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ORIGINAL RESEARCH

Study on serum uric acid in patients with Metabolic Syndrome at a tertiary care hospital in Tamilnadu

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ABSTRACT

Background: Metabolic Syndrome (MetS) is a set of interrelated clinical disorders, including dyslipidemia, central obesity, glucose intolerance, and high blood pressure. Hyperuricemia is known to cause various inflammatory diseases via uric acid deposition in the joints. Present study was aimed to study serum uric acid in patients with metabolic syndrome at a tertiary care hospital in rural Tamilnadu. Material and Methods: Present study was comparative, observational study, conducted in patients of age > 18 years, either gender, case of metabolic syndrome (cases) & healthy, age & gender matched subjects (controls). Results: In present study 400 cases & age, gender matched 400 controls were participated. We noticed that systolic blood pressure, diastolic blood pressure, fasting blood sugar & triglycerides were significantly higher among patients with metabolic syndrome as compared to controls & difference was statistically significant (p<0.001). While, high-density lipoprotein, total cholesterol & low-density lipoprotein (mg/dL) were comparable in both groups & difference was not significant statistically (p>0.05). In patients with metabolic syndrome higher levels of uric acid (6.78 ± 1.05) were noted as compared to controls (5.16 ± 0.95), difference was statistically significant (p<0.001).In patients of metabolic syndrome higher levels of uric acid were noted in patients with BMI > 30 kg/m^2 (6.17 ± 1.02 vs 4.81 ± 0.92), Fasting Blood Sugar ≥100 (6.29 ± 1.09 vs 4.92 ± 0.99), blood Pressure ≥130/85 (6.27 ± 1.13 vs 5.29 ± 1.01) & triglycerides > 150 mg/dL (6.05 ± 0.99 vs 5.53 ± 1.21), difference was statistically significant (p<0.001). Conclusion: Elevated levels of uric acid were seen in patients with metabolic syndrome and also in components of metabolic syndrome such as body mass index, fasting blood sugar, blood pressure & triglycerides.

Keywords: uric acid, metabolic syndrome, body mass index, fasting blood sugar, blood pressure

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INTRODUCTION

Metabolic Syndrome (MetS) is a set of interrelated clinical disorders, including dyslipidemia, central obesity, glucose intolerance, and high blood pressure. Its presence is involved in the development of various diseases such as fatty liver, diabetes mellitus, cancer, and cardiovascular and infectious diseases.[1] Prior research indicates that insulin resistance plays an important role in the pathophysiology of this condition. Metabolic syndrome is characterized by a large waist size, high triglyceride level, low HDL cholesterol level, increased blood pressure, and/or elevated fasting blood sugar.[2,3]

Hyperuricemia is known to cause various inflammatory diseases via uric acid deposition in the joints but is also recognized as one of the major diseases contributing to metabolic syndrome. Moreover, hyperuricemia is a risk factor for cardiovascular disease and therefore requires long-term management. Physiologically, metabolic syndrome involves insulin resistance, which reduces uric acid excretion and increases uric acid reabsorption in the kidneys, ultimately resulting in elevated blood uric acid levels. In addition, a high uric acid concentration raises blood pressure and triglyceride levels, lowers high-density cholesterol, and causes repeated exacerbation of metabolic syndrome.[4,5,6]

Historically, hyperuricemia was attributed as a secondary consequence to insulin resistance, but more recent studies suggest it may have a contributory causal role, especially since an elevated serum uric acid often precedes the development of insulin resistance.[6,7] Indeed, insulin resistance in patients of metabolic syndrome can be improved by lowering serum uric acid , and uric acid has been shown to block cyclic AMP-activated protein kinase and to stimulate gluconeogenesis. Present study was aimed to study serum uric acid in patients with metabolic syndrome at a tertiary care hospital in rural Tamilnadu.

MATERIAL AND METHODS

Present study was comparative, observational study, conducted in department of General Medicine, Melmaruvathur Adhiparasakthi Institute of Medical Sciences and Research, Melmaruvathur, Tamilnadu, India. Study duration was of 1 years (January 2022 to December 2022). Study approval was obtained from institutional ethical committee.

Inclusion criteria

- Cases - Patients of age > 18 years, either gender, free from severe chronic illness, case of metabolic syndrome according to National Cholesterol Education Program Adult Treatment Panel III[8], willing to participate in present study.
- Controls – Healthy, age & gender matched subjects

Exclusion criteria

- Pregnant women, Lactating mother
- Participants with a history of hepatotoxic drug intake, kidney disease, alcohol intake, self-reported evidence of acute or chronic hepatitis.
- Participants with missing anthropometric data or blood samples
- Lipid lowering therapy in previous 6 weeks, use of allopurinol,
- The presence of diabetes mellitus or other secondary hyperlipidemias,
- Acute infection or trauma,
- Acute cardiovascular event in the last 3 months, heart failure NYHA III and IV

Metabolic syndrome was defined by using the criteria proposed by the National Cholesterol Education Program Adult Treatment Panel III.[8] Metabolic Syndrome was defined to be present when at least three of following criteria were met.

