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Original Article

Investigation of Endocrine Disease Frequency in Dyslipidemia

Dislipidemide Endokrin Hastalık Sıklığının Araştırılması

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ABSTRACT

Objective: The purpose of our research was to investigate the frequency of endocrine disorders like diabetes, high blood pressure, obesity, hyperuricemia, insulin resistance, and thyroid dysfunction, all of which are thought to be critical in the process of diagnosing and treating patients who have dyslipidemia.

Methods: Between December 2010 and May 2012, a total of 200 patients with dyslipidemia and 23 healthy control groups without dyslipidemia who applied to the general internal medicine and subspecialty outpatient clinics at the Atatürk University Faculty of Medicine were included in the study. The mean age of the dyslipidemic patients was 49 ± 15 years, and the mean age of the healthy control groups was 32 ± 17 years. Anthropometric measures were obtained, as well as measurements of triglyceride levels, total cholesterol levels, low-density lipoprotein cholesterol levels, high-density lipoprotein cholesterol levels, free T4 levels, Thyroid-stimulating hormone (TSH), The hemoglobin A1c (HbA1C) levels, serum uric acid levels, fasting insulin levels, fasting blood glucose levels and Hemoglobin A1c (HbA1c) .

Results: It was shown that diabetes mellitus is the most common endocrine condition that occurs in conjunction with dyslipidemia, with a prevalence of 52%. While there was a statistically significant increase in HbA1c, body mass index, and uric acid values of the dyslipidemic group compared to the control group ($P < .05$), no difference was found between the 2 groups in TSH and homeostasis model assessment index-insulin resistance (HOMA-IR) values. Also, 85 of the patients in the dyslipidemic group (42.5%) were found to have systemic hypertension, but only one of the patients in the control group (4.3%) had hypertension ($p < .001$).

Conclusion: The frequency of diabetes, hypertension, obesity, and hyperuricemia in patients with dyslipidemia was significantly higher than in the control group. Considering these diseases when treating dyslipidemia is important for cardiovascular morbidity and mortality.

Keywords: Dyslipidemia, diabetes mellitus, hypertension, obesity, hyperuricemia

ÖZ

Amaç: Çalışmamızda dislipidemi saptanan hastalarda tanı ve tedavi yönetiminde önemli olduğunu düşündüğümüz diabet, hipertansiyon, obezite, hiperürisemi, insülin direnci ve tiroid fonksiyon bozukluğu gibi endokrin hastalıkların sıklıklarının incelenmesi amaçlanmıştır.

Yöntemler: Çalışmaya 2010 Aralık-2012 Mayıs ayları arasında Atatürk Üniversitesi Tıp Fakültesi Genel Dahiliye ve yandal polikliniklerine başvuran yaş ortalaması 49 ±15 yıl olan dislipidemik 200 hasta ile dislipidemisi olmayan yaş ortalaması 32 ± 17 yıl olan 23 sağlıklı kontrol grubu alındı. Antropometrik ölçümlere bakıldı, total kolesterol, trigliserid, LDL (low-density lipoprotein) kolesterol, HDL (high-density lipoprotein) kolesterol, serbest T4, TSH (Tiroid Stimülan Hormon), serum ürik asit, açlık insülin, açlık kan glukozu ve HBA1c (Hemoglobin A1c) düzeyi çalışıldı.

Bulgular: Dislipidemiye eşlik eden endokrin hastalıkların başında %52 oranla diabetes mellitus'un olduğu saptandı. Dislipidemik grubunun HbA1C, VKİ (vücut kitle indeksi) ve serum ürik asid değerlerinde kontrol grubuna göre istatistiksel olarak anlamlı yükseklik saptanırken ($p < .05$), TSH ve HOMA-IR (homeostasis model assessment index) değerlerinde iki grup arasında fark saptanmadı. Ayrıca dislipidemik grupta 85 (%42,5) hastada sistemik hipertansiyon saptanırken kontrol grubunda hipertansiyonu olan 1 hasta (%4,3) tesbit edildi ($p < .001$).

