ORIGINAL INVESTIGATION

Prevalence and Phenotypic Distribution of Dyslipidemia in Type 1 Diabetes Mellitus

Effect of Glycemic Control

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Background: Data on the prevalence of dyslipidemia in type 1 diabetes mellitus are scarce and are based on total triglyceride and total cholesterol concentrations alone.

Objective: To assess the effect of glycemic optimization on the prevalence of dyslipidemia and low-density lipoprotein cholesterol (LDL-C) concentrations requiring intervention in patients with type 1 diabetes.

Patients: A total of 334 adults with type 1 diabetes and 803 nondiabetic control subjects.

Methods: Levels of glycosylated hemoglobin, total cholesterol, total triglyceride, high-density lipoprotein cholesterol (HDL-C), and LDL-C were assessed at baseline and after 3 to 6 months of intensive therapy with multiple insulin doses.

Results: Levels of LDL-C greater than 4.13 mmol/L (>160 mg/dL) and total triglyceride greater than 2.25 mmol/L (>200 mg/dL) and low HDL-C levels (<0.9 mmol/L [<35 mg/dL] in men or <1.1 mmol/L [<45 mg/dL] in women) were found in 16%, 5%, and 20% of patients and 13%, 6%, and 9% of controls, respectively ($P<.001$ for HDL-C). Diabetic women showed more hypercholesterolemia than nondiabetic women (15.6% vs 8.5%; $P=.04$). After glycemic optimization (mean±SD glycosylated hemoglobin decrease, 2.2±1.96 percentage points), the prevalence of LDL-C levels greater than 4.13 mmol/L (>160 mg/dL) became lower in diabetic men than in nondiabetic men (9.7% vs 17.5%; $P=.04$), but women showed frequencies of dyslipidemia similar to their nondiabetic counterparts. The proportion of patients with LDL-C concentrations requiring lifestyle (>2.6 mmol/L [>100 mg/dL]) or drug (>3.4 mmol/L [>130 mg/dL]) intervention decreased from 78% and 42% to 66% and 26%, respectively.

Conclusions: Low HDL-C is the most frequent dyslipidemic disorder in patients with poorly controlled insulin-treated type 1 diabetes, and a high proportion show LDL-C levels requiring intervention. Less favorable lipid profiles could explain the absence of sex protection in diabetic women. The improvement caused by glycemic optimization puts forward intensive therapy as the initial treatment of choice for dyslipidemia in poorly controlled type 1 diabetes.

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ATHEROSCLEROTIC complications are the leading cause of death in people with diabetes.[1] Therefore, identifying risk factors, such as lipid abnormalities, that explain their cardiovascular risk is essential. The lipid profile of patients with type 1 diabetes mellitus is highly dependent on glycemic control. Individuals with poorly controlled type 1 diabetes show high levels of total triglyceride[2-5] and total cholesterol[2,3,5] and variable concentrations of high-density lipoprotein cholesterol (HDL-C)[2,4,5] compared with nondiabetic control subjects, whereas patients with well-controlled type 1 diabetes show similar, and sometimes more favorable, lipid and lipoprotein concentrations than controls.[2-4,6] However, unlike type 2 diabetes, epidemiological data on the prevalence of dyslipidemia and phenotype distribution in type 1 diabetes mellitus are scarce and are mostly based on total triglyceride and total cholesterol concentrations alone.[2,7-9] Furthermore, the cutoff points used for the definition of dyslipidemia vary among different authors, and, to our knowledge, there are no studies that compare the prevalence of dyslipidemia in patients with type 1 diabetes before and after improving glycemic control with that in nondiabetic controls. On the other hand, although aggressive lowering of low-density lipoprotein choles-

PATIENTS AND METHODS

PATIENTS

We studied 334 adults with type 1 diabetes (54% men and 46% women; mean±SD age, 31.3±10.2 years [range, 18-71 years]; mean±SD disease duration, 7.9±9.3 years; and mean±SD glycosylated hemoglobin [Hb A_{1c}] level, 8.5%±2.0%) consecutively seen at our Diabetes Clinic (Endocrinology Department, Hospital de Sant Pau, Barcelona, Spain) and a control group of 803 nondiabetic controls (49% men and 51% women; mean±SD age, 30.7±9.2 years [range, 18-59 years]). The control group was obtained from a background population. Their main clinical features are displayed in **Table 1**.

