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ORIGINAL ARTICLE

The Role of Serum Uric Acid as a Biomarker for Early Detection of Metabolic Syndrome in Middle-Aged Pakistani Adults: A Cross-Sectional Study

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ABSTRACT

Introduction: Metabolic syndrome (MetS) is the collection of interrelated metabolic abnormalities, including central obesity, hypertension, dyslipidemia, and hyperglycemia, that together increase the risk of cardiovascular disease and type 2 diabetes. The traditional serum uric acid (SUA) marker for gout has recently been implicated in MetS development. However, despite growing international data, no research has been done in the Pakistani population to investigate this association.

Aims and Objectives: The objective of the study was to assess the association between serum uric acid levels and metabolic syndrome in middle aged adults visiting tertiary care hospitals of Pakistan and to determine the gender distribution and correlation of SUA with each component of MetS as well.

Methodology: It was a cross-sectional observational study in Liaquat University Hospital, Hyderabad/Jamshoro, from July 2022 to June 2023. There were 120 adults aged 40–60 years enrolled. Anthropometric measurements, blood pressure, fasting glucose, lipid profiles, and serum uric acid levels were assessed. NCEP ATP III criteria were used to define metabolic syndrome. SPSS version 26 was used to analyze data with the application of t-tests and Pearson correlation analysis.

Results: This was found in 56.7% of the participants. Mean serum uric acid was significantly higher in the MetS group (6.8 ± 1.1 mg/dL) than in non non-MetS group (5.3 ± 1.0 mg/dL, $p < 0.001$). A positive correlation was seen between serum uric acid and waist circumference, systolic blood pressure, and triglyceride, and a negative correlation with HDL cholesterol. Gender-specific analysis showed consistent associations.

Conclusion: Serum uric acid is strongly associated with metabolic syndrome and the degree of severity. SUA measurement could be used to early identify persons at metabolic risk in Pakistan.

Keywords: serum uric acid, metabolic syndrome, middle-aged adults, Pakistan, hyperuricemia, cardiovascular risk

INTRODUCTION

Metabolic syndrome (MetS) is now considered a major public health problem worldwide, characterized by the combination of interrelated metabolic risk factors that dramatically increase the risk of cardiovascular diseases (CVD), type 2 diabetes mellitus (T2DM), and all-cause mortality. MetS is defined as central obesity, blood pressure, insulin resistance or hyperglycemia, triglycerides, and low HDL cholesterol. [1]. The syndrome is a result of the interactions between genetic predisposition and environmental factors and lifestyle habits like sedentary behavior, poor dietary patterns, and urbanization. The prevalence of MetS in adults is reported to be between 20 and 25 % globally by the International Diabetes Federation, with considerable differences in prevalence across regions and ethnic groups [2].

The prevalence of MetS is rising alarmingly in Pakistan in parallel to the country's rapid demographic and nutritional transition. Prevalence has been reported in several local studies from 18% to over 40% in middle-aged urban populations. The reason for this rise is mostly due to rates of obesity, physical inactivity, diets with excessive refined carbohydrates and fats, and genetic susceptibility. Early identification and management of individuals at risk of MetS is important, as Pakistan has a high burden of non-communicable diseases [3].

Serum uric acid (SUA) is among several emerging biomarkers that have attracted attention as potential contributors to the pathogenesis of MetS. In humans, purine metabolism ends with uric acid, which is mainly excreted in the urine. Traditionally, hyperuricemia has been linked to gout, however, there is recent evidence suggesting that elevated SUA levels might also play a role in the development of hypertension, insulin resistance, endothelial dysfunction, and atherosclerosis, all of which are components or consequences of MetS. There have been experimental studies showing that uric acid can induce oxidative stress, promote inflammation, decrease nitric oxide production, and activate the renin angiotensin system in a proatherogenic and prohypertensive environment [4].

