



METABOLIC SYNDROME AND THYROID DYSFUNCTION

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ABSTRACT **BACKGROUND:** Prevalence of metabolic syndrome is increasing all over the world, more so in developing countries like India. The plethora of metabolic abnormalities in Metabolic syndrome is associated with increased risk for atherosclerotic cardiovascular disease, Cerebrovascular disease, type 2 diabetes mellitus, Renal disease etc. Metabolic syndrome (MetS) and hypothyroidism are well-established forerunners of atherogenic cardiovascular disease. Relationship between thyroid dysfunction and metabolic syndrome is less known.

MATERIALS AND METHODS: We studied 70 patients (who fulfilled three or more of the NCEP ATP III National Cholesterol Education Programme – Adult Treatment Panel III criteria to define the metabolic syndrome) and 70 healthy individuals as controls. Clinical Examination Anthropometry, Thyroid function Test, Metabolic profile including Insulin levels were done in both groups. All the patients (group I) had insulin resistance as per the HOMA IR (the homeostasis model for insulin resistance) model.

RESULTS: T3 and T4 levels were comparable in patients and controls. There was a significant increase in TSH levels in patients as compared to the controls. This increased TSH is probably due to thyroid receptor resistance to TSH and may be a part of metabolic syndrome rather than a state of hypothyroidism.

KEYWORDS :

INTRODUCTION

Metabolic syndrome (MetS) and hypothyroidism are well-established forerunners of atherogenic cardiovascular disease.¹

There is increased prevalence of metabolic syndrome all over the world.^{2,3} Thyroid disorders are associated with many atherosclerotic cardiovascular disease.^{4,5} Thyroid hormones accelerate metabolic process and may be associated with increased chance of atherosclerosis related heart diseases. Relationship between thyroid dysfunction and metabolic syndrome is less known.^{6,7}

Thyroid dysfunction is defined on the basis of altered serum thyroid stimulating hormone (TSH) level with normal or altered levels of triiodothyronine (T3) and thyroxine (T4).⁸ On the other hand, slow metabolism in subclinical hypothyroidism can result to obesity.⁹ For establishing the diagnosis of subclinical hypothyroidism it was proposed by national academy of clinical biochemistry (NCAB) to lower down the upper range limit of TSH to 2.5 microIU/L.¹⁰

Metabolic Syndrome and thyroid dysfunction share common abnormalities such as central obesity, impaired blood glucose, hypertension, decreased high density lipoprotein and elevated triglycerides and acts as individual risk factors of atherosclerotic cardiovascular disease.^{10,11,12} A cross sectional analyses showed significantly higher risk of CVD in sub clinical hypothyroid subjects than euthyroid subjects.¹³ Subclinical hypothyroidism with a thyroid stimulating hormone more than 10 mIU/l was significantly associated with increased odds of prevalent metabolic syndrome.^{14,15,16}

Present study is conducted to know association between thyroid function tests and metabolic syndrome.

AIMS AND OBJECTIVES

To study the association between Thyroid Function tests and Metabolic syndrome.

METHOD OF COLLECTION OF DATA

70 patients (group I) who presented with features of Metabolic syndrome, as per NCEP ATP III criteria, were evaluated for Thyroid disorder clinically and tested for their TSH, T3, T4 levels. Similarly age and sex matched, 70 control subjects (group II) also were also evaluated for thyroid function tests. The patients were selected from the O.P.D as well as from indoor of Maharishi Markandeshwar Institute Of Medical Science And Research Hospital.

INCLUSION CRITERIA

Patients with features of metabolic syndrome according to NCEP ATP

III criteria {At least 3 out of 5 criteria}
NCEP: ATP III 2001¹⁷

Three or more of the following:

Central obesity: Waist circumference ≥ 102 cm in males or ≥ 88 cm in females

Hypertriglyceridemia: triglycerides ≥ 150 mg/dl

Low HDL cholesterol < 40 mg/dl (males) or < 50 mg/dl (females)

Hypertension : blood pressure ≥ 130 mm systolic or ≥ 85 mm diastolic

Fasting plasma glucose ≥ 100 mg/dl.

Exclusion criteria

Patients With primary Thyroid disorder, who had irradiation of Thyroid gland, who had undergone thyroidectomy / thyroid surgeries or On Anti-thyroid drugs, drugs that alter thyroid functions and lipid levels such as Statins, Lithium, Amiodarone, Oral contraceptive pills, with Liver disorders with Renal disorders, in Congestive cardiac failure, Pregnant women

STUDY DESIGN

Anthropometric parameters, thyroid function tests, lipid profile, blood glucose and serum insulin levels:-

Body weight (kg) and height (m) were measured using standardised techniques and equipments. The BMI were calculated as weight in kgs divided by squared height in metres. $BMI = \text{weight(kgs)} / (\text{height in metres})^2$. The waist circumference were measured with a measuring tape, placed horizontally at the level of umbilicus in standing position. Hip circumference was measured at the level of greater trochanter. Blood pressure was measured from left arm in the sitting position with sphygmomanometer apparatus being placed at the level of heart. Venous blood sample were taken after 8 hours of fasting, separated and frozen at -8 degree Celsius until analysis. The serum levels of TSH (reference range 0.17–4.05 μ IU/ml), T3 (reference range, 70–200 ng/dl) and T4 (reference range 5.5–13.5 μ IU/dl) were measured as indicators of thyroid function by chemiluminescence immunoassay method.

