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ORIGINAL RESEARCH

Association of metabolic syndrome and serum uric acid

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ABSTRACT

Background: Metabolic syndrome, elevated concentrations of uric acid are associated with a variety of cardiovascular conditions. However, the association of uric acid and Metabolic syndrome remains controversial and limited experience exists on this relationship. Given the high prevalence of Metabolic syndrome in Indian population, in the present study we evaluated the association of serum uric acid levels and Metabolic syndrome components in the present study. **Materials & methods:** 273 patients fulfilling IDF Criteria for metabolic syndrome reporting at L.N. Medical College & J. K. Hospital, Kolar Road, Bhopal and satisfied the criteria inclusion criteria were selected for the study. Relevant clinical data was recorded in a structured proforma.Participants consented by endorsing a written consent form before samples were collected.The clinical profile of patients was evaluated as per the proforma.Data was analysed statistically. Analysis was done in the form of percentages, proportions and represented as tables, charts, graphs wherever necessary. Appropriate tests of significance were applied with $p<0.05$. **Results:** The study examined the distribution of 273 subjects across various age groups, finding that the majority (30.4%) fell into the 41-50 years category, followed by the 51-60 years group (27.1%). The study population was predominantly middle-aged and elderly, with a relatively balanced gender distribution (42.85% male, 57.14% female).Uric acid levels varied across age groups, with no clear pattern. Males had slightly higher uric acid levels than females, but the difference was not statistically significant. No significant correlations were found between uric acid levels and HDL cholesterol, waist circumference, or fasting blood sugar. **Conclusion:** In conclusion, this study demonstrates a significant association between metabolic syndrome and serum uric acid levels in middle-aged and elderly individuals. Elevated uric acid levels were found to be positively correlated with increased systolic and diastolic blood pressure, triglycerides, and smoking habits, suggesting a potential link between uric acid and cardiovascular risk factors.

Key words: Metabolic, Syndrome, Uric acid

INTRODUCTION

The term "metabolic syndrome" refers to a group of abnormalities that includes dyslipidemia, dysglycemia, abnormal blood pressure, and central obesity.[1] It is generally defined as a cluster of five components: high blood pressure (BP), high triglyceride level (TG), low high-density lipoprotein cholesterol (HDL), abdominal obesity, and a high glucose level. It was first described in 1988 by Reaven and is also known as insulin resistance syndrome or Syndrome X.[2] Since then, numerous international organizations and expert groups have made an effort to include all the parameters that are used to define metabolic syndrome (Metabolic syndrome). These groups include the World Health Organization (WHO), the National Cholesterol Education Program Adult Treatment Panel III (NCEP:ATPIII), the European Group for the study of Insulin Resistance (EGIR), the American Association of Clinical Endocrinology (AACE), the International Diabetes Federation (IDF), and the American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI).[3] Scientific organizations have listed diagnostic criteria for the definition of the syndrome, with different specific cut-off points of risk values for waist circumference, blood pressure and serum levels of glucose, triglycerides and High Density Lipoprotein (HDL).[4]

According to the International Diabetes Federation (IDF) definition,he or she has the metabolic syndrome if he or she has central adiposity plus two or more of the following four factors [5]: 1) raised concentration of triglycerides: ≥150 mg/dl (1.7 mmol/l) or specific treatment for this lipid abnormality; 2) reduced concentration of HDL cholesterol: <40 mg/dl (1.03 mmol/l) in men and <50 mg/dl (1.29 mmol/l) in

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women or specific treatment for this lipid abnormality; 3) raised blood pressure: systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg or treatment of previously diagnosed hypertension; and 4) raised fasting plasma glucose concentration ≥100 mg/dl (5.6 mmol/l) or previously diagnosed type 2 diabetes. [5]

Moreover, undoubtedly Metabolic syndrome is a common condition, present in about 20–30% of the world's adult population, whose global prevalence is rising also due to current sedentary lifestyle.[4] It is a constellation of an interconnected physiological, biochemical, clinical, and metabolic factors that directly increases the risk of atherosclerotic cardiovascular disease (ASCVD), (T2DM), and all cause mortality. This collection of unhealthy body measurements and abnormal laboratory test results include atherogenic dyslipidemia, hypertension, glucose intolerance, proinflammatory state, and a prothrombotic state.[6] Because of the altered glucose metabolism associated with Metabolic syndrome prevalence and the rising global prevalence of T2DM, there will likely be an alarming increase in the frequency of MS occurrences. [7]

