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The Association of Leptin Levels in Iraqi Women with Newly Diagnosed Thyroid Dysfunction

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ABSTRACT

Background: Leptin changes were observed in thyroid dysfunction patients, yet the evidence is inconsistent.
Objective: This study aimed to find the correlation between leptin and thyroid hormone with lipid profile in Iraqi women who have recently been diagnosed with thyroid dysfunction.
Subjects and Methods: A case-control study that was conducted at Chemistry and Biochemistry department, Medicine College in cooperation with National Diabetes Center (NDC), Mustansiriyah University during the period from January 2021 to February 2022. One hundred thirty two (132) samples were included in this study. All participants were women and aged between (21-54) years. They were divided into three groups: (44) subjects served as a control group, (44) patients with newly diagnosed hyperthyroidism and (44) patients with newly diagnosed hypothyroidism.
Results: The levels of serum leptin have been elevated in the patients who have newly diagnosed hypothyroidism ($p \leq 0.001$) and declined in patients that had newly diagnosed hyperthyroidism ($p \leq 0.0010$) when compared to control group. Patients with hyperthyroidism had low levels of triglycerides, cholesterol, high density lipoprotein, very low density lipoprotein and low density lipoprotein, while patients with hypothyroidism had high levels of triglycerides, cholesterol, high density lipoprotein, very low density lipoprotein and low density lipoprotein. No correlation between leptin and thyroid hormones with lipid profile in both hypothyroidism and hyperthyroidism. **Conclusion:** Leptin levels were high in patients with hypothyroidism, while were low in hyperthyroidism. No correlation between leptin and thyroid hormones with lipid profile.
Keywords: Hyperthyroidism, Hypothyroidism, Leptin.

INTRODUCTION

A hypermetabolic state that is characterized by the increase in the expenditure of resting energy, loss of weight, lower levels of cholesterol, elevated gluconeogenesis, and improved lipolysis, is aided by hyperthyroidism, a condition in which there is too much thyroid hormone. Conversely, hypothyroidism, or low levels of the thyroid hormone, has been related to the hypometabolism, which is distinguished by low resting energy expenditure, gain of weight, low gluconeogenesis, elevated levels of the cholesterol, and low lipolysis [(1)].

Thyroid hormones and adipokines have physiological effects in addition to glucose and lipid metabolism, like controlling energy expenditure [(2)].

Adipokines are a diverse of biologically active materials that are released by adipose tissue in paracrine, autocrine, and endocrine processes [(3)]. Adipokines, including resistin, adiponectin, leptin, and fibroblast growth factor 21, among others, have been demonstrated to play a significant role in controlling energy expenditure and lipid metabolism in some ways [(4)]. Leptin is a protein with 146 amino acids that adipocytes excrete when there is an increase in fat mass. It is a crucial atom in feed-in circle that controls balance of energy. Leptin has two functions: it reduces appetite and increases fat burning by improving energy utilization [(5)]. As adipokine that is released by the adipose tissue, leptin regulates glucose and lipid metabolism along with energy homeostasis. Consequently, it appears that thyroid function and adipose tissue interchange [(6)]. Adipose tissue function could be affected by thyroid dysfunction, which contributes to the growth of metabolic diseases. Additionally, people with thyroid dysfunction have changes in their lipolysis [(7)].

Previous studies point to a connection between leptin and thyroid hormones. TSH could induce leptin release from adipose tissue while leptin can stimulate thyroid-stimulating hormone secretion [(8, 9)].

According to studies, hyperthyroidism patients also have altered profiles of adipokines (such as resistin, adiponectin, and leptin, among others) in addition to aberrant circulating levels of TSH and TH [(10)].

Additionally, adipocytes show high numbers of TH and TSH receptors that operate similarly to thyroid receptors, indicating that TH could play a role in controlling adipocyte functions [(11)].

Therefore, adipokine secretion, which contributes to lipid metabolic disorders, could be impacted by thyroid dysfunction.

Leptin elevates levels of thyroid hormone [(12)]. It impacts on metabolism of thyroid by adipocytes; leptin and thyroid stimulating hormone had a positive association could occur due to this direct effect of TSH, it might also affect thyroid- axis in acute way.

