

## Lipids and leptin level in natives of Kyrgyzstan

### Kırgızistan'ın yerli halkında lipitler ve leptin düzeyi

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#### ABSTRACT

**Objectives:** A possible link between obesity and impaired lipid metabolism is leptin, the 167-amino acid protein, secreted by adipocytes. The content of leptin in the body is closely associated with body mass index (BMI). Data obtained from studies on the association of leptin with dyslipidemia are contradictory. The level of leptin has not been studied in the ethnic Kyrgyz population previously. The purpose of this study was to investigate the relationship between leptin and lipid parameters in a group of ethnic Kyrgyz.

**Study design:** The study included 322 ethnic Kyrgyz (145 males, 177 females) aged  $\geq 30$  years, living in Kyrgyzstan. Measurement of anthropometric parameters (height, weight, waist circumference [WC], hip circumference [HC]) and blood pressure (BP) was done. Laboratory tests included blood glucose (fasting) in plasma, lipid profile (total cholesterol [TC], triglycerides [TG], high-density lipoprotein [HDL] cholesterol, low-density lipoprotein [LDL] cholesterol), and serum leptin.

**Results:** Leptin was positively correlated with BMI, WC and TG in both sexes and with TC in males.

**Conclusion:** Leptin is associated with BMI, WC and TG in both sexes of Kyrgyz and with TC in Kyrgyz males.

Obesity is associated with dyslipidemia and cardiovascular disease.<sup>[1]</sup> However, the underlying mechanisms of this association are not fully understood. A possible link between obesity and impaired lipid metabolism may be found through the molecule leptin, a 167-amino acid protein, secreted by adipocytes.<sup>[2]</sup> Since 1994,<sup>[2]</sup> leptin has attracted the attention of researchers as it was found that its content in the body reflects the amount of energy reserves accumu-

#### ÖZET

**Amaç:** Adipositler tarafından salgılanan 167 amino asitli protein olan leptin obezite ile bozulmuş lipit metabolizması arasındaki olası bağlantıyı oluşturur. Vücutta leptinin içeriği beden kütle indeksiyle (BKİ) yakından ilişkilidir. Leptinin dislipidemiyle ilişkisi konusundaki çalışmalardan elde edilen veriler çelişkilidir. Kırgız halkında leptin düzeyi daha önce araştırılmamıştır. Bu çalışmanın amacı Kırgız ırkında leptin ile lipit parametreleri arasındaki ilişkiyi araştırmaktır.

**Çalışma planı:** Çalışmaya Kırgızistan'da yaşayan  $\geq 30$  yaşlarında Kırgız ırkından 322 kişi (145 erkek, 177 kadın) alındı. Antropometrik parametreler [boy, kilo, bel çevresi (BÇ), kalça çevresi (KÇ)] ve kan basıncı (KB) ölçüldü. Laboratuvar testlerinden açlık kan şekeri (AKŞ), lipit profili [total kolesterol (TK), trigliseritler (TG), yüksek yoğunluklu lipoprotein (YYL) kolesterol, düşük yoğunluklu kolesterol (DYL) ve serum leptin ölçüldü.

**Bulgular:** Serum leptin, her iki cinste BKİ, BÇ, TG ve erkeklerde TK ile pozitif korelasyon göstermektedir.

**Sonuç:** Leptin, Kırgızlarda her iki cinste BKİ, BÇ ve TK, erkeklerde TK ile ilişkilidir.

lated in adipose tissue and is closely associated with body mass index (BMI).<sup>[3]</sup> In contrast, data obtained from studies on the association of leptin with dyslipidemia are contradictory.<sup>[4]</sup>

Some studies have found a positive correlation of leptin with triglycerides (TG)

#### Abbreviations:

AO	Abdominal obesity
BMI	Body mass index
HDL-C	High-density lipoprotein cholesterol
TC	Total cholesterol
TG	Triglycerides
WC	Waist circumference

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and no relation to high-density lipoprotein cholesterol (HDL-C).<sup>[5,6]</sup> On the other hand, some studies have found a correlation of leptin only with HDL-C.<sup>[7]</sup> The level of leptin has not been studied previously in the ethnic Kyrgyz population. Thus, the purpose of this study was to investigate the relationship between leptin and lipid parameters in a group of ethnic Kyrgyz.

## PATIENTS AND METHODS

### Study population

This cross-sectional study assessing the prevalence of cardiovascular risk factors was conducted from April to July 2008 and included adult persons from the general population permanently living in Kyrgyzstan. Exclusion criteria included those who underwent surgery within one month prior to the study; those with severe chronic diseases of the liver and/or kidney; those with thyroid dysfunction; patients currently receiving treatment with corticosteroids, lipid-lowering drugs, or insulin; pregnant women; and persons of non-Kyrgyz ethnicity. In total, 322 native ethnic Kyrgyz (145 males, 177 females) aged  $\geq 30$  years were included in the present study.

