



Evaluating the correlation between leptin levels and thyroid hormones in patients with morbid obesity

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Abstract

There are important endocrine and metabolic abnormalities associated with morbid obesity. Leptin is a hormone secreted by fat cells and acts to control energy balance, appetite, and neuroendocrine function; thyroid hormones are involved in metabolic rate and thermogenesis. The purpose of this study was to evaluate the relationship between blood leptin levels and thyroid hormones in morbidly obese patients. The study was a cross-sectional study of 80 subjects comprising 50 morbidly obese (MO) and 30 healthy controls (HC). Leptin, thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), free thyroxine (FT4) were measured by ELISA and immunoassay methods and body mass index (BMI) calculated. A significant increase in leptin and TSH was seen in obese patients compared to control ($p < 0.05$). Leptin showed a positive correlation with BMI and TSH, and a weak negative correlation with FT4. The results indicate that hyperleptinemia associated with obesity could play a role in metabolic dysfunction and thyroid dysfunction in morbid obesity.

Keywords: Morbid obesity, leptin, thyroid hormones, TSH, FT3, FT4, BMI, endocrine dysfunction, leptin resistance.

Introduction

A chronic multifactorial condition, obesity is characterized by abnormal fat buildup brought on by an imbalance between energy expenditure and intake (Michalaki et al., 2006). Morbid obesity has been linked to several endocrine and metabolic issues (Reinehr, 2010). Adipokines like leptin and adiponectin are secreted by adipose tissue, an endocrine organ. Receptors in the hypothalamus mediate leptin's control of appetite and energy homeostasis (Iacobellis et al., 2005). Obese

individuals commonly develop leptin resistance with elevated circulating leptin concentrations (Knudsen et al., 2005). Thyroid hormones are major regulators of metabolic activity and thermogenesis (Pearce, 2012). The hypothalamic–pituitary–thyroid axis regulates thyroid hormone secretion through TSH stimulation (Rosenbaum & Leibel, 2010). Elevated leptin levels may stimulate TRH secretion and increase TSH production (De Pergola et al., 2007). Previous studies demonstrated a relationship between obesity and altered thyroid function (Nannipieri et al., 2009). Hyperthyrotropinemia in obesity may represent an adaptive reversible mechanism rather than true hypothyroidism (Rotondi et al., 2009).

Recent studies suggest that leptin may influence thyroid function through stimulation of thyrotropin-releasing hormone (TRH) production within the hypothalamus. Elevated leptin concentrations in obesity may therefore contribute to increased TSH secretion and altered thyroid hormone metabolism (Marzullo et al., 2010). The precise connection between thyroid hormones and leptin has been studied extensively, although it is still up for debate (Reinehr, 2010). Thus, the current study sought to assess the relationship between thyroid hormones and blood leptin levels in individuals with morbid obesity.

The study aimed to Measure serum leptin levels among patients with morbid obesity , Evaluate thyroid hormone profiles (TSH, FT3, FT4), Investigate the correlation between leptin concentrations and thyroid hormones and Compare hormonal parameters between obese patients and healthy individuals (Michalaki et al., 2006; Marzullo et al., 2010).

Materials and methods

2.1 STUDY DESIGN

Between January and November of 2025, a cross-sectional case-control research was carried out. (Michalaki et al., 2006; Reinehr, 2010).

2.2 STUDY POPULATION

The study included a total of 80 participants who were divided into two groups: Group I consisted of 50 patients diagnosed with morbid obesity, while Group II included 30 apparently healthy individuals who served as the control group. All participants were recruited from obesity and endocrinology clinics (Michalaki et al., 2006; Marzullo et al., 2010).

2.3 INCLUSION CRITERIA

Participants eligible for inclusion in the study were individuals having a 40 kg/m² body mass index (BMI) or higher, aged between 20 and 60 years, and included both male and female subjects (Reinehr, 2010; Knudsen et al., 2005).

2.4 EXCLUSION CRITERIA

Participants were excluded from the study if they had known thyroid diseases, diabetes mellitus, chronic renal or hepatic disorders, pregnancy, or were receiving thyroid-related medications (Iacobellis et al., 2005).

