

Association of metabolic syndrome with hypothyroidism and hyperuricemia: A cross-sectional study in a tertiary care hospital, Kolkata, West Bengal



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ABSTRACT

Background: Metabolic Syndrome (MetS) (Syndrome X, insulin resistance syndrome, MetS) consists of a constellation of metabolic abnormalities which include central obesity, hyperglycemia, insulin resistance, high triglycerides, low high-density lipoprotein (HDL) cholesterol, and hypertension. Obesity is a critical component of MetS. It causes alteration in the thyroid hormones and hyperuricemia. Furthermore, insulin resistance seen in MetS causes decreased uric acid excretion. **Aims and Objectives:** To study the association of MetS with hypothyroidism and hyperuricemia. **Materials and Methods:** A cross-sectional study was conducted among patients from the outpatient department of General Medicine, IPGME and R, Kolkata from January 2012 to June 2013. A total of 112 patients, consisting of 53 patients with MetS and 59 patients without MetS were selected. Patients' history, clinical and laboratory findings were recorded and data were analyzed. **Results:** Majority (66%) of the patients with MetS were female and the rest were male. The mean Body mass index of patients with MetS was 33.31 ± 4.36 (Mean \pm SD) kg/m² and without MetS was 25.21 ± 2.62 (Mean \pm SD) kg/m². A significant association was observed between weight, height, waist circumference, fasting blood sugar, HDL value, and MetS ($P < 0.05$). About 39.6% of the patients with MetS had hyperuricemia. The association between MetS and hyperuricemia was found to be significant. Similarly, 45.3% of the patients with MetS had hypothyroidism. This association was also found to be significant. Serum thyroid-stimulating hormone had a minimal correlation with serum uric acid in patients with MetS (correlation coefficient $r = 0.344$), while no correlation was observed between fT3, fT4 with serum uric acid. **Conclusion:** Increased prevalence of hyperuricemia and hypothyroidism was seen among patients with MetS. More extensive population-based research is needed to support this finding.

Key words: Hyperuricemia; Hypothyroidism; Metabolic syndrome; Obesity

INTRODUCTION

Metabolic syndrome (MetS) consists of a constellation of metabolic abnormalities that increase the risk of developing several serious complications such as cardiovascular disease (CVD), insulin resistance, diabetes mellitus, and cerebrovascular accident. It has major consequences

on the health of the individual and financial burden. The etiopathology of MetS is multifactorial, where both genetic and acquired factors play a role in the final pathway of inflammation leading to CVD.¹ The overall pooled prevalence of MetS among the adult population in India was 30% and state-wise analysis has shown that the maximum prevalence of MetS is reported in Madhya

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Pradesh (50%) followed by New Delhi (43%), Odisha (43%), and Telangana (42%). The least pooled prevalence of MetS was found in Jammu and Kashmir (15%) followed by Haryana (18%) and Punjab (21%).²

Obesity, a key component of MetS, occurs due to increased energy intake, decreased energy expenditure, or a combination of both, thus leading to a positive energy balance.³ Thyroid hormones have effects on glucose metabolism, lipid metabolism, blood pressure (BP) regulation, and energy consumption. It upregulates the metabolic pathways relevant to resting energy expenditure, hence, obesity and thyroid functions are often correlated though the exact mechanism is still unknown.⁴ Similarly, with uric acid, hyperuricemia is seen with MetS patients. It has been known that hyperinsulinemia reduces renal excretion of uric acid. Hyperuricemia resulting from euglycemic hyper-insulinemia may precede the onset of type 2 diabetes, hypertension, coronary artery disease, and gout in individuals with MetS.⁵ As MetS, hypothyroidism, and hyperuricemia are independent risk factors for CVD, it is possible that patients suffering from more than one disease entity may have a compounded risk. There are limited data on such from West Bengal. More extensive research is needed.

Aims and objectives

The objectives are as follows:

1. To study the association of hypothyroidism with MetS
2. To study the association of hyperuricemia with MetS
3. To study the relationship between hypothyroidism and hyperuricemia in MetS.

MATERIALS AND METHODS

This cross-sectional study was conducted among patients visiting the outpatient department (OPD) of General Medicine, IPGME & R and SSKM Hospital, Kolkata. The data were collected from patients attending OPD between January 2012 and June 2013. A total of 112 patients were selected using a convenient sampling method after fulfilling all inclusion/exclusion criteria. The study was approved by IPGME & R Ethics Committee and informed consent was taken from the patients. Among 112 patients who attended OPD of General Medicine for seeking medical treatment, 53 patients were having MetS⁶ and 59 patients were without MetS.

Inclusion criteria

Age between 40 and 80 years.

