



Comparative Evaluation of Serum Uric Acid Levels in Hypertensive Patients with and Without Metabolic Syndrome.

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Abstract

Background: Serum uric acid has been associated with hypertension and metabolic syndrome, but its relationship among hypertensive patients may be influenced by renal function, medication use and shared metabolic risk factors. Aim: To compare serum uric acid levels in hypertensive patients with and without metabolic syndrome. **Methods:** A hospital-based comparative cross-sectional study was planned among 180 adults with primary hypertension, with 90 participants in each metabolic syndrome group. Metabolic syndrome was classified using harmonized criteria. Fasting serum uric acid was measured by an enzymatic method. Continuous and categorical measures were compared using appropriate tests, and logistic regression was specified to assess the association between uric acid and metabolic syndrome after adjustment for selected confounders. Results: **Results** showed higher mean serum uric acid in participants with metabolic syndrome than in those without it (6.2 ± 1.1 vs 5.1 ± 1.0 mg/dL; mean difference 1.10 mg/dL, 95% CI 0.79–1.41; $p < 0.001$). Hyperuricaemia was present in 46.7% versus 23.3% (RR 2.00, 95% CI 1.31–3.05; $p = 0.001$). Each 1 mg/dL increase in serum uric acid was associated with higher odds of metabolic syndrome (adjusted OR 1.65, 95% CI 1.27–2.15; $p < 0.001$). These values are synthetic and do not represent observed patient data. **Conclusion:** Among hypertensive patients, those with metabolic syndrome had higher serum uric acid levels and a greater prevalence of hyperuricaemia than those without metabolic syndrome. Serum uric acid remained associated with metabolic syndrome after adjustment for selected confounders (adjusted OR 1.65 per 1 mg/dL increase; 95% CI 1.27–2.15; $p < 0.001$). This cross-sectional association does not establish causality.

Keywords: Hypertension; Metabolic syndrome; Serum uric acid.



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INTRODUCTION

Hypertension and metabolic syndrome frequently coexist and substantially increase the lifetime risk of cardiovascular and renal disease. Metabolic syndrome is a cluster of central adiposity, dysglycaemia, raised triglycerides, reduced high-density lipoprotein cholesterol and elevated blood pressure. In people already receiving care for hypertension, identifying additional metabolic abnormalities can help characterize cardiometabolic risk and guide preventive assessment. Serum uric acid (SUA), the end product of purine metabolism in humans, has attracted attention as a readily measurable marker associated with insulin resistance, adiposity, dyslipidaemia, renal handling of sodium and vascular dysfunction. Proposed mechanisms include endothelial nitric-oxide impairment, oxidative stress, activation of inflammatory pathways and altered renal microvascular function; however, observational association does not by itself establish causality or show that urate-lowering treatment improves cardiovascular outcomes [1].

Evidence from population cohorts and clinical samples has repeatedly linked higher SUA with metabolic syndrome and its components. A prospective meta-analysis reported a dose-response association between SUA and incident metabolic syndrome. Other cohort studies found that the association persisted after adjustment for body composition and conventional cardiometabolic factors, although the magnitude varied by sex and population. Among hypertensive patients, SUA has also been associated with metabolic syndrome, renal risk markers and less favourable cardiovascular profiles [2-3].

The relationship remains complex. Reduced kidney function, age, sex, diet, alcohol intake, diuretics and other medicines can affect urate concentrations. Metabolic syndrome definitions also differ in waist thresholds and treatment criteria. A recent systematic review and meta-analysis found higher average urate concentrations among people with metabolic syndrome, although substantial between-study heterogeneity remains. A separate dose-response meta-analysis linked SUA with cardiovascular mortality. Reviews of hyperuricaemia in cardiovascular and metabolic disease therefore describe SUA

as a potentially useful risk marker while emphasizing uncertainty about causal pathways and the clinical benefit of lowering SUA in people without gout [4-5].

AIM

To compare serum uric acid levels in hypertensive patients with and without metabolic syndrome.

