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Research Article

Correlation of Serum Leptin with Thyroid Hormones in Metabolic Syndrome Patients with and without Hypothyroidism

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A B S T R A C T

Introduction: Cardiovascular illnesses, type 2 diabetes mellitus, and other metabolic disorders are linked to metabolic syndrome. The purpose of this study was to examine the connection between thyroid hormone profiles and blood leptin levels in individuals with metabolic syndrome who did not have hypothyroidism.

Methods: A total of 120 participants were included 80 patients with metabolic syndrome (40 with hypothyroidism and 40 without hypothyroidism) and 40 healthy controls. Blood glucose levels, lipid profiles, thyroid hormone levels, and serum leptin concentrations were measured and compared across groups.

Results: Serum leptin levels were significantly higher in metabolic syndrome patients with hypothyroidism (25.18 ± 5.46) compared to those without hypothyroidism (11.55 ± 3.15) and healthy controls (4.05 ± 2.12) (p- 0.0001). A significant positive correlation was observed between serum leptin and thyroid-stimulating hormone (TSH) levels (r = 0.749, p- 0.0001).

Conclusion: These results imply that in patients with metabolic syndrome, leptin metabolism and the pituitary-thyroid axis are strongly correlated. Serum leptin level monitoring may help identify and stop problems in these patients early.

Keywords: Hypothyroidism, Leptin, Metabolic Syndrome, Thyroid-Stimulating Hormone

Introduction

The Metabolic Syndrome (Met S) are more prone to get diabetes mellitus, particularly type 2 diabetes mellitus (T2DM) and heart diseases.[1,2] Particularly, a three-fold rise in metabolic syndrome prevalence is linked to a five-fold increase in the chance of diabetes mellitus, a two-fold increase in the risk of cardiovascular disease fatality, and a 150% increase in overall mortality.[3,4] The recent studies have shown that there is a maximum risk of fact that metabolic syndrome enhances the risk of both diabetes and cardiovascular diseases.[5,6] Early metabolic syndrome diagnosis and the ensuing management plans may help lower the prevalence of these related illnesses.

The major risk factors for Met S are elevated blood sugars, abnormal lipid profile leads to obesity. The significant complications of obesity are metabolic disorders like diabetes mellitus, thyroid diseases and cardiovascular diseases in patients with Met S.[7,8] Obesity pathogenesis involves an imbalance between energy utilisation and consumption. This energy imbalance leads to the synthesis of neuroendocrine multiple neuroendocrine factors, like adipocytokines, which are proteins made by adipose tissue.[9,10]

Leptin constitutes one of the most significant adipocytokines and contains 167 amino acids. It will affect the hypothalamus, which regulates calorie intake and speeds up metabolism.[11] Additionally, this also involves blood sugars homeostasis through insulin and significantly elevated levels of leptin positively correlated with obesity in the body.[12] Elevated levels of leptin have been linked to metabolic, inflammatory, and homeostatic elements implicated in the pathophysiological mechanisms of obesity-related disorders.[13] Because human pituitary glands contain leptin receptors, hypothyroidism patients' serum leptin levels were substantially associated with thyroid stimulating hormone (TSH). Recent studies have reported that thyroid hormones stimulate the production of serum leptin levels and increases obesity, basal metabolic rate (BMR) and oxidative phosphorylation.[14,15] Hence, there is a controversy between leptin and thyroid hormones for energy imbalance in hypothyroid patients and also very less studies on leptin and thyroid status in metabolic patients with and without hypothyroidism. The current study aimed to analyse the correlation between serum leptin and thyroid hormones in metabolic syndrome patients with and without hypothyroidism.

Materials and Methods

Between 2020 and 2023, the current analytical cross-sectional study was carried out at the Medical and Biochemistry Departments of Gayatri Vidya Parishad Medical College in Visakhapatnam, Andhra Pradesh, India. The study comprised 80 individuals with metabolic syndrome (Met S), as defined by the International Diabetes Federation (IDF) guidelines. Depending on their thyroid condition, the patients were further divided into two subgroups:

- **Group 2:** 40 individuals with Met S who do not have hypothyroidism
- **Group 3:** 40 individuals Met S with hypothyroidism

Additionally, 40 healthy individuals who matched in terms of age, gender, and body mass index (BMI) were included as controls; these individuals formed the Group 1.

