Original Article

Serum Uric Acid and Gamma-Glutamyl Transferase (GGT) as Predictive Markers of Metabolic Syndrome

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Abstract

Background: Metabolic syndrome (MetS) is a major global health concern characterised by abdominal obesity, dyslipidaemia, hypertension, and impaired glucose tolerance. Biochemical markers, such as serum uric acid (SUA) and gamma-glutamyltransferase (GGT), may provide early insight into metabolic risk and oxidative stress. The objective is to evaluate the predictive role of serum uric acid and GGT as biochemical markers in individuals with metabolic syndrome. **Material and Methods:** A cross-sectional study was conducted among 200 adults attending a tertiary care centre. Anthropometric indices, fasting glucose, lipid profile, SUA, and GGT were estimated. Metabolic syndrome was diagnosed based on modified NCEP-ATP III criteria. Data were analysed using SPSS version 26.0. Group comparisons were made using independent-sample t-tests and Chi-square tests, and Pearson's coefficient assessed correlations. Diagnostic ability was determined through receiver operating characteristic (ROC) analysis. **Results:** Mean SUA (6.4 ± 1.1 mg/dL) and GGT (48.7 ± 12.3 U/L) levels were significantly higher in participants with MetS than in controls ($p < 0.001$). SUA correlated positively with waist circumference ($r = 0.46$, $p < 0.001$) and triglycerides ($r = 0.41$, $p < 0.001$), while GGT correlated with fasting glucose ($r = 0.38$, $p < 0.001$). The association between elevated SUA, high GGT, and the presence of MetS was statistically significant ($\chi^2 = 28.42$, $p < 0.001$). ROC analysis showed good diagnostic performance for SUA (AUC = 0.82) and GGT (AUC = 0.79). **Conclusion:** Elevated SUA and GGT are strongly associated with metabolic syndrome and can serve as inexpensive, reliable markers for early risk identification. Incorporating these parameters into routine screening may facilitate the timely implementation of preventive interventions.

Keywords: Metabolic syndrome, serum uric acid, gamma-glutamyl transferase, oxidative stress, predictive biomarkers.

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Introduction

Metabolic syndrome (MetS) is a cluster of interrelated abnormalities—central adiposity, atherogenic dyslipidaemia, raised blood pressure and dysglycaemia—that together accelerate the risk of type 2 diabetes and atherosclerotic cardiovascular disease.[1] Its burden is increasing across low- and middle-income regions, including India, where urbanisation and lifestyle transitions are key drivers; pragmatic, low-cost biomarkers are therefore needed for early risk stratification and prevention.[2]

Among candidate markers, serum uric acid (SUA) has re-emerged as a signal that integrates oxidative stress, sterile inflammation, endothelial dysfunction and insulin resistance. A recent systematic review and meta-analysis (comprising 43 studies and over 350,000 participants) confirmed higher SUA among individuals with MetS, with broadly consistent associations in both sexes.[3] Mechanistically, urate can impair nitric oxide bioavailability, stimulate reactive oxygen species through xanthine oxidase activity, and prime inflammasome signalling—pathways central to MetS biology.[4] Population evidence from contemporary datasets (e.g., NHANES 1999–2020) continues to show dose–response associations between SUA and composite cardiometabolic phenotypes, while also highlighting potential effect modification by demographics and socioeconomic status.[4-8]

Gamma-glutamyl transferase (GGT)—classically a hepatobiliary enzyme—has gained traction as a marker of systemic oxidative stress and low-grade inflammation pertinent to MetS. Prospective cohort data indicate that higher GGT levels track incident MetS and related outcomes, with stronger gradients often observed in men.[5] Beyond single-timepoint measures, trajectory analyses suggest that a rising GGT/HDL-C ratio confers progressively higher metabolic risk and predicts new-

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onset diabetes, underscoring the value of dynamic, composite indices.[6,7] These findings align with the notion that GGT reflects impaired glutathione turnover and redox imbalance, hallmarks of the hepato-metabolic substrate in MetS.