Sonuç: Dislipidemili hastalarda diabet, hipertansiyon, obezite ve hiperürisemi sıklığı kontrol grubuna göre anlamlı olarak yüksek saptandı. Dislipidemi tedavi edilirken bu hastalıkların göz önünde bulundurulması kardiyovasküler morbidite ve mortalite için önemlidir.

Anahtar Kelimeler: Dislipidemi, diabetes mellitus, hipertansiyon, obezite, hiperürisemi.

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INTRODUCTION

Ischemic heart disease (IHD) remains the main cause of morbidity and mortality worldwide. Dyslipidemia (defined as an increase in serum total cholesterol (TC), triglyceride (TG), and low-density lipoprotein (LDL) levels, a decrease in high-density lipoprotein (HDL) levels, or a combination of these features) is the major risk factor for IHD.[1] The cardiovascular mortality and morbidity-increasing effect of dyslipidemia is especially increased when it is combined with other risk factors (diabetes, obesity, hypertension, family history, smoking, sedentary lifestyle, etc.).[2] Today, a very rich literature has accumulated about the diseases accompanying dyslipidemia. For example, in a recent study conducted in China investigating the association between obesity, which is a pandemic of our time, and dyslipidemia, it was shown that obese patients, including regional obesity, have a higher prevalence of dyslipidemia.[3]

In a recent study investigating the frequency of relationship between dyslipidemia and diabetes, fasting TG level was determined as an independent risk factor for the development of new-onset diabetes (odds ratio (OR) 2.33, 95% CI 1.61-3.39). Based on the results of this study, it has been reported that hypertriglyceridemia may be an alternative screening tool to identify populations at risk of developing diabetes in the future.[4]

In a study conducted on patients with metabolic syndrome who had dyslipidemia, the prevalence of hypertension was found to be approximately 80%.[5] It was shown in another study that combined treatment of hypertension and dyslipidemia resulted in a significantly greater reduction in the risk of developing ischemic cardiovascular disease (CVD).[6]

In the literature, there are meta-analyses showing that increased serum uric acid levels may be independently and significantly associated with the risk of IHD.[7] Considering the close relationship between dyslipidemia and IHD, the frequency of hyperuricemia becomes important in dyslipidemic patients.

MAIN POINTS

- When paired with other risk factors, dyslipidemia's already significant impact on cardiovascular mortality and morbidity is ratcheted up to an even higher level.
- In our study, the frequency of diabetes, hypertension, obesity, and hyperuricemia in patients with dyslipidemia was significantly higher than in the control group.
- When diagnosing and treating dyslipidemia, taking into account these conditions will be an extremely helpful step that will contribute greatly to the management of the process.

The prevalence of dyslipidemia, IHD, and risk of death in Türkiye are at the top of the world rankings. In a recent prevalence study in our country, it has been shown that in the adult population, approximately 3 out of 10 people have hypercholesterolemia, 1 in 2 people have low HDL cholesterol, and 1 out of 3 people have high TG levels. This was associated with a sedentary lifestyle, widespread smoking and, more importantly, a higher incidence of comorbidities such as diabetes, hypertension, and obesity in both sexes.[8,9]

Therefore, in this study, we aimed to investigate the frequency of endocrine diseases such as diabetes, hypertension, obesity, hyperuricemia, insulin resistance, and thyroid dysfunction in our patient population with dyslipidemia.

METHODS

The study comprised patients with the diagnosis of with who presented to general internal medicine and subbranch outpatient clinics at Atatürk University Faculty of Medicine between December 2010 and May 2012 or were followed up in the clinics. The presence of at least one of the criteria including TC $\geq$ 200 mg/dL, LDL cholesterol $\geq$ 160 mg/dL, TG $\geq$ 150 mg/dL, HDL cholesterol < 50 mg/dL was considered as dyslipidemia.[10] The study groups consisted of 200 dyslipidemic patients with a mean age of 49 $\pm$ 15 years and 23 healthy individuals with a mean age of 32 $\pm$ 17 years, who were not diagnosed with dyslipidemia and were not treated for dyslipidemia. Patients using insulin or insulin secretagogues were excluded from the patient group in the calculation of insulin resistance (HOMA-IR). People with chronic alcohol use or known malignant disease were not included in the patient and control groups. Ethics committee approval for our study was obtained from the local ethics committee of the Atatürk University Faculty of Medicine with the 11/02/2011 dated and 3 numbered decision.

