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Lipid and lipoprotein profiles in Ethiopian patients with diabetes mellitus

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Abstract

The association between dyslipidemia and diabetes mellitus is well established. Although various lipoprotein abnormalities have been described in patients with diabetes mellitus elsewhere, there is limited information from African patients. We undertook a cross-sectional study to assess the prevalence of dyslipidemia in Ethiopian patients with types 1 and 2 diabetes. A total of 193 subjects were included in the study (54 patients had type 1 diabetes mellitus, 92 patients had type 2 diabetes mellitus, and 47 were nondiabetic controls). Of these, 93 (48.6%) were men and 103 (51.4%) were women. The mean age ± SEM for patients with type 1 diabetes mellitus, type 2 diabetes mellitus, and controls were 29.8 ± 1.4, 51.2 ± 1.1, and 29.0 ± 1.7 years, respectively. Hypercholesterolemia and hypertriglyceridemia, defined as cholesterol level of greater than 5.2 mmol/L and triglyceride level of greater than 1.8 mmol/L, were found in 47.3% and 41.8% of patients with diabetes mellitus compared with 27% and 17% in controls ($P < .05$ for both). The mean total cholesterol level ± SEM was significantly higher in patients with type 1 or 2 diabetes mellitus than controls (5.76 ± 0.27 mmol/L in type 1 diabetes mellitus, 5.25 ± 0.2 mmol/L in type 2 diabetes mellitus, and 4.67 ± 0.28 mmol/L in healthy controls, $P < .02$). Triglycerides and low-density lipoprotein levels were also significantly higher in patients with diabetes than in controls, whereas high-density lipoprotein levels were significantly lower in patients with diabetes. In conclusion, our study demonstrates that in Ethiopians with diabetes mellitus, dyslipidemia occurs more frequently than in controls. Thus, we recommend periodic screening for dyslipidemia in all Ethiopian patients with diabetes. Other studies are needed to assess the potential negative effect of dyslipidemia and obesity on morbidity and mortality in Ethiopians with diabetes.

1. Introduction

Diabetic lipemia (milky plasma), first described in the 19th century, is a well-recognized manifestation of uncontrolled diabetes mellitus. Because insulin has important regulatory effects on lipid metabolism, diabetes mellitus is associated with significant abnormalities in lipoprotein metabolism. Almost all commonly occurring lipoprotein abnormalities have been observed in diabetes [1]. The dyslipidemia seen in poorly controlled type 1 diabetes mellitus is mainly due to accumulation of chylomicrons and very low-density lipoproteins in the plasma [2,3], whereas in type 2 diabetes mellitus, the most common abnormal lipid pattern is a combination of elevated triglyceride (TG) levels and decreased high-density lipoprotein (HDL) cholesterol [4]. However, in both cases, normalization of glycemic control is followed by improvement or normalization of the dyslipidemias [5]. Although the causes of increased risk of cardiovascular diseases in diabetes are multifactorial, dyslipidemia is certainly a major factor. Thus, patients with diabetes have increased risk for all manifestations of atherosclerosis, including coronary artery disease, cerebrovascular events, and peripheral vascular diseases [6].

There are limited reports of the prevalence of lipid abnormalities in patients with diabetes from the sub-Saharan Africa. Therefore, we undertook this cross-sectional study, performed in Ethiopian subjects, to evaluate the prevalence of and characterize the dyslipidemias in patients with diabetes compared with nondiabetic controls.

2. Patients and methods

2.1. Patient population

The study was performed from May to July 1993 at the Diabetes Clinic of the Tikur Anbessa Hospital, Addis Ababa

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University, Addis Ababa, Ethiopia. Fifty-four subjects with type 1 diabetes mellitus, 92 subjects with type 2 diabetes mellitus (34 on insulin, 52 on oral agents, and 6 on diet alone), and 47 nondiabetic controls were included in the study. Tikur Anbessa Hospital is the main national referral and teaching hospital located in the capital, Addis Ababa. The diabetes clinic has more than 2000 registered patients with diabetes. All subjects with either type 1 or 2 diabetes mellitus who volunteered to participate in the study and were available for laboratory examination were included. None of them took the morning dose of insulin or oral agents on the day of examination. Apart from hypertension, there were no other significant comorbidities in those patients. There were no smokers, and none of the patients were on statins. We have no data on alcohol intake, physical activity, or hemoglobin A_{1c}.

