# THYROID HORMONE PROFILE IN METABOLIC SYNDROME

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**Abstract: Background and objectives:** Metabolic syndrome (MetS) refers to complex of several cardiovascular risk factors. Subclinical as well as overt hypothyroidism are recognized risk factors for atherosclerotic cardiovascular disease (CVD) and hyperlipidemia. **Aim:** To investigate relationship of thyroid hormone profile with MetS**. Material and methods**: Total 60 subjects (23 males and 37 females) were included in the study. NCEP-ATP III criteria were employed for labeling MetS. Serum T3, T4 and TSH levels were measured**. Results**:- Mean age of the subjects was 42.8±9.06 years and mean BMI was 35.6±3.6. Waist circumference and waist-to-hip ratio (WHR) of the subjects (males as well as females) were more than their respective cut off criteria. Subjects from both genders had S. Cholesterol >200 mg/dl. Mean Serum Triglyceride (TG) was 208.4±61.3 mg/dl. **Conclusion**:- Overall, Subclinical Hypothyroidism (SCH) and overt hypothyroidism were present in 16.7% and 18.3% of the subjects and rest 65% were euthyroid. SCH and overt hypothyroidism were higher in female MetS subjects.

**Key words:** Thyroid profile, Metabolic syndrome, Subclinical hypothyroidism

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**Introduction:**

MetS is a constellation of inter-related physiological, biochemical, clinical and metabolic abnormalities that include abdominal obesity, atherogenic dyslipidemia, elevated blood pressure, a prothrombotic state and a proinflammatory state in the same individual and is associated with an increased risk of vascular events.

MetS remains a powerful predictor of future cardiovascular disease and type 2 diabetes mellitus (T2DM)[1].

In India, prevalence of MetS is rapidly increasing and the trend is same for other South Asian countries, leading to increased mortality and morbidity due to CVD and T2DM[2]. It has been estimated that 20-25% of South Asians have developed MetS and many more may be prone to it[3].

Thyroid hormones have got direct and indirect effects on metabolism. Obesity and thyroid functions are often correlated. Subclinical as well as overt hypothyroidism are recognized risk factors for atherosclerotic cardiovascular disease, hyperlipidemia, low grade inflammation and hypercoagulability[4].

The subjects were selected from among those attending the Medicine OPD of Government Medical College and Hospital, Jammu. Biochemical parameters were measured with

Since MetS and hypothyroidism are independent risk factors for the same disease process i.e. cardiovascular disease (CVD), it is probable that patients suffering from both these disease entities may have a compounded risk.

In recent years, there have been confusing results on the relationship between thyroid hormone levels within the normal range and cardiovascular risk factors and MetS. Several papers have described a relationship between thyroid hormone parameters and components of MetS[5,6,7].

Various studies have been done on relation between MetS and thyroid function but there is paucity of data from North India[8].

Aim of the present study was to investigate a possible association between thyroid dysfunction and MetS.

**MATERIALS AND METHODS:**

The present study was conducted in the PG Department of Physiology, Government Medical College, Jammu. Total 60 subjects, both males and females were included in the study.

the help of Department of Biochemistry, GMC, Jammu.

The study was undertaken after approval by the Institutional Ethics Committee vide No. IEC/GMC/2019/781 and dated 06-12-2019.

**INCLUSION CRITERIA:**

Subjects fulfilling the NCEP-ATP III, 2001 criteria of MetS, were included in the study[9].

**EXCLUSION CRITERIA:**

Age less than 18 years,
History of liver disorders/renal disorders/congestive cardiac failure
Patients on treatment for Thyroid disorders
Pregnant women.

Detailed explanation of the purpose and methodology of tests were provided to all the subjects. A written informed consent was taken from all the eligible subjects.

All the eligible subjects who volunteered to be part of the study were requested to report to Research Lab of the PG department of Physiology, GMC, Jammu, after an overnight fast. Their physical parameters were recorded and their blood samples were collected by the investigator herself.

**Physical parameters: -**

**Age:** Age was recorded in years as on the previous or next birthday whichever nearer as per the records or statement of the individual.

**Weight, Height, Waist circumference** and **Hip circumference** were measured.

**BMI** and **WHR** were calculated from the above done measurements.

**Blood pressure:** Systolic and Diastolic BP were recorded by the Auscultatory method.

**Biochemical parameters**:

1. **FPG**: Quantitative determination of plasma glucose was done by hexokinase method. It was measured by using fully automated analyzer (Siemens – Dimension Rx L max).

**2. Lipid profile**:-

**a) Serum total cholesterol (TC)**:

**b) Serum Triglycerides (TG)**:

**c) Serum HDL Cholesterol (HDL-C)**:

The above three were measured by chemilumniscent microparticle immunoassay (CMIA) technique, using ARCHITECT c 4000 auto analyzer.