OBJECTIVES

1. To describe and compare the sociodemographic and clinical characteristics of hypertensive patients with and without metabolic syndrome.
2. To compare serum uric acid levels and the prevalence of hyperuricaemia between the two groups.
3. To assess the association between serum uric acid and metabolic syndrome after adjustment for selected confounding variables.

MATERIALS AND METHODS

Source of data

Data were obtained from adults with diagnosed primary hypertension attending the outpatient clinics and inpatient services of the study hospital during the study period. Clinical interview, examination, medical records and laboratory investigations were used as sources.

Study design

A hospital-based, comparative cross-sectional study was conducted.

Study location

The study was conducted in the Department of General Medicine at a tertiary care teaching hospital in India. The institution name should be inserted in the final protocol/manuscript.

Study duration

The study was conducted over 12 months, from January to December 2025. The dates should be reconciled with the actual approved protocol and recruitment log before submission.

Sample size

A total sample of 180 participants was planned, with 90 hypertensive patients with metabolic syndrome and 90 without metabolic syndrome. The calculation was based on a two-sided comparison of independent means, using an anticipated standardized difference of 0.46, 5% type I error and 80% power. The calculated minimum was approximately 74 participants per group; allowing approximately 15% for incomplete data gave approximately 87 per group, which was rounded to 90 per group.

n per group = $2 \times (Z\alpha/2 + Z\beta)^2 / d^2$
= $2 \times (1.96 + 0.84)^2 / (0.46)^2 = 73.9$, rounded up to 74 per group; after 15% allowance, $74 / 0.85 = 87.1$. The target was rounded to 90 per group, giving a total sample of 180.

Inclusion criteria

- Adults aged 18–70 years of either sex.
- Known or newly diagnosed primary hypertension, based on documented diagnosis or current antihypertensive treatment.
- Ability and willingness to provide written informed consent.
- Availability of fasting biochemical measurements and waist circumference for classification of metabolic syndrome.

Exclusion criteria

- Secondary hypertension, pregnancy or lactation.
- Known gout, recent acute gout flare, or current urate-lowering therapy.
- Estimated glomerular filtration rate (eGFR) below 60 mL/min/1.73 m², acute kidney injury, or severe hepatic illness.
- Current chemotherapy, active malignancy, or another acute condition likely to alter urate or metabolic measurements.
- Use of medicines known to substantially affect SUA, where a reliable medication history or stable exposure could not be established; diuretic use was recorded and considered during analysis rather than automatically excluding otherwise eligible patients.
- Incomplete essential clinical or laboratory data.

Procedure and methodology

After written informed consent, eligible participants underwent a structured interview and examination. Age, sex, residence, tobacco and alcohol history, diet-related history, physical activity, duration of hypertension, antihypertensive medicines, diabetes history and relevant comorbidities were recorded. Height and weight were measured without shoes using calibrated equipment; body mass index was calculated as weight in kilograms divided by height in metres squared. Waist circumference was measured at the midpoint between the lowest rib and iliac crest at the end of normal expiration. Blood pressure was measured after at least five minutes of seated rest using an appropriately sized cuff; two readings were taken at least one minute apart and the average was recorded.

Metabolic syndrome was classified using the Joint Interim Statement approach: at least three of five components were required. Components were central obesity using Asian waist cut-offs (≥ 90 cm in men or ≥ 80 cm in women), triglycerides ≥ 150 mg/dL or relevant treatment, HDL cholesterol < 40 mg/dL in men or < 50 mg/dL in women or relevant treatment, fasting glucose ≥ 100 mg/dL or glucose-lowering treatment, and elevated blood pressure or treatment. Because all participants had hypertension, blood pressure was recorded but was not sufficient by itself to classify metabolic syndrome. Hypertensive participants were assigned to the metabolic syndrome group if they met at least two of the other four metabolic components in addition to hypertension; this operational rule is equivalent to meeting at least three total components when hypertension is present. The definition and cut-offs were specified before analysis.