1) WC: ≥ 90 cm for men and ≥ 85 cm for women.
2) TG level ≥ 150 mg/dL.
3) HDL cholesterol level: ≤ 40 mg/dL for men and ≤ 50 mg/dL for women.
4) Fasting glucose level ≥ 100 mg/dL or receiving treatment for diabetes mellitus.

5) SBP ≥ 130 mmHg or DBP ≥ 85 mmHg.

Study was explained to all subjects in local language & written consent was taken for participation & study. A standard questionnaire was used to collect demographic and lifestyle information from the participants. Individual anthropometric data such as age, gender, weight and height were recorded in the questionnaire form.

Blood pressure was measured in the left arm of the participants with an automated sphygmomanometer in the seated position after at least 10 minutes of rest. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured three times, and the averages of the second and third measurements were subjected to analyses.

Body mass index was calculated as weight in kilograms divided by height in square meters (kg/m^2). Waist circumference (WC) was measured using general tape that was placed midway between the lowest border of the ribs and iliac crest. Hip circumference (HC) was measured at the largest circumference of the buttocks to the nearest 0.5 cm. Waist-hip ratio (WHR) was measured as waist circumference divided by hip circumference. 10 ml of Venous blood samples were collected after an overnight fast from each subject and sent for estimation of serum uric acid, FBS, PPBS, HBA1C, RFTs, LFTs & lipid profile.

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi-square test or Fisher exact test as applicable. P value less than 0.05 was considered as statistically significant.

RESULTS

In present study 400 cases & age, gender matched 400 controls were participated. We noticed that systolic blood pressure, diastolic blood pressure, fasting blood sugar & triglycerides were significantly higher among patients with metabolic syndrome as compared to controls & difference was statistically significant ($p<0.001$). While, high-density lipoprotein, total cholesterol & low-density lipoprotein (mg/dL) were comparable in both groups & difference was not significant statistically ($p>0.05$).

Table 1: Blood pressure & Biochemical Parameters of Study Subjects

Parameter	Metabolic Syndrome (Mean ± SD)	Non-Metabolic Syndrome (Mean ± SD)	p value
Systolic blood pressure (mm of Hg)	134.7 ± 11.64	114.17 ± 7.52	0.001*
Diastolic blood pressure (mm of Hg)	86.44 ± 6.48	75.57 ± 6.37	0.001*
Fasting blood sugar (mg/dL)	134.27 ± 31.26	96.56 ± 18.49	0.01*
Triglycerides (mg/dL)	152.01 ± 43.91	104.67 ± 20.51	0.001*
High-density lipoprotein (mg/dL)	41.35 ± 7.31	38.76 ± 9.13	0.053
Total cholesterol (mg/dL)	203.9 ± 45.51	194.45 ± 23.21	0.062
Low-density lipoprotein (mg/dL)	154.3 ± 30.38	148.4 ± 32.47	0.073

In patients with metabolic syndrome higher levels of uric acid (6.78 ± 1.05) were noted as compared to controls (5.16 ± 0.95), difference was statistically significant ($p<0.001$).

Table 2: Association of Metabolic and Non-Metabolic Syndrome with Hyperuricaemia

Uric acid (mg/dl)	Metabolic Syndrome (n=60) (%)	Non-Metabolic Syndrome (n=60) (%)	P value
<4.0	7 (1.75 %)	33 (8.25 %)	
4.1-5.0	47 (11.75 %)	120 (30 %)	
5.1-6.0	87 (21.75 %)	147 (36.75 %)	
6.1-7.0	153 (38.25 %)	93 (23.25 %)	
>7.0	106 (26.5 %)	7 (1.75 %)	
Mean (mg/dl)	6.78 ± 1.05	5.16 ± 0.95	< 0.001

In patients of metabolic syndrome higher levels of uric acid were noted in patients with BMI > 30 kg/m^2 (6.17 ± 1.02 vs 4.81 ± 0.92), Fasting Blood Sugar ≥100 (6.29 ± 1.09 vs 4.92 ± 0.99), blood Pressure ≥130/85 (6.27 ± 1.13 vs 5.29 ± 1.01) & triglycerides > 150 mg/dL (6.05 ± 0.99 vs 5.53 ± 1.21), difference was statistically significant (p<0.001).