Fasting serum concentrations of triglycerides were measured by using TGL method on Dimension® clinical chemistry system and HDL will be measured using Automated HDL cholesterol method on the Dimension® clinical chemistry system.

Blood sugar levels (reference range, 60–100 mg/dl) were estimated by the glucose oxidase-peroxidase (GOD-POD) method using the glucose analyzer. Serum insulin levels were measured by

chemiluminescence immunoassay method. To define the insulin resistance, homeostasis model assessment for insulin resistance (HOMAIR) were calculated by following formula: (Fasting blood glucose mg/dl x fasting serum insulin mIU/l).

RESULTS

Among 70 patients, 25 (35.7%) were males and 45 (64.3%) were females. 32 (45.7%) of patients were between 30-45 years, followed by 31 (44.3%) subjects between 46-60 years.

Table 1 : Distribution Of Patients According To The Thyroid Status

| Thyroid status | Frequency | Percent |
|--------------------------|-----------|---------|
| Euthyroid | 40 | 57.1 |
| Hypothyroid | 8 | 11.4 |
| Subclinical Hyperthyroid | 6 | 8.6 |
| Subclinical Hypothyroid | 16 | 22.9 |
| Total | 70 | 100.0 |

Table 2: Comparison Of Variables Between Metabolic Syndrome And Control Group

| | Group | N | Mean | Std. Deviation | Mean difference | P-value |
|--------|---------|----|--------|----------------|-----------------|---------|
| BMI | Control | 70 | 21.641 | 1.689 | -8.905 | <0.001* |
| | Mets | 70 | 30.546 | 2.445 | | |
| WC(cm) | Control | 70 | 82.871 | 7.991 | -11.343 | <0.001* |
| | Mets | 70 | 94.214 | 6.752 | | |

Difference In Components Of Metabolic Syndrome Among Thyroid Dysfunction Subgroups

| | Euthyroid (n=40) | | Hypothyroid (n=8) | | Subclinical Hyperthyroid (n=6) | | Subclinical Hypothyroid (n=16) | | F-value | P-value |
|---------|------------------|----------------|-------------------|----------------|--------------------------------|----------------|--------------------------------|----------------|---------|----------|
| | Mean | Std. Deviation | Mean | Std. Deviation | Mean | Std. Deviation | Mean | Std. Deviation | | |
| WC(Cms) | 92.98 | 7.395 | 94.63 | 4.984 | 91.33 | 3.615 | 98.69 | 4.990 | 3.460 | 0.021* |
| SBP | 140.60 | 13.581 | 134.50 | 6.024 | 131.67 | 4.082 | 138.50 | 5.774 | 1.597 | 0.199 NS |
| DBP | 89.98 | 6.294 | 92.50 | 8.864 | 88.17 | 4.997 | 89.31 | 6.478 | 0.599 | 0.618 NS |
| FBS | 144.65 | 42.122 | 141.00 | 21.831 | 150.33 | 45.680 | 144.75 | 20.940 | 0.074 | 0.974 NS |
| HDL | 46.83 | 5.957 | 44.50 | 5.099 | 44.17 | 4.262 | 44.56 | 6.880 | 0.893 | 0.450 NS |
| TGL | 196.60 | 83.263 | 186.63 | 65.589 | 178.33 | 32.807 | 237.19 | 95.414 | 1.299 | 0.282 NS |

* denotes significant if p-value <0.05 NS- denotes not significant if p-value >0.05

This table shows the comparison of different components of metabolic syndrome between thyroid dysfunction groups using One-Way ANOVA. Only the waist circumference showed statistically difference between the different thyroid group with p-value 0.021.

Table 3 Comparison According To The Metabolic Syndrome Criteria And Thyroid Status

| Criteria | No Of Patients | Euthyroid | Subclinical Hypothyroid | Hypothyroid | Subclinical Hyperthyroid |
|----------|----------------|-----------|-------------------------|-------------|--------------------------|
| 3 | 20 | 19 | 0 | 1 | 0 |
| 4 | 27 | 18 | 6 | 1 | 2 |
| 5 | 23 | 3 | 10 | 6 | 4 |

There are 23 patient fulfilling all the 5 criteria. Among them the maximum patient are of subclinical hypothyroid, followed by hypothyroid, subclinical hyperthyroid and then euthyroid. Then there are 20 patients fulfilling 3 criteria. Among them maximum patients that is 19 are having euthyroid status followed by hypothyroid.

