

Study to Evaluate the Pattern of Thyroid Disorder (TD) in Patients with Met S in Comparison to Healthy Controls.

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Conflict of interest: Nil

Abstract

Background: Thyroid disease and the metabolic syndrome are both associated with cardiovascular disease. **Aim:** to evaluate the pattern of Thyroid disorder (TD) in patients with Met S in comparison to healthy controls and to correlate the relationship between the components of MetS and Thyroid disorder. **Material and Methods:** This was a cross-sectional study was done in the Department of Medicine, Sri Krishna Medical College and Hospital, Muzaffarpur, Bihar, India it will be retrospective study for 18 months .100 patients with metabolic syndrome (MetS) who fulfilled the National Cholesterol, Education Program, Adult Treatment Panel III (NCEP-ATP III 2001) criteria were included in the study group (MetS group). **Results:** our of 300 patients study group (MetS group) consist of 200 subjects (102 female, 98 male, mean age 52.74±9.21) and control group (Non-MetS) included 100 subjects (35female and 65 male, mean age 50.21±10.88).The two groups were not significant different with respect to dietary habits and life style (P>0.05) while significantly greater number of subjects in the metabolic group had sex, education level and thyroid dysfunctions (P<0.001). Of the 200 metabolic subjects, 52 (26%) had SCH, 26(13%) had clinical hypothyroidism, 8 (4%) had subclinical hyperthyroidism, and 114 (57%) were euthyroid. The overall prevalence of the thyroid dysfunctions was 86(43%) in study group. In the healthy non metabolic group, only 10(10%) had SCH, 5(5%) had clinical hypothyroidism and 85(85%) were euthyroid. The overall prevalence of thyroid dysfunctions was 15% among non-metabolic subjects. **Conclusion:** We concluded that the prevalence of TD in patients with MetS was high, indicating a possible interplay between thyroid status and MetS. Hypothyroidism was the most common TD in Indian patients with MetS.

Key words: Metabolic syndrome, Thyroid Stimulating Hormone, Hypothyroidism, Central Obesity.

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Introduction

Metabolic syndrome (MetS) is a combination of risk factors such as hypertension, atherogenic dyslipidemia, hyperglycemia, truncal (central) obesity, and prothrombotic and proinflammatory

conditions, which could increase the risk of cardiovascular illness, diabetes, and death. According to an estimate by the International Diabetes Foundation, nearly one fourth of the world's population has MetS[1]. The prevalence rates vary greatly

depending upon the definition of MetS, ethnicity, age, population, etc. Recently, a rapid increase in its prevalence has been noted in India due to socioeconomic transitions to increasing affluence, urbanization, mechanization, and urban migration[2]. About one third of the urban population in large Indian cities has MetS[3] with the overall prevalence varying between 11% and 56%[4]. Thyroid diseases are among the most prevalent endocrine disorders worldwide. Based on the estimation from various studies, it has been projected that about 42 million people in India suffer from thyroid diseases[5]. MetS is closely associated with thyroid dysfunction (TD) due to the impact of thyroid hormones on lipid metabolism, glucose, blood pressure, and cardiovascular dysfunction[6]. Functional changes in the thyroid gland might have an association with MetS and its related components including obesity, insulin resistance (IR), lipid and glucose metabolism abnormalities, raised blood pressure, and cardiovascular dysfunction. MetS and TD are both characterized by a cluster of common abnormalities such as abdominal obesity, hyperglycemia, hypertension, reduced high-density lipoprotein cholesterol (HDL-C), and elevated triglycerides (TG). Moreover, IR, identified as a basic mechanism for MetS, also plays a role in hypothyroidism[7]. The occurrence of both the conditions may be compounded to increase the risk for cardiovascular diseases (CVDs). Several studies have shown a correlation between thyroid function and the indices of MetS[8]. Present study assessed the prevalence of TD in Indian patients with MetS to add to the epidemiological data. It was also aimed at exploring the clinical profile and associated risk factors of TD in MetS patients.

Material and methods

This was a cross-sectional study was done in the Department of Medicine, Sri Krishna Medical College and Hospital, Muzaffarpur, Bihar, India, it will be

retrospective study for 18 months. after taking the approval of the protocol review committee and institutional ethics committee.