Leptin taking inverts the fasting-induced suppression of hypothalamus pituitary- thyroid axis at the central level by expression of upregulating TRH in the hypothalamus [(13)]. This study aimed to find the correlation between leptin level and thyroid hormone

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with lipid profile in Iraqi women with newly diagnosed of thyroid dysfunction.

MATERIALS AND METHODS

Subjects

A case-control study that was performed at chemistry and biochemistry Department, Medicine College in cooperation with National Diabetes Center (NDC), University of Mustansiriyah during the period from January 2021 to February 2022. 132 women aged between (21-54) years were included in this study. They were divided into three groups: 44 subjects served as a control group, 44 patients with newly diagnosed hyperthyroidism and 44 patients with newly diagnosed hypothyroidism. Blood samples were transferred into a gel tube and allowed to clot at room temperature. Then centrifuge at 3000 rpm for 10 min. for separation of the serum. Some of the fresh serum was used for determination of thyroid function test (TSH ,T4,T3,). The rest of serum was transported to the Eppendorf tubes and stored in a deep freezer (-20ºC) to be used for determination of leptin.

Exclusion criteria: Tobacco chewers, smokers, subjects with hepatic illness, renal disease and malabsorption syndrome, people with any other endocrine diseases such as diabetes, people taking nutritional and antioxidant supplements, and people who were unwilling to give their consent.

BIOCHEMICAL MEASUREMENTS

Leptin was measured By (ELIZA), thyroid stimulating hormone, triiodothyronine and thyroxine were measured by (ELFA) and lipid profile (TC, TG, HDL-c) was measured by spectrophotometer. LDL and VLDL were estimated by calculation.

Ethical approval: This study was permitted by The Scientific Committee of Chemistry and Biochemistry Department, College of Medicine, Mustansiriyah University. The objectives and methodology were clarified to all participants and verbal agreement had been taken, in addition to that all patients have the right to withdraw at any time they feel like to do.

Statistical analysis

The statistical analyses had been performed with the use of MedCalc@ v. 19.5 and IBM SPSS 26 program (IBM SPSS Inc., Chicago). Tables and figures have been presented using Microsoft Excel 2019 software. The $p \leq 0.05$ for statistical significance was selected and the means ± standard deviation was shown. ANOVA has been undertaken in order to discover whether there have been significant differences in various variables among the groups.

RESULTS

Table (1) displayed the biochemical and clinical features of the study subjects. The mean age of patients with hyperthyroidism, hypothyroidism, and control subjects were 35.89 ± 8.12 year, 35.25 ± 8.40 year and 35.57 ± 8.16 year respectively. There was no significant differences regarding age amongst these 3 groups, proving that the patients and controls were age-matched. Patients with hyperthyroidism had lower levels of leptin **(**18.89 ± 7.17 mg/dl**)**, body mass index (24.73 ± 3.16 kg/m^2), cholesterol (132.14± 22.38 mg/dl**)**, triglycerides (89.47 ± 25.70 mg/dl), high density lipoprotein (34.99± 9.10 mg/dl**)**, low density lipoprotein (71.05 ± 17.02 mg/dl) and very low density lipoprotein (17.74 ± 5.15 mg/dl**)**. Whereas, patients with hypothyroidism had higher levels of leptin (125.34 ± 6.47 mg/dl**)** body mass index (31.39 ± 6.17 kg/m^2), cholesterol (271.46 ± 18.73 mg/dl**)**, triglycerides (292.28 ± 42.68 mg/dl), high density lipoprotein (38.83 ± 9.31 mg/dl**)**, low density lipoprotein (168.65 ± 11.39mg/dl) and very low density lipoprotein (59.88 ± 9.89 mg/dl**)** levels as shown in table (1) and figure (1). Between the case groups and controls, there have been highly significant differences (p less than 0.001). As indicated in table (2), there was non-significant correlation between leptin and either hypothyroidism or hyperthyroidism.