Type 1 diabetes mellitus was diagnosed according to the National Diabetes Data Group criteria.[10] Smoking was defined as the consumption of 1 or more cigarettes or other form of tobacco presentation per day. Patients were considered to have hypertension if they received antihypertensive drug treatment or if their blood presure was 140/90 mm Hg or higher on 2 or more occasions. Peripheral vascular disease was defined by the existence of symptoms consistent with intermittent claudication, absence of distal lower limb pulses, abnormal Doppler examination results, or a history of reconstructive vascular surgery or amputation. Patients who had experienced angina pectoris (retrosternal squeezing or pressure-type discomfort relieved by nitroglycerin therapy and/or accompanied by typical electrocardiographic changes [Minnesota code 5-1 or 5-2]) or had a history of acute myocardial infarction or electrocardiographic signs of necrosis (Minnesota code 1-1) were considered to have ischemic heart disease. The diagnosis of diabetic retinopathy was established if the assisting physician or ophthalmologist described the presence of microaneurysms, with or without hemorrhages, hard exudates, or new vessels in funduscopic examination with complete pupillary dilation or by a history of laser treatment. To assess the presence of diabetic nephropathy we measured 24-hour protein excretion after ruling out infection. Proteinuria or established nephropathy was defined as protein excretion greater than 300 mg/d and advanced nephropathy by nephrotic range proteinuria or creatinine concentrations higher than the reference range. Neither patients nor controls received lipid-lowering drugs.

STUDY DESIGN

Patients were included in an intensive therapy program, with regular insulin administration before main meals and isophane insulin administration before dinner or at bedtime. They received an isoenergetic diet, providing 50% to 55% of energy as carbohydrates and 30% to 35% as fat. All patients underwent a specific diabetes education program and were seen in the outpatient unit every 2 to 4 weeks for 3 to 6 months. Assessment was carried out at baseline and after achieving an improvement of at least 1 percentage point in their Hb A_{1c} level. They were compared with the nondiabetic control group in both metabolic situations.

Patient history was taken, physical examination was performed, and concentrations of the following laboratory values were determined: serum glucose, fructosamine, Hb A_{1c}, total triglyceride, total cholesterol, HDL-C, and LDL-C.

LABORATORY MEASUREMENTS

Blood samples were drawn after an overnight fast (10-12 hours) at baseline and after achieving good glycemic control. Blood samples remained at room temperature for 30 minutes, and serum was separated by centrifugation (at 3000*g* for15 minutes). Glucose concentrations were measured using the routine glucose-oxidase method; fructosamine levels were measured using a colorimetric method, with glycated albumin as standard (reference interval, 205-285 µmol/L); and Hb A_{1c} levels were determined using high-performance liquid chromatography with a Hi-AutoA1c HA-8121 analyzer (Dic-Kioto, Kioto, Japan) (reference range, 3.7%-5.8%). Total triglyceride and total cholesterol concentrations were measured using commercial fully enzymatic methods, and HDL-C levels were determined, after precipitation of apolipoprotein B– and apolipoprotein E–containing particles, using polyethylene glycols (Boehringer Mannheim, Mannheim, Germany). Values for LDL-C were calculated using the Friedewald formula (adapted to millimoles per liter) when triglyceride levels did not exceed 3.45 mmol/L (≤300 mg/dL) and otherwise using the combined ultracentrifugation and precipitation method recommended by the Lipid Research Clinics.[11]

DEFINITION OF DYSLIPIDEMIA, DYSLIPIDEMIC PHENOTYPES, AND RECOMMENDED LDL-C CONCENTRATIONS

The cutoff points used for the definitions of hypercholesterolemia and hypertriglyceridemia (LDL-C >4.13 mmol/L [>160 mg/dL] and triglyceride >2.25 mmol/L [>200 mg/dL], respectively) were those recommended by the National Cholesterol Education Program.[12] Low HDL-C concentrations were less than 0.9 mmol/L (<35 mg/dL) for men and less than 1.1 mmol/L (<45 mg/dL) for women.[13] Patients and controls were classified into different dyslipidemic phenotypes according to the algorithm shown in **Figure 1**. Following the recommendations of the American Diabetes Association,[13] LDL-C concentrations of 2.6 mmol/L or lower (≤100 mg/dL) were considered a desirable goal, whereas LDL-C levels greater than 2.6 mmol/L (>100 mg/dL) and greater than 3.4 mmol/L (>130 mg/dL) were regarded as eligible for lifestyle and pharmacological treatment, respectively.

