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Research Article

Study of thyroid function in patients with metabolic syndrome

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ABSTRACT

Background: Thyroid disease and the metabolic syndrome are both associated with cardiovascular disease. The aim of this study was to explore the study of thyroid function in patients with metabolic syndrome.
Methods: This cross-sectional study was conducted at department of physiology, M P shah medical college Jamnagar, Gujarat. It included 200 patients with metabolic syndrome (MetS) (National Cholesterol Education Program's-Adult Treatment Panel III Criteria) in the study group and 100 subjects without metabolic syndrome in the control group. Anthropometric variables and blood pressure were taken using standardized technique and body mass index was calculated. Fasting blood sample was analyzed for total cholesterol (TC), triglycerides (TG), high density lipoproteins cholesterol (HDL-C), blood glucose (FBG) and TSH, T_4 and T_3 were measured using electro-chemiluminescence immuno assay. Statistical analysis was performed using SPSS windows version 20.0 software (SPSS Inc., Chicago, Illinois).
Results: The overall prevalence of thyroid dysfunction in patients with MetS was 41.5% with high prevalence of sub clinical hypothyroidism (27%). TSH (P<0.001) was significantly higher in the study group than in control group (P <0.01) but T_3 and T_4 values of study group were significantly lower than those of control group (P< 0.01). Metabolic components waist circumference, blood pressure, fasting blood glucose and triglycerides were significantly higher in metabolic subject (P<0.001), while HDL-C was significantly lower in study group (P<0.001) then control group.
Conclusion: Hypothyroidism brawny associated with components of metabolic syndrome, therefore increased multifaceted risk of cardiovascular disorders with elevate TSH levels.

Key words: Metabolic syndrome, Thyroid stimulating hormone, Hypothyroidism, Central obesity

INTRODUCTION

The metabolic syndrome (syndrome X or insulin resistance syndrome) is one of the major public health issues of this century.

It is a constellation of physical conditions and metabolic abnormalities which include central obesity, hyperglycemia plus insulin resistance (IR), hypertension, dyslipidemia and pro-inflammatory conditions, usually occurring together that increases an individual's risk for development of type 2 diabetes mellitus and cardiovascular disease.[1] Thyroid has ubiquitous effects and influences the function of most organs. Thyroid hormones play an important role in regulating energy homeostasis, carbohydrate, lipids and protein metabolism. This hormone appears to serve as a general pacemaker accelerating metabolic processes and may be associated with metabolic syndrome. Hyperthyroidism is usually associated with low cholesterol and glucose intolerance; whereas hypothyroidism is associated with high cholesterol tendency, and patients are prone to weight gain and cardiac signs like bradycardia.[2] Thyroid functions affect the components of MetS including HDL–cholesterol (HDL-C), triglycerides (TG), blood pressure and plasma glucose. The impact of various degree of thyroid dysfunction (TD) on components of MetS, however, continues to be debatable.[3] These metabolic disorders associate with cardiovascular

diseases and other abnormalities like diabetes mellitus. Therefore MetS syndrome and Hypothyroidism both are recognized risk factors for atherosclerotic cardiovascular disease and increased risk for cardiovascular morbidity and mortality. As metabolic syndrome and hypothyroidism are independent risk factors for the same disease process, namely cardiovascular disease, it is possible that patients suffering from both these disease entities may have a compounded risk.[4] There is limited information available in literature regarding status of thyroid functions in relation to components of metabolic syndrome. Therefore the present study was an effort to investigate the study of thyroid function in patients with metabolic syndrome in population of Saurashtra region Gujarat, India.

METHODS

This cross sectional study was conducted as a part of Ph.D. research program for duration of three years (from July 2011 to June 2014) at the Department of physiology, M.P Shah Medical College, Jamnagar, Gujarat, India. The patients were randomly selected from the outpatient clinic and diabetes centre of Department general Medicine, M.P Shah Medical College and associate hospital.

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).[5]

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. Patients were also be excluded which under treatment of any thyroid related disorders.