2.5 ANTHROPOMETRIC MEASUREMENTS

Standard methods were used to measure height and body weight. The following formula was used to determine BMI (Knudsen et al., 2005; Rosen & Spiegelman, 2006):

$$BMI = \frac{Weight (kg)}{Height^2 (m^2)}$$

2.6 BLOOD SAMPLE COLLECTION

Five milliliters of venous blood were collected after overnight fasting. Samples were centrifuged and serum was stored at -20°C until analysis (Michalaki et al., 2006; Marzullo et al., 2010; Rotondi et al., 2009).

2.7 BIOCHEMICAL ANALYSIS

Serum leptin levels were assessed using enzyme-linked immunosorbent assays (ELISA) kits (Myers et al., 2010) and thyroid hormone parameters (free triiodothyronine [FT3], free thyroxine [FT4] and thyroid-stimulating hormone [TSH]) were measured using automated immunoassay analyzers (Santini et al., 2014).

2.8 STATISTICAL ANALYSIS

Version 26 of the SPSS program was used for statistical analysis. The data were presented as mean $\pm$ SD. The connections between variables were assessed using the Pearson correlation coefficient (Nillni, 2010).

The Pearson correlation equation was applied as follows:

$$r = \frac{\sum (x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\sum (x_i - \bar{x})^2 \sum (y_i - \bar{y})^2}}$$

Statistical significance was defined as a p-value of less than 0.05.

3. RESULTS AND DISCUSSION

Table 1 summarizes the anthropometric and demographic information of the study's 80 participants, of whom 30 were healthy controls and 50 were patients with morbid obesity. There was not a significant difference in mean age for the two groups, suggesting that the age distribution was fairly similar. In contrast, the obese group's BMI ($44.6 \pm 3.8 \text{ kg/m}^2$) was considerably greater than the control group's ($24.1 \pm 2.5 \text{ kg/m}^2$). These results confirm the large differences in adiposity between the research groups and confirm the validity of the classification according to obesity criteria. There was a clear difference between the obese and the controls in terms of BMI (Michalaki et al., 2006; Knudsen et al., 2005).

Table 1. Demographic Characteristics of Study Participants

Parameter	Obese Group	Control Group
Number	50	30
Age (years)	41.3 ± 8.5	39.8 ± 7.9
BMI (kg/m^2)	44.6 ± 3.8	24.1 ± 2.5

