Original Article

Relationship of serum leptin levels with body mass index and gender

Nazish Rafique, Mohammad Nasir Afzal

ABSTRACT

Objective
To evaluate the relationship between hyperleptinemia, obesity and gender in males and females.

Methods
This was an observational study carried out at Shifa College of Medicine from January 2007 to June 2007. Serum leptin levels of ninety five healthy male and female subjects were measured. Height and weight was recorded and BMI was then calculated. Leptin levels were measured by DRG Leptin (sandwich) ELISA EIA-2395.

Results
Serum leptin levels were significantly higher in the females (25.37±22.82 ng/ml) as compared to the males (11.12±10.68 ng/ml). They were also higher in the overweight and obese (BMI ≥25kg/m²) individuals (26.78±19.13 ng/ml) as
compared to the normal weight (BMI <25kg/m^2) subjects (6.30±5.06 ng/ml) (P value < 0.05).

**Conclusion**

Serum leptin levels of females were two times higher as compared to males. Overweight and obese individuals showed higher serum leptin levels as compared to lean and normal weight individuals. This indicates that gender and BMI are the major determinants of serum leptin levels. (Rawal Med J 2009;34: ).

**Key words**

Leptin, body mass index, obesity, adiposity, gender.

**INTRODUCTION**

Leptin is a 16 K Da (167-amino acid) protein expressed mainly by adipocytes and released in the blood in proportion to the size of adipose tissue and relays a satiety signal to the hypothalamus.\(^1\) It’s concentrations are highly correlated with body fat storage and exhibit sexual dimorphism, with women having higher concentrations at every level of relative or absolute adiposity.\(^2,3\) The significant relationship between the serum leptin concentration and the percentage of body fat suggests that adipocytes signal the brain about the size of the adipose-tissue depots resulting in decreased appetite and increased energy expenditure, which together will result in weight loss.\(^4,5\)
The *ob* gene is an adipocyte-specific gene that encodes leptin and an increase in its expression in obese subjects has been found. The finding of hyperleptinemia in obese subjects suggests that these increased leptin levels do not induce the expected responses (i.e., reduction in food intake and increase in energy expenditure) thereby, indicating that obese humans are resistant to the effects of endogenous leptin. For any given measure of obesity, leptin levels are 3 fold higher in women than in men and umbilical cord leptin levels suggest that the gender-based differences are established during the intrauterine period. Adipose tissue of females secrete significantly higher amounts of leptin than that of men and estrogen may be involved in its regulation. Lower leptin levels in males are due to testosterone anabolic action which increases lean body mass, but not adipose tissue, the source of leptin. This study aims to investigate the effect of gender and BMI on leptin levels from representative samples of Pakistani women and men.

**SUBJECTS AND METHODS**

This was an observational study carried out at Shifa College of Medicine and Shifa International Hospital Islamabad from January 2007 to June 2007 and included 96 healthy subjects. There were 48 male and 47 female. Detailed history and physical examination was carried out to rule out any physical or mental
illness. Patients with hypertension, diabetes mellitus, metabolic disorders other than obesity and those with any inflammatory disorder were excluded from the study.

Weight, height, blood pressure, and fasting glucose levels were taken at the time of the collection of blood samples. BMI was calculated as weight (kg) divided by height (m$^2$). The subjects with BMI less than 18 kg/m$^2$ were considered as lean, those with BMI greater than 25 kg/m$^2$ were considered as overweight, whereas subjects with BMI greater than 30 kg/m$^2$ were considered as obese. Blood glucose levels were measured with glucose test strips and leptin levels were determined with ELISA (enzyme-linked immunosorbent assay) method using DRG Leptin (sandwich) ELISA EIA-2395 kit Germany.

The protocol was approved by the ethics committee and institutional review board of Shifa College of Medicine and written informed consent was taken from each subject. Data were analyzed on SPSS version 15. Mean serum leptin levels between the overweight and obese group and normal weight and lean group, as well as the mean leptin levels between the male and female group were compared by t-test. A p value less than 0.05 was regarded as statistically significant and a p value < 0.001 was regarded as highly significant.
RESULTS

Mean serum leptin concentration in the overweight and obese subjects were higher as compared with in the normal-weight and lean subjects. (P<0.001) (Table 1). The lowest serum leptin concentration detected in a subject from overweight and obese group was 13.35ng/ml whereas, the highest serum leptin concentration detected in a subject from normal weight and lean group was 21.72 ng/ml.