Table 3: Association of Mean Uric Acid Levels with components of MetS

Variables	Groups	n (%)	Uric acid (mg/dl) (Mean ± SD)	p value
BMI	<30	43 (71.67 %)	6.17 ± 1.02	0.001*
	>30	17 (28.33 %)	4.81 ± 0.92	
Fasting Blood Sugar	≥100	40 (66.67 %)	6.29 ± 1.09	0.001*
	<100	20 (33.33 %)	4.92 ± 0.99	
Blood Pressure	≥130/85	32 (53.33 %)	6.27 ± 1.13	0.049
	<130/85	28 (46.67 %)	5.29 ± 1.01	
HDL	Low	46 (76.67 %)	5.93 ± 1.31	0.35
	High	14 (23.33 %)	5.45 ± 1.12	
Triglycerides (mg/dL)	>150	23 (38.33 %)	6.05 ± 0.99	0.001*
	<150	37 (61.67 %)	5.53 ± 1.21	

DISCUSSION

Metabolic Syndrome is a premorbid condition that develops in the setting of insulin resistance and factors such as poor diet, physical inactivity, obesity, and genetics play a contributing role. MetS consists of a cluster of risk factors for cardiovascular disease (CVD), chronic kidney disease (CKD), type 2 diabetes mellitus and hypertension.[9] The results of a meta-analysis strongly suggest MetS is associated with an increased incidence of CVA and an increase in mortality.[10]

Plasma uric acid (UA) is a circulating marker of oxidative damage in a variety of pathological conditions such as ischemic liver injury, hyperlipidemia, chronic heart disease, atherosclerosis, ischemic reperfusion injury, and diabetes.[11] The serum uric level depends on gender, lifestyle, meals, and previous use of diuretics.[12] Multiple mechanisms are involved in the relationship between UA and obesity. Obesity, especially its abdominal type, increases the activity of xanthine oxidase in the adipose tissues and would result in higher UA production and lower UA renal clearance.[13,14] However, insulin resistance (HOMA index) has been reported to be improved by benzbromarone and allopurinol in two small randomized trials. In addition, one study reported an improvement in hemoglobin A1C levels in normotensive diabetic subjects treated with allopurinol.[15]

K Gunanithi et al.,[16] noted that serum uric acid levels were significantly higher in patients with diabetic metabolic syndrome when compared with normal healthy controls with level of significance (p = 0.0001). Serum uric acid levels showed positive correlation with various components of the metabolic syndrome including fasting plasma glucose, post prandial plasma glucose, serum total cholesterol, serum LDL cholesterol, serum triglycerides (pearsons correlation significant at $p<0.05$) except for serum HDL cholesterol.

Jose J et al., [17] noted metabolic syndrome in 50.9% of obese patients. The mean serum uric acid levels were 6.07±1.61 and 4.62±1.33 in metabolic and non-metabolic syndrome respectively and were found to be statistically significant. The association of mean uric acid levels with BMI, FBS and triglycerides were statistically significant.

Mundhe SA[18] studied 150 patients of type 2 DM patients, metabolic syndrome was diagnosed in 68 patients (45.3%) with higher prevalence in males (53.4%) than females (33.9%). Hyperuricemia was found in 38 patients (25.3%) with higher prevalence in males (33%) than females (14.5%). Hyperuricemia and metabolic syndrome was found in 32 (21.3%) patients with higher prevalence among males (27.3%) than females (12.9%). Prevalence of hyperuricemia is higher in patients of type 2 diabetes with metabolic syndrome and is positively correlated with BMI, blood pressure and triglycerides and negatively correlated with HDL-C.

In study by Reddy M et al.,[19] mean serum uric acid levels in cases were 7.9 mg/dL in men and 6.8 mg/dL in women. Mean serum uric acid levels in controls were 4.8 mg/dL in men and 3.9 mg/dL in women. This difference was statistically significant (p= 0.001). Among the subjects having metabolic syndrome, 28 subjects (65%) had hyperuricemia. Among the controls 10 subjects (25%) had hyperuricemia.

Karmakar S et al.,[20] noted that hyperuricemia significantly increases with an increase in age and BMI. Subjects of MS (Cases) significantly have more systolic and diastolic blood pressure, fasting plasma glucose, raised serum triglyceride, uric acid, and low HDL than their healthy counterparts (control). Hyperuricemia is significantly associated with MS cases irrespective of sex after menopause of females, but males are more affected than females when the age group is not considered.

A meta-analysis[21] of 11 cohort studies suggested that the combined RR of MetS risk was 1.72 (1.45, 2.03) comparing the top SUA level category to the lowest SUA level category, and dose–response analysis indicated that the risk of developing MetS increased 1.30 (1.22, 1.38) times for per 1 mg/dL SUA increment.

Overwhelming evidence suggests that hyperuricemia is linked to obesity, hypertension, reduced HDL cholesterol, hypertriglyceridemia, hyperinsulinemia and reduced insulin sensitivity, components of the metabolic syndrome, chronic kidney disease, etc.[22] There is agreement on the association between high SUA levels and cardiovascular-related mortality in the general population.[23] Early diagnosis & management of various components of MetS patients is rewarding by improvement in the metabolic parameters as well as reducing the cardiovascular risk; thereby improving the quality of life of these patients. Prevention and treatment MetS should be a public health priority to reduce cardiovascular diseases.

CONCLUSION

Elevated levels of uric acid were seen in patients with metabolic syndrome and also in components of metabolic syndrome such as body mass index, fasting blood sugar, blood pressure & triglycerides. However, further studies are required to study role of uric acid lowering agents, in the management of metabolic syndrome.

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