STATISTICAL ANALYSIS

Quantitative data are expressed as mean±SD and qualitative variables are expressed as frequencies. Student *t* (gaussian distribution) and Mann-Whitney *U* (nongaussian distribution) tests were used for quantitative variables when comparing patients with type 1 diabetes with controls, and the Student *t* test for paired data (gaussian distribution) and the Wilcoxon rank sum test (nongaussian distribution) were used when comparing diabetic patients with good vs poor control. Frequencies between patients and controls and between patients with poor vs good control were compared using χ^2 and McNemar tests, respectively. All tests were 2-tailed, and $P<.05$ was considered significant. All analyses were performed using statistical software (SPSS for Windows, version 8.0; SPSS Inc, Chicago, Ill).

Table 1. Clinical Features of Patients With Type 1 Diabetes Mellitus and the Nondiabetic Control Group*

	Diabetic Patients (n = 334)	Nondiabetic Control Subjects (n = 803)
Sex, M/F, %	54/46	49/51
Age, mean ± SD, y	31.3 ± 10.2	30.7 ± 9.2
BMI, mean ± SD, kg/m^2	22.6 ± 3.2†	24.8 ± 4.4
Time since diagnosis, mean ± SD, y	7.9 ± 9.3	NA
Smoking, %	54	53
Hypertension, %	4.8	5.7
Retinopathy, %	27	0
Overt proteinuria, %	7	0
Creatinine, mean ± SD, µmol/L (mg/dL)	89 ± 14 (1.0 ± 0.2)	86 ± 14 (0.9 ± 0.2)
CHD, %	1.2	0
Peripheral arteriopathy, %	1.2	0

**BMI indicates body mass index; CHD, coronary heart disease; and NA, not applicable.*
†P<.001 compared with nondiabetic controls.

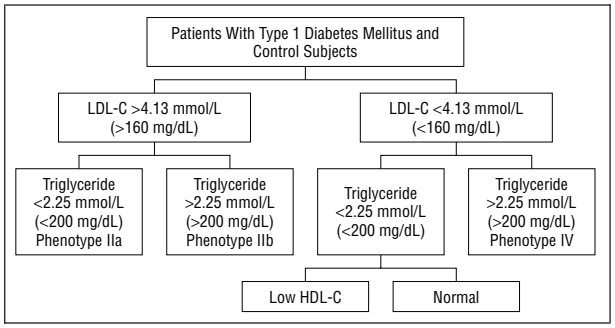

Figure 1. *Algorithm used for classification of patients and control subjects into the different dyslipidemic phenotypes. LDL-C indicates low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.*

terol (LDL-C) levels is advised in diabetic patients, limited data are available on the frequency with which the recommended goals are achieved. Thus, the aim of our study was to assess the effect of improving glycemic control on the prevalence of dyslipidemia and LDL-C concentrations greater than recommended goals in patients with type 1 diabetes compared with a control group of similar age.

RESULTS

CLINICAL FEATURES, GLYCEMIC CONTROL, AND LIPID CONCENTRATIONS

Patients and controls showed similar age, sex distribution, and frequency of tobacco consumption and hypertension, but their mean body mass indexes were different (Table 1). Similar results were obtained when comparing diabetic men and women with their nondiabetic counterparts (data not shown). Body mass index, markers of glycemic control, and lipid and lipoprotein concentrations in diabetic patients before and after glycemic optimization and in controls are shown in **Table 2**. Compared with the nondiabetic population, patients with poorly controlled diabetes displayed similar total cholesterol and total triglyceride levels but higher LDL-C and lower HDL-C concentrations. When grouping patients according to sex, men and women displayed lower HDL-C concentrations than their nondiabetic counterparts (1.16±0.32 vs 1.28±0.33 mmol/L [45±12 vs 50±13 mg/dL]; $P<.001$ and 1.42±0.40 vs 1.53±0.34 mmol/L [55±15 vs 60±13 mg/dL]; $P=.008$, respectively), but only diabetic women had higher LDL-C levels than control women (3.25±1.02 vs 2.88±0.89 mmol/L [125±40 vs 110±35 mg/dL]; $P=.001$).

