ORIGINAL ARTICLE

CORRELATION OF THYROID STIMULATING HORMONE LEVELS WITH COMPONENTS OF METABOLIC SYNDROME IN TYPE 2 DIABETES MELLITUS PATIENTS IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Metabolic syndrome is a cluster of conditions including central obesity, high blood pressure, high blood sugar, and dyslipidemia which collectively heighten the risk of cardiovascular diseases and type 2 diabetes. Thyroid stimulating hormone, a pivotal regulator of thyroid gland activity, plays a crucial role in maintaining overall metabolic homeostasis. This study was conducted to investigate and establish the correlation between thyroid stimulating hormone (TSH) levels and the various components of metabolic syndrome in type 2 diabetic patients. This observational study was conducted in a tertiary care hospital, from July 2014 to June 2015. A total 200 subjects were selected with the age range from 18 to 70 years meeting the International Diabetic Federation criteria for metabolic syndrome and not on any medications. Baseline assessments of demographic data, physical examinations, and measurements such as body weight, height, BMI, waist circumference, blood pressure, FBG, total cholesterol, triglycerides, HDL-C, and TSH levels were done. Correlation between variables were determined by Pearson's correlation coefficient with significance set at $P < 0.05$.

This study shows BMI, waist circumference (WC), SBP, total cholesterol (TC), triglycerides (TG), and FBS exhibited a significant positive linear correlation ($P < 0.05$) with thyroid stimulating hormone (TSH) levels. Conversely, age and high-density lipoprotein cholesterol (HDL-C) displayed a non-significant negative correlation ($P > 0.05$) with TSH levels. This study revealed significant associations between TSH levels and metabolic syndrome, emphasizing a potential link between thyroid function and metabolic health. These findings underscore the importance of considering thyroid function in the assessment and management of metabolic disorders. However, further research is warranted to establish causation and elucidate the underlying mechanisms of this association.

Key words: Metabolic syndrome, Thyroid dysfunction, Subclinical hypothyroidism, Overt hypothyroidism, Hyperthyroidism.

Introduction

Metabolic syndrome, recognized as a cluster of cardiovascular risk factors, poses a significant global public health challenge[1,2]. It increases the likelihood of cardiovascular disease, diabetes, and specific types of cancer[1,3]. As per the National Cholesterol Education Program's Adult Treatment Panel III definition, metabolic syndrome is characterized by the presence of abnormal values in at least three of the following criteria: waist circumference, serum triglycerides, high-density lipoprotein cholesterol (HDL-C), blood pressure, and fasting glucose[1,3].

Thyroid hormones play a crucial role in regulating metabolism[1,4]. Disruptions in thyroid hormone levels can lead to changes in metabolism, sharing common pathophysiological mechanisms with metabolic syndrome. Consequently, thyroid dysfunction has the potential to influence metabolic syndrome. These hormones exert direct and indirect effects on the cardiovascular system, and individuals with thyroid disorders, particularly hyperthyroidism, frequently exhibit cardiovascular related signs and symptoms[1,5,6]. The impact on lipid metabolism and blood pressure regulation by thyroid hormones may contribute to these observed cardiovascular changes[4-6].

These hormones seem to function as a general regulator, accelerating metabolic processes and potentially being linked to metabolic syndrome. Both metabolic syndrome (MetS) and thyroid dysfunction (TD) are correlated with an increased risk of atherosclerotic heart disease and a cluster of common abnormalities, including abdominal obesity, hyperglycemia, hypertension (HTN), reduced high-density lipoprotein cholesterol (HDL-C), and elevated triglycerides (TG). Investigating thyroid dysfunction in the metabolic syndrome population can illuminate the extent of overlap between these two conditions. It may underscore the significance of thyroid function tests in implementing effective management strategies, leading to a substantial reduction in cardiovascular morbidity and mortality associated with metabolic syndrome and thyroid dysfunction. The current study aimed to assess the prevalence of thyroid dysfunction in individuals with metabolic syndrome and its correlation with the various components of MetS.

Materials and Methods

This observational study was carried out in the Department of Biochemistry, Mymensingh Medical College (MMC) and the subjects were collected from the Department of Endocrinology, Mymensingh Medical College Hospital spanning from July 2014 to June 2015. All eligible patients meeting the specified inclusion and exclusion criteria were recruited for participation. The study included a total of 200 individuals age ranging from 18 to 70 years who met the criteria for metabolic syndrome according to the International Diabetic Federation (IDF) and were not currently on any medications-encompassing newly identified cases of metabolic syndrome. Those already on medications for diabetes mellitus, hypertension, thyroid disorders, or dyslipidemia were excluded from the study.