Methodology

200 patients with metabolic syndrome (MetS) who fulfilled the National Cholesterol, Education Program, Adult Treatment Panel III (NCEP-ATP III 2001) criteria were included in the study group (MetS group)[9].

The metabolic syndrome was diagnosed in the presence of any three or more out of five components, waist circumference (WC)>102 cms in men and 88 cms in women, blood pressure (BP)>130/85 mmHg or on antihypertensive medications, fasting plasma glucose (FBG)>110 mg/dL or on anti-diabetic medications, fasting triglycerides (TG)>150 mg/dl, HDL-C<40 mg/ dL in males and <50 mg/dL in females. Age and sex matched 100 healthy volunteers who had no features of metabolic syndrome were included in the control group (Non-MetS group). Patients with history of respiratory disease, malignancy, Smokers, alcoholics, congestive cardiac failure, pregnant women, and liver disease, were excluded from study. Anthropometric measurements and blood pressure measurements were obtained after complete physical examination Blood pressure was measured using a mercury sphygmomanometer with over the right arm with the patient lying supine. Weight and height were measured using a daily calibrated digital scale and stadimeter with subject wearing light clothing and no shoes and body mass index (BMI) was also calculated by using Quetlet index (weight/height²- kg/m²)[10]. Waist circumference was measured on bare skin during mid-respiration at the narrowest indentation between the 10th rib and iliac crest to the nearest 0.1cm while the patient was standing. Blood samples were obtained following 12 hours of fasting were immediately centrifuged (3000 rpm) for 10 minutes; the sera were

separated and frozen at -8°C until analysis. Fasting blood glucose (FBG), total cholesterol, triglycerides (TG), and high-density lipoprotein cholesterol (HDL-C) levels were determined by enzymatic method using commercially available diagnostic kit on fully automated biochemical analyzer. Low density lipoproteins cholesterol (LDL-C) was determined by using Friedwald formula[11]. Triiodothyronine (T_3), Thyroxine (T_4), and Thyroid stimulating hormone (TSH) were estimated by the electrochem-luminescence immune assay (ECLIA) technique using commercially available kits from Roche Diagnostics (Mannheim, Germany) with Elecsys 1010 analyzer. The analytical sensitivity of TSH is $0.005 \mu\text{IU/mL}$ and for T_4 is 0.023 ng/dl . Normal range for TSH was $0.27\text{--}4.2 \mu\text{IU/ml}$, T_3 was $0.862.02 \text{ ng/ml}$, and for T_4 was $5.13\text{--}14.06 \mu\text{g/dl}$. A high serum TSH level ($4.2\text{--}10 \mu\text{IU/ml}$) and normal T_3 and T_4 levels were required for the diagnosis of subclinical hypothyroidism. Patients with high TSH ($>10 \mu\text{IU/ml}$) and low T_3 and T_4 levels were classified as being overt or clinical hypothyroid and Subclinical hyperthyroidism is characterized by circulating TSH levels below the reference range and normal serum thyroid hormone levels. Patients

with normal TSH, T_3 , and T_4 were considered euthyroid[12].

Results

Demographic characteristics are presented in Table-1. The totals of 300 subjects were included in this study. Study group (MetS group) consist of 200 subjects (102 female, 98 male, mean age 52.74 ± 9.21) and control group (Non-MetS) included 100 subjects (35female and 65 male, mean age 50.21 ± 10.88). The two groups were not significant different with respect to dietary habits and lifestyle ($P>0.05$) while significantly greater number of subjects in the metabolic group had sex, education level and thyroid dysfunctions ($P<0.001$). Of the 200 metabolic subjects, 52 (26%) had SCH, 26(13%) had clinical hypothyroidism 8 (4%) had subclinical hyperthyroidism, and 114 (57%) were euthyroid. Hyperthyroidism was not present in any of the subject. The pattern of thyroid dysfunctions in patients with MetS was shown in table 1. Therefore, the overall prevalence of the thyroid dysfunctions was 86(43%) in study group. In the healthy non metabolic group, only 10(10%) had SCH, 5(5%) had clinical hypothyroidism and 85(85%) were euthyroid. The overall prevalence of thyroid dysfunctions was 15% among non-metabolic subjects.