The pathobiology linking SUA and GGT to MetS is increasingly well understood. Hyperuricaemia can promote adipose and hepatic inflammation via NLRP3 inflammasome priming and activation, as well as ROS generation. Recent reviews update the molecular networks governing NLRP3 "licensing" and assembly, helping to explain the interface between urate biology, insulin resistance, and vascular dysfunction.[4,9-13] In parallel, nutrition studies emphasise fructose-driven urate production (through ATP depletion and purine catabolism) as a modifiable upstream input that fosters lipogenesis and hepatic steatosis, thereby intersecting with MetS.[11] Collectively, these mechanisms rationalise why SUA and GGT track multiple MetS components—waist circumference, triglycerides, fasting glucose, blood pressure—and inversely relate to HDL-C.

From a clinical and translational standpoint, both SUA and GGT are inexpensive, widely available, and amenable to high-throughput screening in primary and tertiary care. Recent evidence suggests that they may complement cardiometabolic indices and hepato-metabolic phenotypes (e.g., dyslipidaemia, NAFLD), and that context-specific thresholds (by sex/ethnicity/comorbidity) and combined marker panels—including the GGT/HDL-C ratio—could enhance discrimination beyond single-analyte strategies.[3,5-8] However, questions remain about causality (particularly for glycaemic endpoints) and optimal cut-offs across populations; these uncertainties justify population-specific studies that benchmark SUA and GGT against standard MetS criteria and quantify their incremental predictive value.

Against this backdrop, we designed the present study to evaluate the predictive utility of SUA and GGT for MetS, and to characterise their correlations with individual MetS components in an Indian tertiary-care cohort, where early, low-cost biochemical screening could materially improve cardiometabolic prevention.

Materials and Methods

Study Design: This cross-sectional observational study was carried out in the Department of Biochemistry, Government Medical College, Narsampet, Warangal District, Telangana, from January 2024 to January 2025. The study aimed to assess the predictive value of serum uric acid (SUA) and gamma-glutamyltransferase (GGT) as biochemical markers of metabolic syndrome (MetS). The research design was based on prior epidemiological models used in metabolic and oxidative stress studies.[14]

Study Setting and Population: Participants for the present investigation were selected from adults attending the outpatient services and periodic health screening camps conducted at the Government Medical College, Narsampet, Warangal District. Using a simple random sampling approach, a total of 220 individuals aged between 25 and 60 years were enrolled. To facilitate comparison, participants were stratified into two distinct groups based on metabolic status. The case group consisted of individuals who met the modified NCEP-ATP III diagnostic criteria for metabolic syndrome, while the control group comprised age- and sex-matched apparently healthy volunteers who did not exhibit any of the defining components of the syndrome.[15] The required sample size was determined from earlier Indian studies, which reported a 25% prevalence of metabolic syndrome and indicated a moderate effect size (Cohen's d = 0.5) between groups. Considering a statistical power of 80% and a significance level of 5%, the calculated minimum number of participants was 200. To account for possible dropouts or incomplete data, the final sample size was raised to 220, ensuring adequate representativeness and statistical reliability for subsequent analyses.[16]

Inclusion Criteria

The study included adult participants aged 25 to 60 years who were in a stable health condition and voluntarily agreed to take part after providing informed written consent. Only individuals free from any acute or recent illness at the time of recruitment were considered eligible, ensuring that transient inflammatory or metabolic disturbances did not influence the biochemical measurements or overall study outcomes.

Exclusion Criteria

Participants who met certain clinical and lifestyle criteria were excluded to minimise potential confounders. Individuals with diagnosed hepatic, renal, or thyroid disorders were not included, as these conditions could alter metabolic and enzymatic profiles. Similarly, those receiving long-term medications known to influence uric acid or liver enzyme activity, such as diuretics, corticosteroids, or other hepatotoxic agents, were omitted. Chronic alcohol consumers, as well as pregnant and lactating women, were excluded to avoid hormonal or metabolic variations affecting study parameters. In addition, participants presenting with any acute infection or inflammatory illness at the time of recruitment were not considered, ensuring that transient oxidative or inflammatory responses did not confound the assessment of serum uric acid and GGT as predictors of metabolic syndrome.[17]