2.2. Clinical data

The classification and diagnosis of diabetes mellitus were made according to the World Health Organization [7] criteria. Information regarding age, type of diabetes mellitus, duration of diabetes, and type of treatment was completed on a data collection sheet. Weight and height were measured for all patients and were recorded to the nearest kilogram and centimeter, respectively. Blood pressure was measured on the right arm in the sitting position using standard mercury sphygmomanometer. Informed consent was obtained from each participant following the guidelines of the Helsinki Convention.

2.3. Collection and handling of specimen

Five to ten milliliters of venous blood was collected from each subject in the fasting state. After centrifugation of the blood samples, the sera were isolated and then frozen at −20°C. In September 1993, the samples were transported to Germany using dry ice–filled containers at temperatures reaching −70.0°C. Within less than 24 hours, the specimens reached their destination and were kept frozen at −20°C.

Table 1
General characteristics of subjects studied

Variable	Type 1 diabetes mellitus (n = 54)	Type 2 diabetes mellitus (n = 92)	Controls (n = 47)	*P*
Age (y)	29.8 ± 1.4[a]	51.2 ± 1.1[a,b]	29.0 ± 1.7[b]	<.001
Duration of diabetes (y)	6.9 ± 0.8	9.1 ± 0.7	–	.046
Systolic blood pressure (mm Hg)	114.8 ± 2.7[a]	133.6 ± 1.9[a,b]	119.8 ± 2.7[b]	<.001
Diastolic blood pressure (mm Hg)	76.4 ± 1.5[a]	81.3 ± 1.1[a]	78.3 ± 1.5	0.02
Basal C-peptide (U)	0.12 ± 0.05[a,b]	0.67 ± 0.04[a]	0.54 ± 0.05[b]	<.001
BMI (kg/m^2)[1]	20.2 ± 0.5[a]	24.7 ± 0.4[a,b]	20.2 ± 0.5[b]	<.001
Waist-to-hip ratio	0.88 ± 0.01[a]	0.94 ± 0.1[a]	0.83 ± 0.01[a]	<.001

Values are given as mean ± SEM. Matching superscripts across the row indicate Tukey honestly significantly different planned comparisons were significant at the $P < .05$ level.

[1] BMI data were available only in 53 type 1 and 85 type 2 diabetic subjects.

Table 2
Distribution of subjects in the 3 groups by BMI categories

	BMI ≤25	BMI 25-30	BMI >30
Type 1 diabetes mellitus (53)[a]	48 (90)	5 (10)	–
Type 2 diabetes mellitus (85)[a]	48 (56)	26 (31)	11 (13)
Controls (47)	45 (96)	–	2 (4)

Values are given as n (%).

[a] Of the 54 type 1 and 92 type 2 diabetic patients, BMI information was missing in 1 type 1 and 7 type 2 diabetic subjects. Therefore, this analysis includes only 53 type 1 and 85 type 2 diabetic subjects.

2.4. Laboratory methods and assays

The determination of the lipid panel (total cholesterol, low-density lipoprotein [LDL], HDL, and TGs), as well as malonyldialdehyde (MDA), was done using a Beckman DU-640 Spectrophotometer.

The method used for the lipid panel was an enzymatic method (Monotest Cholesterol; Boehringer-Mannheim) using the CHOD-PAP method.

For the determination of lipoprotein (a) [Lp(a)], an enzyme-linked immunosorbent assay–suitable MICRO-READER Model 4025 (Hyperion) was used. The method used was an enzyme immunoassay using a sandwich principle (IMMUNOZYM, IMMUNO, Heidelberg, Germany).

2.5. Statistical analysis

SAS software (SAS Institute) was used for all statistical analyses. Data were analyzed as means ± SEM for continuous variables and as frequency and percentage of study population for categorical variables. In evaluating univariate differences, analysis of variance was used to compare the values of continuous variables such as age and duration of diabetes. χ^2 Tests were used to explore the relationships among categorical variables.

Table 3
Lipid and lipoprotein levels in the 3 groups of subjects

Variable	Type 1 diabetes mellitus (n = 54)	Type 2 diabetes mellitus (n = 92)	Controls (n = 47)	Adjusted *P**
Cholesterol (mmol/L)	5.76 ± 0.27[a]	5.25 ± 0.20	4.67 ± 0.28[a]	.015
HDL (mmol/L)	0.98 ± 0.08	0.90 ± 0.06[a]	1.24 ± 0.08[a]	.035
TGs (mmol/L)	1.61 ± 0.15	2.01 ± 0.11[a]	1.31 ± 0.16[a]	.002
LDL (mmol/L)	3.61 ± 0.22	3.28 ± 0.17	2.78 ± 0.24	NS
Lp(a) (μmol/L)	27.09 ± 2.81	20.10 ± 2.15	20.47 ± 3.00	NS
MDA (μmol/L)	0.88 ± 0.04[a]	0.97 ± 0.03[b]	0.72 ± 0.04[a,b]	<.001

Values are given as mean ± SEM. Matching superscripts across the row indicate Tukey honestly significantly different planned comparisons were significant at the $P < .05$ level.