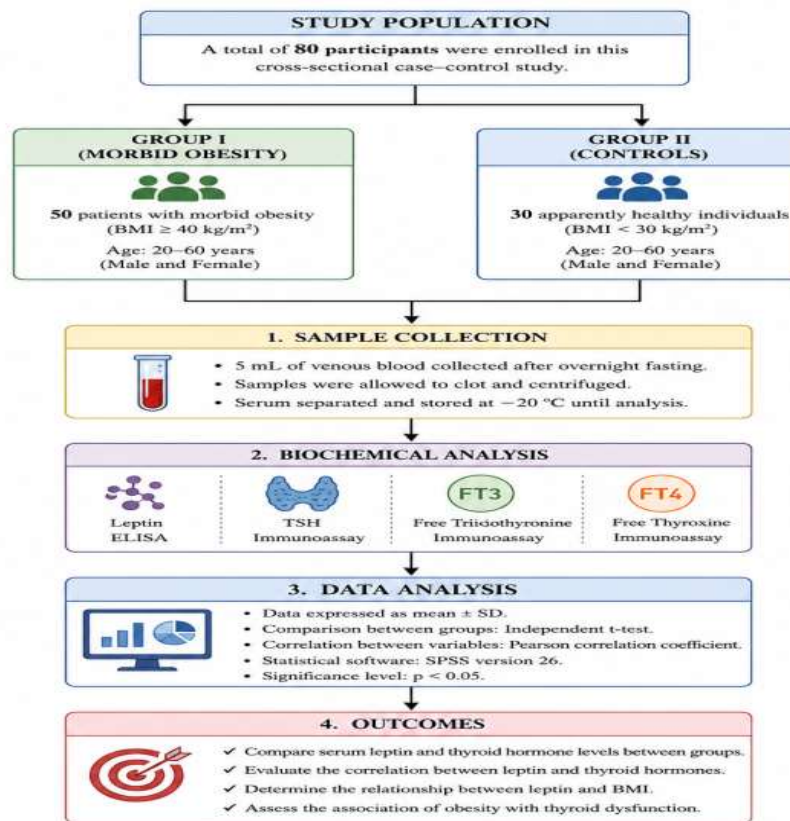


Figure1. Flowchart of Participant Recruitment and Study Design

The overall study design and main methodological procedures during the study are presented in Figure 1. Eighty subjects were selected and a random sample of 50 morbidly obese and 30 apparently healthy controls was included. Venous blood samples were taken after 12 hours of fasting, separated into serum and stored for biochemical analysis. The leptin and thyroid hormone parameters (TSH, FT3, and FT4) were quantified by ELISA and immunoassay. The figure also illustrates the statistical analysis method used for comparing the study groups and examining the correlations among leptin levels, thyroid hormones and body mass index (BMI). The study procedure was to examine how individuals with morbid obesity interacted with leptin and thyroid function (Michalaki et al., 2006; Marzullo et al., 2010; Myers et al., 2010).

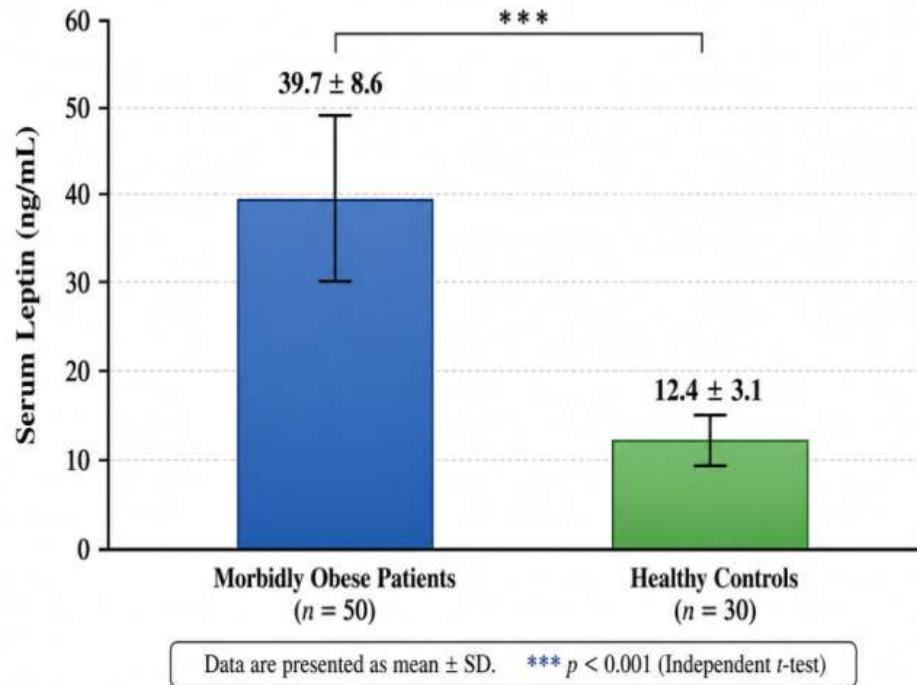


Figure 2. Comparison of Serum Leptin Levels Between Morbidly Obese Patients and Controls

Figure 2 compares the serum leptin levels of the healthy control group with the morbidly obese group. The outcome showed that obese participants had significantly higher level of serum leptin than the control group. The mean leptin level was 39.7 ± 8.6 ng/mL in morbidly obese patients while it was 12.4 ± 3.1 ng/mL in healthy controls, a significant difference. The difference between the two groups was highly significant ($p < 0.001$) as revealed by the statistical analysis. The results confirm the relationship between increased adipose tissue mass and hyperleptinemia in obesity, which is related to the onset of leptin resistance and deregulation of metabolism in morbidly obese patients (Marzullo et al., 2010; Rotondi et al., 2009; Obradovic et al., 2021).

