Different types of dyslipidemia in type 2 diabetes and the associated factors

Tip 2 diyabette farklı dislipidemi türleri ve ilişkili faktörler

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Abstract

Aim: Diabetes and dyslipidemia are common diseases that can be seen together. In this study, we aimed to investigate factors affecting the type of dyslipidemia in diabetic patients.

Methods: The cross-sectional study included a total of 596 patients with type 2 diabetes who visited the outpatient diabetes clinic of the Istanbul Medeniyet University between January 2017 and December 2019. Patient laboratory, clinical, and sociodemographic data were retrieved from medical records.

Results: Of all patients, 52% were diagnosed with hypercholesterolemia (total cholesterol ≥200 mg/dL) and 56.4% had a history of hypertriglyceridemia. Four hundred and forty-four (74%) patients had abnormal low-density lipoprotein cholesterol (LDL-C) levels (≥100 mg/dL). Eighty percent of the female patients and 67.4% of the male patients had abnormal LDL-C levels, and the difference between the two sexes was statistically significant (p<0.001). Triglyceride levels were higher in the patients with a hemoglobin A1c (HBA1c) level ≥7% (p<0.001). Smokers had significantly higher levels of LDL-C (p=0.03) and lower levels of high-density lipoprotein cholesterol (p=0.038) than non-smokers. The mean body mass index was higher for the group of non-smokers than for the smokers (p<0.001). The rates of hypertriglyceridemia and obesity were significantly higher in patients with hypertension than in those without (p=0.036 and p=0.013, respectively).

Conclusion: Dyslipidemia is common in diabetic patients, especially women. A complete examination of the patient should include the consideration of conditions associated with dyslipidemia.

Keywords: diabetes; dyslipidemia; hypercholesterolemia; hypertriglyceridemia

Öz

Amaç: Diyabet ve dislipidemi birlikte görülebilen yaygın hastalıklardır. Bu çalışmada diyabet hastalarında görülen dislipidemi tipini etkileyen faktörleri incelemek amaçlanmıştır.

Yöntem: Kesitsel araştırmamız Ocak 2017—Aralık 2019 döneminde İstanbul Medeniyet Üniversitesi'nin diyabet polikliniğine başvuran toplam 596 tip 2 diyabetli hasta içerdi. Hastaların laboratuvar, klinik ve sosyodemografik verileri tıbbi kayıtlardan elde edildi.

Bulgular: Hastaların %52'si hiperkolesterolemi (total kolesterol ≥200 mg/dL) tanısı almıştı ve %56,4'ünde hipertrigliseridemi öyküsü vardı. Dört yüz kırk dört (%74) hastada anormal düşük yoğunluklu lipoprotein kolesterol (DYL-K) seviyeleri (≥100 mg/dL) görüldü. DYL-K düzeyi kadınların %80'inde, erkeklerin %67,4'ünde anormaldi ve iki cinsiyet arasındaki fark istatistiksel olarak anlamlıydı (p<0,001). Hemoglobin A1c (HBA1c) düzeyi ≥%7 olan hastalarda trigliserit düzeyleri daha yüksekti (p<0,001). Sigara içmeyenlere kıyasla, sigara içenlerde DYL-K seviyeleri anlamlı biçimde daha yüksek (p=0,03), yüksek yoğunluklu lipoprotein kolesterol seviyeleri ise anlamlı biçimde daha düşüktü (p=0,038). Sigara içenlere kıyasla sigara içmeyen hasta grubunda ortalama vücut kitle indeksi daha yüksekti (p<0,001). Hipertansiyonu olmayan hastalara kıyasla, hipertrigliseridemi ve obezite oranları hipertansiyonlu hastalarda anlamlı biçimde daha yüksekti (sırasıyla p=0,036 ve p=0,013).

Sonuç: Dislipidemi diyabetik hastalarda, özellikle kadınlarda yaygındır. Yapılacak bütüncül incelemelerde dislipidemi ile ilişkili durumlar da göz önünde bulundurulmalıdır.

