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The relationship between high HDL levels and certain metabolic and anthropometric variables.

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Abstract

There is a common opinion that a higher level of HDL is better. It is reported that HDL particle involved significant defects in Turkish adults. We aimed to determine whether there was a relationship between high levels of HDL and certain metabolic and anthropometric variables. In the present study, patients ≥ 18 years of age who had HDL levels >60 mg/dl were the target group of the study. Randomly selected 259 patients were retrospectively evaluated. Patient files in archives were analyzed. Patients with high levels of HDL were predominantly female (89.2%). Mean HDL level was 69.6 ± 8.8 mg/dL. More than half of the patients were not diabetic (51.9%); however, 50.8% had a family history of diabetes mellitus. The mean HDL value of non-smokers was higher (p=0.03). Parameters were compared according to the gender, males were found to be older than females (p=0.02) and taller (p<0.001). There was a negative and weak correlation between triglyceride and HDL (r=-0.166) (p=0.01). There was no relationship between gender and anthropometric measurements and HDL. In non-smoking participants, HDL levels were higher than the smokers. Simple linear regression model for triglyceride might be acceptable as a good model in the prediction of HDL value.

Keywords HDL, Diabetes Mellitus, Triglyceride, Smoking.

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Introduction

There is a common opinion that a higher level of HDL is better for health better over the years. Medical advices enhancing HDL levels, such as statin, niasin, diet, exercise, cholesteryl ester transfer protein (CETP) inhibitors and bariatric surgery, are frequently applied in case of necessity [1].

However, it must be known that there are two different definitions for HDL; HDL quantity (circulating plasma levels of HDL) and HDL quality (atheroprotective properties of HDL) [2]. Besides, studies showed that high levels of HDL might lead to negative results as in high levels of LDL. Onat et al. reported that HDL particles having the most preservative function against atherogenesis and inflammation involved significant defects in Turkish adults which might cause diabetes mellitus in both genders, and as well as, metabolic syndrome and coronary diseases [3]. In certain studies, structurally altered and high levels of Apo A-I ratio were found to be associated with type 2 diabetes mellitus in cases of high-HDL levels [4,5]. In the present study, it was aimed to determine whether there was a relationship between high levels of HDL and certain metabolic and anthropometric variables.

Patients and Methods

In the present study, patients ≥ 18 years of age who were treated for any reason between the dates of December 2013 and June 2015 in Samsun Training and Research Hospital, and who had HDL levels >60 mg/dl were the target group of the study. According to the power analysis performed by considering the patient population, the minimum number of cases must be 250 within the scope of 5% acceptable error limit and 90% confident interval. In our study, randomly selected 259 patients were retrospectively evaluated. Demographic data, anthropometric measurements, history of diabetes mellitus and drug use, complete blood count (CBC), the values of blood lipid and glucose were analyzed from patient files in archives. Patients who were using drugs affecting HDL levels (especially statin) or patient having a disease (especially dyslipidemia) were excluded from the study.

Normolipidemic blood levels included in the study were based on the criteria of NCEP ATPIII (Triglyceride <150 mg/dl, LDL-C <130 mg/dl and HDL-C 40-60 mg/dl) [6]. The range of impaired fasting glucose was accepted according to ADA 2003 criteria as 100-125 mg/dl [7]. Patients were considered as under-weight, normal, over-weight, obese and morbid in accordance with the BMI classification of <18.5 kg/m^2, 18.5 -

24.9 kg/m^2, 25 - 29.9 kg/m^2, ≥ 30 kg/m^2 and ≥ 40 kg/m^2, respectively [8]. Further examination was not requested from the patients. Statistical analyses were performed by using SPSS v.22 package program and the significance level was considered as 0.05. Normal distribution of measurable values was examined by visual (Histogram and possible graphics) and analytical (Kolmogorov-Smirnov) methods. Quantitative data were presented as mean ± standard deviation; categorical data were presented as number and percent. Chi-squared test was used for comparison of categorical variables. For comparison of numerical data, Student's-t test was used. The relationship between triglyceride and HDL were examined by using Pearson correlation test. The effect of triglyceride on HDL was investigated by using simple linear regression model. All the procedures in the study were designed in accordance with the Helsinki Declaration and Good Clinical Practice guidelines and approved by the OMU Institutional Ethical Committee (May 14, 2015).