During the initial assessment, demographic information was collected, and a thorough physical examination was conducted. Body weight (in kilograms) and height (in meters) were measured using standardized methods and equipment. Body Mass Index (BMI) was calculated as the weight divided by the square of height (kg/m^2). Waist circumference was measured at the midpoint between the lower margin of the least palpable rib and the top of the iliac crest, employing a stretch-resistant tape. Blood pressure was measured from the left arm while the patient was seated, and the apparatus was positioned at the heart level. Fasting plasma glucose (FPG) was determined using the glucose oxidase and peroxidase method described by Sackhs[6,7]. Total serum cholesterol levels were assayed by enzymatic end point method outlined by Allain et al[8]. The serum triglyceride level was estimated using the enzymatic GPO-PAP method provided by McGowan et al[9] and HDL-C was determined by precipitation method specified by Burstein et al[10]. Quantitative determination of thyroid stimulating hormone (TSH) was conducted using enzyme immunoassay and commercially available kits. The acquired data were organized in the SPSS-25 spreadsheet, and all results were presented as mean $\pm$ standard deviation.

Student's t-test was utilized to determine any significant relationship between the components of metabolic syndrome and TSH levels. Pearson's correlation coefficient was employed to assess the strength of associations. All tests were two-tailed, and statistical significance was recognized at $P < 0.05$.

Results

In this observational study, total 200 subjects aged 18 to 70 years were enrolled on the basis of their clinical and laboratory diagnostic criteria. Among them 132 (66%) were females and 68 (30%) were males. The age group of 60-69 exhibited the highest proportion (31%) of patients with metabolic syndrome (MetS) within the 18-69 age range (Table I).

Table I: Distribution of the study subjects according to age (n=200)

Age in years	Number	Percentage	Mean±SD
20–29	12	6	
30–39	22	11	50.77±12.23 yrs
40–49	53	26.5	
50–59	51	25.5	
60–69	62	31	

Table II shows that subclinical hypothyroidism (SCH) was identified in approximately one-fifth of MetS patients, with 24.2% in females and 10.3% in males, followed by five cases of overt hypothyroidism (OHT) (2.3% in females and 2.9% in males). No instances of subclinical hyperthyroidism or overt hyperthyroidism were observed in our study.

Table II: Distribution of thyroid dysfunction patients according to sex (n=200)

Thyroid dysfunction	Male (n=68)		Female (n=132)		Total No (%)	P values
	No	%	No	%		
Euthyroid	59	86.8	97	73.5	156 (78)	0.257
Overt Hypothyroidism	2	2.9	3	2.3	5 (2.5)	0.672
Subclinical Hypothyroidism	7	10.3	32	24.2	39 (19.5)	0.016

In terms of thyroid dysfunction, BMI, SBP, DBP, TG, HDL-C and FBS, showed significant difference ($P < 0.05$), while age and waist circumference, were not significantly correlated ($P \geq 0.05$), as illustrated in Table III.

Table III: Baseline characteristics of study population

MetS components	Euthyroidism	Overt Hypothyroidism	Subclinical hypothyroidism	P values
Age (years)	48.9 ± 11.2	50.84 ± 8.9	51.2 ± 21.8	0.391
BMI (Kg/m^2)	25.7±1.8	32±0.7	26.8±2.1	0.005
WC (cm)	87.6± 5.3	87±2.8	87.2±5.9	0.929
SBP	131.8±12.9	167±11.3	145.1±15.8	0.001
DBP	87.2±8.6	97.4±4.9	91.9±8.6	0.016
TC (mg/dL)	165.3±42.8	237±34.1	211.4±37.9	0.001
HDL (mg/dL)	40.9±6.9	34.7±2.5	37.4±6.9	0.041
TG (mg/dL)	171.3±39.4	191.8±39.6	198.3±45.1	0.009
FBS (mg/dL)	118.3±26.2	188.4±5.8	145.2±51.9	0.003

Values are expressed as Mean±SD. *WC: waist circumference; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC: Total cholesterol; HDL high density lipoproteins; TG: triglycerides; FBS: fasting blood sugar. P value between thyroid dysfunction (OHT and SCH) and euthyroid.

Table IV shows BMI, WC, SBP, DBP, TC, TG, and FBS exhibited a significant positive linear correlation ($P < 0.05$), while age and HDL-C displayed a non-significant negative correlation ($P > 0.05$) with TSH levels.

