

# Leptin in Goitrous patients

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## **Abstract:**

**Objective:** To evaluate the relationship between serum Leptin levels and metabolic syndrome, in (obese, non-obese) control subjects, untreated hypothyroid and hyperthyroid patients.

**Methods:** A study was made on 63 goitrous patients and 25 control subjects. Body mass index (BMI) was calculated. Serum T3, T4, TSH were measured by RIA method, serum lipid profile was measured by spectrophotometric method, serum Leptin was measured by ELISA method.

**Results:** The mean serum Leptin level was significantly higher in obese than in non-obese control subjects (29.1 vs. 5.8 ngm / ml) and higher in hypothyroid patients (27.9 ngm /ml), and lowest levels in hyperthyroid patients (3.4 ngm /ml).

**Conclusion:** Leptin reduce body weight by decreasing food intake (appetite), fat deposition and increasing energy expenditure. Serum Leptin is highly correlated with the body mass index (BMI), other indices of adiposity (lipid profile) in normal obese human and hypothyroid patients.

**Key Words:** Leptin Hormone, Obesity, lipid profile, Thyroid Hormone.

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## **Introduction:**

Leptin acting on its receptors in hypothalamus and other several peripheral tissues exerts diverse biological effects. It is a neuromodulator protein of 167 amino acids, 16 KDa cytokine-like hormones and mainly secreted from adipose tissue. Due to sex differences in body fat distribution and testosterone level, females have higher Leptin level than males when matched by age, weight and body fat<sup>(1)</sup>. Like other hormones, Leptin is secreted in a pulsatile way and has a substantial diurnal variation with an increase of about 50% in the late evening and early morning hours that might be related to an intrinsic circadian component, meal timing and the sleep-wake<sup>(2)</sup>.

Several factors regulate the synthesis and secretion of Leptin from adipose tissue, including nutrients, hormones and the sympathetic nervous system (SNS)<sup>(3)</sup>. Insulin, steroid hormones and noradrenaline are important regulators of Leptin production and secretion<sup>(4,5)</sup>.

The changes in Leptin expression in response to fasting and feeding are mediated by insulin. Fasting can inhibit Leptin expression, while after feeding Leptin synthesis is increased<sup>(6)</sup>.

Leptin receptors isoforms can be divided into three classes: secreted, short and long forms<sup>(7)</sup>.

Individuals with mutations in the Leptin gene or in the Leptin receptor gene characterized by severe early onset obesity with marked hyperphagia, hypogonadotropic, hypogonadism, sympathetic nervous system underactivity, defects in immune functions, this syndrome is called Leptin deficiency syndrome<sup>(3)</sup>.

Leptin is taken up into the central nervous system (CNS) by a saturable transport mechanism and binds to the long form of the Leptin receptor (Ob Rb), which is principally located in the arcuate nucleus of the hypothalamus<sup>(4)</sup>.

Within the arcuate nucleus, Leptin is able to directly inhibit the expression of orexigenic neuropeptide like neuropeptide Y and Agouti-related peptide (AGRP), peptides that increase food

intake and decrease energy expenditure <sup>(8)</sup>. In contrast, expression of anorectic peptides that decrease food intake, such as cocaine and amphetamine regulated transcript (CART) and pro-opiomelanocortin (POMC) are increased (3). The Leptin effect is most probably mediated by the melanocortin pathway, as alpha melanocyte-stimulating hormone (MSH), which secondary to Leptin falls during fasting <sup>(9)</sup>.

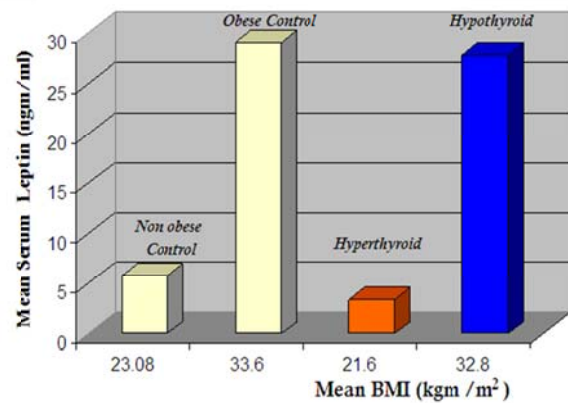
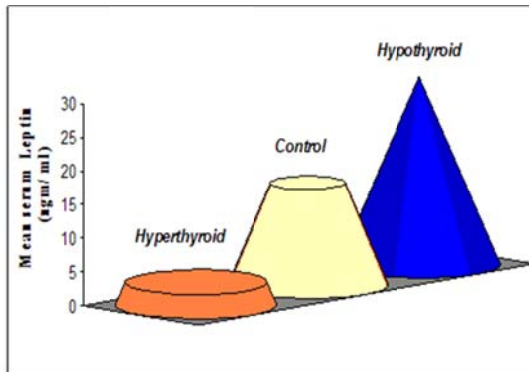
**Patients and Methods:**

A study was made of 25 control (12 female, 3 male) aged (25 – 35) year, mean BMI= 27.3 kg /m <sup>2</sup> and 33 of untreated hyperthyroid (18 female, 15 male) aged (30 – 40) year, mean BMI= 21.6 kg /m <sup>2</sup> and 30 of untreated hypothyroid (17female, 13 male) aged (30–40) year, mean BMI=32.8 kg/m<sup>2</sup> patients.