Anahtar sözcükler: dislipidemi; diyabet; hiperkolesterolemi; hipertrigliseridemi

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INTRODUCTION

Hypertension, dyslipidemia, diabetes, obesity, smoking and family history, and microalbuminuria are among the leading causes of cardiovascular diseases (1,2). The significance of dyslipidemia in cardiovascular diseases has been stated in large international studies, such as the INTERHEART and INTERSTROKE studies (3,4). Coronary artery disease is 2 to 4 times more common in individuals with diabetes than in non-diabetic individuals, and the risk is even greater in the coexistence of dyslipidemia and diabetes (5). The PROCAM study found that levels of low-density lipoprotein cholesterol (LDL-C) were slightly higher in hypertensive men and diabetic women, while rates of elevated triglycerides were higher in all hypertensive and diabetic patients, regardless of sex. High-density lipoprotein-cholesterol (HDL-C) has been found to be low in diabetic and hypertensive women (6). In this study, we aimed to investigate factors affecting the type of dyslipidemia in diabetic patients.

MATERIALS AND METHODS

Sample selection

The cross-sectional study included a total of 596 patients with type 2 diabetes (T2D) who visited the outpatient diabetes clinic of the Istanbul Medeniyet University between January 2017 and December 2019. The patient laboratory, clinical, and socio-demographic data were retrieved from the medical records. These included data on patient age and sex, levels of hemoglobin A1c (HbA1c), HDL-C, LDL-C, total cholesterol (TC) and triglyceride (TG), body mass index (BMI), waist circumference, and history of smoking and hypertension. Patients with type 1 diabetes, under the age of 18 years, and with incomplete records were excluded. The T2D diagnosis was made based on an HbA1c level >6.5% (7). An HbA1c level >7% was defined as poorly controlled T2D.

Measurements

The TG, TC, HDL-C and LDL-C levels were measured using an Architect c8000 analyzer (Abbott Diagnostics, Illinois, USA). Our laboratory is not accredited, but it is a registered public laboratory under the supervision of the Ministry of Health, operating according to the "Quality Standards in Health".

Cholesterol can be determined by chemical methods or enzymatically. These methods are either direct or indirect. In direct methods, serum or plasma is used directly. Direct methods are preferred as they are simpler and applicable to autoanalysis. Triglycerides are determined using a commercial kit based on enzymatic methods. In our study, we used commercial kits for the lipid tests. HbA1c was assessed by high-performance liquid chromatography using a Primus high-performance liquid chromatography device. The dyslipidemia definitions were made according to the European Society of Cardiology dyslipidemia guidelines (8): hypercholesterolemia (TC ≥200 mg/dL), hypertriglyceridemia (TG ≥150 mg/dL), low HDL-C (≤40 mg/dL in males, ≤50 mg/dL in females), and high LDL-C (≥100 mg/dL). BMI was calculated by dividing the participant's weight (kg) by the square of the height (m^2). A BMI <25 kg/m^2 was defined as normal weight, 25–29.9 kg/m^2 overweight, and ≥30 kg/m^2 obese.

Statistical analysis

Statistical analysis was performed using the 2007 version of the Number Cruncher Statistical System (Utah, USA). Normality of the data was checked using histograms and the Kolmogorov–Smirnov and Shapiro–Wilk tests. Intergroup comparisons were made using the Kruskal–Wallis and Mann–Whitney U tests. Intervariable correlations were tested by Pearson's and Spearman's correlation analyses. The Bonferroni test and one-way analysis of variance were used to compare normally distributed parameters between three or more groups. Pearson's chi-square test, the Fisher–Freeman–Halton test, and Fisher's exact test were used for qualitative analysis. $p<0.05$ was considered statistically significant.

Study ethics

The study protocol was approved by the local ethics committee of of the Istanbul Medeniyet University Goztepe Training and Research Hospital (2020/0772). After written informed consent was obtained from all participants, the study was conducted in accordance with the principles of the Declaration of Helsinki.

