

# Thyroid Status Effect on Leptin Hormone and Lipid Profile in Female Patients with Thyroid Dysfunction

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## ABSTRACT

**Background:** Thyroid gland is one of the most important glands in the human body which responsible for the secretion of Thyroxin (T4) and Triiodothyronine (T3) hormones. These hormones in addition to Thyroid Stimulating Hormone (TSH) have a great effect on other hormones like leptin. So, the objective of this study is to assess any correlation between thyroid hormones, lipid profile, and leptin in female patients with thyroid dysfunction.

**Methods:** This cross-sectional study was conducted for 50 women diagnosed with hypothyroidism (25) and hyperthyroidism(25) attending AL-Karamah Teaching Hospital in Wasit. All of them ranged between 20-55 years. The researchers obtained verbal consent and then took a serum sample from all of them to test the level of thyroid hormones (T4, T3), TSH, leptin hormone and lipid profile (TG, HDL-C, LDL-C and cholesterol) were determined. Data were analyzed by SPSS version 23 using descriptive statistic for quantitative variables. Independent t-test, correlation and regression analysis were also used.

**Results:** This study found that both the leptin level and lipid profiles (Cholesterol, TG, LDL and HDL) were significantly higher ( $P<0.01$ ) in hypothyroid patients relative to hyperthyroid. A significant negative correlation was found between T4, T3 and leptin ( $P<0.01$ ). The leptin can be significantly mainly predicted by TSH ( $P<0.001$ ) in female patients with thyroid dysfunction. Also found that there is a strong and significant ( $P<0.01$ ) correlation between all studied variables with leptin.

**Conclusion:** Although the leptin hormone level in patients with thyroid dysfunction showed a strong correlation with lipid profiles, TSH, and thyroid gland hormones. The only significant predictor for leptin was the TSH.

**Keywords:** Hypothyroidism, Hyperthyroidism, Leptin, Lipid Profile, TSH.

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## INTRODUCTION

Considering Hyperthyroidism and hypothyroidism as the main dysfunctions that can occur in thyroid gland due to disturbances in the levels of TSH, T3, and T4 hormones. These thyroid hormones playing a controlling role for many body processes like heat production, metabolism, and cell multiplication in addition to controlling the action of other hormones. Abnormalities in thyroid hormones make an effect on appetite which leading to changing in the number of fat cells and finally change body weight. Cardiovascular diseases and type 2 diabetes mellitus can also be presented in patients with thyroid dysfunction (1).

The thyroid gland can effect on the level of leptin hormone because it is responsible for the production of both triiodothyronine (T3) and thyroxin (T4) which play an important role in keeping metabolic rate in a proper running. So, any disturbances in the secretion of these hormones may lead to an obvious change in the number of fat cells in the body and the energy outflow and it seems to act on leptin level.(2)

The leptin hormone still attracts the attention of many scientists, since its discovery and the researches are still ongoing up to date (3). The leptin hormone is the product of obesity gene and consists of 761 amino acid, followed by a cytokine while in mice family it is consisting of five spiral parts (4). The obesity gene in human is like that in a mouse as it located on chromosome 7 and secreted by the fatty acid gland. Besides, leptin is also produced by some tissue non-

fatty sorts such as the stomach wall, cells of the breast, muscle cells, and the placenta. (5).

The leptin hormone is presented in the blood with two images, either free or as conjugated protein. However, lean individuals have a hormone in the form of proteins, while those fatty individuals have the free form hormone. The leptin hormone reaches its peak in the middle of the night because of the luteinizing hormone increases at night leading to reversing effect on the level of the cortisol hormone which reaches its peak at the beginning of the day (6). The secretion of leptin is also affected by the number and size of fat cells, so in obese people, there is an increase in size and number of these cells leading to produce leptin in a larger amount in reverse to thin people. However, it was found that women have an exceeding level of leptin hormone than and this possibly may be due to the increasing proportion of fat. (7). It was also found that androgen deficiency reduces the secretion of the leptin hormone. Organizing factors to secrete the leptin hormone: the hormone estradiol increases.