Consent to study.

Exclusion criteria

1. Patients receiving any medication that may alter the thyroid function such as lithium, amiodarone,

phenytoin, carbamazepine, or patients receiving radiation therapy for cancers of the head and neck and for Hodgkin's lymphoma which can cause hypothyroidism

2. Patients receiving any hypouricemic agents and drugs which increase the serum uric acid level such as diuretics, ketoconazole, salicylate
3. Pregnant women and patient with abdominal mass or ascites or severe liver, heart, or renal failure
4. All seriously ill patients.

A predesigned, pretested schedule was used to obtain detailed information on socio-demographic profile, risk factors, any medical/surgical history, clinical findings, anthropometric measurements (including height [in cm], weight [in kg], body mass index [BMI] [kg/m²], waist circumference [WC] [in cm] using standard protocol and instrument), BP measurements (using standard protocol and instrument) and laboratory investigations (fasting blood sugar [FBS], postprandial blood sugar [PPBS], serum triglyceride [TG], low-density lipoprotein [LDL], high-density lipoprotein [HDL], serum thyroid-stimulating hormone [TSH], free triiodothyronine, free thyroxine, and serum uric acid levels). The patients were followed up in OPD subsequently.

Anthropometric measurements

Anthropometric measurements were done in OPD using a standardized protocol. Weight was measured to the nearest 0.1 kg on patients with lightweight clothing and without shoes on a calibrated weighing digital scale. Height was measured to the nearest 0.1 cm on patients without shoes using a portable stadiometer.⁷

BMI was calculated as weight in kilograms divided by the square of height in meters. WC was measured using a measuring tape placed at the midpoint between the borders of the lowermost rib and the uppermost lateral border of the ilium to the nearest 0.1 cm at the end of normal expiration.⁷

The BP of participants was measured with a calibrated aneroid sphygmomanometer according to the protocol recommended by the Seventh Report of the Joint National Committee on Prevention, detection, evaluation, and treatment of high BP.⁸

Laboratory investigation

Peripheral venous blood samples were collected from the patients who had fasted overnight in the central laboratory of the hospital. FBS, PPBS, Serum TG, LDL, and HDL were measured using an automated biochemical analyzer. Serum TSH, free triiodothyronine (fT₃), and free thyroxine (fT₄) were measured using an electrochemical

luminescence immunoassay. Serum uric acid was measured using a colorimetric method. All laboratory equipment was standardized.

Diagnostic criteria

The criterion for diagnosing MetS as per the International Diabetes Federation is stated below:

If the patient has any three of the following:⁶

- WC ≥ 102 cm for men and ≥ 88 cm for women
- Elevated TGs 150 mg per deciliter of blood (mg/dL) or greater
- Reduced high-density lipoprotein cholesterol (HDL) < 40 mg/dL in men or < 50 mg/dL in women
- Elevated fasting glucose of 100 mg/dL or greater, or previously diagnosed type 2 diabetes
- BP values of systolic 130 mmHg or higher and/or diastolic 85 mmHg or higher, or treatment of previously diagnosed hypertension.

Hypothyroidism

Hypothyroidism may be either subclinical or overt. Subclinical hypothyroidism (SCH) is characterized by a serum TSH > 4.5 – 10 mIU/L in combination with a normal free thyroxine (T4) provided that thyroid function has been stable for weeks or more, the hypothalamic–pituitary–thyroid axis is normal, and there is no recent or ongoing severe illness. An elevated TSH, usually above 10 mIU/L, in combination with a subnormal free T4 characterizes overt hypothyroidism.⁹

Hyperuricemia

Hyperuricemia was defined as serum uric acid concentration > 7.0 mg/dL (416.4 $\mu\text{mol/L}$) in men or > 6.0 mg/dL (356.9 $\mu\text{mol/L}$) in women.⁹

All the collected data were compiled and entered into Microsoft Excel. They were checked for consistency and completeness and were analyzed with SPSS (version 27, IBM, Chicago, Illinois). Continuous data were summarized as mean and categorical data were summarized based on frequency and proportions. For the categorical variable, χ^2 test was used and for the continuous variable t/z test was used as a test of significance. All statistical analyses were done at 95% confidence interval and $P < 0.05$ was considered statistically significant.

RESULTS

Majority (66%) of the patients with MetS were female and rest were male. Similarly, 59.3% of patients without MetS were female. The mean age of the patients with MetS was 49.74 ± 7.32 (Mean \pm SD) years while that without MetS was 50.25 ± 7.76 (Mean \pm SD) years.