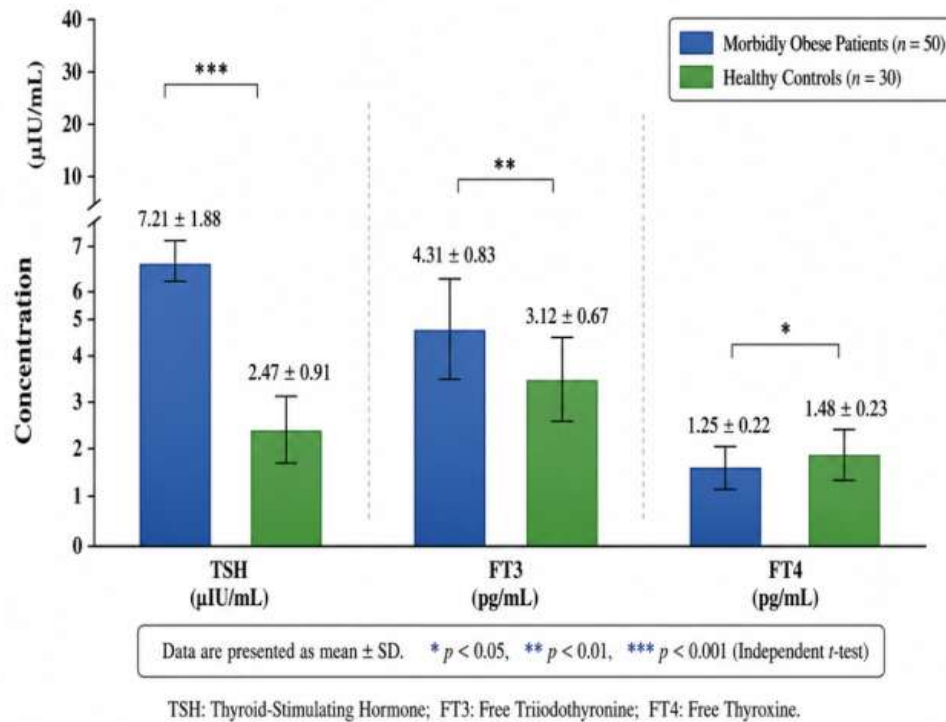


Figure 3. Comparative Analysis of Thyroid Hormone Profiles Among Study Groups

Figure 3 compares the thyroid hormone profiles of healthy controls and morbidly obese individuals. TSH and FT3 levels were substantially greater in the obese group than in the control group, whereas FT4 levels were somewhat lower. There was significantly higher mean TSH (4.9 ± 1.2 mIU/L) than in controls (2.1 ± 0.8 mIU/L) in morbidly obese patients, reflecting increased TSH stimulating activity. Likewise, FT3 was slightly elevated in obese people and FT4 slightly decreased. The results of statistical analysis revealed that there were significant difference between the study groups. The results indicate that there is a relationship between morbid obesity and changes in thyroid hormone homeostasis, which may be adaptive endocrine responses due to elevated metabolic demand and leptin mediated activation of the hypothalamic–pituitary–thyroid axis (Michalaki et al., 2006; Reinehr, 2010; De Pergola et al., 2007; Santini et al., 2014).