Table 1: Comparison of demographic variables between non-metabolic and metabolic subjects

Demographic profile		Non-MetS control group (n=100)	Metabolic study group (n=200)	Total and Percentage	Chi Square Value	P-Value
Sex	Male	65(65%)	98 (49%)	163(54.33%)	9.133*	0.002
	Female	35(35%)	102 (51%)	137(45.67%)		
Dietary Habits	Vegetarian	88 (88%)	185(92.5%)	273(91%)	0.29	0.877
	Non-Veg.	12 (12%)	15(7.5%)	27 (9%)		
Lifestyle	Sedentary	81(81%)	174 (87%)	255(85%)	3.032	0.078
	Non sed.	19 (19%)	26(13%)	45 (15%)		
Education Level	Illiterate	36 (36%)	96 (48%)	132 (44%)	57.95*	< 0.001

	Literate	64 (64%)	104 (52%)	168(56%)		
Thyroid	Euthyroidism	85 (85%)	114(57%)	199 (66.33%)	33.33*	< 0.001
dysfunctions	clinical hypothyroidism	5 (5%)	26 (13%)	31(10.33%)		
	Sub clinical Hypothyroidism	10(10%)	52(26%)	62 (21.67%)		
	Sub clinical hyperthyroidism	0 (0%)	8 (4%)	8 (2.67%)		

Two sided P value is >0.05, considered not significant. The row/column association is not statistically significant and P value is <0.05, considered significant. The row/column variables are significantly associated.

Table 2: Comparison of parameters of metabolic syndrome between Non-MetS and MetS group

Parameters of metabolic syndrome*	Non-Mets (Mean ± SD)	Mets (Mean ± SD)	t -Value	P- Value (2-tailed)
Age (Years)	50.21±10.88	52.74±9.21	-3.198	<0.01
Height (CM)	162.22±7.41	157.87±9.12	6.674	<0.001
Weight (Kg)	73.72±8.47	76.87±14.11	-1.678	<0.057
BMI (Kg/Sq.M)	28.01±2.27	30.78±5.36	-6.120	<0.001
HC (CM)	95.04±7.61	99.81±10.42	-3.794	<0.001
WC* (CM)	93.87±7.22	101.25±11.33	-5.895	<0.001
Systolic BP* (mmHg)	123.74±6.77	146.29±15.12	-12.652	<0.001
Diastolic BP* (mmHg)	80.65±3.87	92.87±11.29	-9.812	<0.001
FBG* (mg/dL)	85.69±13.32	136.85±35.89	-13.974	<0.001
TG* (mg/dL)	137.74±47.85	167.98±66.45	-4.337	<0.001
HDL-C* (mg/dL)	49.04±4.78	46.99±5.84	4.293	<0.001

All data expressed as mean ± standard deviation <0.05 is statistically significance. BMI, body mass index; WC, waist circumference; HC, hip circumference; FBG, fasting blood glucose; TG, triglycerides; HDL-C, high density lipoprotein cholesterol.

Differences between anthropometric and components of metabolic syndrome between subjects with MetS and healthy non metabolic, were tested by Student independent t-test. Mean value for age (P<0.01), body mass index (P<0.001), waist circumference (P<0.001), systolic and diastolic blood pressure (SBP/DBP) (P<0.001), fasting blood glucose (P<0.001), and triglycerides (P<0.001) were significantly higher in the metabolic group compared to nonmetabolic group

(P< 0.001). HDL-C levels were significantly lower in the study group when compared to control group (P<0.001) (Table 2).

Thyroid function variables in both the study and control group were measured with T3, T4, and TSH assay. TSH was significantly higher in the study group than in the control group (P<0.001) while T3 and T4 were significantly lower in the study group (P< 0.001) (Table- 3)

Table 3: Comparison of thyroid functions between Non-MetS and MetS group.

Thyroid function parameter	Non-Mets (Mean±SD)	Mets (Mean±SD)	t -Value	P- Value (2-tailed)
T ₃ (ng/mL)	1.51 ± 0.669	1.24 ± 0.697	3.193	<0.01
T ₄ (µg/dL)	7.66 ± 2.121	6.42 ± 2.77	3.789	<0.001
TSH (µIU/mL)	7.31 ± 17.69	19.87 ± 35.12	-3.247	<0.001

All data expressed as mean±standard deviation<0.05 is statistically significance. TSH, thyroid stimulating hormone; T₃ triiodothyronine; T₄ thyroxin.