The syndrome has been linked to three times the risk of cardiovascular disease (CVD), five to seven times the risk of type 2 diabetes mellitus (T2DM), and 1.5 times the risk of all-cause death. Given that almost 25% of people worldwide suffer from Metabolic syndrome, it is crucial to thoroughly investigate the epidemiology of the disease in a variety of demographic groups.[8] The incidence of type 2 diabetes mellitus and coronary heart disease (CHD) is remarkably elevated in South Asians. Compared to white Caucasians, South Asians frequently have smaller waist circumferences (WC) and body mass indices (BMI) and higher prevalence, earlier onset, and more complications from T2DM and CHD. Twenty to twenty-five percent of South Asians were thought to have acquired Metabolic syndrome, and many more might be susceptible.[7] Recently, a meta-analysis has reported that almost one in three adults in India suffer from metabolic syndrome (MS) with prevalence of 30% of MS among adult population in India with a steady increase in the burden across the age groups from 13% (18–29 years group) to 50% (50–59 years).[9]

Thus above mentioned data throws insight that nowadays in Asia, life style has been dramatically westernized. The consequence of this change is the increase of obesity. Indirectly affected by this phenomenon, the incidence of Metabolic syndrome and hyperuricemia also become higher. [10]

Uric acid is an enzymatic end product of purine metabolism in humans.[11] Hyperuricemia is a metabolic disease caused by purine metabolic abnormalities related to metabolic syndrome. It happens as a result of either decreased excretion or increased production of uric acid. However, uric acid is not defined as part of the metabolic syndrome.[1] Alterations in serum uric acid homeostasis have been correlated with several diseases such as gout, metabolic syndrome, cardiovascular disease, diabetes, hypertension and kidney disease.[11] Although serum uric acid levels are often associated with Metabolic syndrome, hyperuricaemia is not included among the diagnostic criteria that have been proposed internationally for the definition of this pathology. However, the pro-oxidant action of hyperuricaemia may induce inflammation and endothelial dysfunction by decreasing the availability of nitric oxide, thus promoting the development of the pathologies.[11]

It is suggested that hyperuricemia and Metabolic syndrome may have common pathophysiology. In addition to Metabolic syndrome, elevated concentrations of uric acid are associated with a variety of cardiovascular conditions. However, the association of uric acid and Metabolic syndrome remains controversial and limited experience exists on this relationship.[12] Given the high prevalence of Metabolic syndrome in Indian population, in the present study we evaluated the association of serum uric acid levels and Metabolic syndrome components in the present study.

MATERIAL AND METHODS

273 patients fulfilling IDF Criteria for metabolic syndrome reporting at L.N. Medical College & J. K. Hospital, Kolar Road, Bhopal and satisfied the criteria inclusion criteria.

Patients fulfilling IDF Criteria for metabolic syndrome and age more than or equal to 18 years were included in the study whereas Patient currently on medication which cause alteration in serum uric acid level, Chronic alcoholics, have a history of mental illness or who do not agree to participate in this research and women during pregnancy or lactation were excluded from the study. Patients fulfilling the inclusion criteria were selected for study. Relevant clinical data was recorded in a structured proforma.The clinical profile of patients was evaluated as per the proforma.

Criteria for diagnosis

For diagnosing Metabolic syndrome IDF criteria was used. Patient must have criteria (a), and any 2 criteria out of remaining 4 criteria. [Ford ES.]

a. Waist circumference ≥90 cm for male and ≥80 cm for female
b. Triglyceride ≥150 mg/dl
c. HDL <40 mg/dl in male &< 50 mg/dl in female
d. Blood pressure ≥130/85 mmhg
e. Fasting blood glucose ≥100 mg/dl

For diagnosing Hyperuricemia Serum Uric acid, in adults, serum uric acid >7.0 mg/dL is widely used as the definition of hyperuricemia, considering the solubility of uric acid.[58-59]

Laboratory investigations

A venous blood sample of participants was taken after

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a 12–14 h overnight fast, centrifuged within 2 h, and refrigerated at −10 °C. Following lab investigations were carried out:

- Fasting lipid profile
- Fasting blood sugar level
- Serum uric acid level
- Complete hemogram
- L.F.T
- R.F.T

Body Mass Index, Waist circumference and blood pressure was measured as follows:

- BMI (Body Mass Index) (kg/m2) – Body weight and height was measured and the BMI was calculated by dividing the weight (in kg) by the height (in m) squared.
- Waist circumference-It was measured halfway between the costal margin and iliac crest and at the end of the second expiration.
- Blood pressure -The blood pressure wase measured according to the American Heart Association's recommendations. Blood pressure measurements were obtained from both arms in the supine position after a 15-min resting period and the highest measurement was used for analysis.

