lipoprotein. Previous work also has shown that a sex-specific lipoprotein distribution exists in diabetics.[31] Further work in this area from Africa would need to take these factors into account.

Our data suggest that compared with other populations, Ghanaian diabetics and hypertensives may be at reduced risk for coronary artery disease. Regional differences in lipid profiles are to be expected, and it is not surprising that our findings are at variance with the study of Oyelola et al[11] reporting from Nigeria. Dietary and other differences may account for some of the variations seen. There is no doubt that in addition to diet, other lifestyle factors such as extent of physical activity can play a significant role in determining levels of lipids and lipoprotein within a population.

CONCLUSION

Serum total cholesterol and lipoprotein levels in adult Ghanaians with diabetes mellitus and hypertension are not significantly different from their age-matched healthy controls. The results obtained in this study suggest a reduced risk for coronary artery disease in the sample population. More work needs to be done in attempting to define factors responsible for regional variations in lipoprotein levels in Africans in health and in disease.

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