Trained interviewers, using a structured questionnaire, interviewed the all participants to obtain the information on socio-demographic characteristics, physical activity, smoking, alcohol drinking habits, dietary characteristics, personal and family history of diseases and hospitalization. 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).[6]

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.[7] 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 [8]. Informed consent was obtained from all the participants prior to start the study. The study protocol was approved by institutional ethics committee and research development council of Saurashtra University, Rajkot, India.

Statistical analysis

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. Statistical analysis was performed using SPSS windows version 20.0 software (SPSS Inc., Chicago, Illinois).

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 (111 female, 89 male, mean age 52.34±8.56) and control group (Non-MetS) included 100 subjects (37 female and 63 male, mean age 48.62±10.48).

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

Socio-demographic Variables		Non-MetS control group (n=100)	Metabolic study group (n=200)	Total and Percentage	Chi Square Value	P-Value
Sex	Male	63 (63%)	89 (44.5%)	152 (50.6%)	9.128*	0.003
	Female	37 (37%)	111 (55.5%)	148 (49.3%)		
Dietary Habits	Vegetarian	92 (92%)	183 (91.5%)	275 (91.5%)	0.22	0.883
	Non-Veg.	8 (8%)	17 (8.5%)	25 (8.5%)		
Life style	Sedentary	83 (83%)	180 (90%)	263 (90%)	3.021	0.082
	Non sed.	17 (17%)	20 (10%)	37 (10%)		
Education Level	Illiterate	33 (33%)	90 (45%)	123 (41%)	57.62*	< 0.001
	Literate	67 (67%)	110 (55%)	177 (59%)		
Thyroid dysfunctions	Euthyroidism	91 (91%)	117 (58.5%)	208 (69.3%)	33.25*	< 0.001
	clinical hypothyroidism	3 (3%)	26 (13%)	29 (9.6%)		
	Sub clinical Hypothyroidism	6 (6%)	54 (27%)	60 (20%)		
	Sub clinical hyperthyroidism	0 (0%)	3 (1.5%)	3 (1%0		

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)	48.62±10.48	52.34±8.56	-3.280	<0.01
Height (CM)	164±7.24	157.59±9.27	6.686	<0.001
Weight (Kg)	74±8.44	76.99±13.92	-1.970	<0.050
BMI (Kg/Sq.M)	27.48±2.56	30.74±5.08	-6.037	<0.001
HC (CM)	95.2±6.97	99.52±10.28	-3.783	<0.001
WC* (CM)	94.1±6.99	100.51±10.78	-5.746	<0.001
Systolic BP* (mmHg)	122.72±6.49	145.15±15.72	-13.684	<0.001
Diastolic BP* (mmHg)	81.02±3.73	92.52±11.02	-9.940	<0.001
FBG* (mg/dL)	85.17±12.19	135.02±35.102	-13.780	<0.001
TG* (mg/dL)	136.48±48.29	168.89±66.25	-4.348	<0.001
HDL-C* (mg/dL)	48.67±4.94	46.86±5.51	4.301	<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.

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, 54 (27%) had SCH, 26 (13%) had clinical hypothyroidism, 3 (1.5%) had subclinical hyperthyroidism, and 117 (58.5%) were euthyroid. Hyperthyroidism was not present in any of the subject. The pattern of thyroid dysfunctions in patients with MetS was shown in Figure 1. Therefore, the overall prevalence of the thyroid dysfunctions was 83 (41.5 %) in study group. In the healthy non metabolic group, only 6

(6 %) had SCH, 3 (3%) had clinical hypothyroidism and 91 (91%) were euthyroid. The overall prevalence of thyroid dysfunctions was 9% among non-metabolic subjects.