RESULTS

Of the 596 patients included, 261 were male (43.8%) and 335 were female (56.2%). The mean patient age

Table 1. Patient sociodemographic characteristics, anthropometric measurements, and serum lipid profiles (N=596)

	Mean±SD (min.–max.)
Age (year)	60.72±10.28 (23–88)
Height (cm)	162.98±9.30 (142–192)
Weight (kg)	82.99±13.77 (53–133)
Waist circumference (cm)	101.75±11.19 (58–150)
BMI (kg/m^2)	31.33±5.21 (17–52)
HbA1c (%)	8.79±2.24 (5.5–17.8)
TG (mg/dL)	182.03±112.823 (45–1420)
HDL-C (mg/dL)	42.95±11.80 (11–105)
LDL-C (mg/dL)	128.13±39.44 (46–402)

BMI: body mass index; HbA1c: hemoglobin A1c; HDL-C: high-density lipoprotein-cholesterol; LDL-C: low-density lipoprotein-cholesterol; max.: maximum; min.: minimum; SD: standard deviation; TG: triglyceride

was 60.72±10.2 years (61.42±10.1 years in females, 59.8±10.4 years in males). The mean HbA1c level for all patients was 8.89±3.3%. Patient sociodemographic, anthropometric, and biochemical characteristics are summarized in Table 1.

Table 2 presents the rates of different types of dyslipidemia in male and female patients. Of all patients, 52% were diagnosed with hypercholesterolemia with a TC level ≥200 mg/dL and 56.4% were diagnosed with hypertriglyceridemia. Four hundred and forty-four (74%) patients had abnormally elevated LDL-C levels (≥100 mg/dL). Two hundred and sixty-eight (80%) of the female patients and 176 (67.4%) of the male patients had abnormal LDL-C levels, and the difference between the two sexes was statistically significant (p<0.001). The HDL-C level was below 50 mg/dL in 62.1% of the male patients and below 40 mg/dL in 65.7% of the female patients. No significant difference was found between the two sexes in terms of levels of abdominal obesity and abnormal triglyceride (p=0.966 and p=0.619, respectively).

Table 3 presents the prevalence of types of dyslipidemia according to glycemic control status. The participants were divided into 2 categories based on their HbA1c levels: patients with an HbA1c level <7.0% and those with an HbA1c level ≥7%. The triglyceride levels were significantly higher in the latter group than in the first group (p<0.001).

The participants were also divided into 3 groups according to smoking status: Smokers, Non-smokers, and Ex-smokers. Smokers had significantly higher LDL-C and lower HDL-C levels than Non-smokers (p=0.03 and p=0.038, respectively). Non-smokers had higher BMIs than smokers (p<0.001). While Non-smokers had a higher rate of obesity than Smokers, the number of overweight patients was greater in Smokers (Table 4).

Table 2. The prevalence of types of dyslipidemia in male (n=261) and female (n=335) patients, shown in n (%)

	Total	**Males**	**Females**	***p***
Triglyceride (mg/dL)				
<150	260 (43.6)	120 (46)	140 (41.8)	0.619
≥150	336 (56.4)	141 (54)	195 (58.2)	
LDL-C (mg/dL)				
<100	152 (26)	85 (32.6)	67 (20)	*<0.001*
≥100	444 (74)	176 (67.4)	268 (80)	
Low HDL-C				
Yes	382 (64.1)	162 (62.1)	220 (65.7)	*<0.001*
No	214 (35.9)	99 (37.9)	115 (34.3)	
BMI (kg/m$^{2)}$				
<25	53 (8.2)	34 (13)	19 (4.5)	*<0.001*
25–29.9	216 (36)	121 (46.4)	95 (28.7)	
≥30	327 (54.8)	106 (40.6)	221 (66.8)	
TC (mg/dL)				
<200	283 (48)	153 (58.6)	130 (38.8)	*<0.001*
≥200	313 (52)	108 (41.4)	205 (61.2)	
Abdominal obesity				
No	58 (9.7)	52 (19.9)	6 (1.8)	0.966
Yes	538 (90.3)	209 (80.1)	329 (98.2)	

BMI: body mass index; HbA1c: hemoglobin A1c; HDL-C: high-density lipoprotein-cholesterol; LDL-C: low-density lipoprotein-cholesterol; TC: total cholesterol

In the comparison of diabetic patients with and without hypertension, the rates of hypertriglyceridemia and obesity were found to be higher in the hypertensive diabetic patients (p=0.036 and p=0.013, respectively) (Table 5).