Table 1: Clinical features of subjects included in the subjects of this study

Variables	Control subjects(n=44)	Hypothyroidism subjects (n=44)	Hyperthyroidism subjects (n=44)	P value ANOVA
Age (Years)	35.57± 8.16	35.25± 8.40	35.89± 8.12	0.94
BMI (kg/m²)	27.55± 3.61	31.39± 6.17	24.73± 3.16	< 0.001**
TSH (uIU/L)	2.34± 0.97	10.46± 1.55	0.11± 0.03	< 0.001**
T4 (nmol/L)	93.71± 13.70	27.16± 4.05	159.44± 14.26	< 0.001**
T3 (nmol/L)	1.53± 0.35	0.23± 0.06	3.34± 0.45	< 0.001**
Leptin (ng/ml)	84.85± 5.41	125.34± 6.47	18.89± 3.17	< 0.001**
Chol. (mg/dl)	159.60± 27.97	271.46± 18.73	132.14± 22.38	< 0.001**
TG (mg/dl)	133.65± 26.82	292.28± 42.68	89.47± 5.70	< 0.001**
HDL (mg/dl)	49.95± 8.09	38.83± 9.31	34.99± 9.10	< 0.001**
VLDL (mg/dl)	26.81± 5.54	59.88± 9.89	17.74± 2.15	< 0.001**
LDL (mg/dl)	91.05± 19.21	168.65± 11.39	71.05± 7.02	< 0.001**

Results have been shown as mean ± SD;; Chol; cholesterol, TG; Triglycerides, BMI: Body Mass Index, HDL; High Density Lipoprotein, VLDL; Very Low Density Lipoprotein, LDL; Low Density Lipoprotein, **Significant at the values of p<0.001.

Table 2: Pearson correlation between leptin and thyroid hormones, lipid profile in study groups

Parameters	Hypothyroidism		Hyperthyroidism	
BMI(kg/m²)	r	-0.080	r	0.110
	p	0.600	p	0.470
TSH(uIU/L)	r	0.140	r	0.040
	p	0.360	p	0.790
T4(nmol/L)	r	0.030	r	0.070
	p	0.850	p	0.630
T3(nmol/L)	r	0.150	r	-0.170
	p	0.350	p	0.270
Chol. (mg/dl)	r	-0.170	r	-0.130
	p	0.260	p	0.390
TG (mg/dl)	r	-0.060	r	0.160
	p	0.680	p	0.300
HDL (mg/dl)	r	-0.150	r	-0.120
	p	0.320	p	0.440
VLDL (mg/dl)	r	-0.080	r	0.160
	p	0.630	p	0.310
LDL(mg/dl)	r	-0.160	r	0.040
	p	0.310	p	0.820