Results

Patients with high levels of HDL were predominantly female (89.2%). Mean age, mean height and mean weight of the patients were 53.4 years, 163.4 cm and 75.4 kg, respectively. Accordingly, mean BMI was calculated as 28.27 kg/m^2. Mean HDL level was 69.6 ± 8.8 mg/dL.

More than half of the patients were not diabetic (51.9%); however, 50.8% had a family history of diabetes mellitus. It was interesting that 39.7% of the patients had thyroid function disorder and 83.1% were using drugs due to a chronic diagnosis. The rate of smoking was 15.3%, and the rate of patients doing regular sports was 10.2%. Demographic data and their mean HDL values were presented in Table 1. Accordingly, mean HDL values in diabetic patients were found as 69.7 mg/dL; whereas it was 73.7 mg/dL and 70.7 mg/dL in patients with impaired fasting glucose and non-diabetics, respectively. The mean HDL value of non-smokers was higher (p=0.03). Besides these, no significant relationship was detected between HDL and the variables including the association of patient's herself/himself or his/her family member with diabetes mellitus, patient's existing diagnosis, drug use and sports. When the analyzed parameters were compared according to the gender, males were found to be older than females (M: 59.8 years, F: 52.6 years, p=0.02) and taller (M: 176.3 cm, F: 161.9 cm, p<0.001). No significant results were detected in other analysis expect that one. Mean HDL value was approximately 69 mg/dL in both genders. The values of LDL and triglyceride were within the normal limits. Mean blood glucose levels (~112 mg/dl) are the indicator of impaired fasting glucose. Mean arterial blood pressures of the patients were within the normal ranges. The waist circumference was 95 cm and 98 cm in females and males, respectively. The hip circumference was 106 cm and 111 cm in females and males, respectively (Table 2).

Table 1. Demographic data and mean HDL values.

Parameter		Frequency	HDL		
			Mean	SD	P value
Gender	Female	89.20%	69.6	8.9	
	Male	10.80%	69.3	7.9	0.93
	DM	32.70%	69.7	1.2	0.48
Association with DM	Impaired Fasting Glucose	15.40%	73.7	9.7	
	No association	51.90%	70.7	8	
Familial DM	Present	50.80%	70.1	9.6	
	Absent	49.20%	70.6	8.1	0.87
	Hypertension	15.50%	71	8.3	
Diagnosis, Other	Thyroid Function Disorder	39.70%	71.8	8.9	0.67
	Other	6.90%	71.2	15.9	
	No	37.90%	68.2	7.8	
	Antı DM	20.30%	68.8	9.9	
	Antı HT	11.90%	71.9	10.2	
Drug use	Levothyroxine	25.40%	73	9.3	
	Other	25.40%	69	8.5	0.46

	No	16.90%	69.3	6.5	
Smoking	Yes	15.30%	68.2	6.7	
	No	84.70%	70.7	9.1	0.03
Sport	Yes	10.20%	73	10	
	No	89.80%	70	8.7	0.67

Table 2. *Measurable variations according to gender.*

	Gender				
	Female		Male		p value
	Mean	± SD	Mean	± SD	
Age (year)	526	16.1	59.8	18.3	0.02
Height (cm)	161.9	6.6	176.3	7.0	<0.001
Weight (kg)	74.5	14.5	83.3	14.8	0.16
BMI (kg/m2)	28.4	5.5	26.8	5.0	0.41
HDL (mg/dl)	69.6	8.9	69.3	7.9	0.88
LDL (mg/dl)	122.0	40.6	108.1	35.9	0.08
Triglyceride (mg/dl)	116.1	70.9	104.9	63.9	0.42
Blood glucose (mg/dl)	112.4	50.8	112.9	40.2	0.95
Waist (cm)	95.2	10.9	98.3	12.5	0.66
Hip (cm)	106.0	13.0	111.6	12.5	0.49
Systolic TA (mmHg)	127.5	20.4	121.6	2.8	0.63
Diastolic TA (mmHg)	79.5	8.8	81.6	2.8	0.92