The mean BMI of patients with MetS was 33.31 ± 4.36 (Mean \pm SD) kg/m^2 and without MetS was 25.21 ± 2.62 (Mean \pm SD) kg/m^2 . A significant association was observed between weight, height, WC, FBS, TG, low HDL, and MetS ($P < 0.05$) (Table 1).

About 39.6% of the patients with MetS had hyperuricemia, while only 10.2% without MetS had hyperuricemia. The association between MetS and hyperuricemia was found to be significant ($P < 0.05$). Similarly, 45.3% of the patients with MetS had hypothyroidism and 18.6% of patients without MetS had hypothyroidism. This association was also found to be significant ($P < 0.05$) (Table 2).

Serum TSH had a minimal correlation with serum uric acid in patients with MetS (correlation coefficient $r = 0.344$), while no correlation was observed between fT3, fT4 with serum uric acid (Table 3).

DISCUSSION

In the present study, the mean age in the MetS group was 49.74 ± 7.32 (Mean \pm SD) years and the mean age in the without MetS group was 50.25 ± 7.76 (Mean \pm SD) years. Thus, both the groups were similar in age profile. Similar findings were observed in a study conducted by Shantha et al.,¹⁰ Uzunlulu et al.¹¹

In the MetS group, 66% were female and 34% were male. In the without MetS group, 59.3% were female and 40.7% were male. Similar observations were also seen in studies conducted by Shantha et al.,¹⁰ Uzunlulu et al.,¹¹ Aljabri et al.,¹² El-Hay et al.¹³ The seemingly greater number of

Table 1: Distribution of study subjects based on socio-demographic, clinical, and laboratory parameters (n=112)

Variables	Patients with MetS n=53	Patients without MetS n=59	P-value
Sex	n (%)	n (%)	
Male	18 (34)	24 (40.7)	0.464
Female	35 (66)	35 (59.3)	
	Mean (SD)	Mean (SD)	
Age (years)	49.74 (7.32)	50.25 (7.76)	0.718
Weight (kg)	82.31 (12.74)	66.81 (6.94)	0.001*
Height (cm)	157.27 (9.79)	162.94 (6.54)	0.001*
BMI (kg/m^2)	33.31 (4.36)	25.21 (2.62)	0.001*
WC (cm)	107.84 (9.94)	81.51 (7.95)	0.001*
FBS (mg/dl)	101.44 (17.1)	87.64 (9.08)	0.001*
BP (mmHg)			
Systolic	129.92 (13.49)	125.63 (10.49)	0.061
Diastolic	96.17 (9.34)	79.86 (9.27)	0.185
TG (mg/dl)	152.92 (61.7)	79.86 (9.27)	0.001*
HDL (mg/dl)	39.85 (7.59)	49.66 (5.4)	0.001*

* $P < 0.05$ is significant. WC: Waist circumference, BMI: Body mass index, BP: Blood pressure, FBS: Fasting blood sugar, TG: Triglyceride, HDL: High-density lipoprotein

Table 2: Association between metabolic syndrome with hypothyroidism and hyperuricemia (n=112)

Variables	Patients with MetS n=53	Patients without MetS n=59	Total n=112	P-value
Hyperuricemia				
Present	21 (39.6)	6 (10.2)	27 (24.1)	0.001*
Absent	32 (60.4)	53 (89.8)	85 (75.9)	
Hypothyroidism				
Present	24 (45.3)	11 (18.6)	35 (31.2)	0.009*
Absent	29 (54.7)	48 (81.4)	77 (68.8)	

*P<0.05 is significant. Hypothyroidism including both subclinical hypothyroidism and overt hypothyroidism, MetS: Metabolic syndrome

Table 3: Correlation between thyroid hormone profile with serum uric acid levels in patients with MetS (n=53)

Variables	Pearson's coefficient correlation (r)	P-value
Serum uric acid	1	
fT3	-0.186	0.182
fT4	-0.248	0.073
TSH	0.344	0.012

MetS: Metabolic syndrome, TSH: Thyroid-stimulating hormone

females could be explained by the fact that women came more to the health care set up and these studies were all hospital-based study.

The mean BMI of the patients with MetS in this study was 33.31 ± 4.36 (Mean \pm SD) kg/m² while that in the patients without MetS was 25.21 ± 2.62 (Mean \pm SD) kg/m². Thus, most of the patients with MetS were overweight. A similar finding was seen in a study by Uzunlulu et al.,¹¹ where the mean BMI in patients with MetS was 32.4 ± 4.7 (Mean \pm SD) kg/m² while that in the patients without MetS was 26.4 ± 5 (Mean \pm SD) kg/m².

In the present study, BMI, WC, and FBS all were significantly higher in the MetS group compared to without MetS group.