After receiving clearance from the Institutional Ethics Committee (IEC; Ref No: GVPIHCMT/IEC/20201012/02), the study was carried out. All subjects gave their signed, informed permission before being recruited.

Inclusion Criteria

Individuals between the ages of 30 and 70 who satisfied the International Diabetes Federation's (IDF) criteria for metabolic syndrome were included.[16] The diagnosis was made on the basis of hypertension, aberrant lipid profiles, and elevated fasting blood glucose levels. While hypothyroidism was identified based on low T4 levels and increased thyroid-stimulating hormone levels (> 10 µIU/mL), healthy controls were those who were healthy.

Exclusion Criteria

Those who were hesitant to engage, had acute or chronic infectious disorders, liver, kidney, or heart conditions, hyperthyroidism, subclinical hypothyroidism, overt hypothyroidism, or urinary tract infections were not allowed to participate.

Blood Sample Collection

A total of 5 mL of overnight fasting blood was collected from each participant. The samples were divided as follows:

1. 1 mL into a fluoride tube
2. 1 mL into EDTA tubes
3. 3 mL into plain tubes

Serum and plasma were separated via centrifugation and stored in labelled aliquots at -50 °C until analysis.

Laboratory Investigations

Blood glucose and lipid profile analysis (total cholesterol, triglycerides, and high-density lipoprotein) using conventional laboratory techniques were among the routine laboratory procedures. The immunoturbidometric technique was used to test glycated haemoglobin (HbA1c). The Enzyme-Linked Immunosorbent Assay (ELISA) was used to measure the serum levels of Total T3, T4, Thyroid-Stimulating Hormone (TSH), and leptin utilising automated analysers (Chem Ultra-Euro, Mindray CL-1200i, and Immuno Assay Automatic Analyser).

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Statistical Analysis

The Kolmogorov-Smirnov test was used to assess the data distribution, and the results were reported as mean ± standard deviation (SD). Analysis of variance was used to compare variables between groups (ANOVA). Pearson's correlation analysis was used to evaluate the relationships between serum leptin and other factors. Statistical significance was defined as a p- value of less than 0.05. Microsoft Excel and SPSS were used to conduct statistical analysis.

Results

The research subjects' anthropometric, demographic, biochemical, and experimental characteristics are shown in Table 1. The research participants' blood pressure, BMI, and age all differed significantly (p-0.05). When compared to controls, metabolic syndrome with and without hypothyroidism showed a substantial rise in fasting blood sugar, postprandial blood sugar, TGL, TC, VLDL, and LDL (p-0.05). Furthermore, we found that individuals with metabolic syndrome, both with and without hypothyroidism, had significantly lower HDL levels than controls (p-0.05). When comparing metabolic syndrome with hypothyroidism to metabolic syndrome without hypothyroidism and controls, there was a substantial rise in TSH levels and a drop in T4 levels (p-0.0001**). Additionally, T3 levels did not significantly differ between controls and those with metabolic syndrome with or without hypothyroidism (p-0.973,904). Additionally, we found that patients with and without hypothyroidism had significantly higher blood leptin levels than controls (p-0.0001**).