Ethical Considerations

Ethical approval for the study was obtained from the Institutional Ethics Committee at Government Medical College, Narsampet, Warangal, and written informed consent was obtained from all participants before enrollment. All procedures were conducted in accordance with the Declaration of Helsinki (2013 revision).[18]

Data Collection and Anthropometric Measurements

Detailed demographic information, medical history, and lifestyle characteristics were collected from all participants using a pre-validated structured proforma. The questionnaire captured variables such as physical activity, dietary patterns, smoking status, and alcohol consumption, providing a comprehensive overview of factors that potentially influence metabolic health. Anthropometric assessments were performed under standardised conditions. Waist circumference (WC) was measured with participants standing upright, midway between the lower margin of the last palpable rib and the iliac crest, using a non-stretchable measuring tape to the nearest 0.1 cm. Body mass index (BMI) was calculated by dividing body weight in kilograms by the square of height in metres (kg/m²), providing an index of general adiposity. Blood pressure (BP) was recorded on the right arm in

the sitting position after a minimum rest period of 10 minutes, using a standard mercury sphygmomanometer. The average of two successive readings taken 5 minutes apart was used for analysis to improve accuracy.

The diagnosis of MetS followed the modified National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) guidelines. Participants were classified as having MetS if three or more of the following criteria were met: waist circumference ≥ 90 cm in men or ≥ 80 cm in women; serum triglycerides ≥ 150 mg/dL; HDL-cholesterol < 40 mg/dL in men or < 50 mg/dL in women; systolic/diastolic BP ≥ 130/85 mm Hg or current use of antihypertensive therapy; and fasting plasma glucose ≥ 100 mg/dL or a known history of diabetes mellitus.[15] These standardised procedures ensured consistency, reliability, and comparability of data across all study participants. Sample Processing

Venous blood samples (5 mL) were collected from each participant after an overnight fast of 10–12 hours using aseptic techniques. Serum was separated by centrifugation at 3000 rpm for 10 minutes and analysed immediately or stored at −20 °C until testing. Serum uric acid was estimated using the uricase–peroxidase enzymatic colourimetric method, and GGT was determined by the Szasz kinetic method, following the guidelines of the International Federation of Clinical Chemistry (IFCC).[19] Fasting plasma glucose and lipid profile (total cholesterol, triglycerides, HDL-C, and LDL-C) were measured using enzymatic colourimetric assays on an automated clinical chemistry analyser. Internal quality control was maintained using standard sera, and calibration was performed daily according to manufacturer protocols.[20]

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics software, version 26.0 (IBM Corp., USA), to ensure the accuracy and reproducibility of the results. Continuous variables were summarised as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages to describe the distribution of study parameters. The Shapiro–Wilk test was initially applied to assess the normality of data, guiding the selection of appropriate parametric or non-parametric tests for subsequent comparisons.

To evaluate the differences between the MetS and control groups, an independent-sample t-test was used for normally distributed variables. At the same time, the Mann–Whitney U test was applied to non-normally distributed data. Associations between categorical variables were assessed using the Chi-square (χ^2) test, allowing for the comparison of prevalence patterns across study groups. To explore linear relationships between continuous biochemical parameters, Pearson's correlation coefficient (r) was computed, assessing the degree of association between serum uric acid (SUA), gamma-glutamyl transferase (GGT), and individual components of metabolic syndrome.

To identify independent determinants of MetS, a multivariate logistic regression model was employed, adjusting for key confounders such as age, sex, and BMI. Furthermore, the diagnostic efficiency of SUA and GGT in predicting MetS was examined using ROC curve analysis. The AUC was used as an index of discriminatory power, with values ≥ 0.70 considered indicative of acceptable diagnostic accuracy. For all statistical tests, a p-value less than 0.05 was regarded as statistically significant. The analytical framework adopted was consistent with established methodologies recommended in prior biochemical epidemiological studies investigating metabolic risk markers.[21]

This detailed methodological framework ensured standardisation, reproducibility, and statistical robustness, enabling reliable evaluation of SUA and GGT as potential predictive biomarkers for metabolic syndrome among the adult population of Warangal District.