So the main objective of our study is to find if there is any correlation between thyroid hormones, lipid profile, and leptin hormone level in hyperthyroidism and hypothyroidism female patients.

**MATERIALS AND METHOD**

**Study Design and Setting**

An analytic cross-sectional study was conducted over fifty females patients between the age of (20 - 55) years old and recently diagnosed with thyroid dysfunction diseases. Twenty-five of them have hyperthyroidism and the remaining 25 were with hypothyroidism.

The patients were recruited from Al-Karamah Teaching Hospital, Endocrine consultation unit during the period from 1st September 2019 till the end of December 2019 and all variables of interest were tested.

**Case Definition**

Diagnoses of both hyper and hypothyroidism depends on clinical features and thyroid function test. In hyperthyroidism patients presented with weight loss despite increased appetite and heat Intolerance, skin wetness, increasing heart rate, nervousness, tremor, eye protrusion in addition to high serum T3, T4 level and low Thyroid Stimulating Hormone(TSH). While hypothyroidism patients suffer from weight gain despite the loss of appetite and cold Intolerance, dry skin, slow heart rate, swelling of the face, noticeable or obvious thyroid gland. There is an elevated serum TSH (more than twice normal), low serum T3 or natural and low Serum T4 level.

**Laboratory Tests**

Measurement of serum leptin and thyroid function test (T3, T4, TSH) by enzyme-linked immunosorbent assay (ELISA). Estimation of total cholesterol (TC) and triglycerides (TG) by Enzymatic Colorimetric Method. (12).

Estimation of high-density lipoprotein cholesterol (HDL-C) by Separation method (precipitant Method) (Burstein et al., 1980). Estimation of low-density lipoprotein cholesterol (LDL-C)

Serum level of LDL\_C was calculated according to friedwold 's formula.)

**Ethical Consideration**

Formal approval was obtained from the directory of health and patients were verbally consent to be involved in this study.

**Data Analysis**

Data were analyzed by SPSS software program version 23 using mean and standard deviation for descriptive purpose, the mean difference between hyperthyroidism and hypothyroidism patients was obtained by independent sample t-test considering P-value 0.005. A correlation test was performed to assess any correlation between the study variables. Multiple regression analysis and factor analysis were done to define leptin hormone predictors in the sample.

**RESULT**

The result of this study depended on the analysis of data obtained from 50 female patients aged (20-55) years old.

Table 1 shows the level of T4, T3 is low in hypothyroidism with a high level of TSH and high level of leptin and all lipid profiles while in hyperthyroidism group the levels of T3, T4 are high with a low level of TSH and low level of leptin and

lipid profile with statistically significant differences between the mean values of leptin, T3, T4, TSH, Cholesterol, triglyceride, HDL, and LDL between two groups.

**Table 1:** Mean, Standard deviations and mean differences in leptin, thyroid hormones, and lipid profile between hyperthyroidism and hypothyroidism

Variables	Hyperthyroidism Mean (SD)	Hypothyroidism Mean (SD)	t-value	P-value
Leptin hormone (ng/ml)	14.6(1)	84.9(3)	-10.78	<0.01
TSH(mIu/ml)	0.28(0.02)	16(0.6)	-11.64	<0.01
T3(nmol/l)	3.96(0.06)	0.79(0.01)	24.88	<0.01
T4(nmol/l)	262.9(4.2)	49.5(0.5)	24.78	<0.01
Cholesterol (mg/dL)	138(1.4)	251(18.6)	-30.3	<0.01
Triglyceride(mg/dL)	126(1.1)	181(1.9)	-12.21	<0.01
HDL (mg/dL)	34(1.5)	54(1.4)	-47.7	<0.01
LDL(mg/dL)	78.9(1.2)	153.7(0.8)	-25.51	<0.01

The leptin hormone, TSH, Cholesterol, Triglyceride, HDL, and LDL appears to be significantly higher in patients with Hypothyroidism than Hyperthyroidism patients.

In table 2, the leptin hormone showed a significant negative correlation with T3 and T4 hormones, while, there was a positive correlation with TSH hormone, also there was a strong correlation of leptin with other studied variables.