Table 1.Comparison of Clinical Characteristics between the Study Subjects

Parameter	Controls			Metabolic Syndrome without Hypothyroidism			Metabolic Syndrome with Hypothyroidism			p- Value
	Mean	±	SD	Mean	±	SD	Mean	±	SD	
Age (years)	39.13	±	5.31	47.00	±	10.78	45.63	±	4.23	0.0001**
BMI (kg/m^2)	20.94	±	2.95	42.97	±	7.94	31.80	±	4.85	0.0001**
SBP (mmHg)	124.38	±	5.25	151.58	±	4.31	165.10	±	5.31	0.0001**
DBP (mmHg)	75.45	±	3.37	95.15	±	2.71	89.33	±	9.71	0.0001**
FBS (mg/dL)	83.93	±	83.93	137.10	±	19.37	144.93	±	36.70	0.0001**
PPBS (mg/dL)	133.55	±	5.98	159.33	±	13.06	182.73	±	30.82	0.0001**
TGL (mg/dL)	115.15	±	12.28	304.23	±	40.46	301.78	±	27.04	0.0001**
TC (mg/dL)	149.75	±	12.42	317.25	±	32.99	297.90	±	41.59	0.0001**
HDL (mg/dL)	57.28	±	4.54	28.55	±	2.75	29.10	±	2.98	0.0001**
VLDL (mg/dL)	23.03	±	2.46	60.85	±	8.09	60.36	±	5.41	0.0001**
LDL (mg/dL)	69.45	±	12.74	227.86	±	33.31	208.45	±	41.81	0.0001**
T3 (ng/dL)	98.35	±	28.71	98.93	±	29.16	99.90	±	31.38	0.973
T4 (µg/dL)	6.96	±	1.68	7.01	±	1.58	4.13	±	1.82	0.0001**
TSH (µIU/mL)	2.49	±	1.21	2.19	±	1.28	11.10	±	3.42	0.0001**
Leptin (ng/mL)	4.05	±	2.12	11.55	±	3.15	25.18	±	5.46	0.0001**

**: Highly Significant.

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Table 2 shows the pearson correlation analysis between serum leptin and other parameters Serum leptin had a significant negative correlation with HDL and T4, and a significant positive correlation with age, BMI, SBP, DBP, FBS, PPBS, TGL, TC, VLDL, LDL, and TSH. The P values were less than 0.05. There is no significant difference between the groups in the T3 ($p > 0.05$).

Table 2.Pearson Correlation Analysis between Serum Leptin and Other Parameters

Parameter	R	p-Value
Age (years)	0.241	0.008*
BMI (kg/m^2)	0.250	0.006*
SBP (mmHg)	0.836	0.0001**
DBP (mmHg)	0.420	0.0001**
FBS (mg/dL)	0.487	0.0001**
PPBS (mg/dL)	0.635	0.0001**
TGL (mg/dL)	0.690	0.0001**
TC (mg/dL)	0.631	0.0001**
HDL (mg/dL)	-0.674	0.0001**
VLDL (mg/dL)	0.690	0.0001**
LDL (mg/dL)	0.617	0.0001**
T3 (ng/dL)	-0.049	0.593
T4(µg/dL)	-0.015	0.0001**
TSH (µIU/mL)	0.749	0.0001**