Anthropometric Measurements

Body mass index (BMI) was calculated with the following formula: BMI (kg/m^2) = (body weight (kg)/(height (m^2). Patients with BMI >30 kg/m^2 were considered obese.

Blood Pressure Measurements

Patients with systolic and diastolic blood pressure >140/90 mmHg and/or using antihypertensive drugs were considered to be hypertensive.

Determination of Insulin Resistance

Insulin resistance (HOMA-IR) was calculated using the homeostasis model assessment index (HOMA-IR) formula: [HOMA-IR = fasting plasma insulin (μU/mL) × fasting plasma glucose (mmol/L)/22.5]. HOMA-IR > 3 was considered as insulin resistance.

Laboratory Investigations

All tests were studied from a blood sample taken after at least 10 hours of fasting. Serum TSH, FT4, and insulin levels were measured on an E170 automated analyzer using the electrochemiluminescence immunoassay method, Japan. Serum TC, HDL cholesterol, LDL cholesterol, TG, glucose and uric acid levels were measured using the spectrophotometric method on the C800 automatic analyzer. Blood HBA1c measurements were made on an ADAMS A1C HA8160 automatic analyzer using high performance liquid chromatography method (ARKRAY Factory, Japan). Those with an HBA1c value >7 were considered diabetics. Serum uric acid levels >7 mg/dL in men and >6 mg/dL in women were considered cut-off. Serum TSH value was considered abnormal if it was outside the 0.27-4.2 μIU/mL range, which is the reference range of our hospital.

Statistical Analysis

Data were calculated as percentage or mean ± standard deviation. Statistical Package for the Social Sciences software 15.0 (IBM Inc, Chicago, IL, USA) package program was used in the analysis of the obtained data. Parametric and non-parametric "*t*-test" was used for the significance in the difference of the means, and the "chi-square" test was used for the differences in the proportional data. $P < .05$ values were considered statistically significant.

RESULTS

A total of 200 dyslipidemic patients who met the inclusion criteria were included in the study. Of the patients, 109 (54.5%) were female and 91 (45.5%) were male. The mean age of the patients was 49 ± 15 years. The control group consisted of 23 healthy volunteers, 12 (52%) female, 11 (48%) male, and the mean age was 32 ± 17 years.

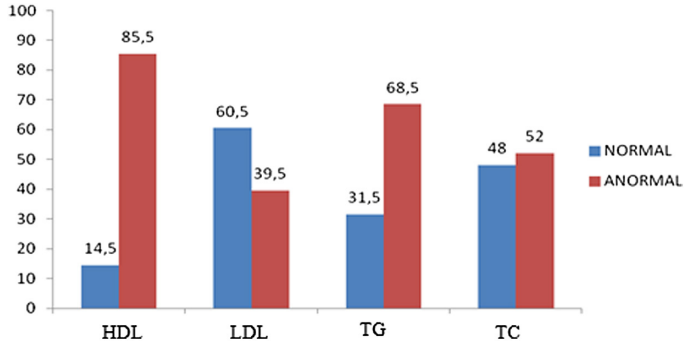

Figure 1. Percentage of lipid profile distribution in dyslipidemic patients (anormal means; low HDL, high LDL, TG and TC levels).

Considering the lipid profile in the dyslipidemic population, it was determined that the subgroup of patients with low HDL cholesterol levels was in the majority. In 85% of the patients diagnosed with dyslipidemia, serum HDL levels were below the cut-off value (Figure 1). The clinical and laboratory findings of the patient and control groups are summarized in Table 1.

While HbA1C, BMI, and uric acid values of the dyslipidemic group were statistically significantly higher compared to the control group ($P < .05$), there was no difference between the groups in TSH and HOMA-IR values ($P = .419$, $P = .912$, respectively) (Table 1). While hypertension was found in 85 (42.5%) patients in the dyslipidemic group, hypertension was found in 1 patient (4.3%) in the control group. There was a statistically significant difference in the incidence of hypertension between the patient and control groups ($P < .001$) (Table 1).