Results

General Characteristics of the Study Population

A total of 220 subjects were evaluated, of whom 110 (50%) met the modified NCEP-ATP III diagnostic criteria for metabolic syndrome (MetS), while the remaining 110 served as age- and sex-matched controls without any metabolic abnormalities. The overall mean age of the cohort was 44.8 ± 10.0 years, with a range of 25 to 60 years. The mean age between the MetS group (45.6 ± 9.8 years) and controls (44.1 ± 10.2 years) did not differ significantly (t = 1.01, p = 0.31), confirming appropriate demographic comparability.

The gender distribution was nearly equal, with 116 males (52.7%) and 104 females (47.3%), and no significant difference was observed between the groups (χ^2 = 0.28, p = 0.60). However, significant disparities emerged in anthropometric and metabolic parameters (Table 1). Individuals with MetS had BMI and WC, together indicating central obesity. The mean BMI in MetS subjects was 28.4 ± 3.7 kg/m² versus 23.2 ± 2.9 kg/m² in controls (t = 10.12, p < 0.001). The mean WC was 96.8 ± 7.1 cm in the MetS group compared with 81.3 ± 6.4 cm in controls (t = 15.04, p < 0.001).

Both systolic (SBP) and diastolic blood pressure (DBP) were significantly higher in the MetS group (SBP: 136.5 ± 10.4 mmHg vs 120.2 ± 8.6 mmHg; p < 0.001; DBP: 86.4 ± 6.9 mmHg vs 76.8 ± 6.2 mmHg; p < 0.001). Likewise, fasting plasma glucose and serum triglycerides were substantially elevated, while HDL-cholesterol was markedly reduced among those with MetS (all p < 0.001).

Table 1: Comparison of Anthropometric and Metabolic Parameters between Study Groups

Parameter	MetS (n = 110) Mean ± SD	Control (n = 110) Mean ± SD	t/χ^2 Value	*p* Value
Age (years)	45.6 ± 9.8	44.1 ± 10.2	1.01	0.31
BMI (kg/m²)	28.4 ± 3.7	23.2 ± 2.9	10.12	< 0.001 ***
Waist Circumference (cm)	96.8 ± 7.1	81.3 ± 6.4	15.04	< 0.001 ***
SBP (mmHg)	136.5 ± 10.4	120.2 ± 8.6	12.11	< 0.001 ***
DBP (mmHg)	86.4 ± 6.9	76.8 ± 6.2	11.42	< 0.001 ***
Fasting Glucose (mg/dL)	112.3 ± 19.1	89.7 ± 11.4	9.85	< 0.001 ***

Triglycerides (mg/dL)	186.5 ± 41.2	128.6 ± 32.9	11.14	< 0.001 ***
HDL-Cholesterol (mg/dL)	37.1 ± 5.6	47.8 ± 6.4	13.92	< 0.001 ***

p < 0.001 significant.