Statistical analysis

Data was analysed statistically. Analysis was done in the form of percentages, proportions and represented as tables, charts, graphs wherever necessary. Appropriate tests of significance were applied with $p<0.05$.

RESULTS

The majority of the subjects fall into the 41-50 years group (30.4%), followed closely by the 51-60 years group (27.1%). The next largest group is the 61-70 years category, accounting for 20.1%. Younger age groups, such as 21-30 years (4.4%) and 31-40 years (11.7%), are less represented, with the smallest group being those above 70 years (6.2%). Of the total 273 subjects, 42.85% are male, and 57.14% are female, making the gender distribution relatively balanced. This equal representation helps ensure that the health conditions being studied can be adequately analyzed for both genders. Cholesterol levels, HDL, and triglycerides are measured. The average HDL is 59.7 mg/dL, which is within the recommended range for good cholesterol. The mean triglyceride level is 158 mg/dL, indicating that some individuals might have elevated triglycerides, a risk factor for heart disease. Hypertension (HTN) is the most common, affecting 60.07% of the subjects, followed by diabetes mellitus (DM) in 47.25%. Hypothyroidism affects 10.26% of participants. This high prevalence of chronic diseases, particularly cardiovascular and metabolic disorders, emphasizes the population's health challenges. Smoking is prevalent in 19% of the subjects, and alcohol use is slightly lower at 18.3%. The relatively significant portion of subjects with these habits suggests potential impacts on their overall health and comorbid conditions. Active (44.69%) and sedentary (55.31%). A larger portion of the study population leads a sedentary lifestyle, which may contribute to the higher rates of metabolic syndrome, hypertension, and diabetes observed in the other tables. The distribution is relatively even, with no statistically significant relationship (p-value = 0.200). Both active and sedentary individuals have similar uric acid levels.

Table 1: Lifestyle wise distribution of study subjects

Lifestyle	Frequency	Percent
Active	122	44.69
Sedentary	151	55.31

Table 2: Relation of various uric acid level with SBP of study subjects (Mean)

Uric acid level	Mean	Std. Deviation
1-1.9	142.00	0.00
2-2.9	151.83	14.81
3-3.9	142.67	14.21
4-4.9	144.63	15.23
5-5.9	150.44	14.53
6-6.9	153.78	17.74
7-7.9	145.27	16.93
8-8.9	148.19	17.33
>9	145.27	7.96

F value – 2.237; p value – 0.025*

Higher uric acid levels generally correspond to increased SBP, with the highest mean SBP (153.78 mmHg) found in the 6-6.9 mg/dL uric acid group. The relationship is statistically significant (p-value = 0.025), indicating that higher uric acid is associated with elevated blood pressure.

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Table 3: Relation of various uric acid level with DBP of study subjects (Mean)

Uric acid level	Mean	Std. Deviation
1-1.9	90.00	0.00
2-2.9	92.92	8.82
3-3.9	89.69	8.26
4-4.9	88.96	7.55
5-5.9	91.64	6.91
6-6.9	95.02	8.42
7-7.9	88.00	6.93
8-8.9	87.05	9.33
>9	89.55	1.51

F value – 3.150; p value – 0.002*

There is a trend of higher DBP in the 6-6.9 mg/dL uric acid group (95.02 mmHg), with statistical significance (p-value = 0.002). This suggests a link between higher uric acid levels and increased DBP.

Table 4: Relation of various uric acid level with HDL of study subjects (Mean)

Uric acid level	Mean	Std. Deviation
1-1.9	20.00	0.00
2-2.9	39.67	6.76
3-3.9	49.35	32.22
4-4.9	44.53	20.94
5-5.9	45.11	23.96
6-6.9	39.83	11.29
7-7.9	46.82	13.80
8-8.9	36.73	14.88
>9	28.84	7.42

F value – 1.749; p value – 0.087

Interestingly, higher uric acid levels do not consistently correlate with lower HDL. The highest HDL levels are found in the 7-7.9 mg/dL uric acid group, while the lowest are in the 1-1.9 mg/dL group. The relationship is not statistically significant (p-value = 0.087).

