Original Research Article

To evaluate the pattern of Thyroid disorder (TD) in patients with Met-S: A case-control study

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Abstract

Background: Metabolic syndrome (Met S) comprise of a group of interconnected metabolic abnormalities, including increased waist circumference, glucose intolerance, systemic hypertension, and dyslipidemia. Recent evidences show metabolic syndrome being increasingly linked to other endocrine abnormalities like diabetes, polycystic ovary disease including thyroid disorder. Undiagnosed TD in patients of MetS may compound to the cardiovascular risk already posed by the components of MetS, thereby increasing mortality rates. **Aim and objectives:** Our study aims 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 TD. **Material and Methods:** This Cross-sectional study was done the Department of Medicine, Vardhman Institute of Medical Sciences, Pawapuri, Bihar, India for 10 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:** The totals of 150 subjects were included in this study. Study group (MetS group) consist of 100 subjects (53 female, 47 male, mean age 53.04±8.31) and control group (Non-MetS) included 50 subjects (19 female and 31 male, mean age 49.14±11.07).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 100 metabolic subjects, 28 (28%) had SCH, 14 (14%) had clinical hypothyroidism, 3 (3%) had subclinical hyperthyroidism, and 55 (55%) were euthyroid. Hyperthyroidism was not present in any of the subject. The overall prevalence of the thyroid dysfunctions was 45(45%) in study group. **Conclusion:** We concluded that the prevalence of thyroid dysfunction was high in the patients with MetS.

Keywords: Metabolic syndrome, Thyroid stimulating hormone, Hypothyroidism, Central obesity.

Introduction

A cluster of interlinked metabolic abnormalities comprising of increased waist circumference, insulin resistance, hyperglycemia, systemic hypertension, deranged lipid profile with increased triglyceride levels and low HDL are collectively represented as Metabolic syndrome (Met S) or Syndrome X[1,2]. Though there is slight variation in the criteria for diagnosis of Met S suggested by various expert groups, it is well established that clustering of such physiological and biochemical risk factors accelerates the risk of developing atherosclerotic cardiovascular disease[3,4]. International Diabetes Federation estimate s an alarming rate of one in four individuals having Met S. Met S patients have twice the mortality rate and three times the risk of developing atherosclerosis or stroke compared to normal population[4].Central obesity is considered to be a key causal factor in the pathophysiology of Met S[5].Increased free fatty acid mobilisation from the intra abdominal fat is postulated as a cause of insulin resistance which in turn leads to the development of hyperglycemia, hypertriglyceridemia and hypertension[6]. Hypertriglyceridemia favours a procoagulant state by activating the coagulation cascade, increasing LDL oxidation and platelet aggregation clearly increasing the risk of developing cardiovascular.

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Risk[5].Thyroid hormone has an indispensable role in cellular growth and differentiation and energy homeostasis. Thyroid hormone regulates appetite via hypothalamus and increases thermogenesis by its action on white and brown adipose tissue[7].Thyroid hormone has diverse metabolic effects including increased gluconeogenesis, glycogenolysis, regulation of cholesterol synthesis and fat mobilisation[8].Thyroid dysfunction resulting in cardiovascular abnormalities by its effect on cardiac output and cardiac rhythm is well documented[9,10].It is thus evident that there is considerable overlap in the pathophysiology of Met S and the metabolic effects of thyroid hormone on carbohydrate and lipid. Our study aims 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 TD. Undiagnosed TD in patients of MetS may compound to the cardiovascular risk already posed by the components of MetS, thereby increasing mortality rates.

Material and methods

This Cross-sectional study was done the Vardhman Institute of Medical Sciences, Pawapuri, Bihar, India for 10 months.

Methodology

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)[11].

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 50 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/height^2-kg/m^2)[12].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 minute; 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 commercial available diagnostic kit on fully automated biochemical analyzer. Low density lipoproteins cholesterol (LDL-C) was determined by using Friedwald formula[13]. Triiodothyronine (T_3), Thyroxine (T_4), and Thyroid stimulating hormone (TSH) were estimated by the electrochem-iluminescence 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 µIU/mL and for T_4 is 0.023 ng/dl. Normal range for TSH was 0.27–4.2 µIU/ml, T_3 was 0.86-2.02 ng/ml, and for T_4 was 5.13-14.06 µg/dl. A high serum TSH level (4.2–10 µIU/ml) and normal T_3 and T_4 levels were required for the diagnosis of subclinical hypothyroidism. Patients with high TSH (>10 µIU/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, T3, and T_4 were considered euthyroid[14].

Statistical analysis

Statistical analysis was performed using SPSS windows version 20.0 software (SPSS Inc., Chicago, Illinois). Baseline characteristics of the study participants were expressed in mean±SD. Independent Student's 't' test was used to compare differences in baseline characteristics between the study group and the control group. Chi-square test and Fischer's exact chi-square test were used for the comparison of qualitative data. P< 0.05 was considered statistically significant.