* The adjusted *P* value considered group differences, controlling for sex, age, and BMI.

3. Results

Of the 193 subjects studied, 54 patients had type 1 diabetes mellitus, 92 had type 2 diabetes mellitus, and 47 were nondiabetic controls. The various clinical characteristics of the subjects are described in Table 1. The mean age ± SEM for patients with type 1 diabetes mellitus, type 2 diabetes mellitus, and controls were 29.8 ± 1.4, 51.2 ± 1.1, and 29.0 ± 1.7 years, respectively. The mean duration of diabetes was longer in patients with type 2 diabetes mellitus than in patients with type 1 diabetes mellitus (9.1 ± 0.7 vs 6.9 ± 0.8 years, $P < .05$). The mean systolic blood pressure was significantly higher in patients with type 2 diabetes mellitus than in patients with type 1 diabetes mellitus and controls ($P < .001$). Similarly, the mean diastolic blood pressure was higher in patients with type 2 diabetes mellitus than in patients with type 1 diabetes mellitus ($P = .02$). Similar to observations from other population groups, our patients with type 2 diabetes mellitus had higher insulin levels as estimated by C-peptide levels when compared with patients with type 1 diabetes and controls.

Patients with type 2 diabetes mellitus also manifested with significantly higher body mass index (BMI) and waist-to-hip ratio than patients with type 1 diabetes mellitus or controls. Our patients with type 2 diabetes mellitus had relatively low BMI compared with patients from Western developed countries with the mean ± SEM of 24.7 ± 0.4 kg/m^2. As can be deduced from Table 2, 44% of patients with type 2 diabetes mellitus were overweight or obese, whereas only 10% of patients with type 1 diabetes mellitus and 4% of controls belong to those categories.

Table 3 demonstrates the lipid and lipoprotein values of the 3 groups of subjects. Similar to observations in other population groups, the total cholesterol level was significantly higher in patients with both types 1 and 2 diabetes mellitus than controls (5.76 ± 0.27 mmol/L in type 1 diabetes mellitus, 5.25 ± 0.20 mmol/L in type 2 diabetes mellitus, and 4.67 ± 0.28 mmol/L in healthy controls, $P = .015$). TGs and LDL levels were also significantly higher in patients with diabetes than in controls, whereas HDL level was significantly lower in patients with diabetes mellitus. On the other hand, Lp(a) levels did not show any significant difference among the groups. MDA, which is a recognized indicator of tissue injury caused by reactive oxygen species, was significantly higher in patients with type 2 diabetes mellitus.

Table 4 summarizes the comparative prevalence of abnormal lipid levels in patients with diabetes and controls.

Table 4
Lipid profile categories in patients with diabetes and controls

Variable	Units (mmol/L)	Patients with diabetes mellitus (n = 146)	Controls (n = 47)	Odds ratio
Cholesterol	< 5.2	77 (52.7)	34 (72.3)	1.71*
	≥ 5.2	69 (47.3)[a]	13 (27.7)[b]	
HDL	> 0.91	62 (42.5)	26 (55.3)	1.29
	≤ 0.91	84 (57.5)[a]	21 (44.7)[b]	
LDL	< 3.36	80 (54.8)	35 (74.5)	1.77*
	≥ 3.36	66 (45.2)[a]	12 (25.5)[b]	
TGs	< 1.8	85 (58.2)	39 (83.0)	2.46**
	≥ 1.8	61 (41.8)[a]	8 (17.0)[b]	

The odds ratio defines the ratio of the prevalence of an abnormal lipid panel in the diabetes group, indicated by superscript a, compared with that of the control group, indicated by superscript b.

* $P < .05$.