For descriptive classification only, hyperuricaemia was defined as SUA > 7.0 mg/dL in men or > 6.0 mg/dL in women. These thresholds were applied consistently, but SUA was also analysed as a continuous variable because cut-offs can vary across laboratories and populations. Treatment history, especially diuretics and losartan, was recorded because these agents may alter urate concentrations.

Sample processing

After an overnight fast of 8–12 hours, venous blood was collected using aseptic precautions. Serum was separated by centrifugation according to laboratory standard operating procedures. SUA was measured using the uricase-peroxidase enzymatic method on an automated biochemistry analyser. Fasting plasma glucose was measured by a validated enzymatic method, and triglycerides and HDL cholesterol were measured using the institution's routine enzymatic assays. Internal quality-control material was run according to laboratory policy. eGFR was estimated using the CKD-EPI equation from serum creatinine. Specimens were processed promptly; delayed samples were stored and handled according to the laboratory protocol.

Statistical methods

Data were entered into a password-protected database and analysed using standard statistical software. Continuous variables were assessed for distribution using graphical methods and the Shapiro–Wilk test. Normally distributed data were summarized as mean (standard deviation) and compared using the independent-samples *t* test; skewed data were summarized as median (interquartile range) and compared using the Mann–Whitney *U* test. Categorical variables were summarized as number (percentage) and compared using the chi-square test or Fisher exact test, as appropriate. Mean differences, risk differences, odds ratios and 95% confidence intervals were reported where suitable. Binary logistic regression was used to estimate the association between SUA and metabolic syndrome, adjusting *a priori* for age, sex, eGFR and smoking status. SUA was entered per 1 mg/dL increase. Multicollinearity and model fit were checked. Two-sided *p* values < 0.05 were considered statistically significant.

Data collection

A pretested structured data-collection form was used. It captured participant identifiers in coded form, consent, demographic details, anthropometry, blood pressure, hypertension history, medication use, comorbidities, laboratory values, metabolic syndrome components and the final group classification. Completed forms were checked for missing or inconsistent entries before database entry. Access to the linking file was restricted to the study team.

RESULTS

Table 1. Demographic and clinical characteristics by metabolic syndrome status (N=180)

Characteristic	With MetS (n=90)	Without MetS (n=90)	Test statistic	Difference (95% CI)	p value
Age, years, mean (SD)	54.8 (10.7)	52.1 (11.4)	<i>t</i> =1.67	2.7 (-0.5 to 5.9)	0.097
Male sex, n (%)	48 (53.3)	49 (54.4)	$\chi^2=0.02$	RD -1.1% (-15.7 to 13.5)	0.881
Hypertension duration, years, mean (SD)	6.2 (4.1)	5.7 (3.8)	<i>t</i> =0.86	0.5 (-0.7 to 1.7)	0.391

Current tobacco use, n (%)	19 (21.1)	22 (24.4)	$\chi^2=0.29$	RD -3.3% (-16.2 to 9.5)	0.591
eGFR, mL/min/1.73 m ² , mean (SD)	82.4 (13.5)	88.6 (12.8)	t=-3.20	-6.2 (-10.0 to -2.4)	0.002
Waist circumference, cm, mean (SD)	96.8 (9.2)	84.1 (8.1)	t=10.11	12.7 (10.2 to 15.2)	<0.001

The two groups had similar age, sex distribution, hypertension duration and tobacco use in dataset. Mean eGFR was lower in the metabolic syndrome group, while mean waist circumference was higher, consistent with the group definition. The between-group eGFR difference was 6.2 mL/min/1.73 m² (95% CI 2.4–10.0; p=0.002).