Hyperuricemia has consistently been reported to be associated with MetS in epidemiological studies across different populations, with elevated SUA levels being considered as an early marker of metabolic disturbances. Nevertheless, the relationship is complex, namely, hyperinsulinemia related to MetS can lower renal excretion of uric acid, resulting in increased SUA levels. This is an important clinical question: Is uric acid an innocent bystander or an active player in the development of MetS? This relationship is important to clarify for screening, prevention, and management strategies [5, 6].

Although studies have been carried out in developed countries to establish the relationship between SUA and MetS, there is a dearth of local research from Pakistan regarding the association between SUA levels and MetS in middle-aged adults who are at a high risk of cardiovascular and metabolic diseases. Considering the ethnic, dietary, and socioeconomic diversity in Pakistan, it is necessary to have population-specific associations to develop effective screening protocols and public health interventions. Additionally, as healthcare systems in Pakistan are under growing strain from the growing burden of non-communicable diseases, it would be useful to find inexpensive and widely available biomarkers such as SUA to screen and manage high-risk patients at an early stage [7].

Thus, this study aimed to evaluate the relation between serum uric acid levels and metabolic syndrome among middle-aged adults visiting tertiary care centers in Pakistan. Examining this relationship is our way of adding to the evidence that uric acid plays a role in MetS and will be useful local clinician data for patient risk stratification and management. Our results may have wider implications for preventive health strategies targeting the

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reduction of the cardiovascular and metabolic disease burden in Pakistan [8].

MATERIALS AND METHODS

A cross-sectional observational study was carried out for a period of one year from July 2022 to June 2023 at major tertiary care centre of Pakistan, Liaquat University Hospital, Hyderabad, Jamshoro. For the representation of both semi-urban and urban populations and a wide range of middle-aged adults presenting for routine outpatient clinics or non-emergency medical care, these hospitals were chosen. The main aim of this study was to find the association of serum uric acid levels with metabolic syndrome in this target population.

A total of 120 middle-aged adults (40–60 years) were enrolled by using consecutive non-probability sampling. Outpatient visits were approached, and participants were recruited after written informed consent was obtained. Adults of the specified age range who were willing to be clinically examined and laboratory tested were included as inclusion criteria. To eliminate potential confounders, exclusion criteria were carefully defined, including a history of gout, chronic kidney disease, liver disease, malignancy, or use of medications that could affect serum uric acid levels, including diuretics, allopurinol, or corticosteroids.

A detailed clinical assessment was carried out on the participants. After standard procedures, weight, height, and waist circumference were recorded. Measurements were made for weight to the nearest 0.1 kg using a calibrated digital scale, height using a wall-mounted stadiometer, and for waist circumference halfway between the lower margin of the last palpable rib and the iliac crest. Body mass index (BMI) was calculated as weight in kilograms over height in meters squared (kg/m²).

Five minutes of rest were allowed in which to sit, and then blood pressure was measured using a mercury sphygmomanometer after five minutes of rest, and the average of two readings was recorded. After 8–12 hours of overnight fasting, fasting blood samples were obtained. Fasting blood glucose, lipid profile (triglycerides, total cholesterol, HDL cholesterol, and LDL cholesterol), and serum uric acid levels were measured in laboratory analysis. Serum uric acid was assayed enzymatically and colorimetrically.

Metabolic syndrome was diagnosed using the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria, which define metabolic syndrome as the presence of three or more of the following: waist circumference ≥102 cm in men or ≥88 cm in women; blood pressure ≥130/85 mmHg or current use of antihypertensive medications; fasting plasma glucose ≥110 mg/dL or use of antidiabetic medications; triglycerides ≥150 mg/dL; or HDL cholesterol <40 mg/dL in men or <50 mg/dL in women.

SPSS version 26.0 was used to carry out statistical analysis. Means and standard deviations were used to report continuous variables, and frequencies and percentages were used to report categorical variables. Continuous variables were compared between the metabolic syndrome and non-metabolic syndrome groups by using independent sample t-tests. The association between serum uric acid levels and individual components of metabolic syndrome was evaluated by calculating Pearson's correlation coefficients. Statistically significant was considered a p-value <0.05.