Table 2. Results of Laboratory Tests Comparing Patients With Type 1 Diabetes Mellitus Before and After Achieving Good Glycemic Control With Nondiabetic Controls*

	Diabetic Patients		Nondiabetic Controls (n = 803)
	Poor Control (n = 334)	Good Control (n = 334)	
BMI, kg/m^2	22.6 ± 3.2†	23.1 ± 3†‡	24.8 ± 4.4
Glucose, mmol/L¶	9.02 ± 3.97†	7.86 ± 3.85†§	5.02 ± 0.79
Fructosamine, µmol/L	438 ± 114	304 ± 66‡	. . .
Hb A_{1c}, %	8.5 ± 1.97	6.25 ± 1.25‡	. . .
Total cholesterol, mmol/L#	5.0 ± 1.1	4.76 ± 1.0†‡	4.99 ± 1.1
Triglycerides, mmol/L**	1.13 ± 1.07	0.94 ± 0.8‡‖	1.11 ± 0.96
HDL-C, mmol/L#	1.27 ± 0.38†	1.36 ± 0.37‡‖	1.41 ± 0.36
LDL-C, mmol/L#	3.3 ± 1.0†	3.01 ± 0.9‡	3.02 ± 0.9

**Data are given as mean ± SD. BMI indicates body mass index; Hb A_{1c}, glycosylated hemoglobin; HDL-C, high-density lipoprotein cholesterol; and LDL-C, low-density lipoprotein cholesterol.*
†P≤.001 vs nondiabetic controls.
‡P≤.001 vs patients with poorly controlled diabetes.
§P = .01 vs patients with poorly controlled diabetes.
‖P = .04 vs nondiabetic controls.
¶To convert glucose from millimoles per liter to milligrams per deciliter, divide millimoles per liter by 0.05551.
#To convert cholesterol from millimoles per liter to milligrams per deciliter, divide millimoles per liter by 0.02586.
***To convert triglycerides from millimoles per liter to milligrams per deciliter, divide millimoles per liter by 0.01129.*

After optimization of glycemic control (Hb A_{1c} concentration decrease of 2.23±1.96 percentage points; $P<.001$), all lipid variables showed significant improvement (Table 2). Compared with nondiabetic controls, total triglyceride and total cholesterol concentrations became and HDL-C concentrations remained significantly lower in the diabetic group. Under these same conditions, triglyceride and total cholesterol levels were lower in diabetic men (1.04±1.0 vs 1.36±1.20 mmol/L [92±88 vs 120±106 mg/dL]; $P<.001$ and 4.69±1.0 vs 5.13±1.10 mmol/L [180±40 vs 200±40 mg/dL]; $P<.001$, respectively) but not in diabetic women (0.83±0.50 vs 0.88±0.50 mmol/L [73±44 vs 80±44 mg/dL] and 4.84±1.0 vs 4.87±1.0 mmol/L [190±40 vs 190±40 mg/dL], respectively) compared with their nondiabetic counterparts.

PREVALENCE OF DYSLIPIDEMIA, DYSLIPIDEMIC PHENOTYPES, AND RECOMMENDED LDL-C CONCENTRATIONS

The prevalence of the different lipid disorders in patients with type 1 diabetes before and after optimization of glycemic control and in the nondiabetic group are de-

picted in **Figure 2**. Low HDL-C concentration was the most prevalent lipid abnormality in diabetic patients with poor glycemic control. It was the only quantitative alteration significantly more prevalent in the diabetic group than in the control group. When considering the sexes separately, similar results were found, except that diabetic women also showed a higher prevalence of hypercholesterolemia than nondiabetic women (**Table 3**). After achieving good glycemic control, the frequency of hypercholesterolemia became similar in diabetic and nondiabetic individuals. Although hypercholesterolemia became less frequent in diabetic men than in nondiabetic men, in diabetic women with optimal glycemic control, the prevalence of dyslipidemia did not differ from that observed in nondiabetic women.

The distribution of dyslipidemic phenotypes in patients and controls according to the algorithm displayed in Figure 1 is depicted in **Figure 3**. Most patients were normolipidemic. The most prevalent dyslipidemic phenotypes in patients with type 1 diabetes, regardless of metabolic control, were IIa and low HDL-C concentration. Nevertheless, with improved metabolic control, the frequency of each dyslipidemic phenotype decreased, with the proportion of normolipidemia becoming more prevalent than in nondiabetic controls.

