ORIGINAL ARTICLE

The prevalence of **thyroid dysfunction** among South Indian women with **Metabolic Syndrome**

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ABSTRACT

Metabolic syndrome and thyroid dysfunction are independent risk factors of atherosclerotic cardiovascular disease and the co-existence of the two will substantially increase cardiovascular risk.

In the present study, our aim was to investigate the prevalence of thyroid dysfunction in women with metabolic syndrome in a South Indian population.

This study was carried out in a tertiary care teaching hospital in Chennai city, South India. The study protocol was approved by the institutional ethics committee and informed consent was obtained from all the participants at the start of study. Seventy six females with metabolic syndrome (NCEP – ATP III criteria) were included in the study. After obtaining the demographic data, fasting blood samples were obtained from the subjects and glucose, total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL) and triglyceride levels were estimated. The serum thyroid stimulating hormone and free thyroxine levels were also measured.

Of the seventy six patients 53% had subclinical hypothyroidism, 25% had overt hypothyroidism and 22% were euthyroid. Overt hyperthyroidism was not present in any of the patients. The mean age of the study group was 52.68, with a standard deviation of 10.20. Women in the 40-60 year age group had a higher incidence of thyroid dysfunction as compared to those in the other age groups.

Our study indicates the higher prevalence of thyroid hypofunction in South Indian women with metabolic syndrome and thus it necessitates the need for evaluating the thyroid status in women with metabolic syndrome.

Key Words: Metabolic syndrome, Thyroid dysfunction, Subclinical hypothyroidism

INTRODUCTION

Metabolic syndrome (MetS) is generally characterized as a clustering of the abnormal levels of blood lipids (low HDL and high triglycerides), impaired fasting glucose, elevated blood pressure, and excess abdominal obesity [1].

Insulin resistance is supposed to be the central pathophysiological phenomenon underlying this clustering [2].

Obesity, insulin resistance, physical inactivity, advanced age and hormonal imbalance have been suggested as the underlying risk factors for the development of this syndrome [3].

Metabolic syndrome (MetS) affects approximately one quarter of the population in developed countries. People with metabolic syndrome are at an increased risk of atherosclerotic cardiovascular disease and type 2diabetes [4].

Several studies have reported that higher TSH (thyroid stimulating hormone) concentrations are associated with a higher likelihood for the occurrence of metabolic syndrome, especially in females. Additionally, thyroid disease, especially overt hypothyroidism, is associated with atherosclerotic cardiovascular disease. Since metabolic syndrome and thyroid dysfunction are independent risk factors of atherosclerotic cardiovascular disease (CVD), the concurrent existence of the two will substantially increase the risk of CVD. Several studies have shown a significant association which links metabolic syndrome with subclinical and overt hypothyroidism and the association seems to be more in females. Uzunlulu et al [5] reported that the prevalence of subclinical hypothyroidism was more in females with metabolic syndrome. The HYOGA study reported that hypercholesterolaemic women above 50 years of age with subclinical hypothyroidism, had symptoms of hypothyroidism and a poorer quality of life, even when the TSH value was less than 10mIU/L[6].

In a study by Bauer DC et al, it was shown that among older white women, high TSH levels were associated with deleterious changes in serum lipids and that women with multiple lipid abnormalities were twice as likely to have increased TSH levels [7].

The present study was carried out to assess the prevalence of thyroid dysfunction in female patients with metabolic syndrome in a South Indian population.

MATERIALS AND METHODS

This study included seventy six female patients who attended the medicine outpatient department at a tertiary care teaching hospital in Chennai, who were diagnosed with metabolic syndrome. The study protocol was approved by the institutional ethics committee and informed consent was obtained from all the participants at the start of the study. The diagnosis of metabolic syndrome was based on the criteria by the American National Cholesterol Education Program Adult III Treatment Panel (NCEP-ATP III) [8].