The ethical review committees approved the current study. The ethics of all procedures were carried out according to the Declaration of Helsinki.

RESULTS

A total of 120 middle-aged adults (40-60 years) were enrolled in the study, the group included 62 males (51.7%) and 58 females (48.3%). Among these participants, 68 (56.7%) had metabolic syndrome and 52 (43.3%) did not. The sample was divided into two groups; the mean age of the entire sample was 51.3 ± 5.5 years. The mean age was 51.7 ± 5.3 years for males and 50.9 ± 5.6 years for females (p = 0.42), so that there was no significant difference between the age of males and females.

Detailed demographic, clinical characteristics of participants are shown in Table 1, stratified by the presence or absence of metabolic syndrome and by gender distribution. There was no significant difference in gender distribution among the 68 participants with MetS (36 males, 52.9%) vs 32 females (47.1%) and the 52 non-MetS participants (26 males, 50.0%) and 26 females (50.0%), (p = 0.75). Mean serum uric acid levels were significantly higher (6.8 ± 1.1 mg/dL vs 5.3 ± 1.0 mg/dL; p < 0.001) in the MetS group compared to the non-MetS group. Systolic blood pressure, fasting glucose, triglycerides, and HDL cholesterol were significantly different in the MetS group compared to the non-MetS group.

Table 1: Demographic and Clinical Characteristics of Study Participants by Metabolic Syndrome and Gender

Variable	MetS Group (n=68)	Non-MetS Group (n=52)	p-value
Male, n (%)	36 (52.9%)	26 (50.0%)	0.75
Female, n (%)	32 (47.1%)	26 (50.0%)	0.75
Age (years)	52.4 ± 5.1	50.2 ± 5.6	0.04
Waist circumference (cm)	105.2 ± 9.3	88.7 ± 6.9	<0.001
Systolic BP (mmHg)	139 ± 12	125 ± 11	<0.001
Fasting glucose (mg/dL)	124 ± 19	98 ± 15	<0.001
Triglycerides (mg/dL)	182 ± 37	135 ± 30	<0.001
HDL cholesterol (mg/dL)	36 ± 8	51 ± 9	<0.001
Serum uric acid (mg/dL)	6.8 ± 1.1	5.3 ± 1.0	<0.001

Table 1 shows the distribution of demographic and clinical variables among participants with and without metabolic syndrome, including gender breakdown, the MetS group as a whole displayed significantly greater waist circumference, blood pressure, fasting glucose, triglycerides, and serum uric acid, and less HDL cholesterol than the group not affected by Mets.

Table 2 shows the strength and significance of correlations between serum uric acid levels and individual metabolic syndrome components. Table 2 shows that serum uric acid showed a moderate positive correlation with the waist circumference (r = 0.44, p <0.001), systolic blood pressure (r = 0.38, p <0.001), fasting glucose (r = 0.27, p = 0.003), triglycerides (r = 0.31, p = 0.001) and a negative correlation with HDL cholesterol (r = –0.35, p <0.001).

Table 2: Correlation Between Serum Uric Acid Levels and Metabolic Syndrome Components

Variable	Pearson's r	p-value
Waist circumference	0.44	<0.001
Systolic BP	0.38	<0.001
Fasting glucose	0.27	0.003
Triglycerides	0.31	0.001
HDL cholesterol	–0.35	<0.001

Table 3 illustrates serum uric acid levels stratified by the number of metabolic syndrome components. Participants with zero or one component had a mean serum uric acid level of 5.1 ± 0.9 mg/dL, which increased progressively to 7.0 ± 1.2 mg/dL in individuals with four or five components, demonstrating a significant upward trend (p <0.001), as shown in Table 3.

