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# Serum Leptin levels in Obese Post Menopause Women

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## الخلاصة

الهدف من هذه الدراسة هو إيجاد العلاقة بين هرمون النحافة وحالة السمنة في النساء ما بعد سن اليأس.

تم قياس مستوى هرمون النحافة في مصل الدم بطريقة الامتزاز المناعي المرتبط بانزيم. كذلك تم قياس منسب كتلة الجسم باستخدام الوزن (كغم)/المتر المربع, وقياس محيط الخصر بالسنتيمترات.

تم اخذ هذه المعايير من 100 سيدة ما بعد سن اليأس والتي قسمت تبعا للسمنة الى مجموعتين: 60 سيدة مصابة بالسمنة و 40 سيدة غير مصابين بالسمنة.

لقد وجد فرق معنوي عالي في مستويات هرمون النحافة في مصل الدم ومنسب كتلة الجسم ومحيط الخصر في النساء المصابات بالسمنة ما بعد سن اليأس مقارنة بالنساء الغير مصابات بالسمنة ($p \leq 0.01$).

كما وجد ارتباط عالي بين هرمون النحافة و منسب كتلة الجسم ($r=0.739$, $p \leq 0.01$) وكذلك بين هرمون النحافة ومحيط الخصر ($r=0.684$, $p \leq 0.01$).

## Abstract

The objective of this study is to find the relationship between leptin and obesity in post menopause women. Serum leptin level was determined by using the Enzyme Linked Immuno Sorbant Assay (ELISA) technique, The Body Mass Index (BMI) was measured by weight (kg)/square height ($m^2$), and waist circumference was measured in centimeters.

These parameters where taken from 100 post menopause women who were divided according to BMI into two groups: 60 obese women and 40 non-obese women.

A highly significant difference in Serum Leptin levels, BMI and Waist circumference was found in the obese post menopause women compared with non-obese subjects ($p \leq 0.01$). And a highly significant positive correlation between serum leptin levels and BMI ($r=0.739$, $p \leq 0.01$), and between serum leptin levels and waist circumference ($r=0.684$, $p \leq 0.01$).

## Introduction

Leptin was discovered as a result of studies on ob/ob mice, a strain of hyperphagic obese mice that were known to lose weight when their circulation was attached to normal mice (parabiosis) [1]. Subsequent studies revealed that ob/ob mice had a mutation that results in inability to produce a protein, first called the ob protein and later Leptin, which regulates food intake [2]. In addition to being very obese, these mice grew poorly and had infertility due to gonadal hypofunction. Administration of Leptin to these animals resulted in a marked decrease in food intake, weight loss, and improved growth [3].

Leptin is a member of the cytokine family, and its receptor is a member of the gp130 group of cytokine receptors, there are at least five forms of the Leptin receptor [4]. The most widely distributed is the short form of the receptor, which is present in most tissues and may serve to transport Leptin into the brain. The long form of the receptor is located in areas where Leptin is thought to act, including hypothalamic nuclei. There may also be a circulating form of the Leptin receptor that binds Leptin [4].

Circulating factors that bind Leptin might also contribute to Leptin resistance [5]. In one study, C-reactive protein was identified as a circulating factor that binds to Leptin, impairs its signaling, and attenuates its physiologic effects (in cultured cells and an ob/ob mouse model). In addition, physiologic concentrations of Leptin stimulated C-reactive protein expression in vitro [5].

Food intake is reduced by systemic Leptin administration in normal-weight experimental animals, but the response decreases as the animals become obese. However, when Leptin is injected into the ventricular system of the brain of obese animals, they remain responsive [6]. Since Leptin is transported across the blood-brain barrier to act within the brain, the processes controlling the entrance of Leptin into the brain are pivotal determinants of its action on food intake [7].

Most obese people, however, are not Leptin deficient, and serum Leptin concentrations are directly related to their amount of body fat. In several surveys of obese subjects, no mutations in the Leptin gene were detected [8, 9]. Given the high serum Leptin concentrations and apparent Leptin resistance in obese subjects [10, 11], little response to exogenous Leptin might be expected. However, in a study of the effect of recombinant Leptin (0.01, 0.03, 0.1, or 0.3 mg/kg per day) or placebo in normal-weight subjects for four weeks and obese subjects for 24 weeks, there was a very modest dose-dependent decrease in weight in both groups [12]. After weight loss, Leptin administration prevents the decline in metabolic rate and circulating concentrations of thyroid hormone [13].

Postmenopausal women are at increased risk of coronary heart disease (CHD), partly because of the decline in estrogen production and concurrent elevations in total and low-density lipoprotein (LDL) cholesterol level [14]. Obesity, weight gain, and adverse changes in body fat distribution and composition are part of this phenomenon [15, 16]. Moreover, the rise in LDL

cholesterol levels and onset of other CHD risk factors (e.g. high blood pressure, high total cholesterol and triglyceride levels, and insulin resistance) is directly influenced by weight gain [16,17].

Several longitudinal studies also suggest that menopause increases central adiposity, although these studies used waist circumference or waist-hip ratio (WHR), a less precise technique [15, 18].

