A cross-sectional study of thyroid dysfunction in metabolic syndrome patients and its correlation with the components of metabolic syndrome

H L Vishwanath¹, V Supriya¹,*, Anitha M¹

¹Dept. of Biochemistry, Bangalore Medical College and Research Institute, RGUHS, Bangalore, Karnataka, India

ABSTRACT

Introduction: 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.

Objectives: To assess the thyroid status in MetS in comparison to healthy controls. To correlate the components of MetS with thyroid status.

Materials and Methods: This study was conducted on 35 patients with metabolic syndrome (NCEP ATP III criteria) and 35 healthy controls in Bowring & Lady Curzon Hospital, attached to BMCRI, Bangalore. Waist circumference and blood pressure were measured. Fasting blood glucose (FBS), lipid profile were assayed in auto analyser and thyroid function test was performed by immunoassay. Statistical data analysis was done using Student t-test and Pearson correlation coefficient.

Result: The mean value of the factors of MetS showed significant differences between the cases and controls. TSH was significantly higher (P = 0.0307) in the MetS group than in the control group, whereas T₃ and T₄ levels were not significant. Increased waist circumference positively correlated with increased TSH and was statistically significant. FBS, HDL, blood pressure negatively correlated with higher TSH while triglyceride positively related with increased TSH but none of them were statistically significant.

Conclusion: Thyroid dysfunction, predominantly subclinical hypothyroidism was seen more frequent in patients with metabolic syndrome. Hence it is important to screen patients having metabolic syndrome for thyroid dysfunction in order to prevent the cardiovascular related mortality.

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LDL oxidation and platelet aggregation clearly increasing the risk of developing cardiovascular risk.4

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.8 Thyroid hormone has diverse metabolic effects including increased gluconeogenesis, glycogenolysis, regulation of cholesterol synthesis and fat mobilisation.9 Thyroid dysfunction resulting in cardiovascular abnormalities by its effect on cardiac output and cardiac rhythm is well documented.10,11

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.

2. Materials and Methods

The study was a cross sectional study carried out in May-July 2018 at Bowring & Lady Curzon Hospital, attached to BMC&RI on subjects aged between 18 -70 years attending outpatient department. Patients with diabetes related complications, those having liver and renal dysfunction, on corticosteroids or other medication that alters lipid, glucose or thyroid parameters, pregnant women, those with history of cardiovascular disease were excluded from the study. After obtaining consent, the waist circumference and BP measurements were taken. Study group were requested to give sample after overnight fasting. Under aseptic conditions, 5ml blood was drawn in plain vacutainers and was assayed after centrifugation. Fasting blood glucose and lipid profile was estimated by enzymatic assay in fully automated clinical chemistry analyser (Beckman Coulter AU480). Subjects who as per NCEP ATP III criteria had the presence of any 3 of the 5 following components namely

1. Waist circumference more than 40 inches (102 cm) in male and 35 inches (88 cm) in female
2. Fasting blood glucose more than 100 mg/dl or on treatment
3. Triglycerides more than 150 mg/dl or on treatment
4. HDL cholesterol less than 40 mg/dl in males and less than 50 mg/dl in females.
5. Systolic more than 130 mmHg and diastolic more than 85 mmHg or on treatment

were grouped as cases and subjects who were healthy and normal were grouped as controls. A total sample size of 70 (35 cases of MetS matched with 35 controls) were included in the study. T3, T4 and TSH was analysed by chemiluminiscence assay in Access-2 hormone analyser. The biochemical assays were routinely monitored through internal and external quality programs. Subjects were classified into one of the following 5 groups: euthyroid, hypothyroid, hyperthyroid, subclinical hypothyroid or subclinical hyperthyroid based on guidelines of diagnosing thyroid dysfunction.12

The factors of Met S were expressed as mean ± SD and significance was tested by Student t test. Pearson correlation coefficient was used to correlate the components of Met S and thyroid function test.