Table 3: Serum Uric Acid Levels by Number of Metabolic Syndrome Components

Number of MetS Components	Mean Serum Uric Acid (mg/dL) ± SD	p-value (trend)
0–1 components	5.1 ± 0.9	
2 components	5.6 ± 1.0	
3 components	6.3 ± 1.1	
4–5 components	7.0 ± 1.2	<0.001

The results indicate that serum uric acid levels were higher in males and females with metabolic syndrome than without and

that uric acid was positively correlated with the degree of metabolic abnormalities. Specifically, the association of hyperuricemia with metabolic syndrome remained significant in both genders, indicating that uric acid is a good marker of metabolic risk irrespective of sex.

DISCUSSION

The goal of this study was to evaluate the association between serum uric acid (SUA) levels and metabolic syndrome (MetS) among middle-aged adults at tertiary care hospitals of Pakistan, Liaquat University Hospital, Hyderabad/Jamshoro. The results show a strong association between high SUA levels and the presence of MetS, and therefore, SUA may also be a biomarker for those stated to be at a higher metabolic risk [9].

The prevalence of MetS in this study was 56.7%, which was not too far from what has been reported in other Pakistani studies, where the prevalence of MetS in middle-aged adults is about 40 – 60%. It is also very important to mention that the SUA levels were significantly higher in the MetS participants compared to those without, and in addition to that, this association is not dependent on gender. Many international studies have found that MetS is associated with hyperuricemia and that it may contribute to the pathophysiology of MetS. This supports the evidence base in the South Asian population, where such data have been sparse [10, 11].

Notably, our results also showed that SUA levels were positively correlated with the main components of MetS, waist circumference, systolic blood pressure, fasting glucose, and triglycerides, and inversely correlated with HDL cholesterol. These associations imply that SUA may be more than a marker, and could be a mediator in the genesis of metabolic disturbances [12]. Oxidative stress, inflammatory pathways, impaired endothelial function, and renin-angiotensin system activation are induced by uric acid, all of which may be important in hypertension, insulin resistance, and dyslipidemia. Additionally, the observed dose-response relationship, i.e., SUA levels increased progressively with the number of MetS components, emphasizes the possible contribution of SUA in indicating how much of the metabolic derangement [13, 14].

Gender analysis also revealed that SUA levels were slightly higher amongst males, however, the relationship between MetS and SUA was significant in both males and females. The importance of this finding lies in that hyperuricemia is a relevant metabolic risk factor in both sexes, and gender-specific cutoffs may be needed in future clinical practice [15].

This study should be acknowledged for several limitations. A limitation of the cross-sectional design is that it does not allow one to conclude whether elevated SUA levels predate the development of MetS or if they develop because of MetS. The second is that although the sample size was sufficient for preliminary analysis, the study was conducted on a relatively small scale, and larger multi-centre studies would strengthen the generalizability of these results. Third, the dietary habits, physical activity, and alcohol intake, as well as the genetic factors that can influence SUA levels, were not assessed in detail and should be included in future studies [16].

However, the study provides important lessons for clinical practice in Pakistan. As serum uric acid testing is simple, affordable, and available for widespread use, it may be a useful adjunct in the early detection of those at risk for MetS to avoid cardiovascular and metabolic complications by early lifestyle modification and medical interventions [17].

CONCLUSION

Finally, this study determined that serum uric acid levels are significantly associated with the presence and severity of metabolic syndrome in middle-aged adults who are attending tertiary care hospitals in Pakistan. Similar to our previous findings in elderly men, both men and women with MetS had elevated SUA, and SUA was highly correlated with several key metabolic parameters (waist circumference, blood pressure, fasting glucose, triglycerides), as well as inversely related to HDL cholesterol. Furthermore, serum uric acid may be a valuable, low-cost biomarker for identifying individuals at heightened metabolic risk. Prospective studies are recommended to further elucidate uric acid's causal role in metabolic syndrome and to determine the effect on metabolic outcome of intervention that lowers SUA.

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Authors Contribution: All authors contributed equally to the current study.