All participants gave written informed consent for the study. The study protocol was approved by the Ethical Committee of the National Center of Cardiology and Internal Medicine. All persons were examined by a cardiologist with collection of complaints, medical history, and physical examination, including measurement of anthropometric parameters (height, weight, waist circumference [WC], hip circumference) and blood pressure (BP). BMI was calculated using the formula:  $BMI = \text{weight (kg)} / \text{height (m)}^2$ . Obesity was defined if BMI was  $\geq 30$  kg/m<sup>2</sup> and abdominal obesity (AO) if WC was  $\geq 102$  cm in males and  $\geq 88$  cm in females.<sup>[1]</sup>

### Laboratory analysis

Blood samples for laboratory tests were taken in the morning on an empty stomach. Biochemical analyses were carried out in the *Dir Adjoint du Département Hommes, Natures, Musée de l'Homme* (Paris, France) and included blood glucose in plasma and serum lipid profile (total cholesterol (TC), TG, HDL-C). The concentration of low-density lipoprotein cholesterol (LDL-C) was calculated with the Friedewald formula.<sup>[8]</sup> Serum leptin level was assessed using solid-

phase enzyme immunoassay (ELISA) (DRG Instruments GmbH, Germany). Hypertriglyceridemia was defined if TG level was  $\geq 1.7$  mmol/L and low HDL level if  $< 1.03$  mmol/L in males and  $< 1.3$  mmol/L in females.

### Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) 12.0 (SPSS, Inc., Chicago, IL). Comparison of variables with a normal distribution was performed using a set Student t test and results are presented as mean  $\pm$  standard deviation. Variables with nonparametric distribution were compared using the Mann-Whitney test and are presented with median values (25th and 75th percentile). Kruskal-Wallis ANOVA test was used to compare the differences among three groups. The relationship between variables was assessed by Spearman rank correlation. A p-value  $< 0.05$  was considered to be statistically significant.

## RESULTS

Clinical characteristics of the patients enrolled in the

**Table 1. Clinical characteristics of patients**

	n	%	Mean $\pm$ SD
Age (years)			51.7 $\pm$ 9.6
Sex (male)	145	45	
Obesity	94	29.2	
Body mass index (kg/m <sup>2</sup> )			27.4 $\pm$ 4.8
Abdominal obesity	136	42.2	
Waist circumference (cm)			91.2 $\pm$ 11.5
Arterial hypertension	135	41.9	
Systolic BP (mmHg)			135 $\pm$ 22
Diastolic BP (mmHg)			85 $\pm$ 12
Type 2 diabetes mellitus	22	6.8	
Fasting glucose* (mmol/L)	5.48	(5.1; 5.9)	
Total cholesterol (mmol/L)			5.1 $\pm$ 1.1
HDL-C (mmol/L)			1.1 $\pm$ 0.3
LDL-C (mmol/L)			3.2 $\pm$ 0.9
Triglycerides* (mmol/L)	1.2	(0.9; 1.9)	
Leptin* (ng/ml)	7.8	(4.0; 14.7)	

\* - Data are presented as median (25th; 75th percentile). BP: Blood pressure; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol.

study are presented in Table 1.

The mean age was 51.7±9.6 years, and the median leptin level was 7.8 ng/ml. 29.2% of the included persons had obesity, 41.9% had arterial hypertension, 42.2% had AO, and 6.8% suffered from type 2 diabetes (Table 1). Analysis of lipids showed hypertriglyceridemia in 30.1% of patients and low HDL-C in 59.9% of the study participants.

In order to evaluate the association of leptin lev-

els with cardiometabolic risk factors, all participants were stratified into three groups based on tertile of leptin (males: <3.0; 3.0-5.51; ≥5.52 ng/ml (Table 2); females: <9.6; 9.6-16.6; ≥16.7 ng/ml (Table 3).