3. Results

The study population comprised of 54.2% male and 45% female among controls whereas cases had a slight female predominance with 57.1% being female and 42.8% being male. The mean age of the study population was 50.4 ± 10.1 among cases and 47.5 ± 9.15 among controls. The mean fasting blood glucose, waist circumference, triglyceride levels, high density lipoprotein, systolic and diastolic blood pressure which are the components of Met S in cases and controls are shown in table 1. Difference of each of the component of Met S between the patients of Met S and control was tested using Student t-test. Significant difference with p value < .00001 was observed in each of the component of Met S between cases and controls as shown in Table 1.

Thyroid profile comprising of T3, T4 and TSH was assessed in the study group. TSH showed significant difference (p= 0.03) with the mean TSH in cases group as 8.16 ± 2.96 and in control as 2.4 ± 0.34 whereas T3 and T4 showed no significant difference between both the groups shown in Table 2. Subclinical hypothyroidism (SCH) is the predominant pattern of thyroid dysfunction observed in 22.8 % of patients having Met S, followed by overt hypothyroidism in 5.7% as shown in while there where were no cases of overt hyperthyroidism as in Figure 1.

The correlation of TSH with the components of Met S was assessed using Pearson correlation coefficient. Waist circumference positively correlated with high TSH and was statistically significant (p = 0.03). Fasting blood glucose, HDL and blood pressure negatively correlated while triglyceride showed positive correlation with high TSH but none of them were statistically significant as given in Table 3.

4. Discussion

Our study showed significant difference in the mean values of the baseline characteristics of Met S between the cases and controls. Similar finding s were obtained in study by Meher et al13 and Gywali et al14 where all the biochemical and anthropometric measurement relating to the components of Met S was significantly higher in the
The comparison of components of MetS among cases and controls is shown in Table 1:

| Parameters                      | Cases (Mean ± SD) | Controls (Mean ± SD) | ‘p’ Value |
|--------------------------------|------------------|---------------------|-----------|
| Fasting blood glucose (mg/dl)  | 216 ± 76.6       | 88.7 ± 9.4          | <.00001**** |
| Waist circumference (inches)   | 39.9 ± 2.66      | 31.9 ± 2.19         | <.00001**** |
| Triglycerides (mg/dl)          | 203.75 ± 72.2    | 110.2 ± 30.08       | <.00001**** |
| HDL (mg/dl)                    | 32.79 ± 7.2      | 40.5 ± 6.7          | <.00001**** |
| Systolic blood pressure (mmHg) | 142.8 ± 8.98     | 121.4 ± 8.08        | <.00001**** |
| Diastolic blood pressure (mmHg)| 95.41 ± 5.2      | 79 ± 4.6            | <.00001**** |

Table 2: Comparison of thyroid profile among cases and controls

| Parameters  | Cases (Mean ± SD) | Controls (Mean ± SD) | ‘p’ Value |
|-------------|------------------|---------------------|-----------|
| T3 (ng/ml)  | 0.84 ± 0.17      | 0.88 ± 0.22         | 0.1       |
| T4 (μg/dL)  | 9.03 ± 2.6       | 9.2 ± 2.2           | 0.3       |
| TSH (μIU/ml)| 8.16 ± 2.96      | 2.4 ± 0.34          | .0307*    |

Table 3: Correlation of TSH with component of MetS

| Parameter 1 | Parameter 2   | ‘r’ Value | P value |
|-------------|---------------|-----------|---------|
| TSH         | Fasting blood glucose | -0.14     | 0.42    |
| TSH         | Waist circumference | 0.36      | 0.03*   |
| TSH         | Triglycerides   | 0.03      | 0.8     |
| TSH         | HDL            | -0.16     | 0.34    |
| TSH         | Systolic blood pressure | -0.107   | 0.54    |
| TSH         | Diastolic blood pressure | -0.166   | 1.34    |