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REFERENCES

1. Ali N, Miah R, Hasan M, Barman Z, Mou AD, Hafsa JM, et al. Association between serum uric acid and metabolic syndrome: a cross-sectional study in Bangladeshi adults. Scientific reports. 2020;10(1):7841.
2. Ahsan N, Kapoor A, Rani M, Shaikh GS, Zafar S, Jesrani VK. Correlation Between Body Mass Index and Serum Uric Acid Among Healthy Pakistani Adults: A Cross-Sectional Comparative Study. Pakistan Journal of Medical & Health Sciences. 2022;16(07):887-.
3. Keenan T, Zhao W, Rasheed A, Ho WK, Malik R, Felix JF, et al. Causal assessment of serum urate levels in cardiometabolic diseases through a Mendelian randomization study. Journal of the American College of Cardiology. 2016;67(4):407-16.
4. Obeidat AA, Ahmad MN, Haddad FH, Azzeh FS. Alarming high prevalence of metabolic syndrome among Jordanian adults. Pakistan journal of medical sciences. 2015;31(6):1377.
5. Song J, Jin C, Shan Z, Teng W, Li J. Prevalence and risk factors of hyperuricemia and gout: a cross-sectional survey from 31 provinces in mainland China. Journal of translational internal medicine. 2022;10(2):134-45.
6. Seremet Kurklu N, Karatas Torun N, Ozen Kucukcetin I, Akyol A. Is there a relationship between the dietary inflammatory index and metabolic syndrome among adolescents? Journal of Pediatric Endocrinology and Metabolism. 2020;33(4):495-502.
7. Khasanova AK, Dobrodeeva VS, Shnayder NA, Petrova MM, Pronina EA, Bochanova EN, et al. Blood and urinary biomarkers of antipsychotic-induced metabolic syndrome. Metabolites. 2022;12(8):726.
8. Zhou H, Ma ZF, Lu Y, Du Y, Shao J, Wang L, et al. Elevated serum uric acid, hyperuricaemia and dietary patterns among adolescents in mainland China. Journal of Pediatric Endocrinology and Metabolism. 2020;33(4):487-93.
9. Robberecht H, Hermans N. Biomarkers of metabolic syndrome: biochemical background and clinical significance. Metabolic syndrome and related disorders. 2016;14(2):47-93.
10. Isnuwardana R, Bijukchhe S, Thadanipon K, Ingsathit A, Thakkinstian A. Association between vitamin D and uric acid in adults: a systematic review and meta-analysis. Hormone and Metabolic Research. 2020;52(10):732-41.
11. Akash MSH, Haq MEu, Qader A, Rehman K. Biochemical investigation of human exposure to aflatoxin M1 and its association with risk factors of diabetes mellitus. Environmental Science and Pollution Research. 2021;28(44):62907-18.
12. Li X, Meng X, Timofeeva M, Tzoulaki I, Tsilidis KK, Ioannidis JP, et al. Serum uric acid levels and multiple health outcomes: umbrella review of evidence from observational studies, randomised controlled trials, and Mendelian randomisation studies. Bmj. 2017;357.
13. Agius R, Pace NP, Fava S. Reduced leukocyte mitochondrial copy number in metabolic syndrome and metabolically healthy obesity. Frontiers in Endocrinology. 2022;13:886957.
14. Khan SH, Shahid R, Fazal N, Ijaz A. Comparison of various abdominal obesity measures for predicting metabolic syndrome, diabetes, nephropathy, and dyslipidemia. J Coll Physicians Surg Pak. 2019;29(12):1159-64.
15. Zheng S, Nie Z, Lv Z, Wang T, Wei W, Fang D, et al. Associations between plasma metal mixture exposure and risk of hypertension: a cross-sectional study among adults in Shenzhen, China. Frontiers in Public Health. 2022;10:1039514.
16. Tahapary DL, Pratisthita LB, Fitri NA, Marcella C, Wafa S, Kurniawan F, et al. Challenges in the diagnosis of insulin resistance: focusing on the role of HOMA-IR and Tryglyceride/glucose index. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2022;16(8):102581.
17. Lin L, Tan W, Pan X, Tian E, Wu Z, Yang J. Metabolic syndrome-related kidney injury: a review and update. Frontiers in endocrinology. 2022;13:904001.

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