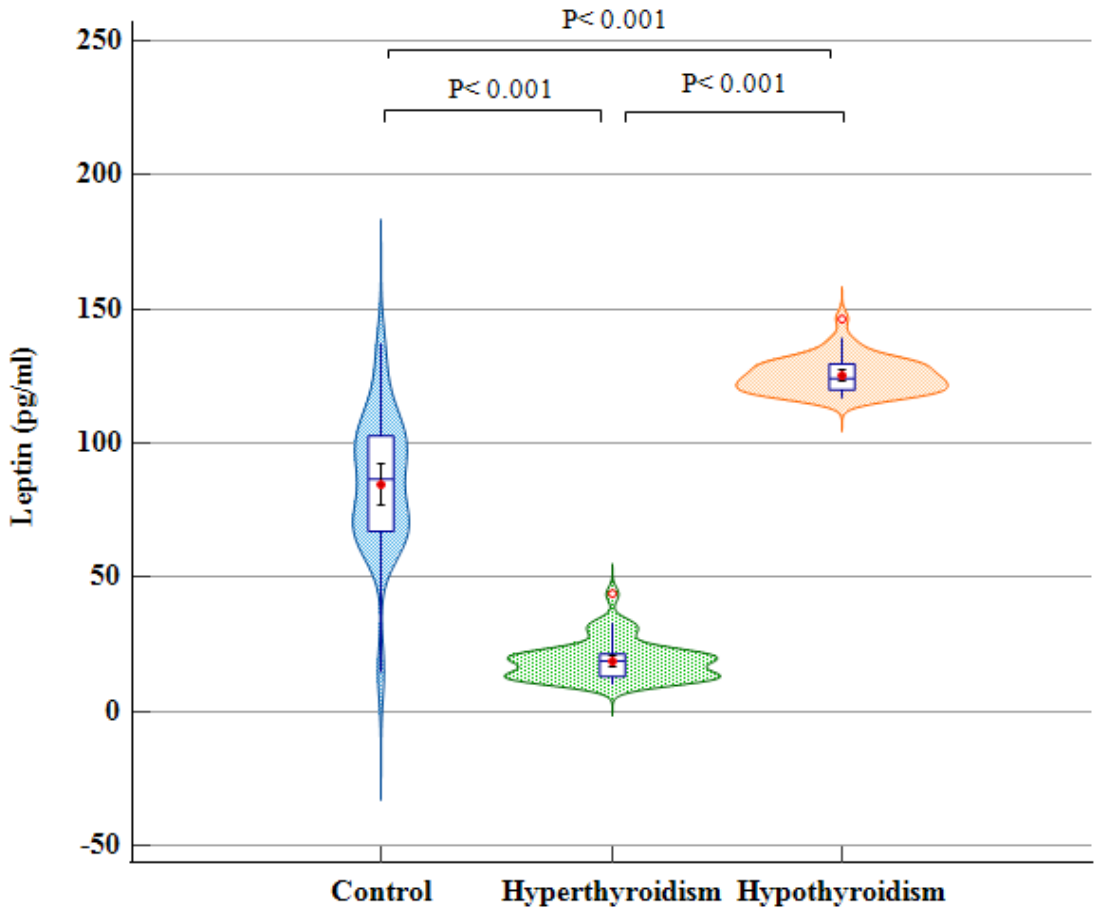

Figure 1 Violin and box plots of serum leptin values in control, hypothyroidism and hyperthyroidism subjects

DISCUSSION

The adipocytokines work as protective or causative operators in the disorders development in the states of dysfunction of thyroid . Abnormal adipocytokines (leptin) levels in hyperthyroidism and hypothyroidism have been reported with controversially results [14].

According to the results of this current study, levels of leptin increased in newly diagnosed hypothyroidism patients and decreased in the patients with newly diagnosed hyperthyroidism. These results agree with **Ibrahim *et al.* [5]** study, which showed that serum leptin in hyperthyroidism group declined than in the control group, while serum leptin level in hypothyroidism group was elevated than in the control group. Other study by **Chen *et al*. [15]** reported increased serum levels of leptin in hypothyroidism group but decreased in hyperthyroidism group**.** Our results disagree with study of **Iglesias *et al.*** [16] who found that serum leptin was declined and **Yaturu *et al.* [17]** who reported that serum leptin was unaltered in hypothyroidism group compared to control group. Also, other studies showed that serum leptin in hyperthyroidism to be normal [18], declined [19], or slightly elevated [20],while In hypothyroidism, serum leptin concentration levels have been described to be elevated [19], unaltered [20], or declined [21].

In the current study, there were no correlation between leptin and TH. This finding agrees with the study of **Saher [22]** who reported no correlation between TH and leptin in hypothyroidism and hyperthyroidism.

There have been conflicting findings about the thyroid hormone effects on leptin serum level, with suggestions indicating they have no effect, an inhibitory effect, or a stimulatory impact. Although both TH and leptin have a role in controlling energy of metabolism, the exact interaction between the two endocrine systems (i.e. TH and leptin) is still unclear and subject to debate. This may be related to the key factors controlling serum leptin concentration, gender and fat mass. The concentration of serum leptin exhibits a substantial association with body fat mass and BMI, and is likely the most significant physiological determinant. Additionally, other research varied with regard to patient characteristics, treatment duration (if used), and the method for measuring serum leptin. Thus, the extreme contrast in the outcomes was not surprising [5].

Hormones of thyroid also appeared to affect levels of leptin. In vitro and vivo sudies on rats established that increased serum T3 leads to a privation in leptin mRNA expression at serum and white adipose tissue [23]. From another side, leptin has a stimulant effect on the TSH relaese [24]. As well as, there is suggestion include the existence of direct stimulant effect of leptin on thyroxine released from thyroid gland [25]. Peripheral and central iodothyronine deiodinase activity and thyroxine to iodothyronine conversion were regulated by leptin. Both thyroid hormones and leptin affect each other and may regulate metabolism and composition of body by mechanisms that are complex.

Studies investigating disorders of thyroid and their consequences on adipokine profiles are limited with extremely variable and conflicting results [26].

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CONCLUSION

According to the current research, patients with newly-diagnosed hypothyroidism have higher leptin levels than those with newly-diagnosed hyperthyroidism.

There was no correlation between thyroid hormone and leptin in hyperthyroidism and hypothyroidism patients. Yet, further researches are required to determine how delicately leptin and thyroid hormones interchanges and to confirm our results.

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