DISCUSSION AND CONCLUSION

Of all participants, 74% had a LDL-C level ≥100 mg/dL, and this abnormal lipid profile was present in 8 out of every 10 women. One of the most important studies showing that dyslipidemia is common in women is the UKPDS study (9), where the fasting plasma lipoproteins and lipids of men and women were compared for the diagnosis of T2D and lipid concentrations were determined for age and sex differentiation. The impact of T2D on the levels of plasma lipids and lipoproteins was determined to be greater in female patients than in male patients. This might help to understand why women have a greater cardiovascular risk than men.

In other studies, the effect of diabetes on dyslipidemia was shown more clearly by way of comparison to non-diabetic control groups. In our study, there was no control group and all of our patients were diabetic. There was no difference between the male and female patients in terms of triglyceride levels. Obesity was found to be more common in the group of female patients. This finding is consistent with results of the UKPDS study, in which the mean BMI was determined

Table 3. The prevalence of types of dyslipidemia in patients with an HbA1c level <7% (n=148) and ≥7% (n=448), shown in n (%)

	HbA1c <7%	HbA1c ≥7%	*p*
Triglyceride (mg/dL)	83 (32)	177 (68)	***<0.001***
<150	65 (19.3)	271 (80.7)	
≥150			
LDL-C (mg/dL)			
<100	42 (27.6)	110 (72.4)	0.355
≥100	106 (24)	338 (76)	
Low HDL-C			
Yes	91 (23.9)	291 (76.1)	0.446
No	57 (26.6)	157 (73.3)	
TC (mg/dL)			
<200	78 (37.6)	205 (72.4)	0.142
≥200	70 (22.3)	243 (77.7)	
Abdominal obesity			
No	15 (25.9)	43 (74.1)	0.848
Yes	133 (24.7)	405 (75.3)	
BMI (kg/m^2)			
<25	15 (30.7)	34 (69.3)	0.333
25–29.9	58 (26.9)	158 (73.1)	
≥30	74 (22.6)	253 (77.3)	

BMI: body mass index; HbA1c: hemoglobin A1c; HDL-C: high-density lipoprotein-cholesterol; LDL-C: low-density lipoprotein-cholesterol; TC: total cholesterol

Table 4. The prevalence of types of dyslipidemia in smokers (n=94), non-smokers (n=496), and ex-smokers (n=6), shown in n (%)

	Smokers	Non-smokers	Ex-smokers	*p*
Triglyceride (mg/dL)				
<150	40 (42.6)	216 (43.5)	4 (66.7)	0.512
≥150	54 (57.4)	280 (56.5)	2 (33.3)	
LDL-C (mg/dL)				
<100	16 (17)	136 (27.4)	0	*0.037*
≥100	78 (83)	360 (72.6)	6 (100)	
Low HDL-C				
Yes	64 (68.1)	317 (63.9)	1 (16.7)	*0.038*
No	30 (31.9)	179 (36.1)	5 (83.3)	
BMI (kg/m^2)				
<25	16 (17.2)	35 (6.5)	1 (16.7)	*<0.001*
25–29.9	45 (48.4)	169 (34.3)	2 (33.3)	
≥30	32 (34.4)	292 (59.2)	3 (50)	
TC (mg/dL)				
<200	36 (38.3)	244 (49.2)	3 (50)	0.151
≥200	58 (61.7)	252 (50.8)	3 (50)	
Abdominal obesity				
No	79 (84)	453 (91.3)	0	0.066
Yes	15 (16)	43 (8.7)	6 (100)	
HbA1c				
<7%	17 (18.1)	128 (25.8)	3 (50)	0.101
≥7%	77 (81.9)	368 (74.2)	3 (50)	

BMI: body mass index; HbA1c: hemoglobin A1c; HDL-C: high-density lipoprotein-cholesterol; LDL-C: low-density lipoprotein-cholesterol; TC: total cholesterol

Table 5. The prevalence of types of dyslipidemia in patients with (n=197) and without (n=399) hypertension, shown in n (%)