Comparative analysis of the groups showed that males in the upper tertile of leptin had high values of BMI, WC, WC/HC and glycemia compared to patients with lower leptin levels. The frequency of obesity and AO increased with higher levels of leptin. The above-

**Table 2. Characteristics of patients in association with leptin level\* (males)**

	1st tertile (n=47)	2nd tertile (n=50)	3rd tertile (n=48)	p<
Age (years)	53.3±11.3	55.9±8.6	51.2±9.2	0.03
Obesity [n (%)]	0 (0)	4 (8)	23 (47.9) <sup>‡§</sup>	0.0001
Body mass index (kg/m <sup>2</sup> )	23.3±2.4	26.4±2.5 <sup>#</sup>	29.4±3.7 <sup>‡§</sup>	0.0001
Abdominal obesity [n (%)]	1 (2.1)	10 (20)	28 (58.3) <sup>‡§</sup>	0.0001
Waist circumference (cm)	84.9±8.5	94.9±6.3 <sup>#</sup>	102.2±10.8 <sup>‡§</sup>	0.0001
WC/HC (cm)	0.92±0.07	0.95±0.05	0.97±0.07 <sup>†</sup>	0.0001
Glucose (mmol/L)	5.3 (5.0; 5.6)	5.6 (5.2; 6.2) <sup>†</sup>	5.7 (5.3; 6.5)	0.003
Total cholesterol (mmol/L)	4.7±0.9	5.6±1.3 <sup>‡</sup>	5.3±0.9 <sup>†</sup>	0.001
Triglycerides (mmol/L)	1.06 (0.8; 1.5)	1.9 (1.2; 2.6) <sup>†</sup>	1.7 (1.2; 2.4) <sup>‡</sup>	0.0001
HDL-C (mmol/L)	1.1±0.3	1.02±0.3	1.04±0.3	NS
LDL-C (mmol/L)	3.03±0.8	3.6±1.3	3.4±0.8	NS

\*: Leptin tertile: 1st <3.0; 2nd 3.0-5.51; 3rd ≥ 5.52; †: p<0.05 compare with 1st tertile; ‡: p<0.001 compare with 1st tertile; §: p<0.001 compare with 2nd tertile; HDL-C: High density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; NS: Non-significant; WC: Waist circumference.

**Table 3. Characteristics of patients in association with leptin level\* (females)**

	1st tertile (n=56)	2nd tertile (n=61)	3rd tertile (n=60)	p<
Age (years)	48.8±11	50.8±7.9	51±8.3	NS
Obesity [n (%)]	4 (7.1)	20 (32.8) <sup>‡</sup>	43 (71.7) <sup>‡§</sup>	0.0001
Body mass index (kg/m <sup>2</sup> )	23.7±3.6	28.3±2.9 <sup>†</sup>	32.5±4.9 <sup>‡§</sup>	0.0001
Abdominal obesity [n (%)]	9 (16.1)	35 (57.4) <sup>†</sup>	53 (88.3) <sup>‡§</sup>	0.0001
Waist circumference (cm)	79.6±9.5	89.9±8.2 <sup>†</sup>	96.5±9.3 <sup>‡§</sup>	0.0001
Waist circumference/HC	0.83±0.07	0.88±0.06 <sup>†</sup>	0.87±0.06 <sup>†</sup>	0.0001
Glucose (mmol/L)	5.2 (4.9; 5.6)	5.5 (5.2; 5.9) <sup>†</sup>	5.6 (5.3; 6.1)	0.0001
Total cholesterol (mmol/L)	4.8±1.09	5.06±0.9	5.05±1.1	NS
Triglycerides (mmol/L)	0.9 (0.7; 1.3)	1.16 (0.9; 1.5)	1.2 (0.9; 1.7)	0.02
HDL-C (mmol/L)	1.3±0.4	1.19±0.3	1.19±0.3	NS
LDL-C (mmol/L)	2.9±0.9	3.3±0.9	3.2±0.8	NS

\*: Leptin tertile: 1st <9.6; 2nd 9.6-16.6; 3rd ≥16.7; †: p<0.05 compared with 1st tertile; ‡: p<0.001 compared with 1st tertile; §: p<0.001 compared with 2nd tertile; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; NS: Non-significant.

**Table 4. Spearman correlation coefficients of leptin level and independent variables**

	Males (n=145)		Females (n=177)	
	r	p<	r	p<
Age (years)	-0.063	NS	0.127	NS
Body mass index (kg/m <sup>2</sup> )	0.72	0.001	0.74	0.001
Waist circumference (cm)	0.684	0.001	0.649	0.001
Total cholesterol (mmol/L)	0.214	0.05	0.09	NS
Triglycerides (mmol/L)	0.301	0.001	0.194	0.05
HDL-C (mmol/L)	-0.079	NS	-0.156	0.05
LDL-C (mmol/L)	0.163	NS	0.126	NS
Glucose (mmol/L)	0.256	0.01	0.306	0.001

HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; NS: Non-significant.

described pattern was traced for females as well, although the age of the groups was comparable.

Analysis of the lipid parameters showed significant differences in TG level in both males ( $p<0.001$ ) and females ( $p=0.02$ ). The other lipid profile components were comparable between tertiles in both sexes, except for TC in males ( $p=0.001$ ) (Tables 2, 3).