When mean age, anthropometric values, blood lipid levels and arterial blood pressure parameters were compared to mean HDL levels, statistically significant result was only detected in triglyceride level (p=0.01) (Table 3). There was a negative and weak correlation between triglyceride and HDL (r=-0.166). The regression model was found to be significant (F (1,256)=7.271, p<0.05, R=0.166, R2=0.024) and the explanation of variation was not dependent on chance. Triglyceride explains 2.4% of HDL. When regression coefficient (β) associated with triglyceride (independent variable), one-unit reduction in triglyceride level led to 0.021-unit reduction in HDL level (p<0.05).

Table 3. *Relationship between measurable variations and HDL.*

			Association with HDL	
Parameter	Mean	± SD	r value	p value
Age (year)	53.4	16.4	-0.015	0.81
Height (cm)	163.4	7.9	0.033	0.81
Weight (kg)	75.4	14.7	-0.082	0.54
BMI (kg/m2)	28.2	5.4	-0.159	0.23
LDL (mg/dl)	120.5	40.3	-0.006	0.92
Triglyceride (mg/dl)	114.9	70.1	-0.166	0.01
Blood glucose (mg/dl)	112.4	49.7	-0.062	0.33
Waist (cm)	95.7	10.9	-0.104	0.65
Hip (cm)	106.8	12.8	-0.026	0.91
Systolic TA (mmHg)	126.5	19.2	-0.238	0.27
Diastolic TA (mmHg)	79.5	8.7	-0.219	0.31

When participants were sorted according to BMI categorization, the frequency of over-weight (38.6%) and obese patients (31.6%) was found to be higher. As BMI increased, the mean HDL was decreased, however this decrease was not statistically significant (p=0.41) (Table 4).

Table 4. *HDL values according to BMI.*

		HDL	
	Frequency (%)	Mean	p value

	Under-weight	1.8	81	
BMI	Normal	28.1	72.1	
Category	Over-weight	38.6	70	0.41
	Obese	31.6	68.5	

Discussion

High levels of HDL might not be a positive health indicator in contrast to general opinion. In the present study, certain variables of patients with high levels of HDL were compared to HDL level.

HDL is the smallest and most intense lipoprotein and is synthesized from liver and intestinal cells. It has a heterogenic structure and consists of apo A1, apo A2, apo AIV, apo C and apo E. There are cardioprotective and atherogenic subgroups [9].

Turkish Adult Risk Factor (TEKHARF) and Turkish Heart Study were reported lower levels of serum HDL in Turkish population in comparison to other populations (average in men ~36, average in women ~42 mg/dl) [10,11]. In Turkish Metabolic Syndrome Study, the mean values of 4,264 cases that were selected as reflecting the truth were found as 46.3 mg/dL in males and 51.9 mg/dL in females [12].

Patients with high levels of HDL were included in our study, and the mean value of ~69 mg/dl and gender differences did not show any influence on HDL. In TEKHARF study, an increase of 1-1.5 mg/dl was reported in HDL levels of males in each decade [10]. In Turkish Heart Study, the level of HDL was increased with age in women ($r=0.14$, $p<0.001$) [13]. There was no significant relationship between age and HDL in our study.

