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# A CROSS -SECTIONAL STUDY OF METABOLIC SYNDROME IN HYPOTHYROID PATIENTS

General Medicine

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## ABSTRACT

Hypothyroidism and metabolic syndrome are well-associated risk factors for atherogenic cardiovascular disease. Insulin resistance, being a common pathogenic mechanism in both, can cause a considerable overlap between hypothyroid and metabolic syndrome population. This cross-sectional study was intended to assess the thyroid function in patients with metabolic syndrome and to investigate the association between hypothyroidism and metabolic syndrome.One hundred patients with metabolic syndrome as per National Cholesterol Education Program-Adult Treatment Panel (NCEP ATP) III criteria and 50 controls (0 out of 5 criteria) attending the internal medicine outpatient clinic were included in the study. Patients were subjected to anthropometry, evaluation of vital parameters, and lipid and thyroid profile, along with other routine laboratory parameters. Students' "*t*" test, Chi-square test, linear regression, and multiple logistic regression models were used for statistical analysis. *P* value <0.05 was considered significant.Body mass index, waist circumference, mean systolic pressure, diastolic pressure, fasting blood sugar, total cholesterol, low density lipoprotein (LDL) cholesterol, triglycerides, and thyroid stimulating hormone (TSH) were significantly higher, and free triiodothyronine (FT3), free thyroxine (FT4), and high density lipoprotein (HDL) cholesterol were significantly lower in the study group compared to the control group. In the metabolic syndrome group, 22 had subclinical hypothyroidism (22%), 4 were overtly hypothyroid (4%), and 74 were euthyroid (74%). Subclinical hypothyroidism was significantly associated with metabolic syndrome group ($P = 0.032$). There was significant linear association between TSH levels and total cholesterol, triglycerides, LDL cholesterol, and HDL cholesterol across the metabolic syndrome group in the linear regression model. Multiple logistic regression analysis recognized the association between body mass index with subclinical hypothyroidism ($P = 0.006$) in the metabolic syndrome group

## KEYWORDS

Body mass index, hypothyroidism, metabolic syndrome, obesity

## INTRODUCTION

Metabolic syndrome (MetS) includes a cluster of risk factors characterized by hypertension, dyslipidemia, hyperglycemia, and prothrombotic and proinflammatory conditions which accelerate the atherogenic process in the body. Hypothyroidism is well known to cause hyperlipidemia, diastolic hypertension, endothelial dysfunction, and cardiovascular disease.Considerable overlap occurs in the pathogenic mechanisms of atherosclerotic cardiovascular disease by MetS and hypothyroidism. Insulin resistance has been studied as the basic pathogenic mechanism in MetS. Role of insulin resistance in development of dyslipidemia in hypothyroidism has been suggested in recent studies.This relationship with insulin resistance can lead to a considerable overlap between the population subsets of MetS and hypothyroidism as well. A study on thyroid dysfunction in MetS population may help us to know the magnitude of overlap of these two groups and may highlight the importance of thyroid function tests in identifying hypothyroid population from MetS.

## MATERIAL AND METHODS

One hundred patients with MetS who fulfilled the National Cholesterol Education Program-Adult Treatment Panel (NCEP-ATP) III criteria [three out of five criteria positive, namely, blood pressure ≥130/85 mm Hg or on antihypertensive medications, fasting plasma glucose >100 mg/dl or on anti-diabetic medications, fasting triglycerides >150 mg/dl, high density lipoprotein cholesterol (HDL-C) <40 mg/dl in males and <50 mg/dl in females, waist circumference >102 cm in men and 88 cm in women] were included in the study group. Fifty patients who had no features of MetS (0 out of 5 criteria for MetS) were included in the control group. The study protocol was approved by institutional ethics committee and informed consents were obtained from the study participants, after they were duly explained about the protocol.

Patients with liver disorders, renal disorders, congestive cardiac failure; pregnant women; patients on oral contraceptive pills, statins, and other medications that alter thyroid functions and lipid levels; and those who were under treatment for any thyroid-related disorder were excluded from the study. Acutely ill patients were excluded taking into account sick euthyroid syndrome. Blood pressure was measured over the right arm with the patient lying supine. Three readings were taken and a mean value of the readings was taken as the final recording. Waist circumference was measured at the plane between anterior superior iliac spines and lower costal margin at the narrowest part of the waistline while the patient was standing and during expiration. Fasting blood samples were obtained (venous blood samples taken after overnight fast of a minimum of 8 h); glucose, total cholesterol, low density lipoprotein cholesterol (LDL-C), HDL-C, and triglyceride levels were determined. Serum thyroid stimulating hormone (TSH), free triiodothyronine (FT3), and free thyroxine (FT4) measurements were made using electrochemiluminescence immunoassay (ECLIA method). Normal range for TSH was 0.27-4.2 μIU/ml, FT3 was 1.4-4.2 pg/ml, and for FT4 was 0.93-1.7 ng/dl. A high serum TSH level (4.2-10 μIU/ml) and normal FT3 and FT4 levels were required for the diagnosis of subclinical hypothyroidism. Patients with high TSH (>10 μIU/ml) and low FT3 and FT4 levels were classified as being overt hypothyroid. Patients with normal TSH, FT3, and FT4 were considered euthyroid. Body mass index (BMI) was calculated by dividing weight in kilograms by height in meters squared.Baseline characteristics of the study participants were expressed in mean ± SD and percentage. Student's "*t* " test was used to analyze differences in baseline characteristics between the study group and the control group. Linear regression model was created to know any significant relationship between the components of MetS and TSH levels. Chi-square test was used to analyze the association between MetS and hypothyroidism. Associations between patient characteristics (age, gender, mean systolic blood pressure, mean diastolic blood pressure, waist circumference, total cholesterol, HDL-C, LDL-C, triglycerides, fasting blood sugar) and subclinical hypothyroidism in the study group were analyzed using multiple logistic regression. *P* value of <0.05 was considered statistically significant.