Table IV: Correlation of components of metabolic syndrome in relation to TSH levels

Variables	r-value	P-value
Age	- 0.036	0.734
BMI (kg/m^2)	0.491	0.001
WC (cm)	0.221	0.024
SBP (mm Hg)	0.391	0.001
DBP (mm Hg)	0.231	0.017
TC (mg/dL)	0.372	0.001
HDL (mg/dL)	-0.104	0.298
TG (mg/dL)	0.261	0.009
FBS (mg/dL)	0.381	0.001

DISCUSSION

The current study was undertaken to assess the prevalence of thyroid dysfunction in individuals with metabolic syndrome and its correlation with the various components of MetS. This investigation uncovered a notably high prevalence of metabolic syndrome (MetS) in female subjects, showing a nearly linear increase with advancing age. PuniaVPS[10] findings aligned with our results, indicating that MetS prevalence rises with age, and he attributed the higher occurrence in women to increased obesity rates and accelerated glucose intolerance over time. PuniaVPS[10] further emphasized the role of cytokines in both disorders[10]. The potential impact of cytokine-mediated injury to thyroid follicles was discussed, highlighting the exposure of enzymes on the apical border to thyroid peroxidase antibodies, which could bind to autoantigens and trigger complement fixation, ultimately leading to hypothyroidism[11].

This study observations, particularly the higher prevalence of low high-density lipoprotein cholesterol (HDL-C) in females, were in line with Punia's work, which noted that elevated triglycerides, low HDL cholesterol, and increased waist circumference were more common in women[10]. This study also noted a substantial prevalence of subclinical hypothyroidism (SCH) in MetS patients. Subclinical hypothyroidism has been associated with atherosclerotic cardiovascular diseases, with various mechanisms such as altered coagulation parameters, hyperhomocysteinemia, and low-grade chronic inflammation potentially contributing to this association. Elevated C-reactive protein (CRP) levels in progressive thyroid failure and metabolic syndrome have been reported[12,13]. Additionally, SCH is known to elevate total and low-density lipoprotein (LDL) cholesterol, blood pressure, and triglyceride levels, while decreasing HDL cholesterol levels. As expected, we found a statistically significant relationship between various MetS components such as BMI, SBP, DBP, TG, and FBS and thyroid dysfunction.

This study found a positive linear correlation between thyroid stimulating hormone (TSH) levels and Body Mass Index (BMI), waist circumference (WC), total cholesterol (TC), triglycerides (TGL), fasting blood sugar (FBS), and systolic blood pressure (SBP). Chugh et al[14] and Gierach et al[15] presented similar findings, noting elevated TSH levels in individuals with metabolic syndrome (MetS) and suggesting a connection to thyroid receptor resistance, potentially a component of MetS. Numerous reports support a correlation between TSH levels and various components of MetS, reinforcing our study findings. Abdominal obesity stands out as a primary risk factor for MetS and cardiovascular disease. It contributes

to insulin resistance, leading to decreased levels of high-density lipoprotein (HDL) cholesterol, elevated triglyceride levels, and the onset of arterial hypertension. Body Mass Index (BMI), a widely used metric for obesity assessment, is a straightforward and practical measure. Obesity, defined as BMI values $\geq$30 kg/m^2, is commonly associated with abdominal obesity.

Several factors may contribute to increased TSH levels in obese individuals, including neuroendocrine dysfunction, alterations in the hypothalamic-pituitary axis induced by leptin, and thyroid hormone resistance due to partially bioinactive TSH protein. Numerous cross-sectional and longitudinal studies have established a correlation between TSH and leptin, with circulating leptin levels being associated with body adiposity and insulin resistance. Consequently, leptin may play a crucial role in linking TSH levels and obesity, potentially through the mechanism of insulin resistance[16,17].

As thyroid hormones play a role in regulating hepatic lipoprotein production, there could be an association between thyroid stimulating hormone (TSH) levels and unfavorable serum lipid concentrations, particularly when TSH levels exceed 10 mU/L[18]. Elevated triglyceride (TG) levels may stem from diminished activity of lipoprotein lipase or impaired clearance of lipoproteins that depend on the function of low-density lipoprotein (LDL) receptors in individuals with hypothyroidism[19].

The presence of a noteworthy correlation between thyroid stimulating hormone (TSH) and both 2-hour post-load plasma insulin (2 hr-PG) and glucose area under the curve (AUC) indicates that elevated TSH levels are linked to hyperglycemia or impaired glucose tolerance[6,20]. Corresponding to our findings, Oh et al[20] also reported a positive and linear association between systolic and diastolic blood pressure and TSH levels. The anti-natriuretic effect of insulin, which promotes renal sodium re-absorption, may be heightened in individuals with insulin resistance. This effect is speculated to play a pivotal role in the development of hypertension in individuals with metabolic syndrome[21].

Conclusion

This study shows that occurrence of thyroid dysfunction (TD) was notably elevated in individuals with metabolic syndrome (MetS), particularly among those with subclinical hypothyroidism (SCH) and elderly females, indicating an increased risk. Moreover, the simultaneous presence of both conditions may significantly amplify the risk of atherosclerotic cardiovascular disease (ASCVD). Therefore, it is advisable to routinely evaluate thyroid function in all individuals with MetS. Such assessments not only aid in preventing mismanagement of these cases but also mitigate the potential risks associated with these coexisting conditions.

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