This present study was designed to evaluate the role of leptin level in obese post menopause women.

## Materials and Methods

### Subjects:

This study included 100 post menopause women from the external laboratory department at Baghdad teaching hospital. Subjects recruited to full fill the criteria of being postmenopausal (at least 6-months history of amenorrhea not due to pregnancy and age range 47-66 years).

Study subjects were divided according to obesity into two groups:

Group 1: 60postmenopausal obese women (body mass index ≥30 kg/m²).

Group 2: 40 postmenopausal non-obese women (body mass index <30 kg/m²).

### Methods:

### Serum leptin:

For each women included in this study venous blood samples were collected to obtain the serum. The Leptin (sandwich) Enzyme immunoassay kit provides materials for the quantitative determination of leptin in serum and plasma. This assay is intended for in vitro diagnostic use only. The leptin (sandwich) ELISA is a solid phase enzyme-linked immunosorbent assay (ELISA) based on the sandwich principle.

The microtiter wells are coated with a monoclonal antibody directed towards a unique antigenic site on a Leptin molecule. An aliquot of patient sample containing endogenous Leptin is incubated in the coated well with a specific rabbit anti Leptin antibody. A sandwich complex is formed. After incubation the unbound material is washed off and an anti rabbit peroxidase conjugate is added for detection of the bound Leptin. Having added the substrate solution, the intensity of color developed is proportional to the concentration of Leptin in the patient sample, reads at 450nm with the microtiterplate reader within 10 minutes after adding the stop solution Normal value in Female = 7.36 ± 3.73 ng/ml and in Male = 3.84 ± 1.79 ng/ml. [19].

### Anthropometric measures:

1- Body Mass Index (BMI) was calculated by weight (in kilograms) divided by the square of height (in meters), weight and height are measured by the same scale for the all sample subjects.
   BMI = Weight (kg)/Square Height ($m^2$) [20].

2 - Waist circumference was measured in centimeters (cm) using a flexible non-elastic measuring tape.

**Statistics:**

To compare the significance of the difference in the mean values of any two groups, Student's t-test was applied; $p \leq 0.01$ was considered statistically highly significant, $p \leq 0.05$ was considered statistically significant.

The Pearson correlation coefficient [r] test is used to describe the association between the different studied parameters; $p \leq 0.01$ was considered statistically highly significant, $p \leq 0.05$ was considered statistically significant.

**Results:**

There was no significant difference in mean age between obese and non-obese subjects ($p = 0.341$) (table 1). Body mass index was higher in obese subjects than non-obese subjects ($p \leq 0.01$) (table 1). Mean waist circumference was higher in obese group than non-obese group ($p \leq 0.01$) (table 1). Mean serum Leptin level was higher in obese group than non-obese group ($p \leq 0.01$) (table 1).

| Characteristic | Obese group | Non-obese group | p value |
|---|---|---|---|
| **Age (year)** | 55.87± 4.38 | 56.65 ± 3.34 | 0.341 |
| **BMI ($kg/m^2$)** | 35.78 ± 5.06 | 25.94 ± 3.22 | ≤0.01 |
| **WC (cm)** | 112.5 ± 8.6 | 85.54 ± 17.16 | ≤0.01 |
| **Leptin (ng/ml)** | 31.41 ± 4.79 | 17.3 ± 5.7 | ≤0.01 |

**Table 1: Mean ± SD values of age, body mass index, waist circumference & Leptin in obese (n = 60) and non-obese (n = 40) subjects.**

Mean waist circumference correlates positively with body mass index [$r = 0.759$, $p \leq 0.01$] (figure 1). Serum Leptin correlates positively and strongly with body mass index [$r = 0.739$, $p \leq 0.01$] (figure 2). Serum Leptin also correlates positively with waist circumference [$r = 0.68$, $p \leq 0.01$] (figure 3).

