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A Study on Association between Thyroid Stimulating Hormone Levels and Metabolic Syndrome Components.

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ABSTRACT

Background: Since metabolic syndrome (MetS) and thyroid dysfunction (TD) are both characterized by a cluster of common abnormalities, it is possible that patients suffering from both disease entities might have compounded risk. This study was aimed to evaluate the pattern of TD in subjects with MetS and its relationship with components of the MetS. **Methods:** One hundred cases defined according to the International Diabetic Federation (IDF) criteria were evaluated for vital parameters, lipid and thyroid profile, along with other routine laboratory parameters. **Results:** There was a significant association of various metabolic syndrome parameters viz. body mass index(BMI), systolic blood pressure (SBP),diastolic blood pressure (DBP), total cholesterol(TC), triglycerides (TG) and fasting blood sugar(FBS) with TD ($P<0.05$). It was found that BMI, waist circumference (WC), SBP, total cholesterol (TC), triglyceride (TG) and FBS had significant ($P<0.05$) positive linear correlation whereas age and high density lipoprotein (HDL) had non-significant ($P>0.05$) negative correlation with thyroid stimulating hormone (TSH) levels. **Conclusion:** The prevalence of TD in patients with MetS was high; while subjects with SCH and elderly females were at increased risk.

Keywords: Metabolic Syndrome, Thyroid dysfunction, Subclinical Hypothyroidism, Overt Hypothyroidism, Hyperthyroidism.

INTRODUCTION

The "deadly quartet" - also known as "metabolic syndrome" is the cluster of metabolic abnormalities characterised by obesity, hypertension, high triglyceride levels, low high density lipoproteins and abnormal fasting glucose levels.[1,2] These patients are at high risk for developing cardiovascular disease and are twice likely to die from and three times as likely to have myocardial infarction and stroke compared with people without this syndrome.[3] Insulin resistance is supposed to be the central pathophysiological phenomenon underlying the clustering.[4] Thyroid disease is associated with atherosclerotic cardiovascular disease[5,6] which may in part be explained by thyroid hormone regulation of lipid metabolism and its effects on blood pressure.

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These hormones appear to serve as a general pacemaker accelerating metabolic process and may be associated with metabolic syndrome. Both MetS and TD are associated with increased risk of atherosclerotic heart disease and a cluster of common abnormalities such as abdominal obesity, hyperglycemia, hypertension (HTN), reduced HDL-C, and elevated TG. A study on TD in MetS population can help to know the magnitude of overlap of these two disease entities and may highlight the importance of thyroid function tests in patients with MetS. This can lead to proper planning and adequate management strategies, resulting in significant reduction in cardiovascular morbidity and mortality due to MetS with TD. The present study was conducted to evaluate the pattern of TD in patients with MetS and its relationship with components of the MetS.

MATERIALS AND METHODS

Source of data

This study was conducted on 100 indoor as well as outdoor patients from Guru Nanak Dev Hospital attached to Government Medical College, Amritsar. All those patients who fulfilled the inclusion and exclusion criteria were enrolled for the present study. The study was carried out for a period of one year after obtaining the approval from the institutional ethics committee.

Inclusion Criteria:

1. Subjects of Age 18 years to 70 years, who fulfilled the criteria for metabolic syndrome by International Diabetic Federation [IDF].
2. Subjects with metabolic syndrome not on any medications–newly detected metabolic syndrome patients.
3. Subjects who gave written informed consent.

Exclusion Criteria:

1. Known hypothyroid or sub-clinical hypothyroid or hyperthyroidism patients.
2. Patients taking medications for diabetes mellitus, hypertension, thyroid disorders, dyslipidemia.
3. Steroids.
4. Individuals less than 18 year's age.
5. Patients lost during follow up.

At baseline, demographic data was collected and a detailed physical examination was done. Body weight (kg) and height (m) were measured using standardized techniques and equipment. The BMI was calculated as weight divided by squared 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, using a stretch resistant tape. Blood pressure was measured from the left arm in the sitting position with apparatus at the level of the heart. FPG was measured by glucose oxidase and the peroxidise method described by Sackhs.[7] Total cholesterol serum cholesterol level was assayed as per method given by Allain et al.[8] The serum triglyceride level was estimated by using enzymatic GPO-PAP method given by McGowan et al[9] and HDL-C was determined by the method given by Burstein et al.[10] The quantitative determination of TSH was done by enzyme immunoassay using commercially available kits.