Table 1. Serum leptin levels and BMI.

<table>
<thead>
<tr>
<th>Serum leptin levels (ng/ml)</th>
<th>Subjects with BMI ≤ 25 kg/m² (n= 47)</th>
<th>Subjects with BMI &gt; 25kg/m² (n= 48)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6.34 ± 5.06</td>
<td>26.78 ± 19.13*</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Serum leptin concentrations were also higher in the female group as compared to the male group (p value < 0.001) (Table 2). The lowest serum leptin concentration detected in a subject from female group was 9.72ng/ml whereas, the highest serum leptin concentration detected in a subject from male group was 21.70ng/ml.
Table 2. Serum leptin levels between males and females.

<table>
<thead>
<tr>
<th></th>
<th>Males (n=48)</th>
<th>Females (n=47)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum leptin levels (ng/ml)</td>
<td>11.12 ± 10.68</td>
<td>25.37 ± 22.82*</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Gender differences remained significant when leptin concentrations were divided by BMI (table 3).

Table 3. Serum leptin levels of males and female and their relationship with BMI.

<table>
<thead>
<tr>
<th>BMI</th>
<th>Leptin levels in males (ng/ml)</th>
<th>Leptin levels in females (ng/ml)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal weight &amp; lean individuals BMI &lt; 25kg/m²</td>
<td>4.43 ± 3.78</td>
<td>11.27 ± 4.71**</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Over weight &amp; obese individuals BMI &gt; 25kg/m²</td>
<td>20.30 ± 10.26</td>
<td>37.71 ± 25.92*</td>
<td>0.003</td>
</tr>
</tbody>
</table>

DISCUSSION

The present study indicated the existence of a strong relationship between serum leptin levels and BMI. Moreover, serum leptin levels were also found to be higher
in the females as compared to males, independent of BMI. Several studies have shown that serum leptin levels are strongly correlated with BMI.\textsuperscript{13,15} It has been observed that the humans lacking this functional protein have severe obesity, greatly increased appetite and reduced metabolic rate.\textsuperscript{16} Moreover; in contrast, the majority of obese persons have high circulating leptin levels suggesting the existence of leptin resistance in hyperleptinemic obese subjects.\textsuperscript{17} Most studies show that that nearly all obese individuals have elevated leptin levels, probably due to increase in leptin gene expression and partly due to greater production because of greater fat cell mass.\textsuperscript{18,19}

The mechanisms leading to leptin resistance in human obesity include limitation of the blood-brain-barrier (BBB) transport system for leptin, alteration in the leptin receptor expression and inhibition of the leptin signaling pathways in leptin-responsive hypothalamic neurons.\textsuperscript{19,20} Long-term (>2 weeks) exposure to a high-fat diet or high leptin levels itself appears to induce multiple defects at the levels of BBB transport, receptor expression and melanocortin pathway, thereby controlling the biological activity of leptin by diet modification may exist as a practical strategy for the treatment of obesity.\textsuperscript{21,22} Another important finding of our study is that the serum leptin levels are about two times higher in the females as compared to the males, and this difference remained significant even after
adjustment for BMI. These results are in consistent with many other studies.\textsuperscript{2,23} This gender difference is maintained even in obesity, as our results showed.

It has been shown that adipose tissue increases leptin release after the administration of estradiol and this may explain the gender differences in leptin levels observed in our study.\textsuperscript{24} Our study showed that males had lower leptin levels than the females. This could be due to serum levels of testosterone in males, which could be an important contributor to the known gender difference in serum leptin levels.\textsuperscript{11} A direct suppressive effect of testosterone on leptin gene expression is also explored, which further justifies the findings of our study.\textsuperscript{11}

**CONCLUSION**

Serum leptin levels were about two times higher in the females as compared to the males and gender differences remained significant when leptin concentrations were divided by BMI. The results showed that the major determinants of serum leptin levels are gender and BMI.

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REFERENCES


13. Lakho GR, Nair K, Chundrigar T, Jabeen N, Qureshi MA. Serum leptin levels in pregnant Pakistani females, relationship with BMI and placental weight. JPMA 200; 51:32-6.