**: Highly Significant & *: Significant.

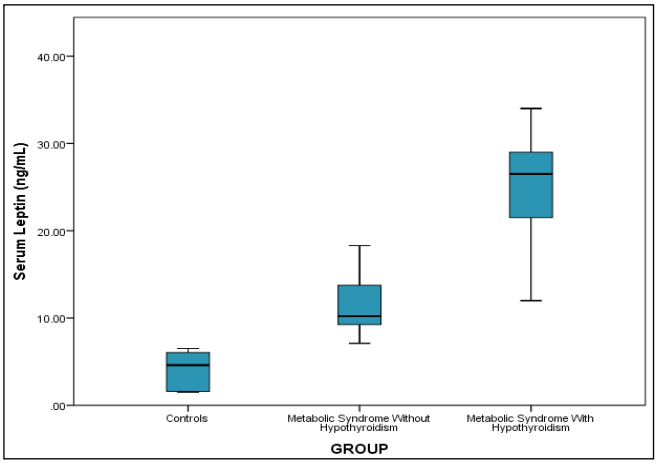

Figure 1.Serum Leptin Concentrations in the Study Groups

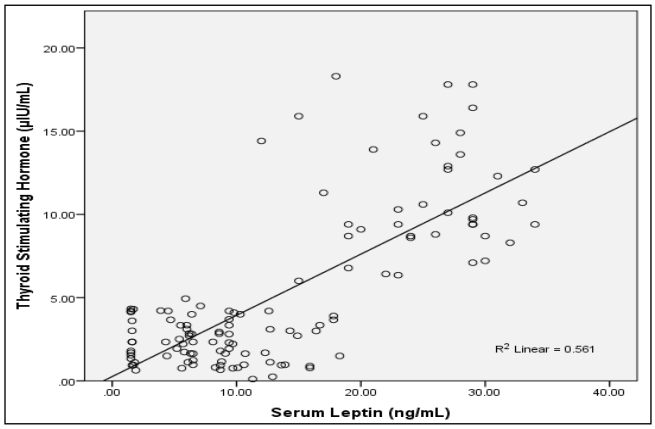

Figure 2.Scatterplot between the Serum Leptin and TSH

Discussion

The current study discovered that individuals with Met S who also had hypothyroidism had significantly higher levels of BMI, SBP, DBP, FBS, PPBS, TGL, TC, VLDL, LDL, and HDL compared to controls. Additionally, recent studies found significantly higher levels of blood sugar, cholesterol, and hypertension when comparing Met S with and without hypothyroidism to healthy controls.[17,18]

Additionally, we discovered that in patients with Met S, both with and without hypothyroidism, and when compared to healthy controls, extremely high levels of TSH were positively connected with blood sugars, dyslipidaemia, and hypertension. According to earlier research, Met S patients with and without hypothyroidism have much higher serum TSH levels than healthy controls. This is because Met S patients have altered lipid and carbohydrate metabolism, which can result in obesity and obesity-related conditions like T2DM and cardiovascular diseases (CVD).[19–21]

The Met S patients were more prone to cardiovascular diseases and there is a need for a biomarker which will serve to identify complications in Met S. Recent studies focused on serum leptin can serve as a potential marker to identify complications like T2DM and CVD in patients with Met S.[22,23] The current study also focused on the serum leptin concentrations in Met S patients with and without hypothyroidism and controls, we observed the serum leptin levels were significantly elevated and positively correlated with blood sugars, lipid profile, and hypertension Met S with or without hypothyroidism and when compared to healthy controls (Figure 1). It is secreted from white adipose tissue and is concerned with the regulation of metabolism due to its neuroendocrine activity.[24] Some of the investigations reported that the circulatory levels of serum leptin concerning energy homeostasis, secretion and activation mainly occurred due to insulin in various tissues such as the brain and other tissues.[25-26] The recent findings

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noticed higher serum levels of leptin, impaired secretion and activation of insulin resulted in increased blood sugars and increased serum levels of TSH.[27-28] The circulatory levels of TSH and leptin complement the action of each other to activate the enzyme involved in the synthesis of blood sugars lead to the condition hyperglycaemia and dyslipidaemia.[29]

The present study found a significant increase in levels of serum leptin positively correlated with blood pressure, blood sugars, lipid profile and TSH in Met S patients with and without hypothyroidism (Figure 1).

Highly elevated levels of serum leptin regulate the outcome of thyroid releasing hormone (TRH), as it increases the production of TSH from the anterior pituitary gland.[30-31] In Met S, the presence of significant amounts of production in leptin levels that accompanies hypothyroidism with the outcome of the study of leptin may function as an emerging potential biomarker.

Conclusion

The results of our study show that thyroid-stimulating hormone (TSH) and serum leptin levels are significantly correlated in individuals with metabolic syndrome, including those with and without hypothyroidism. This emphasises how closely the pituitary-thyroid axis and leptin metabolism are related. For the early identification and treatment of any consequences related to thyroid and metabolic dysfunction, blood leptin levels in individuals with metabolic syndrome may be a useful tool.

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Authors' Contribution: BK: Sample Collection, Sample Processing & Paper Writing, PKD: Data Analysis, Statistics., VG: Paper Correction's, Results & Discussion

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