Statistical Analysis

The data obtained was tabulated on the SPSS-19 spreadsheet. All data were expressed as mean ± standard deviation. Student's t -test was used to know any significant relationship between the components of metabolic syndrome and TSH level. Pearson's correlation coefficient was used to determine the strength of associations. All the tests were 2-tailed and statistical significance was accepted at $P < 0.05$.

RESULTS

The study group consisted of 100 patients (67: 33 females and males) were in the age group of 18-70 years. The age group 50-59 had maximum number (69.2%) of female patients with MetS. Interestingly, the prevalence of MetS in the female patients increased almost linearly with advancing age [Table 1]. Subclinical hypothyroidism(SCH) is present in about one fifth of the MetS patients (16% females and 3.0% males) followed by 3% cases of Overt hypothyroidism(OHT) (2.0% females and 1.0% males). There were no cases of subclinical hyperthyroidism or overt hyperthyroidism in our study [Table 2].

Table 1: Distribution of cases with metabolic syndrome according to age and gender groups.

Age	Total No	Metabolic syndrome	
		Male	Female
20-29	5	2 (40)	3 (60)
30-39	11	4 (36.4)	7 (63.6)
40-49	26	9 (34.6)	17 (65.4)
50-59	26	8 (30.8)	18 (69.2)
60-69	32	10 (31.3)	22(68.8)

The data in parentheses are percentage

Table 2: Pre test and Post Test mnemonic Results -class average score

	Total no	Euthyroid	Overt Hypothyroidism	Subclinical Hypothyroidism
Males	33	29 (88.8)	1 (3.0)	3 (9.0)
Females	67	49 (73.1)	2 (2.9)	16 (23.9)
Total	100	78	3	19

The data in parentheses are percentage

As depicted in [Table 3], among the female patients low HDL (18.4% and 2.6% in SCH and OHT respectively) was the most common MetS abnormality followed by hypertension (17.1% and 2.8% in SCH and OHT respectively), large WC (16% and 2% in SCH and OHT respectively), high TG (16.7% and 1.2 % in SCH and OHT respectively), and high FBS (14.3% and 2.6% in SCH and OHT respectively). Among the male patients, high FBS (3.9% and 1.3 % in SCH and OHT respectively) was most common followed by high TG (3.6% and 1.2 % in SCH and OHT respectively), hypertension (2.8 % and 1.4 % in SCH and OHT respectively) large WC (3.0 % and 1.0 % SCH and OHT respectively) and low HDL (1.3% each in SCH and OHT).

Table 3: Prevalence of MetS components according to gender groups

MetS components	Total No	Euthyroidism		Overt Hypothyroidism		Subclinical Hypothyroidism	
		Male	female	Male	female	male	Female
WC (cm)	100	29 (29)	49 (49)	1(1)	2 (2)	3 (3)	16 (16)
Hypertension	70	21(30.0)	32 (45.7)	1(1.4)	2 (2.8)	2 (2.8)	12 (17.1)
HDL (mg/dl)	76	21(27.6)	37(48.7)	1(1.3)	2 (2.6)	1 (1.3)	14 (18.4)
TG(mg/dl)	84	26 (30.9)	39(46.4)	1 (1.2)	1 (1.2)	3(3.6)	14 (16.7)
FBS(mg/dl)	77	22 (28.6)	38(49.3)	1(1.3)	2(2.6)	3(3.9)	11 (14.3)

The data in parentheses are percentage

The BMI, SBP, DBP, TG and FBS were all significantly related to thyroid dysfunction ($P<0.05$) whereas, age, waist circumference and HDL were non-significantly related to thyroid dysfunction ($P \geq 0.05$) as depicted in [Table 4].

The BMI, WC, SBP, TC, TG and FBS had significant ($P<0.05$) positive linear correlation while

age and HDL had non-significant (P>0.05) negative correlation with TSH levels [Table 5].

Table 4: Baseline characteristics of study population

MetS components*	Euthyroidism	Overt Hypothyroidism	Subclinical hypothyroidism	†*P* value
Age (years)	49.1 ± 10.8	51.2 ± 8.5	51.6 ± 21.7	0.393
BMI (Kg/m^2)	25.5±1.6	31±0.8	26.6±2.0	0.006
WC (cm)	87.9± 5.3	87±2.5	87.0±5.6	0.931
SBP	132.7±13.2	168±10.7	144.6±15.6	0.001
DBP	86.6±8.5	96.6±4.7	92.5±8.3	0.002
TC(mg/dl)	164.4±43.0	238±35.3	210.7±38.4	0.000
HDL (mg/dl)	41.2±6.8	35.3±2.5	38.4±6.9	0.050
TG(mg/dl)	170.2±38.7	192.3±38.5	199.1±44.2	0.010
FBS(mg/dl)	117.9±25.8	187.3±5.2	146.8±52.1	0.005