Table 1. Clinical and Laboratory Findings of the Patient and Control Groups

	Dyslipidemic Group n=200		Control Group n=23		
	No	Range	No	Range	*P*
Total cholesterol (mg/dL)	204 ± 56	(24-382)	158 ± 20	(193-120)	<.001
HDL (mg/dL)	39 ± 12	(11-86)	56 ± 6	(69-50)	<.001
LDL (mg/dL)	146 ± 50	(32-295)	96 ± 20	(136-56)	<.001
Triglyceride (mg/dL)	231 ± 145	(25-831)	83 ± 28	(141-44)	<.001
HbA1C (%)	8.5 ± 3.1	(19-4.3)	5.9 ± 1.5	(13-5)	<.001
HOMA-IR	2.8 ± 2.15	(13-0.2)	2.9 ± 3.31	(17-0.1)	.912
BMI (kg/m^2)	30.2 ± 7	(55-12)	22.2 ± 3.3	(35-19)	<.001
Uric acid (mg/dL)	5.2 ± 1.6	(11-1.9)	4.2 ± 1.2	(7.1-2.5)	<.002
TSH (μIU/mL)	2.09 ± 3.6	(41-0.005)	2.57 ± 2.54	(12-0.2)	.419
Hypertension (No-%)	85 (42.5%)		1 (4.3%)		<.001

BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Table 2. Distribution of Endocrine Disease Incidence Between Groups

	Dyslipidemic Group n=200 No (%)	Control Group n=23 No (%)	P
Diabetes mellitus	105 (52.5%)	1 (4.3%)	<.001
Obesity	91 (45.5%)	1 (4.3%)	<.001
Hyperuricemia	50 (25.0%)	1 (4.3%)	<.001
Hypertension	85 (42.5%)	1 (4.3%)	<.001
Insulin resistance	40 (34.5%)	6 (26.1%)	.434
Thyroid dysfunction	22 (11.5%)	5 (21.7%)	.135

When the incidence of endocrine disease was analyzed between the groups, diabetes mellitus, obesity, hyperuricemia, and hypertension were found to be significantly higher in the dyslipidemic group (Table 2). When frequency of endocrine diseases was examined in the dyslipidemic group, it was found that diabetes mellitus accompanied dyslipidemia in the highest rate (52%) of the patients (Figure 2).

When the lipid profile in the 4 endocrine diseases (diabetes mellitus, obesity, hyperuricemia, hypertension) whose incidence was found to be higher in the dyslipidemic patient arm was evaluated separately, it was observed that especially high TG levels were at the forefront, each of which was summarized in separate tables (Tables 3-6).

DISCUSSION

In our study conducted on 200 dyslipidemic patients and 23 healthy control groups, diabetes mellitus,

Table 3. Lipid Profile in Diabetes Mellitus

	DM (–) n=95	DM (+) n=105	P
Total cholesterol (mg/dL)	203 ± 61	205 ± 52	.805
Triglyceride (mg/dL)	193 ± 127	265 ± 152	<.001
LDL (mg/dL)	145 ± 54	146 ± 46	.868
HDL (mg/dL)	40 ± 11	38 ± 12	.387

DM, diabetes mellitus; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Table 4. Lipid Profile in Obesity

	Obesity (–) n=109	Obesity (+) n=91	P
Total cholesterol (mg/dL)	197 ± 56	212 ± 54	.053
Triglyceride (mg/dL)	209 ± 137	257 ± 150	**.020**
LDL (mg/dL)	136 ± 49	156 ± 49	**.007**
HDL (mg/dL)	39 ± 12	38 ± 11	.641

HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Table 5. Lipid Profile in Hyperuricemia

	Hyperuricemia (–) n=150	Hyperuricemia (+) n=50	P
Total cholesterol (mg/dL)	204 ± 55	204 ± 59	.992
Triglyceride (mg/dL)	222 ±143	257 ± 148	.133
LDL (mg/dL)	146 ± 46	144 ± 59	.803
HDL (mg/dL)	39 ± 11	38 ± 12	.675

HDL, high-density lipoprotein; LDL, low-density lipoprotein.