**Results:**

Hormonal data of serum Leptin (Mean, ±SD) for thyroid patients and control were shown in Tables(3.1) in which high significant decrease of serum Leptin was found in hyperthyroid patients (P < 0.005) and high significant increase was found in hypothyroid patients (P < 0.005) compared with control group, Figure (3.1)

The mean serum Leptin in hypothyroid group is significant increase than that of non obese control group (P < 0.05) ,while the mean serum Leptin in hyperthyroid group is not significant difference than that of non Obese control group. In the control group, serum Leptin level showed a positive correlation with BMI and serum T4, TSH, TG, TC, VLDL –C, LDL– C (P<0.001) and correlated negatively with serum T3 (P<0.05) and HDL-C (P<0.001). In hypothyroid patients serum Leptin level showed a positive correlation with serum TG (P<0.05), TC, VLDL-C, LDL-C (P<0.001) and correlated negatively with serum T3 and HDL-C (P<0.001). In hyperthyroid patients serum Leptin level was unrelated to all parameters (all P=NS).



**Figure3.1**-The serum Leptin level for control, Hyperthyroid and hypothyroid groups

**Figure 3.2**- The serum Leptin level for (non obese and obese) control, Hyperthyroid and hypothyroid groups.

**Table 3.1- The serum Leptin level for (non obese and obese) control, Hyperthyroid and hypothyroid groups.**

	<i>Control</i>		<i>Hyperthyroid</i>	<i>Hypothyroid</i>
	<i>Non obese</i>	<i>Obese</i>		
<b>N</b>	15	10	33	30
<b>Mean BMI</b>	23.08 ±	33.6 ±	21.6 ± 1.3	32.8 ±
<b>(kg/m<sup>2</sup>) ± SD</b>	1.21	2.03		1.74
<b>Range (kg/m<sup>2</sup>)</b>	20.8 – 24.9	30.7 – 36.3	19.1 – 24.5	30.4 – 39
<b>P-value</b>	_____	< 0.005	NS*	< 0.025
<b>Mean serum</b>				
<b>Leptin (ng/ml</b>	5.8 ± 2.78	29.1 ± 6.6	3.4 ± 0.96	27.9 ±
<b>± SD</b>				11.21
<b>Range (ng/ml)</b>	1.8 – 10.5	20 – 39	1.9 – 4.5	10.5 – 61.5
<b>P-value</b>	_____	< 0.05	NS*	< 0.05

NS\* = Non significant difference, P>0.05

### **Discussion:**

Leptin is a pleiotropic hormone that has helped to redefine adipose tissue as an endocrine organ; it plays an essential role signaling energy status to the CNS, high circulating concentrations may contribute to the pathogenesis of some obesity-related conditions, such as hypertension <sup>(3)</sup>, insulin resistance and accelerated atherogenesis <sup>(10)</sup>.

There were no correlation of human Age with serum Leptin level for study groups, these results agreed with <sup>(11)</sup>, another study showed a negative correlation between age and serum Leptin <sup>(12)</sup>.

The findings of hyperleptinemia in obese humans indicate the existence of a defect in either the loop or in the Leptin action. Leptin resistance may occur for one of several reasons: Leptin may fail to cross the blood–brain barrier, the hypothalamic receptors may be down regulated or downstream signaling may be inhibited <sup>(13)</sup>.

There was a significant decrease in mean serum Leptin level in hyperthyroidism; this is agreed with (14) and (15). Other report slightly increased (16). Other reports no change (17).

The thiamazole-treated thyrotoxic patients increased their serum Leptin concentrations during 12 months antithyroid drug treatment <sup>(18)</sup>. An enhanced beta-adrenergic stimulation by thyroid hormones may be responsible for decrease of Leptin levels in patients with hyperthyroidism.

In hypothyroid group there was a significant increase in mean serum Leptin level, this is agree with (16) and (19). Other report lower Leptin level compared with controls (15). Other reports no change (17). Treatment of hypothyroidism resulted in a reduction in the raised plasma Leptin levels (14).

The increase of serum Leptin in hypothyroidism may be associated with Leptin resistance and seems to suppose that these effects are mediated by decrease genes expression, transcriptional regulation of the protein involved due to the decrease thyroid hormone levels.

Leptin rapidly decreases the level of plasma insulin, and causes reduced expression of target genes participating in fatty acid and cholesterol synthesis. The genes required for reverse cholesterol transport (including HDL and bile acid metabolism) are up-regulated by Leptin signaling via an unknown mechanism <sup>(20)</sup>. Leptin has been shown to downregulate hepatic

Hydroxymethyl -glutaryl-CoA reductase, leading to a substantial drop in TC and VLDL-C in plasma (21).

### **Conclusion:**

- 1- The increased serum Leptin level in hypothyroidism may be due to the effect of thyroid hormone on cell membranes signaling of adipocytes cell and Leptin receptor [Leptin resistance].
- 2- The decreased serum Leptin level in hyperthyroidism may be due to the effect of thyroid hormone on up regulation of adrenergic receptors, which tend to decrease Leptin secretion.

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