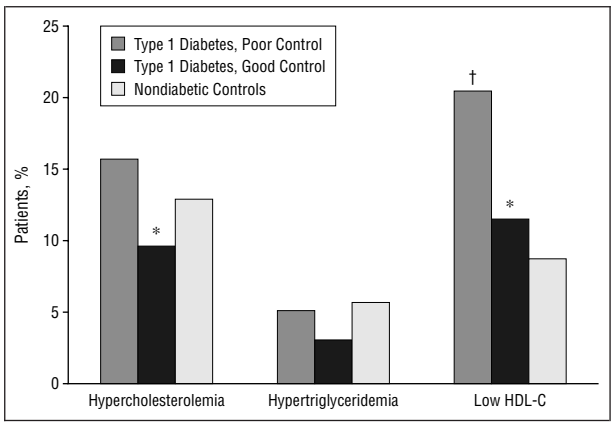

Figure 2. *Prevalence of dyslipidemic disorders in patients with type 1 diabetes mellitus before and after glycemic optimization and in nondiabetic controls. Asterisk indicates* P = *.01 vs patients with poorly controlled type 1 diabetes; dagger,* P< *.001 vs nondiabetic controls. See the "Definition of Dyslipidemia, Dyslipidemic Phenotypes, and Recommended LDL-C Concentrations" subsection of the "Patients and Methods" section for definitions of the dyslipidemic disorders.*

Regarding LDL-C goals, the prevalence of LDL-C concentrations of 2.6 mmol/L or less (≤100 mg/dL) in patients with type 1 diabetes with poor glycemic control was 22.4%, reaching 34.2% after glycemic optimization ($P=.01$). The percentages of patients showing LDL-C values greater than 3.4 mmol/L (>130 mg/dL), thus making them eligible for pharmacological intervention, were 41.9% and 25.9% under poor and good control, respectively ($P<.001$).

COMMENT

The results of this study confirm that total triglyceride and total cholesterol concentrations do not differ, despite poor glycemic control, between patients with insulin-treated type 1 diabetes and nondiabetic controls of similar age. However, LDL-C levels are higher and HDL-C levels are lower in the diabetic group than in the control group. In addition, our findings demonstrate that the most frequent dyslipidemic disorder in diabetic patients with poor glycemic control is low HDL-C concentration and that most patients have undesirable levels of LDL-C, with 1 in 4 requiring drug intervention. These lipid abnormalities improve after glycemic optimization and, except for HDL-C concentrations, become similar to or more favorable than those in controls. Finally, the impact of diabetes on lipid levels seems to be more evident in women than in men.

LIPOPROTEIN CONCENTRATIONS

In agreement with results of previous studies,[2-4,6,14] the degree of glycemic control is the major determinant of lipoprotein profile in our patients with type 1 diabetes. Although increased concentrations of triglycerides are frequently seen in untreated diabetic patients, lipid profiles of patients with poorly controlled insulin-treated type 1 diabetes show normal or mildly increased triglyceride, total cholesterol, and LDL-C levels and decreased, normal, or increased HDL-C levels.[2,5-7,15,16] Glycemic optimization by intensive insulin therapy is associated with normal or better than normal lipid levels.[2-4,6,17] Patients with insulin-treated type 1 diabetes in the present study showed higher LDL-C but not triglyceride or total cholesterol levels and lower HDL-C concentrations than controls. After

Table 3. Prevalence of the Different Dyslipidemic Disorders According to Sex*

	Diabetic Men			Diabetic Women		
	Poor Control (n = 181)	Good Control (n = 181)	Nondiabetic Men (n = 391)	Poor Control (n = 153)	Good Control (n = 153)	Nondiabetic Women (n = 412)
LDL-C >4.13 mmol/L (>160 mg/dL)	15.8	9.7†	17.5	15.6†	9.5	8.5
Triglycerides >2.25 mmol/L (>200 mg/dL)	8.3	5.0	9.7	1.3	0.7	1.9
HDL-C, mmol/L (mg/dL)						
<0.9 (<35)	20.6‡	11.2	8.4	NA	NA	NA
<1.1 (<45)	NA	NA	NA	19.6§	12.0	9.2