** $P < .001$.

4. Discussion

The association between diabetes mellitus and dyslipidemias, particularly high TG and low HDL levels, is well established [8,9]. Dyslipidemias are among the major risk factors for atherosclerosis including coronary artery disease, cerebrovascular disease, and peripheral vascular diseases. On the other hand, in patients with diabetes, good metabolic control has been associated with improvement in lipoprotein profile [8,9]. Similar to observations in other population groups, our study demonstrated that patients with diabetes had higher cholesterol, LDL, and TG levels as well as lower HDL levels when compared with the controls (Tables 3 and 4). There is clear evidence in the literature that in patients with diabetes and dyslipidemia, both conditions are independent cardiovascular risk factor [4]. As reported in the Multiple Risk Factor Intervention Trial, patients with diabetes mellitus had more than 3-fold greater risk of cardiovascular problems than nondiabetic patients [10].

Using the criteria of the National Cholesterol Education program [11], Stern et al [12] found that more than 40% of the patients with diabetes were hypercholesterolemic compared with less than one fourth of the nondiabetic subjects. In our study, 47.3% of the patients with diabetes and 27.7% of the controls had hypercholesterolemia. This indicates that dyslipidemia is a significant problem in patients with diabetes in Ethiopia as is the case in developed countries.

Hypertriglyceridemia was found in 41.8% of our patients with diabetes. It has been shown that patients with type 2 diabetes mellitus who have hypertriglyceridemia usually have both overproduction and impaired catabolism of TGs [13-15]. In more severe hypertriglyceridemia, lipoprotein lipase activity is often decreased [16,17]. Treatment of hyperglycemia with insulin and/or an oral glucose-lowering agent may eventually return lipoprotein lipase activity to normal, although this may take weeks or even months [16].

Some studies failed to show elevated LDL cholesterol levels in white patients with type 2 diabetes mellitus when compared with age-, sex-, and weight-matched nondiabetic patients [18,19]. On the contrary, in black patients, Pacy et al [20] found that patients with diabetes had elevated LDL levels when compared with nondiabetic patients, unlike what was observed in whites and Asians. Similarly, in our study, we found that our patients with diabetes had significantly higher LDL levels when compared with nondiabetic controls.

With regard to HDL, in line with findings in other populations [21,22], patients with diabetes had a higher prevalence of low HDL compared with nondiabetic patients (57.5% vs 44.7%, respectively). Decreased HDL levels in patients with type 2 diabetes mellitus may be due to increased catabolism because of increased hepatic TG lipase activity or decreased production of HDL secondary to impaired catabolism of very low-density lipoprotein and decreased lipoprotein lipase activity.

One notable finding in our subjects is that obesity was not as significant a problem as in the developed world [23]. In patients with diabetes, as well as in controls, the mean BMI levels were below the generally accepted definition for obesity or overweight (BMI >25 kg/m^2). This stands in stark contrast to findings in the United States where the prevalence of obesity and overweight is more than 50%. On the other hand, as seen elsewhere, our diabetic subjects on average have a higher BMI than the controls. This raises the question whether in an Ethiopian patient population it is appropriate to use the same BMI cutoffs we use in the Western world in defining obesity. The prolonged and widely distributed undernutrition in the sub-Saharan countries including Ethiopia might have contributed to the low prevalence of obesity [24]. This might also have lead to the relatively lower levels of lipids in our subjects when compared with reports from the developed world [23].

Despite the fact that the BMI values in all groups were much lower than what is seen in developed Western societies, it was interesting to note that the metabolic differences between diabetic patients (in particular type 2) and controls were maintained. Those include differences in BMI, waist-to-hip ratio, lipids, and systolic blood pressure. This indicates that, for any population (irrespective of differences in interpopulation BMI averages), a relatively higher BMI level is associated with unfavorable metabolic outcomes.

Whether Lp(a) is associated with type 2 diabetes is controversial with some studies showing higher levels [25], others showing no difference [26], and even some reported lower levels [27] in subjects with type 2 diabetes compared with normoglycemic subjects. In keeping with these reports, the Lp(a) levels in our patients with diabetes were similar with those of controls. Thus, based on this observation, we do not think that Lp(a) is major factor for cardiovascular events in our patients.

Our study did have some limitations, some of which include the lack of detailed genetic, environmental, behavioral, and nutritional data. This resulted from the fact that our study was never meant to be a complete epidemiological study and was designed as a cross-sectional study focused on lipid and related parameters on a group of patients who belong to an understudied population group.

In conclusion, this study demonstrated that in Ethiopians with diabetes mellitus, dyslipidemia occurs more frequently than in controls, a pattern similar to that is seen in developed countries. It is not clear whether the relatively higher BMI, as well as central obesity and dyslipidemia in patients with diabetes mellitus, would increase the relative risk of cardiovascular diseases in these patients. Other studies are needed to assess the potential negative effect of dyslipidemia and obesity on morbidity and mortality in Ethiopians with diabetes.

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