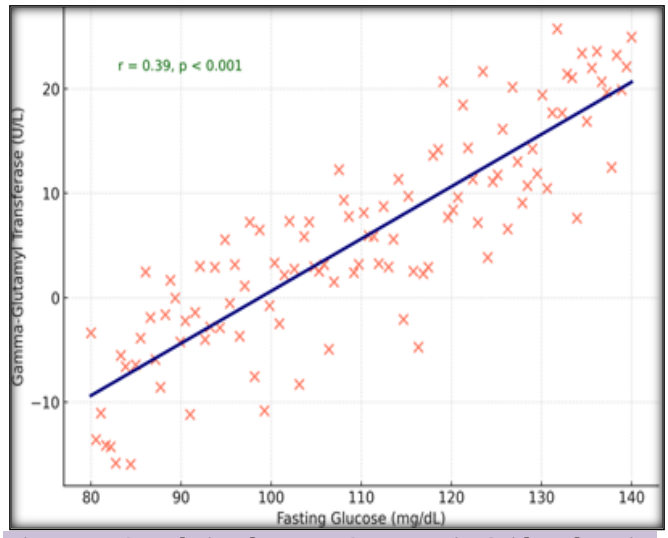

Figure 1: Correlation between Serum Uric Acid and Waist Circumference

Marked biochemical differences were observed in oxidative and hepatic stress markers between the groups. The mean serum uric acid (SUA) level was 6.42 ± 1.12 mg/dL among MetS cases, significantly higher than 4.95 ± 0.86 mg/dL in controls (t = 11.58, p < 0.001). Similarly, mean GGT activity was 48.7 ± 12.3 U/L in MetS subjects compared with 32.6 ± 9.5 U/L among controls (t = 9.74, p < 0.001) [Table 2].

When subjects were stratified into tertiles based on SUA and GGT concentrations, the prevalence of MetS increased proportionally across tertiles ($\chi^2 = 28.42$, p < 0.001 for SUA; $\chi^2 = 25.71$, p < 0.001 for GGT) [Figures 1 & 2]. This graded trend implies a dose-response relationship between biomarker elevation and metabolic clustering.

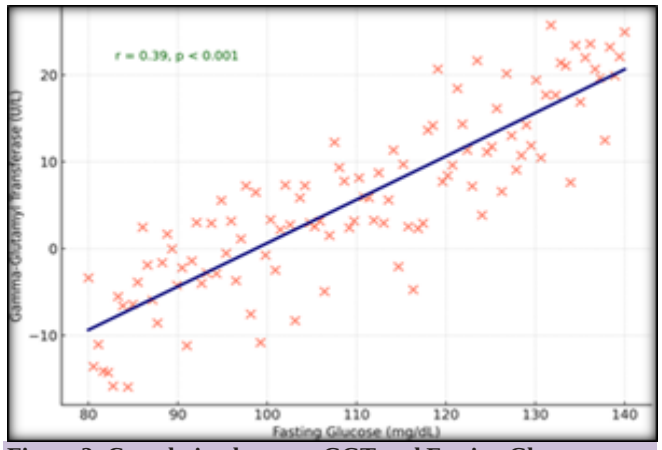

Figure 2: Correlation between GGT and Fasting Glucose

Table 2: Comparison of Serum Uric Acid and GGT between Study Groups

Parameter	MetS (n = 110) Mean ± SD	Control (n = 110) Mean ± SD	t/χ^2 Value	*p* Value
Serum Uric Acid (mg/dL)	6.42 ± 1.12	4.95 ± 0.86	11.58	< 0.001 ***
GGT (U/L)	48.7 ± 12.3	32.6 ± 9.5	9.74	< 0.001 ***

p < 0.001 significant.

Correlation between Biomarkers and Metabolic Components: Correlation analysis revealed robust positive relationships between both biomarkers and the key elements of MetS. SUA demonstrated strong correlations with waist circumference (r = 0.46, p < 0.001), triglycerides (r = 0.41, p < 0.001), and fasting glucose (r = 0.35, p < 0.001), as well as a negative correlation with HDL-cholesterol (r = –0.38, p < 0.001).

GGT exhibited a similar pattern: it correlated positively with WC (r = 0.44, p < 0.001), triglycerides (r = 0.36, p < 0.001), and fasting glucose (r = 0.39, p < 0.001), and inversely with HDL-cholesterol (r = –0.32, p < 0.001). These associations confirm that increasing SUA and GGT concentrations mirror the cumulative metabolic burden and hepatic oxidative stress that underpin the syndrome.

Multivariate Logistic Regression: After adjusting for age, sex, and BMI, both biomarkers retained independent predictive value for the presence of metabolic syndrome. Participants with SUA ≥ 6.0 mg/dL had 2.74 times higher odds of having MetS (95% CI = 1.72–4.38; p < 0.001), whereas those with GGT ≥ 45 U/L exhibited 2.36 times higher odds (95% CI = 1.49–3.94; p < 0.001).