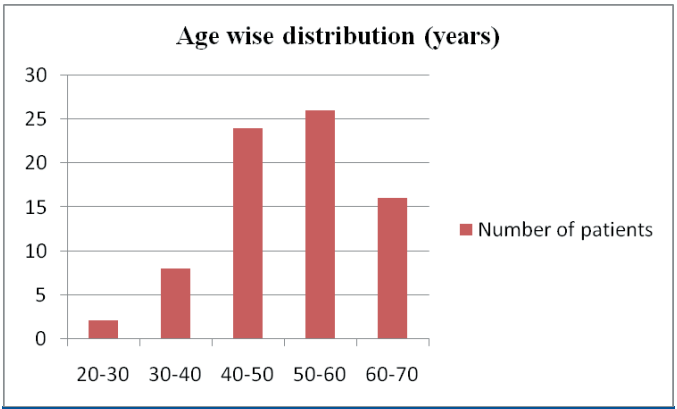
The participants were classified as having MetS if they had at least 3 components of an NCEP ATP III definition of MetS: (1) a fasting glucose level of 110 mg/dL or greater (to convert to mmol/L, multiplied by 0.0555), (2) a fasting triglycerides level of 150 mg/dL or greater, (3) an HDL level less than 50 mg/dL (to convert to mmol/L, multiplied by 0.0259), (4) a blood pressure of 130/85 mm Hg or greater on pharmacological treatment for hypertension, and (5) waist circumference > 88 cms. At the baseline, the demographic data was collected and a detailed physical examination was done.

The blood pressure was measured in the right arm in the supine position. 3 readings were taken and the mean value of the 3 readings was taken as the final recording. If the patient was a known hypertensive or if she was on antihypertensives, one reading was taken as the final one. The waist circumference was measured at the plane between the anterior superior iliac spines and between the lower costal margins at the narrowest part of the waistline while the patient was standing and during slight expiration. The fasting blood samples were collected, following an overnight fast of a minimum of 8 hours and the glucose, total cholesterol, HDL cholesterol, LDL cholesterol and triglyceride levels were estimated. The serum TSH and FT4 measurements were also made.

A high serum TSH level and a normal free thyroxine (FT4) level were required for the diagnosis of sub-clinical hypothyroidism (SCH). The patients were classified as overt hypothyroid when the TSH levels were high (TSH > 10 µIU/ml) and when the FT4 levels were low (FT4 < 0.93 ng/dl). Patients with normal TSH (0.27-4.2 µIU/ml) and FT4 (0.93-1.7)ng/dl levels were considered to be euthyroid. Patients who are taking any medication that could alter the thyroid functions or the lipid levels and pregnant women were excluded from the study, as were patients with renal disorders, liver disorders and congestive cardiac failure. Statistical analysis was done by using the SPSS software, version 17.1

RESULTS

This study included seventy six female patients with metabolic syndrome. Their mean age was 52.68 ± 10.20. The age group distribution is shown in [Table/Fig 1]. The general characteristics of the study patients are described in . [Table/Fig 2]

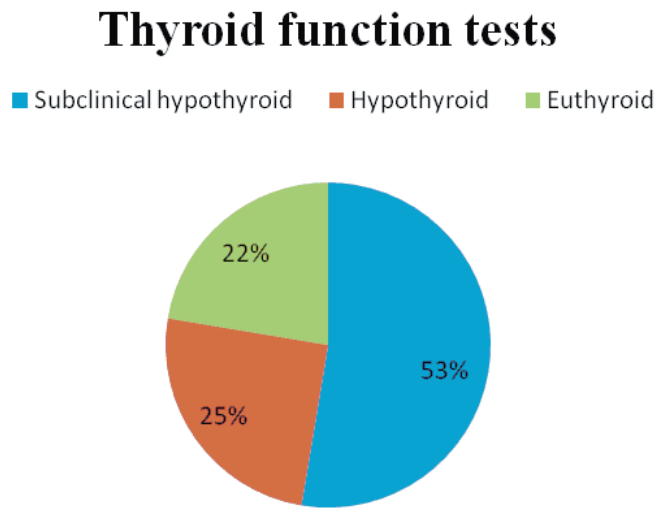


[Table/Fig 1]: Age group distribution is shown

Characteristics	Mean ± SD
Age(years)	52.68 ± 10.20
Waist circumference (inches)	37.76 ± 1.99
Systolic BP (mmHg)	135.26 ± 17.47
Diastolic BP (mmHg)	87.23 ± 12.02
Fasting Blood Glucose (mg/dl)	144.06 ± 51.70
Postprandial Blood glucose (mg/dl)	209.63 ± 63.72
Triglycerides (mg/dl)	182 ± 69.63
HDL (mg/dl)	48.65 ± 25.08
LDL (mg/dl)	122.63 ± 51.67
FT4 (ng/dl)	1.16 ± 0.32
TSH(µIU/ml)	10.92 ± 21.09