Results

Demographic characteristics are presented in Table-1. The totals of 150 subjects were included in this study. Study group (MetS group) consist of 100 subjects (53 female, 47 male, mean age 53.04±8.31) and control group (Non-MetS) included 50 subjects (19 female and 31 male, mean age 49.14±11.07).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 100 metabolic subjects, 28 (28%) had SCH, 14 (14%) had clinical hypothyroidism, 3 (3%) had subclinical hyperthyroidism, and 55 (55%) 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 45(45%) in study group. In the healthy non metabolic group, only 4(8%) had SCH, 2(4%) had clinical hypothyroidism and 44(88%) were euthyroid. The overall prevalence of thyroid dysfunctions was 12% among non-metabolic subjects.

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

Socio-demographic Variables		Non-MetS control group(n=50)	Metabolic study group (n=100)	Total and Percentage	Chi Square Value	P-Value
Sex	Male	31 (62%)	47 (47%)	78 (52%)	9.133	0.002*
	Female	19 (38%)	53 (53%)	72 (48%)		
Dietary Habits	Vegetarian	45 (90%)	92 (92%)	137(91.33%)	0.29	0.877
	Non-Veg.	5 (10%)	8 (8%)	13 (8.67%)		
Life style	Sedentary	42 (84%)	88 (88%)	130 (86.67%)	3.032	0.078
	Non sed.	8 (16%)	12(12%)	20 (13.33%)		
Education Level	Illiterate	17 (34%)	47 (47%)	64 (42.67%)	57.95	< 0.001*
	Literate	33 (66%)	53 (53%)	86 (57.33%)		
Thyroid dysfunctions	Euthyroidism	44 (88%)	55 (55%)	99 (66.67%)	33.33	< 0.001*
	clinical hypothyroidism	2 (4%)	14 (14%)	16 (10.67%)		
	Sub clinical Hypothyroidism	4 (8%)	28(28%)	32 (21.33%)		
	Sub clinical hyperthyroidism	0 (0%)	3 (3%)	3 (2%)		

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 components of metabolic syndrome between Non-MetS and MetS group

Components of metabolic syndrome*	Non-Mets (Mean ± SD)	Mets(Mean ± SD)	t -Value	P- Value (2-tailed)
Age (Years)	49.14±11.07	53.04±8.31	-3.261	<0.01
Height (CM)	163.11±7.33	158.23±9.33	6.576	<0.001
Weight (Kg)	74.12±8.38	77.12±14.05	-1.763	<0.053
BMI (Kg/Sq.M)	27.28±2.31	30.69±5.12	-6.042	<0.001
HC (CM)	94.87±7.88	99.88±10.57	-3.873	<0.001

WC* (CM)	93.98±7.12	101.01±11.12	-5.876	<0.001
Systolic BP* (mmHg)	123.92±6.87	146.22±15.32	-12.674	<0.001
Diastolic BP* (mmHg)	80.12±3.79	92.98±10.98	-9.897	<0.001
FBG* (mg/dL)	85.75±13.24	136.78±35.98	-13.954	<0.001
TG* (mg/dL)	137.41±47.32	167.47±66.21	-4.324	<0.001
HDL-C* (mg/dL)	48.87±4.88	46.88±5.74	4.287	<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 non-metabolic 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 variables	Non-Mets (Mean ± SD)	Mets (Mean±SD)	t -Value	P- Value (2-tailed)
T_3 (ng/mL)	1.45 ± 0.671	1.22 ± 0.671	3.188	<0.01
T_4 (µg/dL)	7.59 ± 2.101	6.32 ± 2.89	3.774	<0.001
TSH (µIU/mL)	7.18 ± 17.44	19.78 ± 34.89	-3.233	<0.001

All data expressed as mean±standard deviation<0.05 is statistically significance. TSH, thyroid stimulating hormone; T_3 triiodothyronine; T_4 thyroxin

Discussion

In this cross-sectional study, we observed that the prevalence of thyroid dysfunctions in MetS subjects was 45% and its pattern showed high prevalence of SCH (28%) followed by hypothyroidism (14%) and subclinical hyperthyroidism (3%). The above results are in agreement with previous studies showing an association between metabolic syndrome and thyroid dysfunctions[15-18]. A study done by Meher LK et al showed a high prevalence of SCH (22%) and overt hypothyroidism (4%) in the MetS subjects[15]. In addition, similar study from India has shown a high prevalence of SCH (21.90%) and overt hypothyroidism (7.40%) in patients with MetS[16]. A recent study in Taiwan by Wang JY et al reported that thyroid dysfunctions were present in 7.21% of Taiwan MetS patients[17].This study had shown 45% had SCH and 3% 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%)[18].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 T_3 mean 1.22 ± 0.671 ng/mL vs 1.45 ± 0.671 ng/mL (P<0.01) and T_4 mean 6.32 ± 2.89 ng/mL vs 7.59 ± 2.101 ng/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.[16,18,19]. 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[20,21]. 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[22].

Conclusion

We concluded that the prevalence of thyroid dysfunction was high in the patients with MetS. Thyroid hormone significantly affects and associated with components of metabolic syndrome. Present study suggests that hypothyroidism is known to be associated with metabolic syndrome and increased compound risk for cardiovascular diseases therefore it should be considered as one of the new component in newly diagnosed metabolic syndrome patients in future.

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