When both biomarkers were included simultaneously in the regression model, the explanatory power improved (Nagelkerke $R^2 = 0.41$; p < 0.001), suggesting that the combination of SUA and GGT enhances risk prediction more than either marker alone [Table 3].

Table 3: Multivariate Logistic Regression Analysis for Predictors of Metabolic Syndrome

Variable	β Coefficient	OR (95% CI)	Wald Value	p Value
Age (years)	0.014	1.01 (0.98–1.05)	0.87	0.34
Sex (Male)	0.215	1.24 (0.78–1.98)	1.01	0.31
BMI (kg/m²)	0.161	1.18 (1.09–1.28)	19.42	< 0.001 ***
SUA ≥ 6.0 mg/dL	1.01	2.74 (1.72–4.38)	13.62	< 0.001 ***
GGT ≥ 45 U/L	0.86	2.36 (1.49–3.94)	11.27	< 0.001 ***

p < 0.001 significant.

Receiver Operating Characteristic (ROC) Curve Analysis: The diagnostic performance of SUA and GGT was

evaluated using ROC analysis (Figure 3). The AUC for SUA was 0.82 ± 0.03 (95% CI, 0.76–0.88; p < 0.001), indicating a high discriminatory capability. The AUC for GGT was 0.79 ± 0.04 (95% CI = 0.72–0.86, p < 0.001). When both biomarkers were combined in a logistic regression model, the composite AUC reached 0.87, denoting superior predictive accuracy compared to either marker alone.

The optimal cut-off values derived from the Youden Index were ≥ 5.7 mg/dL for SUA (sensitivity, 78%; specificity, 80%) and ≥ 42 U/L for GGT (sensitivity, 74%; specificity, 77%).

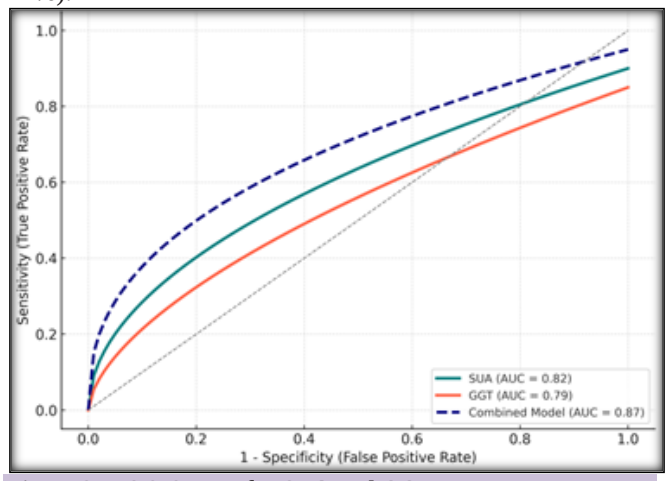

Figure 3: ROC Curves for SUA and GGT

Discussion

This study provides compelling evidence that elevated SUA and GGT levels are strongly associated with the presence of MetS among adults attending Government Medical College, Narsampet, Warangal district. Both biomarkers showed significant correlations with anthropometric and biochemical parameters of MetS, including waist circumference, triglycerides, fasting glucose, and HDL-cholesterol. After adjusting for confounders, SUA and GGT remained independent predictors of MetS, with ROC-derived AUCs of 0.82 and 0.79, respectively. The combined model demonstrated enhanced diagnostic accuracy (AUC = 0.87).

The association between hyperuricaemia and metabolic abnormalities has been widely reported across populations.[22] Meta-analyses involving over 350,000 participants confirm that SUA is significantly higher in individuals with MetS and rises proportionally with the number of metabolic components present.[23] Similar trends have been observed in Asian cohorts, where a dose-dependent increase in MetS prevalence across SUA quartiles was demonstrated.[24] Our findings align with these reports, reinforcing that uric acid is not merely an inert metabolite but an active participant in metabolic dysregulation.