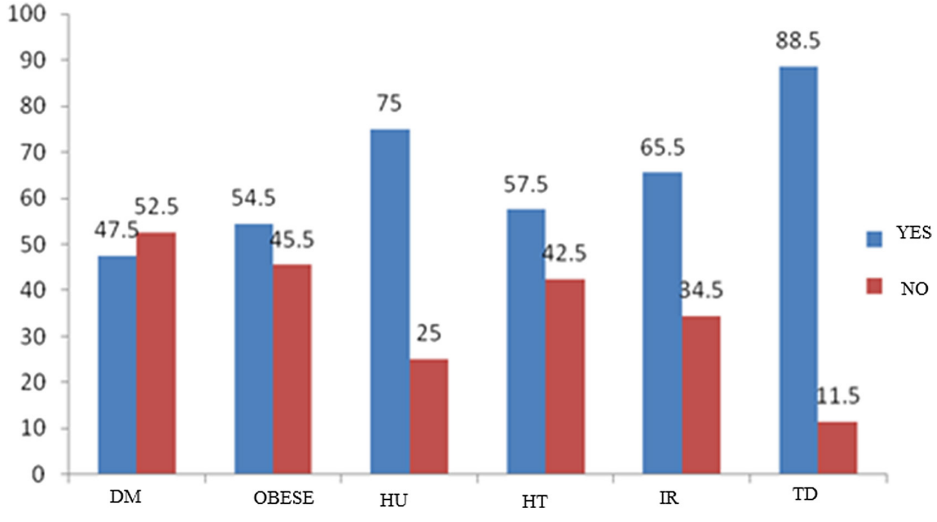

Figure 2. Percentage of endocrine disease frequency detected in dyslipidemic patients. DM, Diabetes mellitus; HT, hypertension; HU, hyperuricemia; IR, insulin resistance; TD, thyroid dysfunction.

Table 6. Lipid Profile in Hypertension

	Hypertension (–)	Hypertension (+)	
	n = 115	n = 85	*P*
Total cholesterol (mg/dL)	207 ± 61	199 ± 48	.307
Triglyceride (mg/dL)	206 ±127	264 ± 161	**.004**
LDL (mg/dL)	148 ± 54	141 ± 43	.378
HDL (mg/dL)	41 ± 12	36 ± 9.8	.004

hyperuricemia, hypertension, obesity, insulin resistance, and thyroid dysfunction were examined under the title of endocrine diseases. In our patient population, a unique lipid profile with low HDL-C was detected.

While the frequency of diabetes, hypertension, obesity, and hyperuricemia was significantly higher in the dyslipidemic group than in the control group, there was no statistical difference between the groups in terms of insulin resistance and thyroid dysfunction.

When lipid parameters in endocrine diseases were examined, TG levels were found to be significantly higher in the diabetic dyslipidemic group than in the non-diabetic group. Again, TG levels were found to be significantly higher in the hypertensive dyslipidemic group. While TG and LDL cholesterol levels were found to be significantly higher in the obese dyslipidemic group compared to the non-obese group, no difference was found among themselves in terms of lipid parameters in other endocrine diseases.

There are plenty of studies in the literature examining the relationship between dyslipidemia and diabetes. In a study by Ascaso et al[11] on 1182 patients with hypertrigl yceridemia, the frequency of diabetes mellitus was found as 33.5%.[11] In our study, the frequency of diabetes in the dyslipidemic group was found as 52.5%. In the healthy group, this value was 4.3% ($P < .001$). Again in our study, when diabetics and non-diabetics were compared in terms of lipid parameters in the dyslipidemic group, the TG value was found to be significantly higher in the diabetic group ($P < .001$). This study, which concluded that hypertriglyceridemia may be useful in the diagnosis of diabetes and metabolic syndrome patients regardless of TG level, is similar in terms of data and results to our study, which found a significantly higher incidence of diabetes in dyslipidemic patients and especially high TG levels in the diabetic group. Vodnala et al[12] investigated the causes of secondary dyslipidemia and found a history of diabetes in 21% of the patients. In our study, the frequency of diabetes was found to be higher at 52.5% in dyslipidemic patients. Al-Meshaweh et al[13] found diabetes mellitus in 32.6% of the patients in their study on a large population of dyslipidemic patients. In our study, the prevalence of diabetes was found to be 52.5% at a higher rate. In a recent retrospective study, the prevalence of dyslipidemia was found to be 86.7% in the diabetic patient population, combined hyperlipidemia was the most common model, and LDL elevation was the most common lipid abnormality.[14] In our study, diabetes was found in 52.5% of dyslipidemic patients, and when diabetic and non-diabetic dyslipidemic patients were compared, the TG level was the highest lipid abnormality, unlike this study ($P < .001$). Our study is in general parallel with the literature in terms of the coexistence of dyslipidemia and diabetes. Considering this coexistence, screening of diabetic patients for dyslipidemia and lowering their lipid levels and screening of dyslipidemic patients for diabetes and regulating their treatment should be applied to reduce the risk of cardiovascular events.