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)	1.42 ± 0.572	1.18 ± 0.640	3.170	<0.01
T_4 (µg/dL)	7.41 ± 2.016	6.25 ± 2.75	3.760	<0.001
TSH (µIU/mL)	6.97 ± 16.54	19.15 ± 35.32	-3.270	<0.001

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

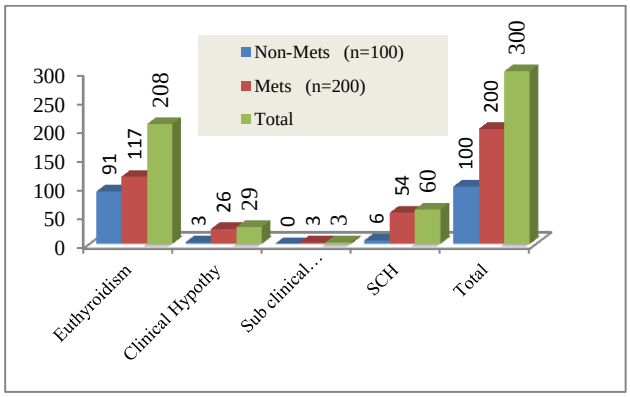

Figure 1: Prevalence of thyroid dysfunctions in Mets and Non-MetS groups.

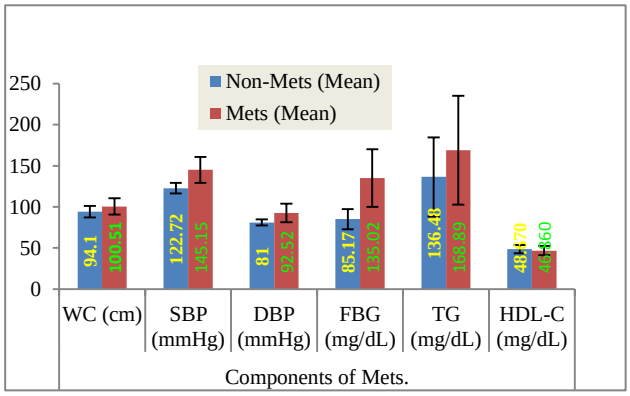

Figure 2: Components of Mets between Non-Mets and Mets groups (Mean±1SD).

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 and Figure 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, Figure 3).

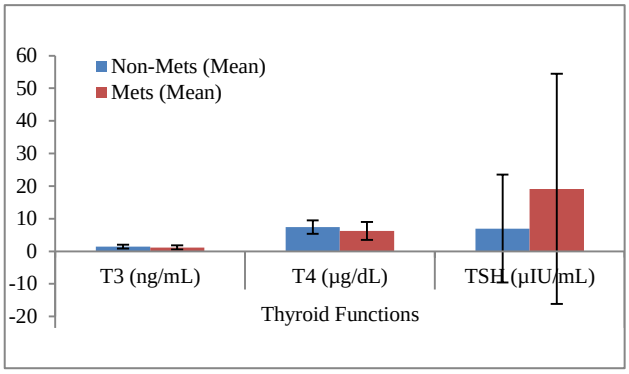

Figure 3: Thyroid functions variables Mean±SD.

DISCUSSION

In this cross-sectional study, we observed that the prevalence of thyroid dysfunctions in MetS subjects was 41.5% and its pattern showed high prevalence of SCH (27%) followed by hypothyroidism (13%) and subclinical hyperthyroidism (1.5%). The above results are in agreement with previous studies showing an association between metabolic syndrome and thyroid dysfunctions.[9-12] A study done by Meher LK et al showed a high prevalence of SCH (22%) and overt hypothyroidism (4%) in the MetS subjects.[9] In addition, similar study from India has shown a high prevalence of SCH (21.90%) and overt hypothyroidism (7.40%) in patients with MetS.[10] A recent study in Taiwan by Wang JY et al reported that thyroid dysfunctions were present in 7.21% of Taiwan MetS patients.[11] This study had shown 4.55% had SCH and 2.64% 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%).[12].

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 (P<0.01) and T_4 (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.[10,12,13]

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.[14,15] 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.[16]

There are few limitations of the study, first is that, this is a cross-sectional study, a cause and effect of relationship could not be determined. Further cohort study is needed to evaluate the deleterious effect of thyroid dysfunctions on cardiovascular disease and metabolic functions.

CONCLUSION

In conclusion, 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. Further investigations are needed to evaluate the mechanism of this correlation.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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