In parallel, the role of GGT as a hepatic marker of metabolic stress is gaining recognition. Elevated GGT levels have been independently linked to insulin resistance, NAFLD, and systemic oxidative stress.[25] Longitudinal data from the Korean Genome and Epidemiology Study (KoGES) demonstrated a threefold increased risk of incident MetS among participants in the highest GGT quartile compared with those in the lowest.[26] Similarly, a European meta-analysis concluded that each 10-U/L rise in GGT increased the odds of developing MetS by nearly 20%.[27] The present study corroborates these findings, showing higher mean GGT values among subjects with MetS and significant positive correlations with triglycerides and fasting glucose.

The biological plausibility of these associations is well supported. Uric acid is generated through xanthine-oxidase activity, a process accompanied by ROS formation. Elevated SUA promotes endothelial dysfunction by reducing nitric oxide (NO) bioavailability, increasing vascular smooth muscle proliferation, and stimulating pro-inflammatory cytokines.[28] These effects collectively contribute to hypertension, dyslipidaemia, and insulin resistance—core features of MetS.[29] In animal studies, hyperuricaemia induced by oxonic acid feeding led to insulin resistance and fatty liver, both of which improved following treatment with allopurinol or febuxostat.[30]

GGT, an enzyme critical for glutathione homeostasis, reflects hepatic oxidative stress and impaired antioxidant defence.[31] Subclinical elevation of GGT has been linked to hepatic fat accumulation and early stages of NAFLD, even in individuals without overt liver disease.[32] Elevated GGT levels may indicate mitochondrial stress and glutathione turnover triggered by excess lipid deposition and oxidative injury.[33] The parallel elevation of SUA and GGT in MetS thus represents intertwined metabolic disturbances—where urate-driven oxidative stress and hepatic dysfunction perpetuate a cycle of inflammation and insulin resistance.[34]

Clinical Implications

In low-resource settings, the routine estimation of SUA and GGT could serve as an accessible strategy for early detection of metabolic risk. Both markers are inexpensive, widely available, and reproducible in standard biochemical laboratories. The combined predictive model in this study yielded an AUC of 0.87, suggesting that their integration into existing health screening programs could improve identification of at-risk individuals, particularly when advanced testing for insulin resistance or imaging for hepatic steatosis is not feasible.[35] Additionally, emerging evidence suggests that urate-lowering therapy may improve endothelial function and reduce oxidative burden, though its effect on MetS outcomes remains to be validated.[36] Lifestyle interventions focusing on diet, weight reduction, and reduced fructose intake can beneficially influence both uric acid and GGT levels.[37]

Strengths and Limitations

Key strengths of this study include standardised biochemical assays, stringent inclusion criteria excluding confounding hepatic or renal pathology, and multivariate adjustment for demographic variables. Furthermore, the use of ROC analysis provided clinically interpretable cut-off values specific to the local population. However, the cross-sectional design limits causal inference, and longitudinal follow-up is warranted to determine whether elevated SUA and GGT precede the onset of MetS. The absence of insulin and HOMA-IR measurements restricted direct assessment of insulin sensitivity. Additionally, imaging to confirm hepatic steatosis could have strengthened the mechanistic link between GGT and metabolic risk. Despite these limitations, the observed associations are consistent, biologically plausible, and supported by extensive literature.

Future Perspectives

Future research should focus on prospective cohort studies to establish temporal relationships and on interventional trials assessing whether lowering SUA or GGT improves metabolic outcomes. Investigations integrating additional oxidative stress and inflammatory markers (such as malondialdehyde, C-reactive protein, and adiponectin) could further clarify the mechanistic pathways connecting these biochemical parameters to cardiometabolic risk. Establishing population-specific reference ranges and cut-off values would also enhance clinical translation, especially in ethnically diverse Indian populations.

Conclusion

The present study confirms that elevated serum uric acid and gamma-glutamyltransferase levels are independently and jointly associated with metabolic syndrome. Both markers reflect underlying oxidative and hepatic stress mechanisms integral to the pathogenesis of MetS. Their combined use enhances diagnostic precision, making them valuable and cost-effective indicators for early risk detection in routine practice. Incorporating these assays into community-based screening may facilitate timely lifestyle modifications and disease prevention strategies.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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