

Research Article

Serum Uric Acid as Biomarker for Diagnosis of Metabolic Dysfunction Associated Steatotic Liver Disease

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Abstract

Metabolic dysfunction-associated steatotic liver disease (MASLD) is the most recent designation for steatotic liver disease linked to metabolic syndrome. It is a widespread condition that currently affects an estimated one third of adults worldwide. This study evaluated serum uric acid levels and their diagnostic significance for Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) among 162 males and 182 females. Mean uric acid levels were significantly higher in males (8.05 mg/dL) compared to females (7.85 mg/dL) ($P = 0.012$). Male values demonstrated slight right skewness, whereas females showed greater variability and heterogeneity. Receiver Operating Characteristic (ROC) analysis revealed excellent diagnostic performance of uric acid for MASLD, with Area Under the Curve (AUC) values of 0.9924 in males and 0.9301 in females, indicating very high predictive accuracy. Cost-threshold and rotated ROC analyses identified gender-specific optimal cutoff values. The most effective diagnostic thresholds were approximately 7.19 mg/dL for males and 6.12 mg/dL for females, highlighting important biological differences in uric acid metabolism between genders. In males, a cutoff around 7.0-7.5 mg/dL achieved high sensitivity with minimal false-positive rates. Elevated uric acid was strongly associated with metabolic dysfunction, insulin resistance, and oxidative stress, supporting its role as a low-cost and reliable biomarker for early MASLD screening. These findings suggest that gender-specific serum uric acid thresholds may improve the diagnostic accuracy and clinical assessment of MASLD.

Keywords: serum uric acid, metabolic dysfunction, steatotic liver disease, major worldwide health issue.

INTRODUCTION

Metabolic dysfunction-associated steatotic liver disease (MASLD) has arisen as a major worldwide health issue, encompassing a range of liver conditions closely associated with metabolic disturbances (Rinella *et al.*, 2023). This condition, recently renamed from non-alcoholic fatty liver disease (NAFLD) and metabolic dysfunction-associated fatty liver disease (MAFLD), encompasses a range of hepatic manifestations including simple

steatosis, steatohepatitis, cirrhosis, and hepatocellular carcinoma (Younossi *et al.*, 2019; Eslam *et al.*, 2020). The change in nomenclature mirrors a fundamental transformation in our comprehension of the disease, highlighting the importance of metabolic dysfunction as its primary aspect rather than just the elimination of alcohol use (Eslam *et al.*, 2021). In addition to hepatic fat accumulation, MASLD is characterized by metabolic abnormalities including insulin

resistance, hypertension, and dyslipidemia (Eslam *et al.*, 2020). In China, various regional factors—including dietary habits high in carbohydrates and purines, genetic susceptibilities, and the increasing incidence of metabolic syndrome (MetS) may play a role in the growing burden of MASLD and underscore the importance of serum uric acid (SUA) as a biomarker. Chinese dietary practices differ greatly by region, affecting SUA levels and metabolic health. Studies have pinpointed different eating habits that are associated with SUA levels (Kong *et al.*, 2023; Zhu *et al.*, 2023). Research has also found genetic polymorphisms, including mutations in ABCG2 and URAT1, that are common in the Chinese population and associated with hyperuricemia risk (Zhang *et al.*, 2021). In addition, MetS is becoming increasingly common in China, impacting nearly 34–45% of adults according to different definitions (Ma *et al.*, 2024; Huang *et al.*, 2022). Components of MetS, including obesity, hypertension, dyslipidemia, and insulin resistance, are strongly linked to increased SUA levels and metabolic disturbances typical of MASLD (Shi *et al.*, 2022). Metabolic dysfunction-associated steatotic liver disease (MASLD) is the most recent designation for steatotic liver disease linked to metabolic syndrome. It is a widespread condition that currently affects an estimated one third of adults worldwide (Wong *et al.*, 2023). MASLD is a prevalent condition characterized by the accumulation of excess fat in the liver, occurring without significant alcohol consumption. Due to globalization and the impact of Western cultures, it is expected that the prevalence of MASLD will increase in the coming decade. There is a parallel between this trend and the increasing prevalence of obesity and type 2 diabetes mellitus (Qi *et al.*, 2024). Significant progress has been achieved in recent years regarding the comprehension of the complex pathophysiological mechanisms underlying MASLD. This disease develops due to multiple factors, with growing attention on the impact of metabolic disorders like hyperuricemia (Wan *et al.*, 2016), insulin resistance (Tanase *et al.*, 2020), and hyperlipidemia (Jones *et al.*, 2024). The recent change in terminology from non-alcoholic fatty liver disease (NAFLD) to MASLD more accurately represents the nature of these complex systemic disorders and their cardiometabolic implications (Targher *et al.*,