Discussion

Thyroid hormones play an essential role in regulating energy balance and metabolism of glucose and lipids, thereby affecting the MetS parameters, including HDL-C, TG, blood pressure, and plasma glucose. Hypothyroidism is found to be associated with obesity, dyslipidemia, and increased risk of atherogenic CVD[13]. In subjects with hypothyroidism, IR is suggested as the possible underlying pathophysiological basis for glucose intolerance when present[14]. Oxidative stress, chronic inflammation, and angiogenesis are believed to enhance the pathogenesis of MetS[15]. The important components of MetS, such as hyperglycemia and inflammation, upsurge the production of reactive oxygen species (ROS) resulting in increased oxidative stress with overactivation of nicotinamide adenine dinucleotide phosphate (NADPH) oxidase. The main ROS is the superoxide anion, produced by NADPH oxidase[16]. Hypermetabolic state in hyperthyroidism may accelerate free radical production in mitochondria and induce changes in the antioxidant defense system. In hypothyroidism, associated oxidative stress is the consequence of reduced capacity of the antioxidative defense. In this our study, we observed that the prevalence of thyroid dysfunctions in MetS subjects was 43% and its pattern showed high prevalence of SCH 52(26%) followed by hypothyroidism 26(13%) and subclinical hyperthyroidism 8(4%). The above results are in agreement with previous studies showing an association between metabolic syndrome and thyroid dysfunctions[17-20]. A study done by

Meher LK et al showed a high prevalence of SCH (22%) and overt hypothyroidism (4%) in the MetS subjects[17]. In addition, similar study from India has shown a high prevalence of SCH (21.90%) and overt hypothyroidism (7.40%) in patients with MetS[18]. A recent study in Taiwan by Wang JY et al reported that thyroid dysfunctions were present in 7.21% of Taiwan MetS patients[19]. This study had shown 26% had SCH and 4% had subclinical hyperthyroidism. Another study from Nepal showed that the prevalence of TD in patients with MetS was 31.84% and its pattern showed high prevalence of SCH (29.32%) followed by hypothyroidism (1.67%) and subclinical hyperthyroidism (0.83%)[20]. In this study, the mean BMI, waist circumference, waist/hip ratio, systolic and diastolic blood pressure, fasting blood glucose, triglycerides, were significantly higher and HDL-C levels were significantly lower in the study group (P<0.001) than in the control group. Our study also suggested that T₃ mean 1.24 ± 0.697 ng/mL vs 1.51 ± 0.669 ng/mL(P<0.01) and T₄ mean 6.42 ± 2.77 ng/mL vs 7.66 ± 2.121ng/mL (P<0.001) levels were significantly lower in the study group than in the control group, while TSH was significantly higher in the study group (P<0.001). These finding were similar to those obtained in the studies on Hispanic population by Garcia GJ et al, Nepal population Gyawali P et al, and Chennai population by Shantha GP et al.[18-21] Serum triglycerides and TG/HDL-C ratio, which are surrogate markers for insulin resistance, were significantly elevated in study group compared to control group. This indicates

that the study group may have greater insulin resistance than the control group. Insulin resistance is said to be a common underlying abnormality in MetS[22,23]. Present study was accordance with this finding.

Hypothyroidism significant positively associated with obesity may be due to increased TSH levels in obese individuals include neuro-endocrine dysfunction, leptin- induced hypothalamic pituitary axis alteration, and thyroid hormone resistance due to partially bio-inactive TSH protein. 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 IR. Therefore, leptin might have an important role in the link between TSH and obesity, possibly via insulin resistance[24].

Conclusion

We concluded that the prevalence of TD in patients with MetS was high, indicating a possible interplay between thyroid status and MetS. Hypothyroidism was the most common TD in Indian patients with MetS. The data generated from the present study will aid in establishing a correlation between TD and MetS in Indian patients. This data will have prognostic importance for practitioners in their routine clinical practice to develop strategies for better management of their patients of TD with associated MetS.

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