In our patient population, the frequency of hyperuricemia in the dyslipidemic arm was found as 25% and it was statistically significant ($P < .001$). It is predicted that chronic elevation of serum uric acid (SUA) level may be a risk factor and acute elevation may be a protective factor.[15] A recent study has shown that transient increases in SUA are positively associated with metabolic syndrome (MetS), even among those with baseline SUA within the normal reference range before MetS has yet developed in the general population. It was also found that those with high baseline SUA and those with greater chronic uric acid elevation were at greatest risk of developing MetS.[16] Peng et al[17] reported that high TG, TC, and LDL cholesterol were significantly associated with high SUA, while HDL cholesterol levels were negatively associated with SUA levels.[17] In a study by Al-Meshaweh et al[13] on a large population of dyslipidemic patients, 23.9% of the patients were found to have hyperuricemia. In our study, the rate of hyperuricemia among dyslipidemic patients was similar at 25%. In the same study, no significant difference was found between the 2 groups in terms of lipid parameters. Similarly, no significant difference was found in terms of lipid parameters in our study.[13] In a recent study in northwest China, hyperuricemia was found to be associated with cardiovascular risk factors, and dyslipidemia was shown to increase the risk of hyperuricemia. In particular, TG and TC elevation were found to be independent risk factors for hyperuricemia in multivariate analysis ($P < .001$). In our study, a significant difference was found between the dyslipidemic group and the control group in terms of uric acid level ($P = .002$). Again, in our study, hyperuricemia was detected in 25% of dyslipidemic patients, while this rate was found to be 1% in the control group ($P < .001$). This comprehensive study, which showed that dyslipidemia and obesity

increase the risk of hyperuricemia, shows parallelism in terms of the results of our study in which the uric acid level was found to be significantly higher in dyslipidemic patients.[18] According to the literature and the results of our study, dyslipidemia is seen as an important disease that increases the burden of hyperuricemia. Although it is not clearly stated in the current guidelines, measurement of serum uric acid levels will be useful in the follow-up of people with dyslipidemia and high risk for IHD.

Looking at the relationship between dyslipidemia and hypertension, it was observed in the Paris Prospective Study that excess non-esterified fatty acids in the blood led to an increase in blood pressure over time. Dyslipidemia is considered one of the major modifiable CVD risk factors, and the term dyslipidemic hypertension has become common in recent years.[6] In a recent study in our country, the association of systemic hypertension and dyslipidemia was found to be remarkably high.[19] In our study, the association of dyslipidemia and hypertension was found as 42%. In addition, when the lipid parameters were examined between the hypertensive and normotensive groups in the dyslipidemic group, TG elevation was found to be significantly higher ($P=.004$). Our study is consistent with this study in terms of showing the coexistence of dyslipidemia and hypertension. In a study conducted on a large population of dyslipidemic patients, hypertension was found in 41.9% of the patients, this value is similar to our study.[13] In the study conducted by Ascaso et al[11] on 1182 dyslipidemic patients, the frequency of patients diagnosed with hypertension (systolic blood pressure >140, diastolic blood pressure >90 mmHg) or receiving antihypertensive treatment was 50.9%.[11] In our study, the frequency of patients diagnosed with hypertension or receiving treatment in the dyslipidemic group was found to be similar as 42.5%. The same value was found as 4.3% in the healthy group ($P < .001$). The opinion that if lipid disorders precipitate hypertension, it is logical that pharmacological treatment of dyslipidemia should lower blood pressure has recently come to the fore; therefore, the importance and necessity of diagnosis and treatment of hypertension in dyslipidemic patients are increasing and our results are in line with this implication.