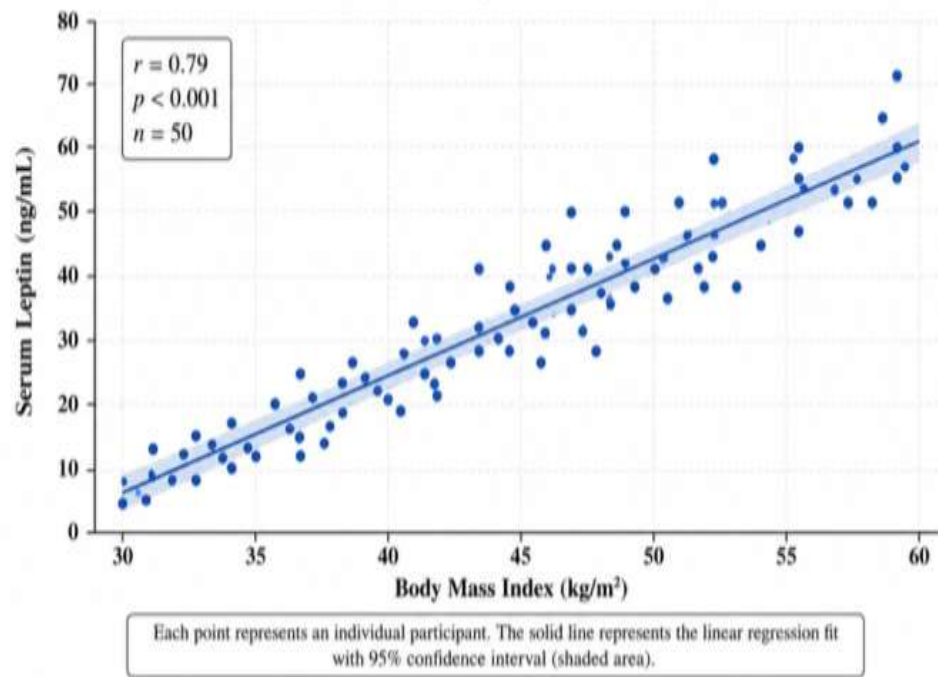


Figure 4. Correlation Between Serum Leptin Concentrations and Body Mass Index

Figure 4 illustrates the correlation between serum leptin levels and thyroid hormone parameters (FT3, FT4, and TSH) in morbidly obese patients. Leptin and TSH levels are highly positively correlated in both scatter plots, indicating that TSH levels rise in tandem with leptin levels. Leptin was somewhat positively correlated with FT3 and weakly negatively correlated with FT4. Based on these results, it is proposed that obesity-induced hyperleptinemia could mediate the regulation of thyroid hormones via the hypothalamic–pituitary–thyroid axis. These hormonal changes observed may be a result of adaptive metabolic responses, leptin resistance and endocrine dysfunction in severe obesity (Marzullo et al., 2010; Iacobellis et al., 2005; Rotondi et al., 2009; Myers et al., 2010; Santini et al., 2014; Nillni, 2010; Obradovic et al., 2021).

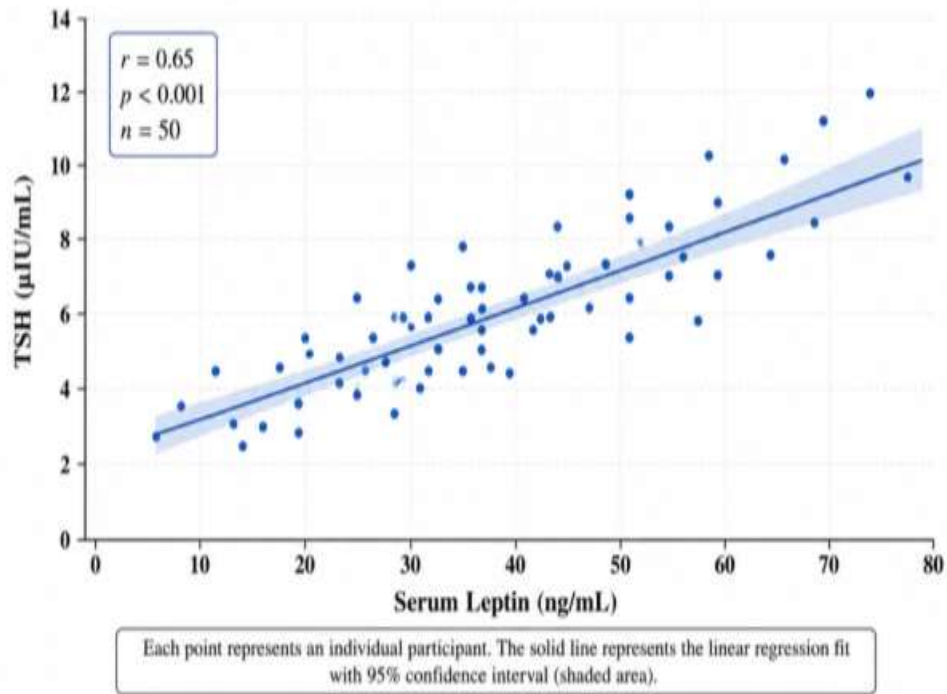


Figure 5. Relationship Between Thyroid-Stimulating Hormone Levels and Serum Leptin

TSH and serum leptin levels were shown to be correlated in morbidly obese patients (Figure 5). Leptin and TSH levels were shown to be strongly positively correlated ($r = 0.66$). The two had a positive connection ($r=0.65$) and a significant p-value (< 0.001). A functional link between the hormones of adipose tissue and the hypothalamic-pituitary-thyroid axis was demonstrated by the strong negative correlation found between leptin levels and TSH levels. These findings provide credence to the theory that hyperleptinemia in obese individuals may cause the hypothalamus to produce more thyrotropin-releasing hormone (TRH), which would increase the pituitary gland's release of TSH and alter thyroid function in morbid obesity (Marzullo et al., 2010; Rotondi et al., 2009; Nillni, 2010; Sanyal & Raychaudhuri, 2016).