	Hypertension +	Hypertension -	*p*
Triglyceride (mg/dL)	74 (37.6)	186 (46.6)	0.036
<150	123 (62.4)	213 (53.4)	
≥150			
LDL-C (mg/dL)			
<100	56 (28.4)	96 (24.1)	0.25
≥100	141 (71.6)	303 (75.9)	
Low HDL-C			
Yes	134 (68)	248 (62.2)	0.16
No	63 (32)	151 (37.8)	
TC (mg/dL)			
<200	96 (48.7)	187 (46.9)	0.66
≥200	101 (51.3)	212 (53.1)	
Abdominal obesity			
No	183 (92.9)	355 (89)	0.12
Yes	14 (7.1)	44 (11)	
BMI (kg/m^2)			
<25	11 (5.6)	38 (9.6)	*0.013*
25–29.9	61 (30.8)	157 (39.3)	
≥30	124 (63.6)	204 (51.1)	
HbA1c			
<7%	47 (23.9)	101 (25.3)	0.69
≥7%	150 (76.1)	298 (74.7)	

BMI: body mass index; HbA1c: hemoglobin A1c; HDL-C: high-density lipoprotein-cholesterol; LDL-C: low-density lipoprotein-cholesterol; TC: total cholesterol

as 28.3 kg/m^2 for men and 30.8 kg/m^2 for women (9). Also, the fact that 7 out of every 10 women were obese in that study indicates that obesity has gradually increased over the years.

A large-scale meta-analysis conducted in Turkey reported a very high prevalence of MetS, especially in women, finding that 1 in every 4 men and 1 in every 3 women had MetS (10). The PURE study, where individuals of low and high socioeconomic status selected from the seven geographical regions of Turkey were followed up for 12 years, also reported that abdominal obesity, low HDL-C levels, high blood pressure, and dysglycemia were more common in women than in men (11).

We also investigated the effect of diabetes regulation on the type of dyslipidemia. Other than elevated triglyceride levels, no significant difference was found between the two groups. Shahwan et al. observed that impaired blood glucose regulation was associated with LDL-C and TG elevation, particularly with the rate of exceeding the LDL-C upper limit of 130 mg/dL (12).

In the present study, smokers had significantly higher LDL-C and lower HDL-C levels than non-smokers. This might be due to a general neglect of personal health and low rate of statin use. A striking finding was that the rate of obesity was significantly lower in the group of smokers than in the non-smokers. The relationship observed between smoking and LDL-C in our study was not seen in a study including 2160 Chinese men.

Also, we determined that TG levels were significantly higher and HDL-C levels were lower in the group of smokers than in the non-smokers and the ex-smokers. However, there was no significant difference among the smokers, non-smokers, and ex-smokers in terms of levels of TC, LDL-C, apolipoprotein B (ApoB), and lipoprotein(a). Surprisingly, another study found that, compared to light smokers, the ApoB levels of very heavy smokers were more commonly abnormal although their LDL-C values were more commonly within the normal range (13).

In our study, high triglyceride levels and obesity were significantly more prevalent in the patients with hypertension than in those without. Hypertension, obesity, dyslipidemia, and diabetes are interrelated comorbidities. For example, it has been shown in the NHANES study that obese patients are 2 times more likely to have dyslipidemia and 4.8 times more likely to have hypertension compared to normal-weight patients. Therefore, the answer to the question of whether dyslipidemia occurs in hypertensive patients or hypertension occurs in dyslipidemic patients is unclear (14).

The main limitations of our study include the lack of a control group and the retrospective design. Although they were socioeconomically heterogeneous, the use of a sample consisting of patients presenting to the outpatient diabetes clinic of a university hospital may be considered another limitation in terms of patient perspectives. Similar studies conducted in Turkey have often been conducted in tertiary and university hospitals and rarely in primary healthcare settings, which affects the nature of the data obtained from patients in Turkey. Accordingly, a comparison with foreign data would not be very useful in terms of evaluating patient perceptions and follow-up quality.

In conclusion, dyslipidemia is quite common in diabetes, especially in diabetic women. It is clear that this is related to abdominal obesity, among other reasons. The treatment processes in diabetic patients should in-

clude careful assessments of lifestyle and dyslipidemia status as well.

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Conflict of interest and financial disclosure

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