2024). Due to the absence of effective treatments specifically aimed at MASLD patients, it is crucial to diagnose and manage MASLD as soon as possible. In modern society, the incidence of hyperuricemia is also increasing rapidly due to high-purine diets and sugary drinks. Uric acid, which is the end product of purine metabolism in humans, has been closely associated with the onset of metabolic syndrome (Andres-Hernando *et al.*, 2021; Kanbay *et al.*, 2016; Maloberti *et al.*, 2024), a collection of conditions that encompasses insulin resistance, dyslipidemia, hypertension, MASLD, gout, and cardiovascular diseases (Li *et al.*, 2023; Stewart *et al.*, 2019).

MATERIAL AND METHODS

Study Type: Cross sectional study

Study Design: Present study was carried out at Department Physiology, CMC, Larkana and outpatient Departments of Hepatology at CMC Teaching Hospital Larkana. Before starting of the study written consent from the subjects were obtained scientific review committee and institutional review board and then Board of Advance Studies and Research for approval for this study was also obtained.

Duration of the Study: Present study was started after approval of the synopsis from the institutional scientific committee and Institutional Review Board.

Study Area: This study was carried out at Department Physiology, Chandka Medical College Larkana and outpatient Departments of Hepatology at Chandka Medical College Teaching Hospital Larkana.

Study Population: According to the guideline given in inclusion and exclusion criteria 344 subjects were selected for the study from outpatient Departments of Hepatology at Chandka Medical College Teaching Hospital Larkana.

Estimation of Uric Acid: Stored serum was used for determination of uric acid. Serum was taken and before analysis sample was allowed to attain room temperature then analyzed by performed on chemiluminescence (Michael F.Holick, 2007).

Statistical analysis Data was analyzed through Statistical package by (SPSS-21).

Analysis: The data was analyzed by the SPSS and Statistic Kingdom software and MS Office and displayed by mean, standard deviation, frequencies, percentages, The inferential statistical test known as Student's t test is

used for the evaluation of difference of the numerical data while taking p value ≤ 0.05 as significant and correlations between Uric acid, lipid profiles in selected populations. The parametric test known as Chi- square test is done for the evaluation the difference in the categories & P Value of ≤ 0.05 which was taken as significant for the comparison of

correlation used, it is the most widely used method of measuring the degree of relationship between to variables.

Presentation: Results generated through analysis are presented in tables, bar graphs, pie charts and correlation tables/ graphs.

RESULT

Table-1. Descriptive Statistics of Serum Total Uric Acid Levels in MASLD Patients

Descriptive Statistics	Uric Acid mg/dL	
	Male	Female
Mean	8.05	7.85
Median	7.8	7.85
Mode	7.21	6
Std. Deviation	1.2	1.53
Minimum	6.12	5.11
Maximum	10.94	11.4
95% Confidence interval of Mean	7.87 - 8.24	7.63 - 8.08
Mean $\pm$ Std.	8.05 $\pm$ 1.2	7.85 $\pm$ 1.53
P Values	0.012	

The study evaluated uric acid levels in 162 males and 182 females. Mean levels were slightly higher in males (8.05 mg/dL) than females (7.85 mg/dL), with a statistically significant difference ($P = 0.012$). Male uric acid levels were slightly right-skewed, indicating a few higher values, while female levels were nearly symmetric but showed greater variability ($SD = 1.53$ vs 1.2 mg/dL). The interquartile range and median absolute

deviation also suggest more heterogeneity among females. These findings indicate that males generally have higher uric acid levels, potentially increasing their risk for hyperuricemia-related conditions such as gout and cardiovascular disorders, while females exhibit a broader distribution, highlighting that some individuals may also be at risk.