DISCUSSION

In the present study there were 70 patients. Among them 35.7 % were male and 64.3 % were female. The maximum patients were female. These observations are in accordance of the studied conducted by Mehra et al in 2017, Jyalal et al in 2015, Shah Y et al in 2015, Uzunlulu et al in 2007.¹⁸ However in the study conducted by Senthil N et al in 2015, Khatiwada S et al in 2016 the maximum number of patients were male.

In our study majority of the patient with metabolic syndrome were seen in the age group of 30-60 years. Similar results were observed in studies conducted by Aggarwal G et al in 2011, Jyalala JA et al in 2015 and Srikanth N et al in 2016.

In the present study comparing the metabolic syndrome criteria, maximum number of patients (27) were fulfilling 4 criteria and out of

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|-----|---------|----|---------|--------|---------|---------|
| SBP | Control | 70 | 124.457 | 9.437 | -14.200 | <0.001* |
| | Mets | 70 | 138.657 | 11.173 | | |
| DBP | Control | 70 | 81.357 | 5.618 | -8.600 | <0.001* |
| | Mets | 70 | 89.957 | 6.513 | | |
| FBS | Control | 70 | 84.414 | 9.819 | -60.329 | <0.001* |
| | Mets | 70 | 144.743 | 36.084 | | |
| HDL | Control | 70 | 51.186 | 5.248 | 5.257 | <0.001* |
| | Mets | 70 | 45.929 | 5.967 | | |
| TGL | Control | 70 | 134.500 | 8.038 | -68.671 | <0.001* |
| | Mets | 70 | 203.171 | 82.406 | | |
| T3 | Control | 70 | 138.443 | 21.311 | -18.429 | <0.001* |
| | Mets | 70 | 156.871 | 24.556 | | |
| T4 | Control | 70 | 6.211 | 1.026 | -0.529 | 0.018* |
| | Mets | 70 | 6.740 | 1.528 | | |
| TSH | Control | 70 | 2.921 | 0.834 | -1.725 | 0.001* |
| | Mets | 70 | 4.646 | 4.321 | | |

*denotes statistically significant p<0.05 NS- denotes not statistically significant p>0.05

In above table when we compared the patient of metabolic syndrome with patient of control group there is statistically significant result of all the criteria except the age.

The Euthyroid subjects age is 50.05±9.640, Hypothyroid subjects age is 47.50±9.666, Subclinical Hyperthyroid subjects age is 47.17±6.795 and Subclinical Hypothyroid subjects age is 47.69±7.956. The age difference is not found statistically significant with p-value 0.72

them 18 were euthyroid and 6 were of subclinical hypothyroidism. Patients fulfilling 3 criteria were 20 in number where almost all the patients were euthyroid. It is observed that hypothyroidism is associated with all the parameters of metabolic syndrome.

More than 60% of hypothyroid patients have obesity, there is decrease in basal metabolic rate and energy metabolism in hypothyroidism¹⁹. In hypothyroidism, systemic vascular resistance is increased and results in hypertension²⁰. Rotterdam study suggested that there was a two fold increase in risk of atherosclerosis in hypothyroid patients²¹. Both the synthesis and degradation of lipids are depressed in hypothyroidism, the latter especially so, the net effect being one of the lipid accumulation, especially of LDL cholesterol and triglycerides²². Glucose intolerance in hypothyroidism is not proved in latest studies, though Shah et al. published insulin metabolism in hypothyroidism in 1975 indicating that glucose intolerance of the hypothyroid state is not characterized by insulin resistance. Aneemieke Ross et al. in 2007 found that free T4 was significantly associated with insulin resistance and with four of five components of the metabolic syndrome (except glucose intolerance)²⁴.

SUMMARY & CONCLUSION

The present study "Study of thyroid function tests in metabolic syndrome" was conducted at M. M Institute of Medical Sciences and Research. In our study 70 patients of metabolic syndrome along with the age and sex matched control group were studied.

Among patients of metabolic syndrome, majority (40) were euthyroid followed by subclinical hypothyroid (16). And subclinical hypothyroid was more common in females than males. The mean value of waist circumference and triglycerides was more in subclinical hypothyroid patients. Diastolic blood pressure was more in hypothyroid group. It is concluded that metabolic syndrome is more common in females and in the age group of 30-60 years. Thyroid dysfunction in patients of metabolic syndrome as seen in present study can predispose them to cardiovascular events and hence, it is suggested that routine screening of thyroid functions especially in females with metabolic syndrome should be done.

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