**Table 2:** Pearson correlation of leptin hormone with thyroid function test and lipid profile in patients with thyroid dysfunction

Variables	Pearson correlation(r)	P-value
TSH(mIu/ml)	.998**	<0.01
T3(nmol/l)	-.998**	<0.01
T4(nmol/l)	-.997**	<0.01
Cholesterol (mg/dL)	.967**	<0.01
Triglyceride(mg/dL)	.996**	<0.01
HDL (mg/dL)	.989**	<0.01
LDL(mg/dL)	.997**	<0.01

Table 3 shows that leptin hormone can be significantly predicted by TSH. The statistical test was to exclude other variables because of multiple Collinearity between the independent variables.

Table 3: Multiple regression and Factor analysis of leptin hormone predictors

Dependent variable	Predictors	R	R <sup>2</sup>	F-value	F-significant	Beta	t-value	t-significant
Leptin hormone	TSH*	0.996	0.993	643.0395	<.001	.9196	80.190	0.001<

\*Thyroid Stimulating Hormone

## DISCUSSION

A lot of studies were suggested the effectiveness of thyroid hormones dysfunction on the function of Adipokines hormones like leptin. It was well known that Thyroid hormones have a great effect in regulation of the energy balance in the human body in addition to its effect on the levels of adipokines especially the Thyroid-stimulating hormone (TSH) which share its receptors in the adipose tissues. (18)

The results of this study showed a significant decrease ( $p < 0.01$ ) in the leptin hormone in a group overactive thyroid gland, may be due to leptin resistance, this low level of the hormone leptin in the blood in the overactive thyroid gland may be caused by the effect of increased thyroid hormone by stimulating device friendly especially for adrenergic receptors which tend to discourage the secretion of leptin by blocking leptin receptors in fat tissue. Fine et al., (21) was observed an increased expression of mRNA Leptin in hypothyroidism in mice, and a decrease in this expression in response to treatment or T3.

The leptin hormone may have a good contributing effect on the appetite-controlling and finally can decrease the adipose tissue mass in the body. And this effect can be explained by the presence of the leptin receptors in the hypothalamus gland. (19).

Results presented in the table (1) found a significant increasing ( $p < 0.01$ ) in the mean serum T3 and T4 and low TSH level in the hyperthyroidism group. While a significant increase ( $p < 0.01$ ) in the level of TSH and decreased T3 levels, T4 in the hypothyroidism group, this is in line with other studies previously published in this area of research.

Decreased Thyroid gland activity causes insufficient production of thyroid hormone and/ or function, with the higher secretion of the TSH hormone caused by the negative feedback to the hypothalamus and the pituitary gland. Hypothyroidism leads to a general slowdown in the metabolism of calories, including declines in all daily energy and oxygen consumption and heat generation.

Some authors have found that there is a decrease in thyroid activity, metabolic energy consumption (ME) and energy expenditure together with increased fat/ fat intake and lower protein Gain/ protein ratio. Thus, the percentage of body fat Significant increase compared to decreased thyroid activity. Mice hypothyroidism first Increased metabolism was balanced with increased intake and energy gain It was similar to that found in euthyroid mice (23).

Because the leptin has an effective role in adjusting the body weight by decreasing the appetite and increasing the heat

production, so the disturbances in these processes occurred in hyperthyroidism patients considering an important issue to be studied by the researchers since mid-1996.

The relationship between the leptin level, thyroids hormone level and lipid profile. Dyslipidemia occurred in patients with Thyroid dysfunction and our results showed a statistically significant increased ( $P < 0.01$ ) in the serum level of (TG and TC and HDL-C and LDL-C) in the hypothyroidism group than the hyperactive thyroid gland group.

When thyroid hormones level decreased lead to weakened of lipoprotein lipase (LPL) enzyme activity, which is responsible for TG-rich lipoproteins clearance. (20).

that leading to an elevation in serum TG. The T3 hormone is controlling LDL receptors via direct attachment to the responsive element of the thyroid hormone (TREs).(25).and regulates sterol controlling protein binding-element.