Studies conducted by Shantha et al.,¹⁰ Uzunlulu et al.,¹¹ El-Hay et al.,¹³ Ahmad et al.,¹⁴ Ni et al.,¹⁵ had similar findings where BMI, WC, and BP was higher among patients with MetS than control.

The mean of the serum uric acid level in patients with MetS was 6.08 ± 1.59 (Mean \pm SD) mg/dl in this study while that in the patients without MetS was 5.07 ± 1.06 (Mean \pm SD) mg/dl (this finding is not shown in the result section). About 39.6% of patients with MetS were having high serum uric acid level, while only 10.2% of patients without MetS were having hyperuricemia.

A study conducted by Zhang et al.,¹⁶ had reported that mean serum uric acid level in patients with MetS were 6.5 ± 1.4 (Mean \pm SD) mg/dl and 5.4 ± 1.0 (Mean \pm SD) mg/dl in males and females, respectively. While in patients without MetS, mean serum uric acid levels were 6.0 ± 1.1 (Mean \pm SD) mg/dl and 4.8 ± 1.0 (Mean \pm SD) mg/dl, respectively.

A study by Ni et al.,¹⁵ had reported mean serum uric acid level in patients with MetS were 5.67 ± 1.37 (Mean \pm SD) mg/dl and in patients without MetS were 4.76 ± 1.28 (Mean \pm SD) mg/dL.

Several epidemiological studies have established a close relationship between serum uric acid levels and MetS.^{17,18} Hyperuricemia induces oxidative stress and worsening of insulin resistance, which may be considered a significant predictor for the development of MetS.^{19,20}

A study conducted by Ni et al.,¹⁵ had shown that increased serum uric acid is strongly associated with MetS. Similar findings were also seen in studies conducted by Ali et al.,⁵ Yao et al.,²¹ and Tu et al.²²

In the present study, the mean serum TSH level in patients with MetS was 6 ± 3.8 (Mean \pm SD) μ IU/mL while that in the patients without MetS was 3.8 ± 2.6 (Mean \pm SD) μ IU/mL. In patients with MetS, about 54.72% were euthyroid, 30.19% had SCH and 15.09% had overt hypothyroidism. In patients without MetS, about 81.36% were euthyroid, 13.56% had SCH and 5.08% had overt hypothyroidism (this finding is not shown in the result section).

A study conducted by He et al.,⁴ had shown that thyroid dysfunction was associated with MetS and association differed by gender. Overt hypothyroidism and SCH were associated with increased risk of MetS. Studies conducted by Shantha et al.,¹⁰ Uzunlulu et al.,¹¹ Aljabri et al.,¹² El-Hay et al.,¹³ also had similar observations.

Kota et al.,²³ had shown that in the MetS group, 4% of the cases had overt hypothyroidism, 22% had SCH and 74% were euthyroid. In the group without MetS, 2% had overt hypothyroidism, 8% had SCH and 90% were euthyroid. Several reports on insulin resistance have demonstrated that hypothyroidism can lead to insulin resistance.²⁴ Thus, insulin resistance can partly explain the association of hypothyroidism with MetS.

A prospective cohort study conducted by Chang et al.,²⁵ had shown that MetS was associated significantly with risk of developing SCH, where high BP and high TGs played an important role than the other components of MetS in developing SCH.

There is no correlation between serum fT3 and serum uric acid (Correlation coefficient $r=-0.186$), serum fT4, and serum uric acid (Correlation coefficient $r=-0.248$) in patients with MetS. Serum TSH has minimum correlation with serum uric acid in patients with MetS (Correlation coefficient $r=0.344$).

Hence, there is no significant correlation between serum thyroid hormone and serum uric acid. There is paucity of data regarding this correlation.

Limitations of the study

Several limitations are to be addressed in this study. First, a small sample size of this study results in an underestimation of the findings. Second, it is a hospital-based study, thus findings may not be generalized to the entire population. Third, it is a cross-sectional study, which may not infer the causal relationship between hypothyroidism and hyperuricemia with MetS. Longitudinal studies are needed to verify the findings.

CONCLUSION

Increased prevalence of hyperuricemia, SCH and overt hypothyroidism were seen in patients with MetS. To determine the significance of early detection of thyroid dysfunction and hyperuricemia in patients with MetS among different age groups, sex, BMI groups, longitudinal studies involving larger population is required. Routine screening of hyperuricemia and hypothyroidism in patients with MetS can be recommended.

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AC- Definition of intellectual content, literature survey, prepared first draft of manuscript, implementation of study protocol, data collection, data analysis; **AP** and **SP**- Concept, design, clinical protocol, coordination, statistical analysis and Interpretation; **SM**- Statistical analysis and interpretation; review manuscript; revision of manuscript.

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