[Table/Fig 2]: Patient Characteristics

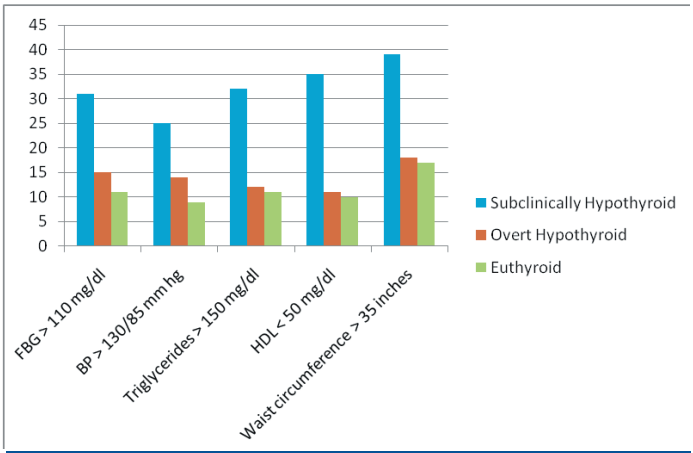
Of the seventy six patients 53% had subclinical hypothyroidism, 25% had overt hypothyroidism and 22% were euthyroid [Table/Fig 3]. None of them had overt hyperthyroidism. shows the distribution of the components of the metabolic syndrome in the study patients. The association of each component of the metabolic syndrome with thyroid dysfunction is demonstrated in [Table/Fig 4]. Women with a waist circumference of more than 88 centimetres (35 inches) had a higher incidence of thyroid dysfunction as compared to the other components. Among the different age groups, women in 40-60 year age group had a higher incidence as compared to the other age groups. [Table/Fig 5]



[Table/Fig3]: Thyroid function tests

Component	Percentage (%)
Blood Pressure > 130/85 mm Hg	63
Triglycerides > 150 mg/dl	72
HDL <50 mg/dl	73
Obesity waist circumference > 35 inches (88cm)	97
Fasting Blood glucose > 110 mg/dl	75

[Table/Fig 4]: Distribution of components of Metabolic Syndrome



[Table/Fig 5]: Association of components of metabolic syndrome with thyroid dysfunction

DISCUSSION

Metabolic syndrome is a cluster of cardiometabolic risk factors and it is characterized by inflammation [5].

Our study revealed that the prevalence of thyroid dysfunction was more among the females with metabolic syndrome. Subclinical

hypothyroidism was present in 53% of the cases and overt hypothyroidism was present in 25% of the patients. Uzunlulu et al also reported a high prevalence of subclinical hypothyroidism among the females with metabolic syndrome in their series. In a study by RV Jayakumar et al [9], it was reported that 60 percent of the cases with metabolic syndrome had thyroid function abnormalities in their case series. In a study by BM Singh et al, they found a significant positive correlation between the TSH and insulin levels, as well as between the TSH and HOMA IR (Homeostasis model of assessment) levels in the female population who was suffering from both SCH and OH [10].

The Rotterdam study [11] found a 10.8 % prevalence of subclinical hypothyroidism among elderly women and The Frementle Diabetes study found a 8.6% prevalence among women with type 2 diabetes [12].

In our study, the females in the 40-60 year age group had a higher incidence of thyroid dysfunction as compared to the other age groups. Our results were comparable with those of the above mentioned study. The incidence of thyroid dysfunction was more in patients with more than three components of the metabolic syndrome. The mean waist circumference which was noted in females with metabolic syndrome and thyroid dysfunction was 37.81 inches as compared to 37.50 inches in euthyroid females with metabolic syndrome. Uzunlulu et al also noted a higher mean waist circumference in patients with metabolic syndrome and subclinical hypothyroidism. In our study, among the components of the metabolic syndrome, women with a waist circumference > 35 inches (88 centimetres) had a higher incidence of thyroid hypofunction.