Table 5: Relation of various uric acid level with TG of study subjects (Mean)

Uric acid level	Mean	Std. Deviation
1-1.9	200.00	0.00
2-2.9	145.81	50.51
3-3.9	150.98	57.33
4-4.9	164.97	53.37
5-5.9	166.22	62.90
6-6.9	181.35	63.59
7-7.9	155.36	46.83
8-8.9	196.62	82.22
>9	227.64	44.85

F value – 3.039; p value – 0.003*

Higher uric acid level generally correspond to higher TG levels, with the highest TG (227.64 mg/dL) observed in the >9 mg/dL uric acid group. The relationship is statistically significant (p-value = 0.003), suggesting a strong link between elevated uric acid and increased triglycerides.

Table 6: Relation of various uric acid level with Waist circumference of study subjects (Mean)

Uric acid level	Mean	Std. Deviation
1-1.9	103.00	0.00
2-2.9	98.08	7.13
3-3.9	100.53	12.67
4-4.9	98.65	7.27
5-5.9	102.05	8.42
6-6.9	101.76	7.09
7-7.9	100.18	5.90
8-8.9	101.24	8.12
>9	102.18	8.07

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F value – .910; p value – 0.509

The waist circumference averages are fairly consistent across uric acid level, with no statistically significant relationship (p-value = 0.509). This suggests that uric acid levels do not strongly influence

Table 7: Relation of various uric acid level with diet of study subjects (Frequency)

Uric acid level	Diet		Total
	Mixed	Veg	
1-1.9	0	1	1
2-2.9	8	4	12
3-3.9	21	28	49
4-4.9	40	28	68
5-5.9	34	25	59
6-6.9	16	25	41
7-7.9	6	5	11
8-8.9	9	12	21
>9	7	4	11
Total	141	132	273

Chi square value – 9.851; p value – 0.276

No clear pattern emerges from the data, and there is no statistically significant difference between subjects following a mixed or vegetarian diet regarding uric acid levels (p-value = 0.276).

Table 8: Relation of various uric acid level with lifestyle of study subjects (Frequency)

Uric acid level	lifestyle		Total
	Active	Sedentary	
1-1.9	1	0	1
2-2.9	2	10	12
3-3.9	25	24	49
4-4.9	37	31	68
5-5.9	24	35	59
6-6.9	15	26	41
7-7.9	4	7	11
8-8.9	8	13	21
>9	6	5	11
Total	122	151	273

Chi square value – 11.029; p value – 0.200

DISCUSSION

Metabolic syndrome is an accumulation of several disorders that raise the risk of atherosclerotic cardiovascular disease, including myocardial infarction, cerebrovascular accidents, peripheral vascular diseases, insulin resistance, and type II diabetes mellitus. The cluster of metabolic disorders that define metabolic syndrome includes central obesity, insulin resistance, hypertension, and atherogenic dyslipidemia. Hyperuricemia and metabolic syndrome (Metabolic syndrome) may share common pathophysiological mechanisms. While elevated uric acid levels are linked to cardiovascular conditions, the uric acid-Metabolic syndrome relationship remains contentious and understudied.[8- 9] Hence, the present study was commenced among patients who met the International Diabetes Federation (IDF) criteria for metabolic syndrome and were aged 18 years or older and a significant association was revealed between metabolic syndrome and serum uric acid levels. Elevated serum uric acid levels were found to be positively correlated with increased systolic blood pressure, diastolic blood pressure, and triglycerides. Additionally, higher uric acid levels were linked to hypertension, showing a marginally significant relationship.

In the present study, liver function is assessed through various tests, including uric acid, SGOT, SGPT, ALP, and albumin levels. The mean uric acid level is 5.27 mg/dL, which is close to the upper normal limit, suggesting that a portion of the population may have hyperuricemia. SGOT (32.86 U/L) and SGPT (30.90 U/L) values suggest generally healthy liver enzyme function. The average ALP level is 95.89 U/L, and albumin is 3.77 g/dL, both within the normal range. High levels of Alanine Aminotransferase (ALT), a liver enzyme, have been linked to an increased risk of developing metabolic syndrome (Metabolic syndrome), diabetes mellitus, and cardiovascular disease. Additionally, elevated ALT levels serve as a predictive marker for non-alcoholic fatty liver disease (NAFLD), also known as steatosis.A study by Molla NH et al revealed that serum levels of alanine aminotransferase (ALT) and gamma-glutamyl transferase (GGT) demonstrated a gradual increase in conjunction with rising serum uric acid (SUA)