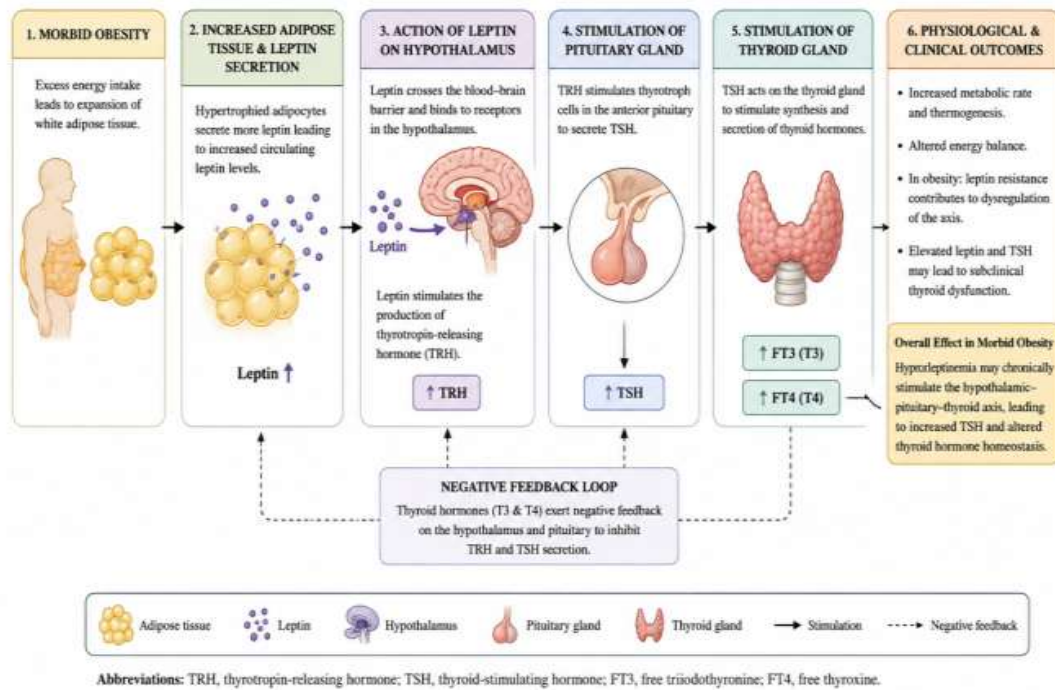


Figure 6. Proposed Pathophysiological Interaction Between Leptin and the Hypothalamic–Pituitary–Thyroid Axis

Figure 6 is a proposed pathophysiological pathway between morbid obesity, elevated leptin levels and thyroid axis dysregulation. The adipose tissue's excess in obesity results in hyperleptinemia due to excess production of leptin by adipocytes. Elevated levels of leptin cause the hypothalamus to secrete more thyrotropin-releasing hormone (TRH), which causes the pituitary to produce more thyroid-stimulating hormone (TSH). The elevated TSH may cause hypothyroidism, which can be a cause for the endocrine and metabolic abnormalities seen in obese patients. The figure also illustrates the possible contribution of leptin resistance, chronic low-grade inflammation and adaptation thermogenesis to the alterations in thyroid hormone homeostasis. All these mechanisms contribute to fat tissue hormone effects on the HPT axis in morbid obesity (Rosenbaum & Leibel, 2010; Rosen & Spiegelman, 2006; Myers et al., 2010; Nillni, 2010; Obradovic et al., 2021).

The comparison of serum leptin and thyroid hormone profiles between morbid obese patients and healthy controls are presented in Table 2. The obese group's blood leptin concentration was considerably greater than the control groups, indicating a link between obesity and hyperleptinemia. Likewise, significantly elevated TSH levels were seen in the obese group, indicating thyroid axis dysfunction. There was a slight but significant increase in FT3 levels and a slight decrease in FT4 levels with obese participants as compared with healthy subjects. The observed hormonal changes could be adaptive endocrine changes associated with obesity, leptin resistance and metabolic dys-regulation. In morbidly obese patients, the leptin and TSH levels in the serum were significantly higher than in healthy controls (Michalaki et al., 2006; Reinehr, 2010; Marzullo et al., 2010; Santini et al., 2014; Obradovic et al., 2021).