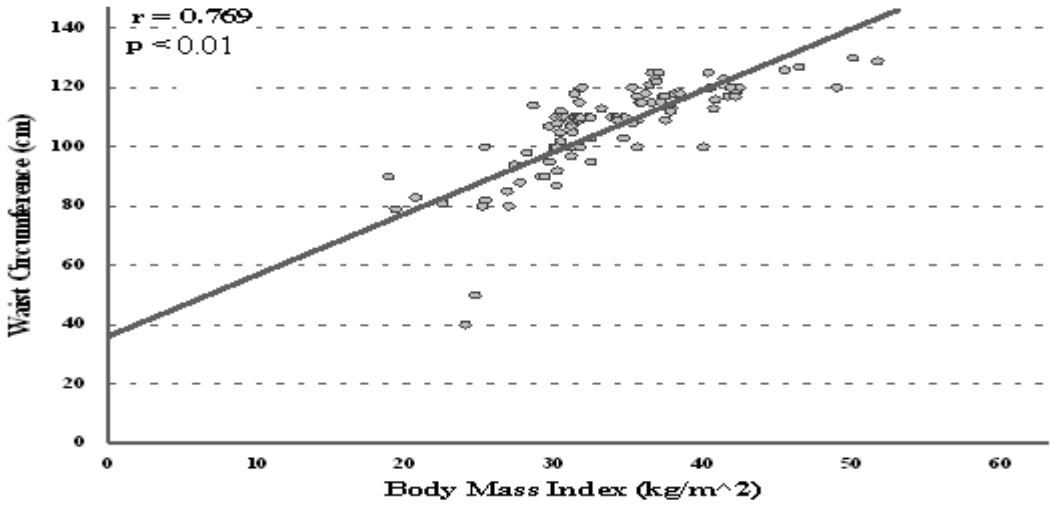


**Figure 1: Correlation between waist circumference and body mass index.**


**Figure 2: Correlation between serum Leptin and body mass index.**

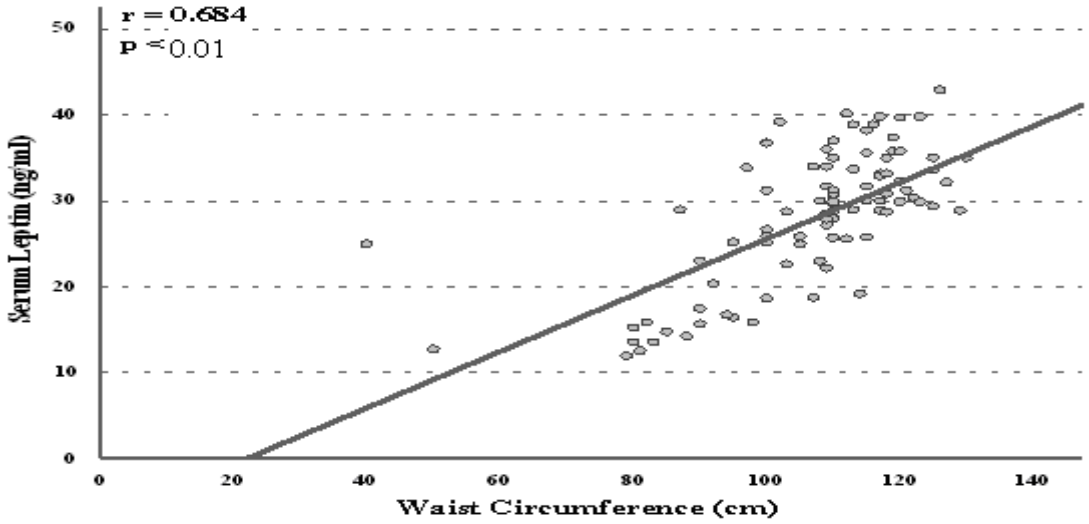


**Figure 3: Correlation between serum Leptin and waist circumference.**

## Discussion

Serum leptin concentration is increased in obese subjects and is closely related to fat mass and BMI [21, 22]. It is regulated by serum insulin concentration[23] and declines with weight loss [21]. Several reports have shown a higher leptin concentration in women than in men [24]. The gender difference has been explained partly by the variable degree and distribution of the amount of body fat depots. Women tend to have a higher overall obesity which is more pronounced in subcutaneous fat than in visceral fat, in contrast to men who have a lower overall but greater visceral adiposity. Serum leptin concentrations are not influenced by menopausal status or serum estradiol level [25].

In the present study of the relationship between serum Leptin and obesity in postmenopausal women, we found that mean serum Leptin level is higher in obese group than non-obese group (Mean ± SD; 31.41 ± 4.79 vs. 17.3 ± 5.7 ng/ml; $p \leq 0.01$), also Serum Leptin correlates positively and strongly with body mass index [$r = 0.739$, $p \leq 0.01$], similar correlation is present in a study done by Marita A.R. et. al. (2005) [26]. In addition, a previous study reported in a cross-sectional study of 3,553 subjects in Netherlands, that BMI and waist circumference are positively associated with serum leptin concentration [27], this is also true in regard for the relation between serum leptin level and waist circumference in our results, as serum leptin level correlates positively with waist circumference [$r = 0.68$, $p \leq 0.01$], another study reported that women who are overweight or had a higher waist circumference (women ≥ 88 cm) have a significantly higher risk of having hyperleptinemia [28].

Other studies concluded that fat distribution contributes to the variability in serum leptin in obese patients. In particular, subcutaneous abdominal fat is a

determinant of leptin concentration, also independently of the amount of fat mass, whereas the contribution of preperitoneal visceral fat is not significant [29].

Most obese individuals are leptin-resistant [30], resistance to the actions of leptin could be cause by decreased leptin transport through the blood-brain barrier [31, 32], or to reduced signaling distal to the leptin receptor [31, 33]. Peripheral signals such as gloucocorticoids may also interfere with leptin's interaction with its receptor and produce central leptin resistance [34, 35].

The mechanism underlying the elevated circulating levels of leptin on obese women, may be due to an accelerated secretion rates of the peptide from adipose tissue because of increased ob gene expression [36].In addition, subcutaneous fat produces more leptin mRNA than visceral fat, which could explain why women have higher leptin levels in as much as they have more subcutaneous fat than visceral fat [37].

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