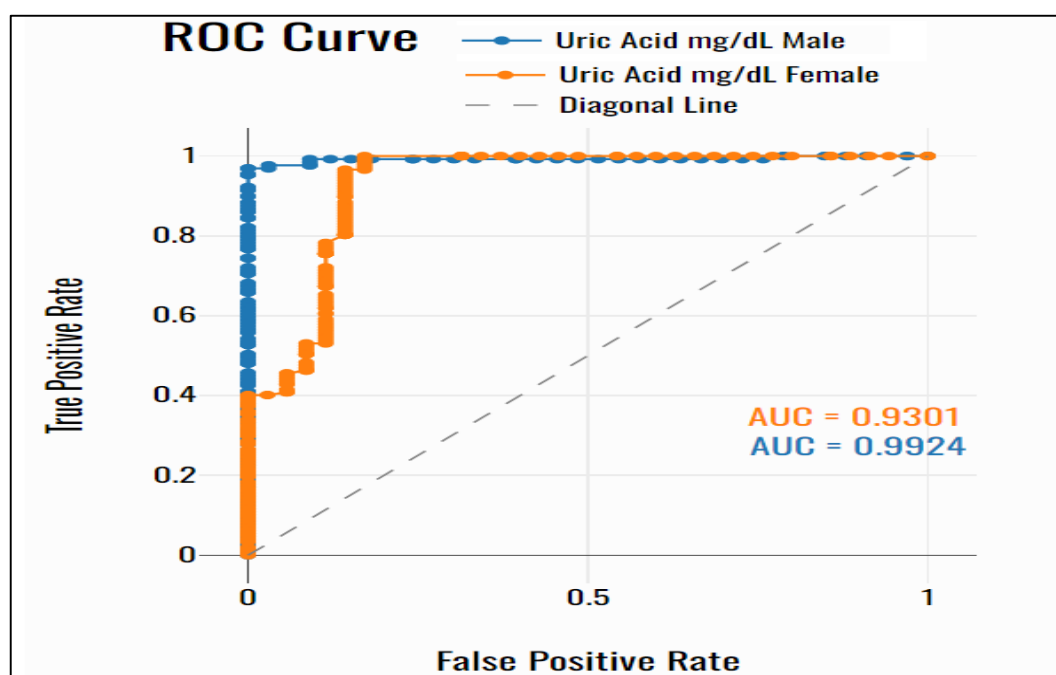


Figure 1. ROC curve evaluates serum uric acid levels (in mg/dL) as a diagnostic biomarker for MASLD

Based on the Receiver Operating Characteristic (ROC) curve provided, it appears that Uric Acid levels are being evaluated as a diagnostic marker for Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD), High Diagnostic Accuracy: The most striking feature of this graph is the Area Under the Curve (AUC). In diagnostic testing, the AUC measures the ability of a test to distinguish between two groups (those with MASLD and those without). Male Patients (Blue Line): With an AUC of 0.9924, Uric Acid is an almost "perfect" predictor for MASLD in this male cohort. It suggests that nearly every male patient with elevated uric acid in this group likely has MASLD. Female Patients (Orange

Line): The AUC of 0.9301 is also excellent. While slightly less "perfect" than the male cohort, it still indicates that Uric Acid is a very strong biomarker for the disease in women. In the context of MASLD, Uric Acid is often considered a proxy for metabolic health. Metabolic Link: High uric acid (hyperuricemia) is strongly associated with insulin resistance and oxidative stress—both of which are primary drivers of fat accumulation in the liver. Early Screening: Because the AUC is so high in both groups, this suggests that monitoring Uric Acid could be a low-cost, effective way to screen for MASLD before resorting to more invasive measures like biopsies or expensive imaging.