In recent years, the concept of "metabolic dyslipidemia" has been extensively discussed in the literature, and insulin resistance and subsequent obesity are held responsible for its etiology. The main driving force in the development of "metabolic dyslipidemia" in obesity is considered to be insulin resistance, and it is thought that the basis of this is impaired adipokine production in adipose tissue and the resulting chronic inflammation.[20] In a study on obesity, insulin resistance, and dyslipidemia, the frequency of dyslipidemia, especially hypertriglyceridemia , was found to be significantly higher in obese individuals compared to non-obese individuals, and HOMA-IR values were significantly higher in the obese dyslidemic group.[21] Similarly, in our study obesity was found in 91 (45.5%) of 200 dyslipidemic patients. The same value was found in 1 patient (4.3%) in the control group. The prevalence of obesity in the patient group was found to be statistically significantly higher than in the control group ($P < .001$). In another study conducted on a large population of dyslipidemic patients, obesity was found in 45.3% of the patients.[13] In our study, the prevalence of obesity was similarly found to be 45.5%. In addition, when we looked at the dyslipidemia profile in obese dyslipidemic patients, it was observed that TG and especially LDL cholesterol levels were significantly higher. Recently, 2 subgroups have received particular attention: healthy obese individuals who, although overweight or obese, who do not have dyslipidemia and fall into the low cardiovascular risk group, the other is non-obese dyslipidemic individuals who have an increase in circulating lipid levels despite being categorized as normal weight, and who are thought to have insulin resistance in particular. Therefore, the evaluation of dyslipidemia and obesity together is important in terms of protection from CVDs.[22]

Considering the association of dyslipidemia and insulin resistance, insulin significantly inhibits the lipolysis process in adipose tissue by suppressing the activity of hormone-sensitive lipase, the key enzyme that affects intracellular lipid metabolism, and thus controls the production of free fatty acids and their secretion into the plasma. Besides this function, insulin can also stimulate the degradation process of apolipoprotein B-48 and apolipoprotein B-100, which ultimately inhibits hepatocyte secretion of chylomicron and very low-density lipoprotein, thereby modulating the prevalence of metabolic-related dyslipidemia.[23] Although obesity can be defined as the main component that leads to the emergence of metabolic syndrome, it has been shown that not all obese people have impaired metabolic profile and insulin resistance and that insulin resistance can also be found in normal-weight individuals.[24,25] In their study, Paramsothy et al[26] found insulin resistance to be significantly higher in the dyslipidemic group ($P < .05$). Nasreddine et al[27] found low HDL cholesterol levels in 96.2% and high TGs in 73.1% of patients in all of whom metabolic syndrome and insulin resistance was detected (HOMA-IR >3.1). In a study evaluating insulin resistance and metabolic parameters in an obese child population, a highly positive correlation was observed between high TC, TG, and LDL cholesterol and insulin resistance (HOMA-IR).[28] In contrary studies, Sala-Vila et al[29] found the rate of patients with insulin resistance to be 25.4% in their study on asymptomatic individuals with primary dyslipidemia in the Mediterranean population. In

the same study, when the groups with and without insulin resistance were compared, a statistically significant difference was found in the group with insulin resistance in terms of TG and HDL cholesterol levels ($P < .001$ and $P < .01$; respectively).[29] In our study, the frequency of insulin resistance in dyslipidemic patients was found as 34.5%. The same rate was found as 26.5% even in the healthy control group ($P = .434$). There was no significant difference in lipid parameters between the groups with and without insulin resistance in dyslipidemic patients. In this study, it was concluded that the Mediterranean diet may have a positive effect on insulin resistance and that olive oil consumption could further reduce this rate.