**Data are given as percentages. LDL-C indicates low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; and NA, not applicable.*
†P = *.04 vs nondiabetic controls.*
‡P< *.001 vs nondiabetic controls.*
§P = *.003 vs nondiabetic controls.*

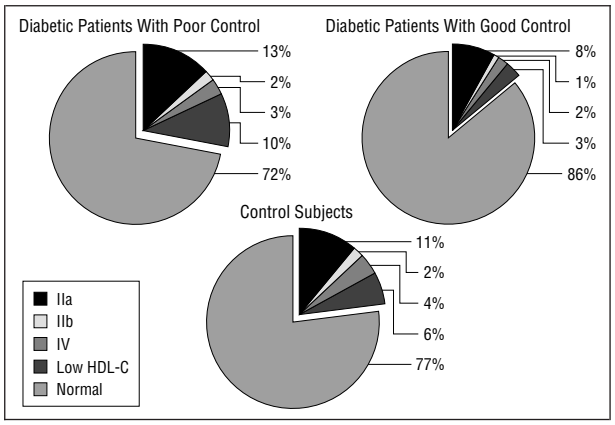

Figure 3. *Distribution of dyslipidemic phenotypes in patients with type 1 diabetes mellitus before and after glycemic optimization and in nondiabetic control subjects. HDL-C indicates high-density liproprotein cholesterol.*

glycemic optimization, all lipidic variables improved significantly (Table 2) to such an extent that total triglyceride and total cholesterol concentrations became lower than those in controls. Nevertheless, HDL-C concentrations remained lower too. Improvements in lipoprotein concentrations are also found in other studies,[3,4,6,17,18] although, unlike what our results show, HDL-C levels do not increase consistently.[19] Previous studies in patients with type 1 diabetes with acceptable or unknown glycemic control show normal or increased levels of HDL-C compared with nondiabetic controls.[14,20-23] However, although HDL-C levels tend to increase with improvement of control, it generally takes several weeks for a change to occur, and it is more often observed in patients with extremely poor previous control who achieve a marked improvement in Hb A_{1c} levels.[4,17,18,24,25] These findings might be related to the fact that, of all lipoproteins, HDL-C has the slowest turnover rate. Furthermore, when accompanied by excessive weight gain, the increase in HDL-C concentration is attenuated.[26] In our study, however, the weight increase that accompanied glycemic optimization after 3 to 6 months of intensive therapy was moderate and patients' body mass indexes remained below those of controls.

PREVALENCE OF LIPIDIC DISORDERS AND THERAPEUTIC GOALS

Data on the prevalence of dyslipidemia in patients with type 1 diabetes are, to our knowledge, limited to 5 cross-sectional studies performed in Northern Europe[2,9] and the United States[7,8,27] and are based on total triglyceride, total cholesterol, or LDL-C concentrations alone. The prevalence of hypertriglyceridemia varies among studies (13%-31%) depending on the cutoff point used to define it and the clinical features of the patients involved.[2,8] On the other hand, hypercholesterolemia is, if anything, less common in diabetic patients than in nondiabetic controls.[2,7-9,27] In the present study, the prevalence of hypercholesterolemia and hypertriglyceridemia, using the cutoff points recommended by the National Cholesterol Education Program[12] (triglyceride >2.25 mmol/L [>200 mg/dL] and LDL-C >4.13 mmol/L [>160 mg/dL]), was similar (under poor glycemic control) or lower (after glycemic optimization) than that observed in age-matched controls. These results are in agreement with those of previous studies, except for the low prevalence of hypertriglyceridemia, which could be accounted for by the clinical features of the population involved (young, lean, and with a low prevalence of nephropathy). In addition to the effect of improved glycemic control on the prevalence of dyslipidemia and thus its role in lowering cardiovascular risk, a particularly novel finding provided by the present study is the prevalence of low HDL-C concentrations in patients with type 1 diabetes. Low HDL-C concentration was the most frequent dyslipidemic disorder regardless of glycemic control. These results are in disagreement with the belief that the level of HDL-C is normal or increased in type 1 diabetes,[8,16,20] which, on the other hand, would make it unlikely that HDL-C concentration had a negative effect on cardiovascular risk in these subjects. Nevertheless, low HDL-C concentration is associated with cardiovascular disease in diabetic[28-30] and nondiabetic[31-33] groups, and recent findings[34] suggest that the rate of coronary events is reduced by raising HDL-C levels and lowering total triglyceride concentrations with gemfibrozil therapy without changing LDL-C concentrations. This probably makes low HDL-C concentration the most important quantitative lipid disorder in type 1 diabetes. The discrepancy between the frequencies of hypertriglyceridemia and low HDL-C levels in our study might be because even mild improvements in glycemic control can result in a decrease in total and very LDL triglyceride, but a prolonged and distinct degree of improvement of glycemic control may be necessary to cause significant changes in HDL-C levels.[4,17,18,25] The difference in prevalence of low HDL-C levels in diabetic patients between the present and previous studies might be due to differences in the diabetic and nondiabetic populations analyzed. Nevertheless, the populations included in this study were large and had similar clinical features with a known effect on lipid metabolism. In addition, this increased prevalence of low HDL-C concentrations cannot be explained by other clinical features such as nephropathy, hypertriglyceridemia, and obesity, the frequency of which was low in these patients.