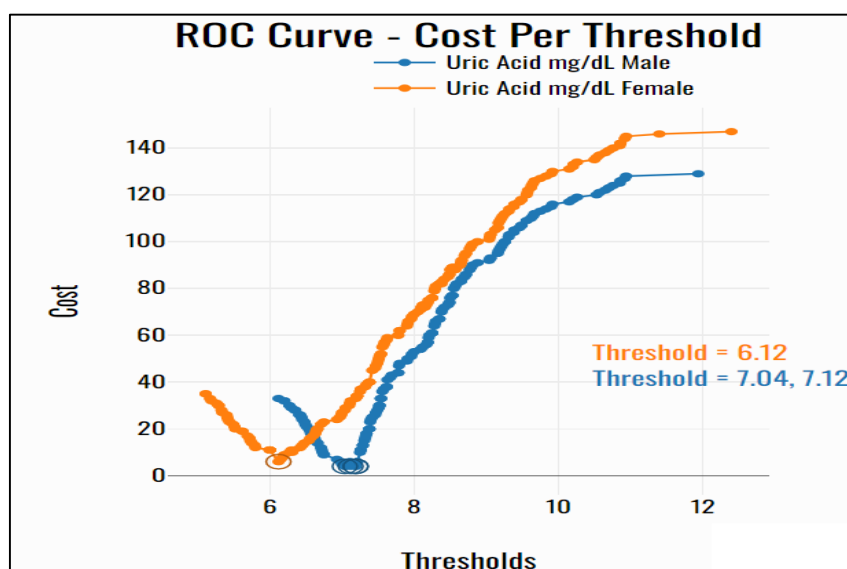


Figure 2. Chart represents a Cost-Threshold Analysis derived from ROC curves.

This chart represents a Cost-Threshold Analysis derived from ROC curves. In the context of MASLD, this is likely being used to determine the optimal serum Uric Acid level to use as a diagnostic cutoff for identifying the disease or its severity. X-Axis (Thresholds): This represents different concentration levels of Uric Acid in mg/dL. Y-Axis (Cost): In medical statistics, Cost doesn't just mean money. Optimal Threshold: Male 6.12 mg/dL and Female 7.04 – 7.12 mg/dL. The best threshold is found at the lowest point of the curve, where the cost to clinical accuracy is minimized. The chart highlights that men and women require different diagnostic thresholds for Uric Acid when assessing MASLD risk. Uric

acid is often elevated in patients with metabolic syndrome. There is a clear biological difference in how uric acid correlates with MASLD between genders. Using a one size fits all threshold (like 7.0 mg/dL for everyone) would likely under-diagnose women or over-diagnose men. Sensitivity vs. Specificity: the threshold lower than the 6.12/7.04 marks, which catch more cases (high sensitivity) but have many false alarms. Threshold higher than 10 mg/dL, the Cost spikes dramatically, meaning miss a massive number of patients who actually have MASLD. For this specific patient population, the most accurate balance to screen for MASLD using Uric Acid is 6.12 mg/dL for females and roughly 7.1

mg/dL for males. Values exceeding these points significantly increase the statistical likelihood of disease presence.

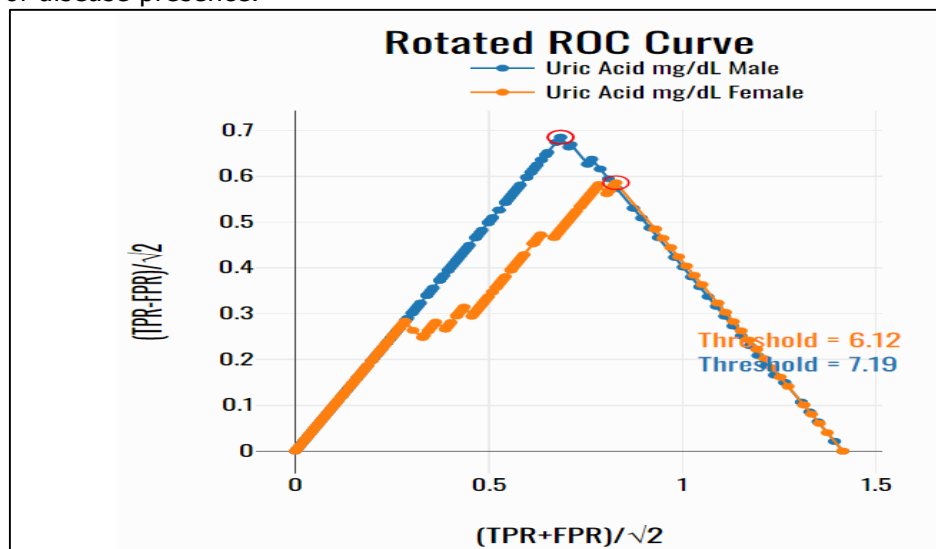


Figure 3. The graph shows a Rotated ROC Curve used to determine the optimal diagnostic thresholds for Uric Acid levels in patients with MASLD