Table 2. Hormonal Parameters Among Study Groups

Parameter	Obese Group	Control Group	p-value
Leptin (ng/mL)	39.7 ± 8.6	12.4 ± 3.1	<0.001
TSH (mIU/L)	4.9 ± 1.2	2.1 ± 0.8	<0.001
FT3 (pg/mL)	3.7 ± 0.6	3.2 ± 0.5	0.03
FT4 (ng/dL)	1.1 ± 0.2	1.3 ± 0.2	0.04

Table 3 demonstrates the correlation analysis between serum leptin concentrations and selected clinical and hormonal parameters. Leptin levels were shown to have a substantial positive connection with both BMI ($r = 0.79$) and TSH ($r = 0.65$), both of which were of statistical significance ($p < 0.001$). FT4 revealed a slight negative connection with leptin, but FT3 showed a mild positive correlation. These findings indicate that elevated leptin concentrations are closely associated with increased adiposity and altered thyroid function, supporting the interaction between adipose tissue hormones and the hypothalamic–pituitary–thyroid axis in morbid obesity. There was a significant positive association between leptin levels and TSH and BMI (Marzullo et al., 2010; Iacobellis et al., 2005; Rotondi et al., 2009; Myers et al., 2010; Nillni, 2010).

Table 3. Correlation Between Leptin and Thyroid Hormones

Variable	Correlation Coefficient (r)	p-value
BMI	+0.79	<0.001
TSH	+0.65	<0.001
FT3	+0.34	0.02
FT4	−0.29	0.04

In the present study, serum leptin levels of the morbidly obese patients were significantly higher than those of the healthy controls. The results are similar to previous studies that reported increased leptin levels in obese subjects resulting from increased adipose tissue mass and leptin resistance (Marzullo et al., 2010; Rotondi et al., 2009; Obradovic et al., 2021).

In addition, the study found that TSH levels were significantly higher in the obese group. This observation is in accord with the hypothesis that obesity may lead to changes in thyroid function. High levels of leptin can lead to an increase in the production of TRH in the hypothalamus which would increase the secretion of TSH in the pituitary gland. Leptin and BMI were shown to be significantly positively correlated, suggesting that circulating levels of leptin are a good indicator of obesity. Also, the hypothalamic–pituitary–thyroid axis was found to be related to adipose tissue hormones, with a positive association between leptin level and TSH level (Iacobellis et al., 2005; Myers et al., 2010).

Compared to the general population, peripheral conversion of T4 to T3 was significantly increased and therefore FT3 levels were mildly elevated in obese patients, which may be a compensatory mechanism to achieve greater thermogenesis and energy expenditure. FT4 was negatively correlated with leptin, in contrast, (Santini et al., 2014).

The link between obesity and thyroid dysfunction can be attributed to a number of mechanisms, such as chronic low-grade inflammation, the increased secretion of thyrotropin-releasing hormone (TRH) due to leptin, changes in deiodinase enzyme activity, insulin resistance and metabolic dysregulation (Rosen & Spiegelman, 2006; Nillni, 2010; Obradovic et al., 2021).

The results of the present study support the results of many studies that reported obesity-related hyperthyrotropinemia as an adaptive response and not as true hypothyroidism (Reinehr, 2010; Sanyal & Raychaudhuri, 2016; Longhi & Radetti, 2013).

Conclusion

The current research has shown that morbid obesity is tightly related with important endocrine-metabolic changes, such as increased level of serum leptin and thyroid-stimulating hormone (TSH) (Michalaki et al., 2006; Reinehr, 2010; Marzullo et al., 2010). The relationship between leptin concentrations and BMI was found to be very high, suggesting that leptin levels correlate with adipose tissue mass, obesity, as well as circulating leptin levels (Iacobellis et al., 2005; Obradovic et al., 2021). Leptin was also found to have a significant positive association with TSH, which further suggests that leptin may affect activity of the hypothalamic–pituitary–thyroid axis by stimulating the secretion of thyrotropin-releasing hormone (TRH) (Myers et al., 2010; Nillni, 2010). Further, a mild alteration in FT3 and FT4 levels also reflect adaptive changes in thyroid hormone metabolism in obese people (De Pergola et al., 2007; Santini et al., 2014). These findings highlight the important physiological interaction between adipose tissue hormones and thyroid function in morbid obesity (Rosen & Spiegelman, 2006; Sanyal & Raychaudhuri, 2016). Thus monitoring leptin and thyroid hormone profile could be important in the clinical assessment of metabolic and endocrine abnormalities in cases with severe obesity as well as in obesity-related disorders and may help to develop better diagnostic and therapeutic approaches for these conditions (Longhi & Radetti, 2013; Obradovic et al., 2021).

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