There is important evidence that the Mediterranean diet is the nutritional habit that should be applied in the prevention of insulin resistance and metabolic syndrome that develops on this basis. In our patient population, the rate of insulin resistance in dyslipidemic patients was higher than in the Mediterranean population. Our study, whose rate of insulin resistance in the healthy control group was equal to the rate of insulin resistance in dyslipidemic individuals fed a Mediterranean diet, raises the idea that this may be due to the genetic background in our region or to common behavior patterns such as diet and lifestyle. In the study by Siqueira et al, HOMA-IR $\geq$ 3.0 values were accepted as insulin resistance. When the groups with and without dyslipidemia were compared, the mean HOMA-IR was found to be insignificant as 2.9 $\pm$ 1.8 and 2.4 $\pm$ 1.5, respectively ($P = .32$). Again, in the same study, when the frequency of patients receiving dyslipidemia treatment in the groups with and without insulin resistance was compared, the frequencies were found to be insignificant as 14% and 9.3%, respectively ($P = .67$). In the same study, no significant difference was observed when lipid parameters were compared in the group with insulin resistance ($P > .005$).[31] Similarly, in our study, no significant difference was found between the dyslipidemic group and the control group in terms of insulin resistance ($P = .912$). Similarly, in our study, when lipid parameters were examined in dyslipidemic patients with insulin resistance, no significant difference was found ($P > .05$). Looking at the literature, studies showing the relationship between insulin resistance and dyslipidemia are in the majority. It is thought that the lack of significant difference between the control group and the control group in terms of insulin resistance in our study and the high incidence of insulin resistance in the healthy control group may be related to the diet and lifestyle in our region.

Thyroid function is closely related to the metabolism of blood lipids. In hypothyroidism and hyperthyroidism, the change in blood lipids is usually the opposite. Some studies have revealed that hypothyroidism can lead to hyperlipidemia, while hyperthyroidism leads to a decrease in blood lipids.[32] In hypothyroidism, lipoprotein lipase and hepatic lipase activity decreases and when thyroid hormone is given, the activity improves. This observation may explain the high fasting TG levels often found in hypothyroidism. Total cholesterol levels increase in hypothyroidism and decrease in hyperthyroidism. Thyroid hormones stimulate the enzyme 3-OH-3-methyl glutaryl CoA reductase, which is the key enzyme in cholesterol biosynthesis, but this effect is dose dependent and the net effect is a decrease in cholesterol, since cholesterol is removed from the liver via LDL receptors in hyperthyroidism. In overt and subclinical hypothyroidism, LDL cholesterol increases, while HDL cholesterol usually remains normal, sometimes even increased. Thyrotoxicosis causes a decrease in plasma concentrations of lipids, including TGs, cholesterol, and phospholipids. Changes also occur in the metabolism of apolipoproteins.[33] While some studies have shown a correlation between HDL, LDL, and TC metabolism and serum TSH levels,[34] there are studies in the opposite direction. In a recent study on 327 thyroid patients, no correlation was found between serum TSH and lipid levels.[35] In our study, thyroid dysfunction was detected in 22 (11.5%) of 200 dyslipidemic patients, but the same value was found in 5 patients (21.7%) in the control group. There was no statistically significant difference between the groups in terms of thyroid dysfunction ($P = .434$). In our study, the frequency of thyroid dysfunction was also found to be higher in the normal group. It was thought that these results might be due to reasons such as the insufficient number of cases in our study, the frequency of thyroid dysfunction in our region, and the use of non-iodized salt. It is known that thyroid disorders negatively affect lipid levels in dyslipidemic patients. Overt or subclinical hypothyroidism has a negative effect on the lipid profile leading to the development of atherosclerosis. Hyperthyroidism may be the underlying cause of the improvement in lipid levels in patients with subsequent hypocholesterolemia and pre-existing dyslipidemia. Thyroid function screening tests should be performed in dyslipidemic patients with improvement or worsening of lipid profile.

Insufficient number of patients and inequality in number and demographic data between groups are the most important limitations of our study. Again, the regional and single-centered nature are the weaknesses of our study.

In conclusion, in our study, the frequency of diabetes, hypertension, obesity, and hyperuricemia in patients with dyslipidemia was found to be significantly higher than in the control group. Considering these diseases when treating dyslipidemia is important for cardiovascular morbidity

and mortality. Considering the environmental conditions and regional characteristics of dyslipidemia, it is clear that we will need to continue the analyses specific to our own community conditions.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Atatürk University Faculty of Medicine (Date: February 11, 2011 , Decision No: 2/3).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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