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 5: Pearson's Correlation coefficient (r) of each component of MetS in relation to TSH levels

Variables*	TSH	
	r	*P* value
Age ,years	- 0.034	0.735
BMI, kg/m^2	0.486	0.000
WC, cm	0.210	0.036
SBP, mm Hg	0.383	0.000
DBP,mm Hg	0.220	0.028
TC, mg/dl	0.360	0.000
HDL, mg/dl	-0.106	0.296
TG, mg/dl	0.253	0.011
FBS, mg/dl	0.377	0.000

*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

DISCUSSION

Our study revealed high prevalence of MetS in the female subjects, which increased almost linearly with advancing age. Punia reported that the prevalence of MetS increased with age and had related its higher prevalence in women to higher rate of obesity as well as rapid glucose intolerance over time. He further highlighted the role of cytokines in both the disorders.[11] Cytokine-mediated injury to thyroid follicles could expose the enzymes on the apical border of follicles to thyroid peroxidase antibodies which may then bind to autoantigens and fix the complement leading to hypothyroidism.[12] Our findings that low HDL was more prevalent in females is supported by the work of Punia who reported that elevated triglycerides, low HDL-C, and increased waist circumference were most common in women.[11]

We observed a high prevalence of SCH in MetS patients. SCH has been found to be associated with atherosclerotic cardiovascular diseases, and multiple mechanisms such as altered coagulation parameters and hyperhomocysteinemia, and low grade chronic inflammation may accompany this process. It has been found that C-reactive protein (CRP) value is elevated in progressive thyroid failure and metabolic syndrome.[13,14] Besides increasing the total and LDL cholesterol, SCH is also known to increase blood pressure and triglyceride levels and to decrease HDL cholesterol levels. As expected a statistically significant relationship of various MetS components viz. BMI, SBP, DBP, TG and FBS was observed with thyroid dysfunction.

A positive linear correlation was observed between TSH levels and BMI, WC, TC, TGL, FBS and SBP. Chugh K et al in a similar study reported high TSH levels in subjects with MetS and attributed the rise to thyroid receptor resistance, which may be a part of MetS.[15] There have been enough reports which support a correlation between TSH levels and components of MetS and thus substantiate our findings. Abdominal obesity is the major risk factor for the development of metabolic syndrome and in the assessment of cardiovascular disease. It is also responsible for the development of insulin resistance, which decreases the levels of the HDL-cholesterol fraction, increases the levels of triglycerides, and leads to the development of arterial hypertension. BMI is the simplest, most practical, and most widely used system of indexing body weight. Obesity is commonly assessed using body mass index (BMI) whose values of ≥30 kg/m^2 determine somatic obesity.[16] Possible causes of increased TSH levels in obese individuals include neuroendocrine dysfunction, leptin-induced hypothalamic-pituitary axis alteration, and thyroid

hormone resistance due to partially bioinactive TSH protein.[17] Many cross-sectional and longitudinal studies have reported a correlation between TSH and leptin, and the circulating leptin levels are correlated with body adiposity and insulin resistance.[18] Therefore, leptin might have an important role in the link between TSH and obesity, possibly via insulin resistance.

Since thyroid hormones regulate the hepatic lipo-protein production, TSH might be associated with unfavourable serum lipid concentrations, especially if the TSH level is > 10mU/L.[19] High TG levels might result from the reduced activity of lipoprotein lipase or the impaired clearance of lipoproteins dependent on LDL receptor function in individuals with hypothyroidism.[20]

A significant correlation between TSH and both the 2-hour post-load plasma insulin (2 hr-PG) and glucose area under the curve (AUC), suggests that elevated TSH levels are associated with hyperglycemia or impaired glucose tolerance. [21]

Similar to our study, a positive, linear association between systolic and diastolic blood pressure and TSH levels was reported by Oh et al.[21] The anti-natriuretic effect of insulin stimulates renal sodium re-absorption, which may be increased in individuals with insulin resistance, and this effect may play an important role for development of hypertension in the metabolic syndrome. [22]

CONCLUSION

The prevalence of TD in patients with MetS was high; while subjects with SCH and elderly females were at increased risk. Furthermore, the coexistence of the two disease entities might have substantially high atheroschlerotic cardiovascular disease (ASCVD), hence it is worthwhile to assess the thyroid function in all patients with MetS because it not only checks the mismanagement of such cases but also reduces the impending risks.

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