- * ‘r’ value is negative correlation, + ‘r’ value is positive correlation

Our study showed that the female subjects with MetS had a increased prevalence of TD than those among male subjects, which is in accordance with previous studies carried out by Gywali et al, Katiwada et al., Shantha et al. Our study showed that the female subjects with MetS had a increased prevalence of TD than those among male subjects, which is in accordance with previous studies carried out by Gywali et al, Katiwada et al., Shantha et al. Thus, there is a strong interlink between the components of MetS. In contrast, our study showed that the female subjects with MetS had a increased prevalence of TD than those among male subjects, which is in accordance with previous studies carried out by Gywali et al, Katiwada et al., Shantha et al. Thyroid function test revealed TSH significantly higher in the MetS group. There was no significant difference in levels of T3 and T4 in both groups. Chugh et al concluded on similar findings in his study of thyroid function test in metabolic syndrome patients wherein only TSH showed significant difference between the two groups. In contrast, our study showed that the female subjects with MetS had a increased prevalence of TD than those among male subjects, which is in accordance with previous studies carried out by Gywali et al, Katiwada et al., Shantha et al. Thus, there is a strong interlink between the components of MetS.
study by Gyawali et al showed both TSH and fT4 significantly altered.\textsuperscript{14} TSH being significantly high and T3, T4 being normal in patients with MetS may imply that Met S is associated with an increased risk of SCH. It is well documented that increased TSH has been linked to weight gain and obesity. Increased TSH levels may be attributed to leptin which is an adipocyte derived hormone which is increased in obesity. It is postulated that leptin regulates the Thyrotropin releasing hormone synthesis by its effect on the hypothalamic pituitary axis leading to the subsequent increase of TSH production.\textsuperscript{22,23}

Our study showed Thyroid dysfunction in 28.5% of Met S patients with a high prevalence of subclinical hypothyroidism (SCH) (22.8%) followed by overt hypothyroidism (5.7%). We did not however find any cases of hyperthyroidism. Study carried out in Nepal by Gyawali et al\textsuperscript{14} reported similar prevalence of thyroid dysfunction (31.8%) in Met S with predominant patients having SCH (29.32%) followed by overt hypothyroidism (1.67%) and subclinical hyperthyroidism (0.83%). Most studies on the pattern of thyroid dysfunction in Met S patients have reported the high prevalence of SCH.\textsuperscript{17,18} SCH downregulates GLUT (glucose transporters) and hence decrease the intracellular glucose uptake and also increases gluconeogenesis thus leading to hyperglycemia.\textsuperscript{8} While it is well known that overt hypothyroidism is a hypometabolic state leading to obesity, recent evidences show SCH also being associated with significant weight gain. Thus, the pathophysiology of Met S and SCH seem to have a considerable overlap.\textsuperscript{24,25}

Relationship between the components of Met S and thyroid dysfunction have been largely varied and still not conclusive based on previous studies.\textsuperscript{15,17,18,26} The diverse ethnicity, lifestyle, race, age, gender of the study population maybe be liable for the discrepancy. We, however found no statistically significant correlation between the components of Met S and thyroid hormones, except for waist circumference. In contrast, other studies have shown association of thyroid function to lipid profile and high insulin resistance in turn leading to hyperglycemia.\textsuperscript{19,27} This could be attributed to the smaller sample size in our study. Thus, epidemiological studies on a large study population are required to clearly establish the association between the TD and the component s of Met S. The other limitation being that this being a cross sectional study the cause and effect of the study could not be investigate. Also fT3 and fT4 could have been more accurate to reflect thyroid status.

5. Conclusion

Thyroid dysfunction, predominantly sub clinical hypothyroidism was more frequent in MetS patients. It is thus imperative to screen MetS patients for thyroid dysfunction in order to prevent cardiovascular related mortality.

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None.

7. Conflict of interest

None.

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**Author biography**

**H L Vishwanath** Professor and HOD

**V Supriya** Post Graduate

**Anitha M** Assistant Professor

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