The thyroid disease is much more prevalent in women than in men. The prevalence of the thyroid disease in patients with diabetes is significantly higher than that in the general population [13].

This indicates a possible interplay between the thyroid status and insulin sensitivity. The main pathophysiological basis underlying the metabolic syndrome has been attributed to insulin resistance. Insulin resistance is a cardinal feature of type 2 diabetes mellitus and an increased risk of dyslipidaemia along with relatively frequently found mild thyroid dysfunction. Insulin resistance leads to an increased production of hepatic cholesterol and very low density lipoproteins (VLDL) and an increased HDL cholesterol (HDL-C) clearance [10].

Bakker et al suggested that insulin resistance augments the deleterious effect of hypothyroidism on the lipid profile [14].

Sub-clinical hypothyroidism (SCH) and overt hypothyroidism (OH) are established risk factors for insulin resistance, hyperlipidaemia, hypercoagulability and low grade inflammation [15], [16].

Several studies have proved the association between insulin resistance and hypothyroidism for overt hypothyroidism, but the association between insulin resistance and subclinical hypothyroidism remains unclear. It is known that overt hypothyroidism leads to an increase in the plasma cholesterol levels. The complex interplay between thyroid function and insulin resistance has been implicated in diabetic dyslipidaemia [10].

In a cross sectional study in 47 healthy euthyroid subjects, it was found that the concentrations of free Tri-iodothyronine (FT3) were associated with insulin production and hyperinsulinaemia [17].

The association between dyslipidaemia with thyroid hypofunction is well established. Over 90% of the overtly hypothyroid patients have hyperlipidaemia. The thyroid hormone is known to play a role in regulating the synthesis, metabolism, and the mobilization of lipids. In patients with overt hypothyroidism, there is an increase in serum total cholesterol, low-density lipoprotein (LDL) cholesterol, apolipoprotein B, lipoprotein (a) [Lp(a)] levels, and possibly, triglyceride levels[18].Normally, thyroid hormones increase the expression of the cell surface LDL receptors, thus leading to LDL clearance from the serum. In hypothyroidism, the depletion of the thyroid hormones leads to a reduced number of LDL receptors in the liver, thereby decreasing the biliary excretion of cholesterol, thus resulting in elevated serum LDL and VLDL levels. It also decreases the lipoprotein lipase activity and causes hypertriglycridaemia [9].

Cardiovascular manifestations are frequent in thyroid dysfunction. Overt hyperthyroidism induces a hyperdynamic cardiovascular state which is associated with an increased heart rate, enhanced left ventricular systolic and diastolic function and an increased prevalence of atrial fibrillation, whereas the opposite changes occur in overt hypothyroidism [9].

Atrial fibrillation, the most common complication of hyperthyroidism, occurs in approximately 15% of the patients. It is more common among men and in those with advancing age (25 to 40% in individuals over the age of 60 years).Subclinical hyperthyroidism (low-TSH) is associated with a > 3 times increase and a risk of developing atrial fibrillation [19].

Patients with subclinical hypothyroidism are at an enhanced risk for atherosclerosis and myocardial manifestations and thus, the thyroxine replacement in these patients has a beneficial effect on the low density lipoprotein cholesterol levels and the clinical symptoms of hypothyroidism. An improvement in the low density lipoprotein cholesterol levels in turn reduces the cardiovascular mortality by 9-31% [20], [21].

Since the prevalence of hypothyroidism (subclinical and overt) is more among females with metabolic syndrome as evident from our study, early detection and thyroxine replacement could reduce the significant cardiovascular risk in these patients. However, there is still a controversy whether the patients with subclinical hypothyroidism would be benefited from thyroxine replacement.

CONCLUSION

It can be concluded that females with metabolic syndrome have a higher prevalence of thyroid dysfunction which predisposes them to cardiovascular events. Therefore, we recommend the routine screening of the thyroid function in females with metabolic syndrome.

FUTURE RECOMMENDATION

This is a preliminary report which was aimed to find the prevalence of thyroid dysfunction among South Indian women with metabolic syndrome. Future studies with a larger sample size may be considered.

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