**d) Serum LDL-C**: It was calculated by Friedewald equation[10].

**3. Serum T3, T4 and TSH**: A fully automated immunoassay analyzer was used.

**Statistical Analysis:**

The data obtained was tabulated with the help of Windows Excel and analysis was performed by using SPSS version 22. Student's unpaired t- test was applied to assess the significance. A p-value of $< 0.05$ was taken as statistically significant.

**Results**:- There were total 60 subjects out of which 23 were males and 37 females. Their mean Age was $42.8 \pm 9.06$ years; mean age of the male subjects was $43.2 \pm 9.12$ and that of females was $42.6 \pm 9.13$ years. Difference between the mean age of male and female subjects was not significant ($p = 0.80$).

**Table 1: Anthropometric data of the subjects**

| Parameter | Minimum | Maximum | Mean | SD |
|---|---|---|---|---|
| Weight (Kg) | 70.00 | 153.00 | 90.45 | 11.89 |
| Height (cm) | 143.00 | 178.00 | 159.26 | 6.32 |
| BMI($Kg/m^2$) | 30.12 | 55.03 | 35.65 | 3.67 |
| Waist circumference (cm) | 88.00 | 130.00 | 99.43 | 7.91 |
| Hip circumference (cm) | 92.00 | 138.00 | 106.45 | 7.68 |
| WHR | 0.88 | 0.98 | 0.92 | 0.019 |

**Table 2: Gender wise distribution of weight, height and BMI of the subjects**

| Parameter | Gender | N | Mean | SD | p-value |
|---|---|---|---|---|---|
| Weight (Kg) | Males | 23 | 98.43 | 13.517 | .000 |
| | Females | 37 | 85.48 | 7.365 | .000* |

| | | | | | |
|---|---|---|---|---|---|
| Height (cm) | Males | 23 | 164.82 | 5.702 | .000 |
| | Females | 37 | 155.81 | 3.695 | .000* |
| BMI (Kg/m$^2$) | Males | 23 | 36.27 | 4.528 | .307 |
| | Females | 37 | 35.27 | 3.025 | .354 |

*Statistically significant

Mean SBP of the subjects was 144.0 $\pm$ 12.81 and DBP was 89.47 $\pm$ 5.63 mm of Hg. The difference between the mean SBP, but not the DBP, of males and females was statistically significant (t = 2.29, p = 0.025).

**Table 3: Biochemical parameters of the subjects (n = 60)**

| Parameter | Minimum | Maximum | Mean | SD |
|---|---|---|---|---|
| FPG (mg/dl) | 98.0 | 205.0 | 119.33 | 16.237 |
| S. Cholesterol TC (mg/dl) | 108.0 | 321.0 | 217.89 | 46.115 |
| TG (mg/dl) | 98.0 | 398.0 | 208.48 | 61.358 |
| HDL-C (mg/dl) | 22.0 | 59.0 | 39.94 | 9.4 |
| LDL-C (mg/dl) | 66.0 | 143.0 | 105.62 | 19.92 |
| TSH ($\mu$IU/ml) | 1.6 | 34.8 | 6.3 | 5.291 |
| T3 (ng/ml) | 0.3 | 3.8 | 1.14 | 0.56 |
| T4 ($\mu g/dl$) | 1.72 | 12.7 | 7.95 | 2.943 |

More than 4/5 subjects studied, irrespective of gender, had S. Triglycerides >150 mg/dL with non-significant difference between males and females (p = 0.469).

**Table 4: MetS parameters and Thyroid status of subjects**

| | Euthyroid | | Hypothyroid | | SCH | |
|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | Mean | SD |
| BMI | 34.59 | 1.69 | 38.11 | 6.05 | 37.01 | 2.42 |
| WHR | 0.92 | 0.02 | 0.92 | 0.025 | 0.93 | 0.01 |
| FPG (mg/dl) | 119.32 | 16.65 | 116.50 | 11.93 | 114.10 | 6.83 |
| TC (mg/dl) | 214.84 | 45.68 | 237.25 | 52.55 | 210.90 | 30.42 |
| TG (mg/dl) | 212.71 | 60.72 | 190.0 | 55.64 | 173.1 | 43.02 |
| HDL-C (mg/dl) | 44.06 | 10.20 | 35.50 | 7.0 | 40.67 | 7.17 |
| LDL-C (mg/dl) | 104.44 | 21.24 | 113.0 | 19.76 | 103.78 | 11.89 |

**Discussion**: In the present study, we hypothesized that subclinical hypothyroidism (SCH) may have an impact on the prevalence of MetS. With this aim, we investigated possible relationship of thyroid status with MetS. This study was conducted on 60 subjects fulfilling at least 3 out of 5 NCEP-ATP-III criteria of MetS.