Table 2. Metabolic and biochemical profile, including the primary outcome (N=180)

Measure	With MetS (n=90)	Without MetS (n=90)	Test statistic	Mean difference (95% CI)	p value
Serum uric acid, mg/dL, mean (SD)	6.2 (1.1)	5.1 (1.0)	t=7.00	1.10 (0.79 to 1.41)	<0.001
Fasting glucose, mg/dL, mean (SD)	119.6 (28.4)	96.8 (14.7)	t=6.88	22.8 (16.2 to 29.4)	<0.001
Triglycerides, mg/dL, mean (SD)	182.3 (61.7)	119.2 (39.8)	t=7.94	63.1 (47.4 to 78.8)	<0.001
HDL cholesterol, mg/dL, mean (SD)	39.8 (8.6)	47.1 (9.2)	t=-5.53	-7.3 (-9.9 to -4.7)	<0.001
Body mass index, kg/m ² , mean (SD)	29.1 (4.2)	24.8 (3.6)	t=7.43	4.3 (3.2 to 5.4)	<0.001

Mean SUA was higher among hypertensive participants with metabolic syndrome than among those without it (6.2±1.1 vs 5.1±1.0 mg/dL; mean difference 1.10 mg/dL, 95% CI 0.79–1.41; p<0.001). As expected from the group definition, fasting glucose, triglycerides and BMI were higher and HDL cholesterol was lower in the metabolic syndrome group.

Table 3. Prevalence of hyperuricaemia and selected metabolic syndrome components (N=180)

Finding	With MetS (n=90)	Without MetS (n=90)	Test statistic	Risk ratio (95% CI)	p value
Hyperuricaemia, n (%)	42 (46.7)	21 (23.3)	$\chi^2=10.31$	RR 2.00 (1.31 to 3.05)	0.001
Central obesity, n (%)	69 (76.7)	24 (26.7)	$\chi^2=45.05$	RR 2.88 (2.00 to 4.13)	<0.001
Raised triglycerides, n (%)	59 (65.6)	22 (24.4)	$\chi^2=30.58$	RR 2.68 (1.82 to 3.93)	<0.001
Low HDL cholesterol, n (%)	53 (58.9)	31 (34.4)	$\chi^2=10.88$	RR 1.71 (1.24 to 2.36)	0.001
Raised fasting glucose / treatment, n (%)	47 (52.2)	19 (21.1)	$\chi^2=18.70$	RR 2.47 (1.59 to 3.84)	<0.001

Hyperuricaemia was present in 46.7% of the metabolic syndrome group and 23.3% of the group without the syndrome, giving risk ratio of 2.00 (95% CI 1.31–3.05; p=0.001). Each metabolic component was also more frequent in the metabolic syndrome group, as expected from its classification criteria. The component comparisons therefore describe group composition and should not be interpreted as independent effects.

Table 4. Multivariable logistic regression for metabolic syndrome among hypertensive participants (N=180)

Predictor	Adjusted OR	95% CI	p value
Serum uric acid, per 1 mg/dL	1.65	1.27 to 2.15	<0.001
Age, per 1 year	1.01	0.98 to 1.04	0.431
Male sex	0.91	0.48 to 1.73	0.779
eGFR, per 10 mL/min/1.73 m ²	0.86	0.73 to 1.02	0.083
Current tobacco use	0.82	0.37 to 1.81	0.622

After adjustment for age, sex, eGFR and current tobacco use, each 1 mg/dL higher SUA was associated with 1.65-fold higher odds of metabolic syndrome (95% CI 1.27–2.15; p<0.001) in the model. This cross-sectional estimate represents adjusted association, not causation. Because the outcome group definition includes metabolic components related to adiposity and glucose/lipids, the interpretation depends on the prespecified model and careful avoidance of overadjustment.

DISCUSSION

Yuan et al. [1] reported a dose-response relationship between SUA and incident metabolic syndrome in prospective studies, supporting the rationale for examining SUA as a continuous exposure. Li et al. [2] found higher SUA associated with hypertension and metabolic syndrome in a large cohort of people with type 2 diabetes. Yu et al. [3] and Al-Daghri et al. [4] likewise reported associations after adjustment for clinical and body-composition variables. These studies support the plausibility of a higher average SUA in the metabolic syndrome group, while differences in population, diabetes status, renal function, sex composition and metabolic syndrome criteria limit direct comparison of effect sizes.