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concentrations across quartile groups. Multivariate regression analysis confirmed that SUA is strongly and independently associated with elevated ALT levels, even after adjusting for potential confounding variables.[13, 14]

The present study found that higher uric acid levels were linked to elevated systolic blood pressure (SBP), with a mean SBP of 153.78 mmHg in the 6-6.9 mg/dL uric acid group (p-value = 0.025) as well as diastolic blood pressure (DBP) also correlated with uric acid levels, with higher DBP in the 6-6.9 mg/dL uric acid group (95.02 mmHg) (p-value = 0.002). Our results stand in line with Nakanishi N et al that found a stronger association between serum uric acid (SUA) levels and the risk of developing hypertension and impaired fasting glucose (IFG) or type 2 diabetes among leaner men (BMI < 24.2 kg/m2) compared to those with higher body mass index (BMI ≥ 24.2 kg/m2). Although the absolute risk was higher in more obese men, these results suggest that SUA levels are significantly linked to an increased risk of hypertension and glucose metabolism disorders, particularly in non-obese individuals. In another alike study, Mazzali M et al that demonstrated a direct correlation between elevated serum uric acid levels and hypertension in rats, with blood pressure increasing proportionally to uric acid concentrations. The study revealed that hyperuricemia triggers hypertension through multiple pathways, including reduced nitric oxide synthase activity in the kidney's macula densa, stimulation of the renin-angiotensin system (RAAS), and decreased renal perfusion. Notably, these effects were mitigated by uric acid-lowering therapies.[15, 16]

The higher uric acid level corresponded to higher triglyceride (TG) levels, with the highest TG (227.64 mg/dL) observed in the >9 mg/dL uric acid group (p-value = 0.003) in the present study. Several associations were found to be non-significant in our study. The Chi-square test revealed no significant association between uric acid level and age groups (p = 0.22). Gender-related differences in uric acid levels were also non-significant (p = 0.167). No clear pattern emerged between uric acid levels and dietary habits (p = 0.276), lifestyle (active vs. sedentary) (p = 0.200), or fasting blood sugar (FBS) levels (p = 0.855). The relationship between uric acid levels and diabetes mellitus (DM) was non-significant (p = 0.769), as was the relationship between gender and raised blood pressure (p = 0.06) and fasting blood sugar (FBS) levels (p = 0.231). Waist circumference averages were consistent across uric acid level, with no significant relationship (p = 0.509). In a comparable study by Uzeli U et al non-significant differences were found between groups w.r.t age and gender distribution across groups (p = 0.066, p = 0.185). Duration of diabetes and FBG values did not differ between patients with T2DM with and without neuropathy (p = 0.825, p = 0.572). HbA1c levels were also comparable between these two groups (p = 0.607). Furthermore, creatinine levels were similar across all three groups. Uric acid levels did not differ significantly between patients with T2DM with neuropathy and healthy subjects or between patients without neuropathy and healthy subjects (p > 0.05). Lastly, UHR values were comparable between patients without neuropathy and healthy subjects.[17]

Hence, the present study indicates that elevated serum uric acid levels are associated with increased cardiovascular risk factors. Lifestyle factors, such as smoking and alcohol consumption, contribute to higher uric acid levels. Moreover, the high prevalence of metabolic syndrome components highlights the need for early detection and management. Middle-aged groups (41-50 and 51-60) were found to have higher frequencies of moderate to high uric acid level, underscoring the importance of targeted interventions.

CONCLUSION

In conclusion, this study demonstrates a significant association between metabolic syndrome and serum uric acid levels in middle-aged and elderly individuals. Elevated uric acid levels were found to be positively correlated with increased systolic and diastolic blood pressure, triglycerides, and smoking habits, suggesting a potential link between uric acid and cardiovascular risk factors. However, no significant correlations were observed between uric acid levels and dietary habits, lifestyle, or diabetes status. The high prevalence of hypertension, diabetes mellitus, and hyperuricemia in this population underscores the need for early detection and management of these conditions. Further research is necessary to confirm causal relationship between raised uric acid and metabolic syndrome.

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