## RESULTS

Of the 100 patients in the study group, 55 were females (55%) and 45 were males (45%). Of the 50 persons in the control group, 26 (52%) were females and 24 (48%) were males. The baseline characteristics of the two groups are depicted in .The two groups were similar with respect to age and sex distribution. Eighteen patients in the study group had goiter with mean TSH of 7.34 ± 4.37 μIU/ml, which was higher than the rest of the patients with no goiter (4.42 ± 3.43 μIU/ml, $P = 0.03$). However, BMI, waist circumference, mean systolic pressure, diastolic pressure, fasting blood sugar, total cholesterol, LDL-C, triglycerides, and TSH were significantly higher in the study group compared to the control group. HDL-C was significantly lower in the study group. In the MetS group, 4 (4%) of the cases had overt hypothyroidism, 22 (22%) had subclinical hypothyroidism, and 74 (74%) were euthyroid. In the control group, 1 (2%) had overt hypothyroidism, 4 (8%) had subclinical hypothyroidism, and the rest 45 (90%) were euthyroid. Subclinical hypothyroidism had significant association with MetS when assessed by Chi-square test, with $P = 0.03$. Subclinical hypothyroidism showed significant association with

BMI when analyzed using logistic regression models in the MetS case group ($P = 0.006$, CI 0.412-0.859).

## DISCUSSION

The MetS group included 100 cases with 45 males and 55 females, while the control group included 50 cases with 24 males and 26 females.

The two groups were similar in their distribution of age ($P = 0.408$) and gender. In this study, the mean systolic pressure, diastolic pressure, fasting blood sugar, total cholesterol, LDL-C, triglycerides, waist circumference, and BMI were significantly higher and HDL-C levels were significantly lower in the MetS group than in the control group. These findings were similar to those obtained in the studies on Hispanic population by Garcia *et al*, and on Chennai urban population by Shantha *et al.* Thyroid function in both the MetS group and control group were assessed with FT3, FT4, and TSH assay FT3 was significantly lower in the MetS group ($P = 0.003$) than in the control group. TSH was significantly higher in the MetS group than in the control group ($P = 0.001$). FT4 was lower in the control group with a $P$ value of 0.217.A linear regression model was created to assess the association between the components of MetS and level of TSH TSH had significant positive linear association with total cholesterol, LDL-C, and triglyceride, and significant negative linear association with HDL-C in the linear regression model. The Nord-Trondelag health (HUNT) study concluded that within the range of TSH that is considered clinically normal, increasing level of TSH is associated with less favorable lipid concentrations. The association with serum lipids was linear across the entire reference range of TSH.Although our study covered groups with both normal and higher TSH (unlike the HUNT study which included only euthyroid individuals), there was a linear relation between lipid concentration and TSH levels across the entire range of TSH, which supports the role of thyroid hormones in the regulation of lipid metabolism, a deregulation of which leads to MetS. A similar study done in MetS group in the Hispanic population has shown linear association of TSH with total cholesterol, LDL-C, triglycerides, and waist circumference, but no association with HDL-C .

The relation between hypothyroidism and cardiovascular disease is not well proven. In a study including 2730 men and women, aged 70-79 years, subclinical hypothyroidism was associated with an increased risk of congestive heart failure among older adults with a TSH level of 7.0 mIU/l or greater, but not with other cardiovascular events and mortality. Another study found that there was no relationship between baseline TSH and cardiovascular mortality.

The prevalence of thyroid dysfunction was analyzed in our study. Our study showed a high prevalence of subclinical hypothyroidism (22%) and overt hypothyroidism (4%) in the MetS group. In the control group, only 8% had subclinical hypothyroidism and 2% had overt hypothyroidism. In a recent population-based study in adult population in India, the prevalence of hypothyroidism was 3.9% while that of subclinical hypothyroidism was 9.4%. According to the report by Shantha *et al*., the prevalence of overt hypothyroidism was 7.4% and that of subclinical hypothyroidism was 21.9% in the MetS population.

Our study showed a significant association of subclinical hypothyroidism with MetS ($P = 0.03$). This study supports the results of Shantha *et al*.'s study, which showed the association of MetS and primary hypothyroidism in the urban population. According to our present study, MetS patients with higher BMI are more prone for having associated subclinical hypothyroidism. Therefore, a TSH below 2.5 mU/l was proposed to be associated with a favorable metabolic profile. Though there have been enough reports earlier on insulin resistance in hyperthyroidism, studies by Rochon *et al* and Stanicka *et al*, have demonstrated that hypothyroidism can also lead to insulin resistance. Subclinical hypothyroidism has also been demonstrated to cause insulin resistance in a few studies.

## CONCLUSION

There is significant association between subclini5al hypothyroidism and MetS. It is advisable to assess the thyroid function in all patients with MetS because unless hypothyroidism is excluded, a large number of patients with thyroid dysfunction will be mislabeled as MetS, which will influence the management of these cases.

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