Studies in younger adults and community cohorts also point to a graded association. Observational work among young adults has linked SUA with metabolic syndrome and hypertension [5], while prospective cohorts have reported increased incidence of metabolic syndrome across higher SUA categories [6,7]. Nagahama et al. [8] observed that higher SUA predicted new-onset hypertension and metabolic syndrome in a Japanese screening cohort. The present study's cross-sectional design, if replicated with real data, would complement these longitudinal observations by describing the association among patients already known to have hypertension; it would not establish whether higher SUA preceded the syndrome.

In hypertensive clinical populations, the relationship may also reflect shared risk factors and renal physiology. Ramirez et al. [9] reported associations between SUA and metabolic parameters in essential hypertension. K-MetS investigators found hyperuricaemia associated with a greater likelihood of uncontrolled blood pressure among treated hypertensive patients [10]. These findings reinforce the need to record kidney function and antihypertensive medications. Thiazide and loop diuretics can raise urate, while losartan may lower it; failure to account for such exposure could bias comparisons.

Multivariable model showed higher odds of metabolic syndrome with increasing SUA. This is compatible with the prospective association reported by Yu et al. [3] and findings from other cohorts [6,7,11]. In women from northeast Brazil, Feitosa et al. [12] reported independent associations between SUA, hypertension and metabolic syndrome. Liu et al. [13] found sex-specific patterns in longitudinal urate change and incident metabolic syndrome, underscoring that pooled estimates may mask effect modification. Future analyses should consider sex-stratified estimates when sample size permits, as well as continuous SUA with flexible modelling rather than relying only on dichotomous hyperuricaemia thresholds.

The difference in group means shown in Table 2 is also broadly consistent with the meta-analysis by Raya-Cano et al. [14], which found higher average urate among people with metabolic syndrome, and the prospective cohort and updated meta-analysis by Chen et al. [15], which linked higher SUA with incident metabolic syndrome. Rahimi-Sakak et al. [11] separately reported an association between SUA and cardiovascular mortality. Borghi et al. [16] and Vareldzis et al. [17] describe plausible links among urate, hypertension, metabolic dysfunction and kidney disease, but emphasize that observational associations and proposed mechanisms do not prove that urate lowering will prevent cardiovascular events. Consequently, SUA may help characterize risk, but treatment decisions should continue to follow established indications such as gout and should not be inferred from a cross-sectional association alone.

CONCLUSION

Hypertensive patients with metabolic syndrome had significantly higher mean serum uric acid levels than those without it (6.2 ± 1.1 vs 5.1 ± 1.0 mg/dL), and hyperuricaemia was twice as prevalent (46.7% vs 23.3%). Higher serum uric acid was independently associated with greater odds of metabolic syndrome after adjustment for age, sex, eGFR and tobacco use. These findings suggest that serum uric acid may help characterize cardiometabolic risk in people with hypertension; however, the cross-sectional design cannot establish a temporal or causal relationship.

LIMITATIONS OF THE STUDY

- A hospital-based cross-sectional design would limit generalizability and cannot establish temporal sequence or causality.
- Residual confounding may remain from diet, alcohol use, physical activity, menopausal status, medication exposure and other renal or metabolic factors.
- SUA and metabolic syndrome components may vary with recent diet, hydration, acute illness and laboratory measurement; a single measurement may not represent long-term exposure.
- Hyperuricaemia thresholds vary by sex, guideline and laboratory; dichotomization can misclassify individuals and loses information relative to continuous SUA.
- Medication effects, particularly diuretics and urate-modifying antihypertensive drugs, could influence SUA and require detailed recording and analytic consideration.
- The sample size calculation used an assumed standardized difference; the final calculation should cite the actual source estimate and be aligned with the approved protocol and available recruitment numbers.

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