The cutoff points that define dyslipidemia differ from therapeutic goals, depending on coexisting cardiovascular risk factors or disease. In diabetic patients, because of high cardiovascular risk, aggressive therapy of dyslipidemia is recommended.[12,13] Even in the absence of previous cardiovascular disease, LDL-C concentrations greater than 2.6 mmol/L (>100 mg/dL) are eligible for lifestyle intervention, and patients with LDL-C concentrations greater than 3.4 mmol/L (>130 mg/dL) should be treated with lipid-lowering drugs.[13] However, limited data are available on the proportion of patients with type 1 diabetes exceeding these cutoff points. In the Pittsburgh Epidemiology of Diabetes Complications Study,[7] the prevalence of LDL-C con-

centrations of 4.13 mmol/L or higher (≥160 mg/dL) in adult women and 3.4 mmol/L or higher (≥130 mg/dL) in men, at that time considered cutoff points for desirable concentrations of LDL-C, was 25% and 40%, respectively. Following current recommendations,[12,13] in the present study, identical cutoff points were used for men and women. After glycemic optimization, the proportion of patients requiring lifestyle or pharmacological intervention decreased from 78% and 42% to 66% and 26%, respectively, the latter percentage being similar to that described by Orchard[7] after excluding patients with nephropathy. Thus, these results support intensive insulin therapy as the initial treatment of choice for dyslipidemia in poorly controlled type 1 diabetes.

SEX DIFFERENCES

Women lose their protective sex effect against development of cardiovascular disease when they have diabetes. They have a prevalence of atherosclerosis that approaches or equals that of men,[35] and once they have coronary heart disease, their prognosis is worse.[36] However, the mechanisms that link diabetes to this risk are poorly understood. The finding of less favorable lipid profiles in women with type 1 diabetes included in this study might explain, at least to a certain extent, their lack of protection. Women, but not men, with type 1 diabetes displayed higher concentrations of LDL-C and a higher prevalence of hypercholesterolemia when glycemic control was poor. After glycemic optimization, diabetic men, but not women, showed lower total triglyceride and total cholesterol concentrations and a lower prevalence of hypercholesterolemia compared with their nondiabetic counterparts. These findings agree with those obtained by some[2,7,9,20] but not all[8] studies. Sex disparities in lipid profile could therefore play a role in the more negative impact diabetes has on cardiovascular risk in women than in men.

CONCLUSIONS

Results of the present study demonstrate that the most prevalent dyslipidemic disorder in insulin-treated poorly controlled diabetes is low HDL-C concentrations and that most patients have undesirable LDL-C levels, with a high proportion requiring pharmacological intervention. In addition, our results prove the beneficial effect glycemic optimization has on diabetic dyslipidemia and confirm that women with type 1 diabetes have less favorable lipid profiles than men. These findings are of considerable interest because they are based on large diabetic and control populations and provide information that, to our knowledge, has not been published previously. Given the association of moderately increased LDL-C[37,38] and low HDL-C concentrations with cardiovascular disease in diabetic[28,30] and nondiabetic[31-34] populations, results of this study reinforce that intensive insulin therapy is the initial treatment of choice for dyslipidemia in poorly controlled type 1 diabetes and prove the importance of including HDL-C in the evaluation of lipid levels in these patients.

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