Mahley et al. stated that the reason of low HDL levels in Turkish population was partially associated with genetics and as well as smoking habits, physical inactivity, triglyceride-rich diet and obesity [11]. In our study, certain variables that were considered to explain the reason of high HDL levels were analyzed, a statistically significant increase was detected in HDL levels in non-smokers and in patients with lower triglyceride values. HDL has anti-inflammatory and antioxidant activities [14]. Increasing HDL levels attenuated the microvascular inflammation. Also, it has potent cytoprotective activity [15,16]. HDL has a protective function in patients with HDL concentration above 75 mg/dl [17-19]. In several studies, lower HDL level has been reported to be associated with increased coronary artery disease risk [20,21]. In our patients, the incidence of cardio-vascular pathologies was relatively rare in line with the literature. Of the patients, 37.9% did not have any chronic disease.

Another matter of option is the functionality of HDL particle in patients with high levels of HDL. HDL loses its preservative function in the presence of a systemic inflammation and it might be pro-inflammatory. This is the main subject desired to search in our study.

The clinical use of the ratio of total to HDL cholesterol as a risk indicator may be misleading in persons with CETP mutations [22]. It was focused on CETP inhibition for the elevation of HDL [23]. CETP exchanges cholesteryl esters of HDL with triglycerides of apo B-containing lipoproteins [24]. Several CETP gene mutations reduce CETP activity and raise HDL but the evidence as to whether they are beneficial is conflicting [25]. The adverse effects of CETP deficiency have been attributed to impairment of reverse cholesterol transport and loss of the anti-atherogenic properties of HDL resulting from its increased cholesterol content and particle size [26]. An increased prevalence of coronary heart disease was seen in men of Japanese ancestry with a different CETP mutation and moderately (but not markedly) raised HDL cholesterol in the Honolulu heart programme's cohort [27].

Population based studies revealed dysfunction of HDL or apo A-I circulating in high concentrations in individuals with diabetes mellitus or coronary heart disease [28]. Ansell et al. were evaluated patients in whom atherosclerosis had been developed despite of their high levels of HDL (≥ 84 mg/dl), and the rates of monocyte chemotaxis, which was the suggestive signs of proinflammatory HDL, were found to be high when compared to healthy controls [29]. Almost half of the patients had diabetes mellitus or impaired fasting glucose. Thyroid function disorder and hypertension were among the other common chronic diseases. The rate of patients associated with diabetes mellitus was higher than the average results in Turkey [30]. This condition was considered that patients with high levels of HDL might be associated with diabetes mellitus by means of mutations. However, the idea of "patients with type II diabetes mellitus have low levels of HDL cholesterol" is common in the literature.

There are studies indicating low HDL levels in patients with hypertriglyceridemia. In both genders, a reverse correlation was shown in between HDL and triglyceride [31,32]. In our study, there was a negative and weak correlation between patients' triglyceride and HDL levels. The high levels of HDL might move ahead of metabolic syndrome either alone or via specific mechanisms by affecting other criteria. Although the criteria of three guidelines developed for metabolic syndrome (NCEP ATP III, WHO, IDF) were considered separately, the mean values of our patients were not met the diagnosis of metabolic syndrome. This indicates the importance of HDL in the diagnosis of metabolic syndrome [33].

It has been known that smoking results in reduction in plasma HDL concentrations [34]. This condition suggested that smoking had a stimulating effect on plasma CETP activity [35]. In our study, the blood levels of HDL cholesterol were found to be higher in non-smokers. HDL becomes normal or increases when smokers quit [36].

Our study was a single-center and retrospective study, therefore HDL subgroups were not able to be evaluated and study data were limited to patients' files in the archives. These could be our limitations. However, a considerable amount of patient would make a great contribution to the literature.

As conclusion, a significant relationship was not determined between HDL levels and diabetes mellitus among the participants; however, the rates of its association with diabetes mellitus were higher than the average in Turkey. There was no relationship between gender and anthropometric measurements and HDL. In non-smoking participants, HDL levels were higher than the smokers. Simple linear regression model for triglyceride might be acceptable as a good model in the prediction of HDL value. Therefore, 1-unit reduction in triglyceride value leads to 0.021 mg/dl decrease in HDL.

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