This graph shows a Rotated ROC (Receiver Operating Characteristic) Curve used to determine the optimal diagnostic thresholds for Uric Acid levels in patients with MASLD. By rotating the standard ROC curve by 45 degrees, researchers can more easily identify the point that maximizes the balance between sensitivity (True Positive Rate) and specificity (1 - False Positive Rate). The graph identifies two distinct optimal cut-off points (red circles) for serum uric acid: Male Patients (Blue): The optimal threshold is 7.19 mg/dL. Female Patients (Orange): The optimal threshold is lower, at 6.12 mg/dL. Peak Height: The y-axis represents TPR - FPR which is a variant of the Youden Index. A higher peak indicates better overall diagnostic accuracy. Male vs. Female: The blue curve (males) reaches a higher peak (0.68) compared to the orange curve

(females, 0.58). This suggests that uric acid is a slightly more robust or cleaner diagnostic marker for MASLD in men than in women. Y-Axis TPR - FPR: Measures the diagnostic gain. The higher the value, the better the test is at distinguishing between those with and without MASLD. X-Axis TPR + FPR: Represents the progression along the ROC curve. In the context of MASLD, elevated uric acid is often linked to insulin resistance and metabolic syndrome. For Men: If uric acid levels exceed 7.19 mg/dL, there is a significantly higher likelihood of MASLD presence or progression. For Women: The threshold is lower (6.12 mg/dL), likely due to physiological differences in metabolic processing and the protective effects of estrogen on uric acid excretion.

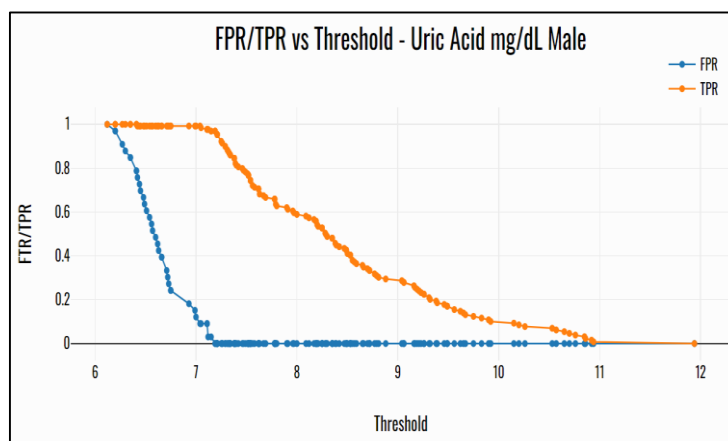


Figure 4. The graph displays the performance of Uric Acid levels (mg/dL) as a diagnostic marker for MASLD in male patients.

This graph evaluates serum uric acid (mg/dL) as a diagnostic marker for MASLD in males by plotting True Positive Rate (TPR/sensitivity) and False Positive Rate (FPR) across different thresholds. Lower thresholds (<6.5 mg/dL): Sensitivity is 100%, but FPR is high—many healthy individuals are misclassified. Higher thresholds (>9.0 mg/dL): FPR approaches 0 (excellent specificity), but sensitivity falls below 30%—most cases are missed. Optimal

cutoff (7.2 mg/dL): FPR is nearly 0 while TPR remains 95%, indicating high diagnostic accuracy with minimal false positives. Overall, the rapid decline in FPR compared to TPR suggests that uric acid is a relatively strong predictor of MASLD in this male cohort. A cutoff around 7.0–7.5 mg/dL appears clinically useful, though diagnosis should always be supported by biochemical tests, imaging, and clinical history.