Shin, (27). In hypothyroidism, a reduction of the thyroid hormones level leads to decreased LDL receptors expression, so increasing cellular LDLC circulatory uptake and LDLC catabolism which contributes to a higher concentration of serum TC. Krotkiewski, (28). While in hyperthyroidism, HDLC and LDLC, TC and TG serum levels are diminished significantly. As mentioned before, the thyroid hormone can control LDL receptor expression, which changes cellular LDL particles uptake and catabolism. Faure(29). Elevated concentrations of thyroid hormones stimulate LPL activity and contribute to diminished serum lipoproteins levels. Thompson, (30). Also, HDLC metabolism modulated by thyroid hormones via elevated cholesteryl ester transfer activity protein, which was exchanges HDL to VLDL (very low-density lipoproteins). (31).

Yu (27) assess thyroid dysfunction (hyper and hypothyroidism) are associated with intermediary alterations of metabolism including body weight changes, and insulin resistance.

Hyperactive thyroid dysfunction is associated with diminished body weight, elevated Glucose and insulin predicting insulin resistance as well as diminished plasma lipid level which is due to the impact of thyroid hormone on the metabolism in the muscle, liver and adipose tissue leading to elevations of energy expenditure. In contrast, hypothyroidism is characterized by lowering levels of thyroxin T4, T3, and elevated TSH thyroid-stimulating hormone which lead to higher body weight and elevated lipoproteins and plasma lipids. So plasma TG, cholesterol LDL and HDL-C are all elevated in hypothyroidism and diminished in hyperthyroidism (21).

Triiodothyronine T3 has an important role in the lipid and energy balance, there is an inverse correlation between serum level of leptin and T3. There is evidence that leptin synthesis in the fat

Inhibited by the sympathetic nervous system, this occurs via B3- adrenergic receptors, also T3 regulates the density of B3- adrenoreceptors density and the white fat sympathetic response. Leptin resistance metabolic impact is decreased TSH production, inhibit T4 to T3 conversion, and elevation

in reverse T3, appetite increase, higher insulin resistance and lipolysis (fat breakdown) suppression.

The majority of people who are overweight or who have difficulty in weight loss have a variable degree of resistance to leptin. Leptin cannot produce natural effects of weight loss, with a magnitude associated with the degree of obesity. The scarcity of leptin in the hypothalamus is causing this leptin resistance that makes the sense of starvation to stimulate different activities for increasing fat storage in response starvation. The leptin resistance also effects on thyroid function test by a fall in both the TSH and T3 levels that cause a decline in metabolic rate which in turn causing weight gain.

Thyroid diseases also presented with changes in lipid profile mainly the LDL-C and HDL-C which appear to be raised in hypothyroidism and the reverse in hyperthyroidism (31). Same results were found by which found an increasing triglyceride in patients with hypothyroidism.

This study also found that there is a strong and significant correlation between all studied variables with leptin hormone and found that TSH was the main predictor for the leptin level in female patients with thyroid dysfunction. Yu (27) also observed that there is a correlation between thyroid function and serum leptin which was mediated by TSH. The mechanism by which TSH effects on the leptin levels is by simulating adipocytes TSH-receptors on the surface of adipocytes which can express this positive correlation (32). Also, the leptin has an acute stimulatory action on the TSH level by acting on the hypothalamus. The leptin has an inhibitory action on the pituitary gland which confirmed by studies conducted on rats to confirm that the rat pituitary leptin may act as an autocrine/paracrine suppresser of TSH production (34). Studies are still continually conducted to confirm more evidence for an association between leptin level and TSH serum concentration with euthyroid young men and in obese peoples (35).

Other researchers also found a significant elevation of leptin in patients with hypothyroidism(36)while others found that there was no effect. (37)(38) (39).

## CONCLUSIONS

In conclusion, this study suggested a high correlation between leptin, lipid profiles and thyroid function test. Hypothyroid patients have an increase in leptin and lipid profile while in hyperthyroidism both are decreased. The TSH was a strong main predictor for the leptin in female patients with thyroid dysfunction.

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## CONFLICT OF INTEREST

None.

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