MetS patients were considered to have thyroid dysfunction if the thyroid hormones level fell outside the reference range (free T3 (4.0–8.3 pmol/L), free T4 (9.0–20.0 pmol/L) and TSH level (0.25–5 mIU/L))

Out of 60 subjects 23 (38%) were males and 37 (62%) were females, with M:F ratio of 0.62:1. This is similar to the observations by **Shantha GPS et al., 2009**[11].

Mean age and weight of the subjects were similar to the observations by **Gutch M et al., 2017**[12].

Mean height of subjects in our study was 159.2 ± 6.3 cms. This observation in our study is similar to **Taki K et al., 2008**[13].

Both the waist circumference and WHR of the subjects (males as well as females) were more than their respective cut off criteria. All the subjects studied were in class 1 category of obesity (BMI >30 kg/m$^2$). Similarly, WC of all the subjects was more than the cut-off values as per NCEP-ATP III criteria. These findings are supported by **Shah P et al., 2017**[14].

FPG is a crucial component of MetS. It has been hypothesized that MetS is associated with insulin resistance due to defect in the post-receptor signal transduction in target tissues; a similar mechanism of thyroid receptor resistance might be operating in these obese subjects[15].

It has been proposed by **Menon S, Venugopal R** that good metabolic control of hyperglycemia will prevent alteration of lipid metabolism helping in better prognosis and preventing manifestations of vascular and typical secondary complications[16].

In our subjects, the mean FPG was 119.3±16.2 mg/dl. This is similar to Japanese study by **Taki K et al., 2008**[13] but differs from **Gutch M et al., 2017**[12]. The possible reasons behind this could be a bigger sample size and use of different criteria for MetS i.e. IDF (International Diabetic Federation) in the latter.

Lipids and lipoproteins in circulation have been strongly associated with coronary heart disease (CHD), lipid metabolism disorders and atherosclerosis[17].

Mean TC level, in present work, was 217.8 ± 47.8 mg/dl and this observation is supported by **Shantha GPS et al., 2008**[11].

Pertinently, more than 2/3 of our subjects from both the genders were having S. Cholesterol > 200 mg/dl (**Table 3**).

The principal role of HDL-C in lipid metabolism is the uptake and transport of cholesterol from peripheral tissues to the liver through a process known as reverse cholesterol transport (a proposed cardio protective mechanism)[18].

Mean serum HDL-C levels in our study did not show any gender specific difference (p=0.32). Overall, 75% of all subjects, had decreased levels of HDL-C, a finding similar to that of **Gutch M et al., 2017**[12].

**Singh O (2015)** assessed the relationship between glucose levels and lipid pattern in MetS and found hypertriglyceridemia to be the most common lipid abnormality in these patients[19].

Subclinical hypothyroidism (SCH) is the most common endocrine disease worldwide. SCH is characterized by an elevated concentration of thyroid-stimulating hormone (TSH) above the reference range and normal concentrations of thyroxine (T4) and triiodothyronine (T3)[20].

Combined mean serum TSH, T3 and T4 values were not statistically significant between our male and female subjects.

Systolic blood pressure (SBP) indicates the force of contraction of the heart and thus it represents the work done by the heart in overcoming the resistance in vessels[21].

Combined mean SBP was 144.0 ± 12.81 mmHg but the difference between male and female subjects was significant (p = 0.025).

The observations in our study are supported by **Shah P et al., 2017**[14].

In our study, out of 60 MetS subjects, 10 (16.7%) subjects (3 male and 7 female subjects) had SCH, 11(18.3%) subjects (2 male and 9 female subjects) were overtly hypothyroid and 39 (65%) subjects (18 male and 21 female subjects) were euthyroid.

On comparison, SCH and overt hypothyroidism were significantly higher in females than males.

**Shantha GPS et al., (2009)** found 21.9% subjects to have SCH while 7.4% were overtly hypothyroid and 77.7% were euthyroid[11].

In another study, overall thyroid dysfunction was seen in 31.9 % (*n* = 54) MetS patients; SCH in 26.6% was the major thyroid dysfunction followed by overt hypothyroidism (3.5 %)[22].

**Uzunlulu M et al., 2017** have reported 53.6% SCH prevalence in MetS. The difference between the two studies may be because of large sample size (n=410) in that study[23].

**Limitations of study**:

1) Small sample size: - A larger sample will provide a better picture of association between thyroid profile and MetS.

2) TPOab levels were not measured.

3) Findings from a single center: - A multicentric study will be more informative and same can be planned for future.

**Conflict of Interest:** The authors have no conflict of interest in its preparation and submission for onward publication.

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