Next, Spearman correlation was performed between leptin, anthropometric data and laboratory parameters (Table 4). No correlation of leptin with age was revealed. In patients of both sexes, leptin positively correlated with BMI, WC, TG, and glucose concentrations. However, leptin correlated with TC in males, and negatively correlated with HDL-C in females (Table 4).

## DISCUSSION

Leptin is secreted mainly by adipose tissue. As an important body weight regulator, it promotes various physiological mechanisms in accordance with the state of energy balance, and informs the hypothalamus about the energy stored in the adipocytes. Leptin plays an important role in the regulation of feeding behavior: its concentration decreases in a state of hunger and increases after a meal.<sup>[9]</sup> It is known that leptin level reflects the amount of adipose tissue in the body, and hyperleptinemia is typical for alimentary obesity and AO.<sup>[10]</sup>

In the present study, serum leptin was significantly associated with general and abdominal obesity. In

addition, a strong correlation was observed between leptin levels and BMI in both sexes. In our study, the leptin level in females was 3.1 times higher than in males. Similar results were shown in other studies.<sup>[11,12]</sup> Gender differences in leptin may be due to the action of sex hormones: it is thought that androgens have a suppressive effect on the leptin concentration.<sup>[13]</sup> The studies on the association of leptin with estrogen and progesterone showed conflicting results.<sup>[14,15]</sup> At the same time, higher leptin levels in females may be due to the influence of other factors, such as the structural differences in the hypothalamus<sup>[16]</sup> and the higher content of subcutaneous adipose tissue in women.<sup>[13,17]</sup> It is known that leptin is predominantly secreted by subcutaneous adipocytes,<sup>[18]</sup> and in some studies, its association with subcutaneous fat tissue was much stronger than with the visceral tissue.<sup>[19]</sup>

Studies on the association of serum leptin and lipids have shown conflicting results. Some studies found no relation of leptin to the parameters of the lipid profile.<sup>[20,21]</sup> Other studies have shown a significant positive correlation between leptin and HDL-C<sup>[7,22]</sup> and TG.<sup>[5,10]</sup> In the present study, a positive correlation was found between leptin and TC in males and a weak negative correlation with HDL-C in females, which is probably due to the higher prevalence of hypercholesterolemia and decreased HDL-C in males and females, respectively. At the same time, among patients of both sexes, leptin level was significantly correlated with TG blood concentration.

Indeed, TG is stored in adipose tissue as the main

form of energy, and there is a strong correlation between the TG blood concentration and adipose tissue deposition. Thus, its association with leptin may be indirect through the presence of obesity.<sup>[23-25]</sup> In addition, some studies have shown that leptin is associated with the factors responsible for lipid metabolism. Hyperleptinemia is associated with increased synthesis and decreased cholesterol absorption.<sup>[26]</sup> Cohen et al.<sup>[27]</sup> also demonstrated that leptin can specifically inhibit the gene encoding stearoyl coenzyme A desaturase-1 - the enzyme involved in the synthesis of TG and a very low-density lipoprotein in the liver. However, the exact mechanisms of leptin regulation of lipid synthesis in the liver are not fully understood and require further research.

Previous studies have shown that leptin levels vary by ethnicity. The highest leptin level was reported in South Asian (Indian) people in several studies,<sup>[28-30]</sup> and was significantly higher compared with persons of Caucasian and Chinese ancestry, independent of age and BMI. African-American subjects were also reported to have greater mean levels of leptin<sup>[31]</sup> compared with Caucasians, Hispanics and those of Chinese origin. In Chinese people, the level of leptin was lower than in other ethnic groups.<sup>[28,31,32]</sup> In addition, it was also shown that the unit change in leptin per unit change in BMI differed across ethnic groups and was significantly higher in the Chinese subgroup.<sup>[31]</sup>

In conclusion, hyperleptinemia, especially in patients with obesity, should be seen as a sign of energy imbalance of carbohydrate and lipid metabolism associated with the development of cardiovascular disease and type 2 diabetes mellitus. Obviously, leptin, as a biomarker for body fat, reflects a hitherto unexplored activity of adipocytes and contains important information about the risk of cardiovascular disease.<sup>[33]</sup> The results of our study show that leptin is associated with general and abdominal obesity and dyslipidemia. However, further large-scale prospective studies are necessary to better understand and closely examine the physiological and pathological functions of leptin.

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**Key words:** Body mass index; leptin; lipids; Kyrgyzstan; waist circumference.

**Anahtar sözcükler:** Beden kütle indeksi; leptin; lipitler; Kırgızistan; bel çevresi.