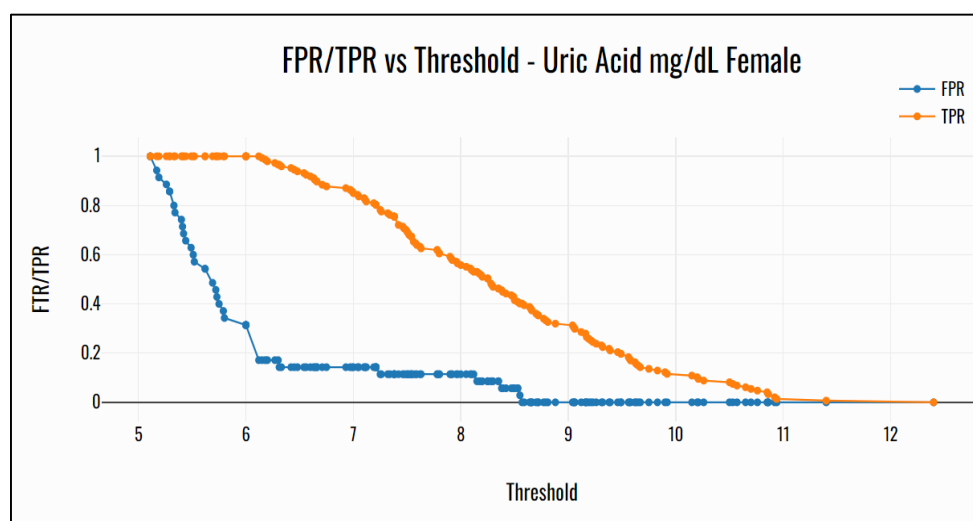


Figure 5. The graph displays the performance of Uric Acid levels (mg/dL) as a diagnostic marker for MASLD in female patients.

This graph shows the trade-off between sensitivity (TPR) and specificity (1–FPR) for serum uric acid as a diagnostic marker of MASLD in females. Low threshold (5.5 mg/dL): TPR 100% (excellent sensitivity) but FPR 0.8—many healthy individuals are misclassified. High threshold (10 mg/dL): FPR 0 (excellent specificity) but TPR 0.1—most MASLD cases are missed. Optimal range (6.0–6.2 mg/dL): TPR remains near 100% while FPR drops to 0.2,

making it suitable for screening. Higher cutoff (8.5 mg/dL): FPR reaches 0, but TPR falls to 0.4 better for confirmatory diagnosis. Lower uric acid thresholds are preferable for screening (maximize case detection), while higher thresholds are more appropriate for confirming MASLD (minimize false positives).

DISCUSSION

The present study demonstrated that serum uric acid is a strong and reliable biomarker for the diagnosis of Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD). Mean serum uric acid levels were significantly higher in males compared to females, indicating gender-related metabolic differences in uric acid regulation and excretion. Similar findings have been reported in previous studies, where males generally exhibited higher uric acid concentrations due to hormonal influences, greater muscle mass, and reduced renal uric acid clearance compared to females (Lonardo et al., 2019). Estrogen in females is considered protective by enhancing uric acid excretion, which may explain the lower threshold values observed in women. Receiver Operating Characteristic (ROC) analysis in the current study showed excellent diagnostic performance, with AUC values of 0.9924 in males and 0.9301 in females. These findings are consistent with studies by Xu et al. (2010) and Li et al. (2009), who reported significant associations between hyperuricemia and fatty liver disease, suggesting that elevated uric acid levels may serve as an independent predictor of hepatic steatosis and metabolic dysfunction. Similarly, Sirota et al. (2013) demonstrated that hyperuricemia is closely linked with insulin resistance, obesity, oxidative stress, and chronic inflammation, all of which contribute to the pathogenesis of MASLD. The present study further identified gender-specific optimal cutoff values of approximately 7.19 mg/dL for males and 6.12 mg/dL for females. These findings highlight the importance of using sex-specific diagnostic thresholds rather than a universal cutoff value. Previous epidemiological studies have also emphasized that a single cutoff may lead to under diagnosis in females and over diagnosis in males (Lonardo et al., 2019). The rotated ROC and cost-threshold analyses additionally confirmed that serum uric acid has greater diagnostic efficiency in males, reflected by a higher peak diagnostic gain compared to females. Biologically, elevated uric acid may contribute to MASLD development through multiple mechanisms, including increased oxidative stress, mitochondrial dysfunction, endothelial injury, and stimulation of inflammatory pathways. Hyperuricemia is also strongly

associated with metabolic syndrome and insulin resistance, which are recognized as major drivers of hepatic fat accumulation (Johnson et al., 2013). Therefore, serum uric acid may not only act as a marker of disease but may also participate in disease progression.

CONCLUSION

Serum uric acid demonstrated excellent diagnostic potential as a biomarker for Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) in both males and females. Significant gender-based differences were observed in uric acid distribution and optimal diagnostic thresholds, with males showing higher mean levels and stronger diagnostic performance. Gender-specific cutoff values of approximately 7.19 mg/dL for males and 6.12 mg/dL for females provided high sensitivity and specificity for MASLD detection. These findings support the use of serum uric acid as a simple, cost-effective, and reliable screening tool for early identification of MASLD, while emphasizing the importance of applying gender-specific reference values in clinical practice.

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