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SERUM URIC ACID TO CREATININE RATIO AS A MARKER FOR SEVERITY OF NON-ALCOHOLIC FATTY LIVER DISEASE

General Medicine

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ABSTRACT

Background: Non-alcoholic fatty liver disease (NAFLD) is one of the most common chronic liver disorders and is closely associated with metabolic syndrome and insulin resistance. Emerging evidence suggests that the serum uric acid to creatinine (sUA/sCr) ratio may reflect both hepatic fat accumulation and renal clearance. **Materials & Methods:** In this cross-sectional study, 100 adult subjects with NAFLD confirmed on ultrasonography were recruited from a tertiary care hospital. Fasting serum uric acid and creatinine were measured and the sUA/sCr ratio was calculated. NAFLD severity was graded on ultrasound and fibrosis stage assessed by FibroScan. Associations between markers and disease severity were analysed using analysis of variance and receiver operating characteristic (ROC) curves. **Results:** Mean age of participants was 41.0±12.1 years and 54 % were male. Obesity (46 %), hypertension (67 %) and dyslipidaemia (96 %) were common. Mean serum uric acid, creatinine and sUA/sCr ratio were 5.90±1.01 mg/dL, 0.93±0.10 mg/dL and 6.35±1.00, respectively. The sUA/sCr ratio increased progressively from mild fatty liver to cirrhosis on ultrasound (5.83±0.86 vs 7.21±0.85; p<0.01) and from fibrosis stages F0–F1 to F4 on FibroScan (5.74±0.80 vs 7.11±0.83; p<0.01). ROC analysis showed that the sUA/sCr ratio (AUC 0.888, best cut-off >6.23) outperformed uric acid alone in predicting significant fibrosis (≥F2). **Conclusion:** The sUA/sCr ratio rises significantly with increasing NAFLD severity and fibrosis and provides a simple, low-cost biomarker for risk stratification in NAFLD patients.

KEYWORDS

NAFLD, Serum Uric Acid, Serum Creatinine, sUA/sCr ratio, FibroScan

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) represents the most prevalent chronic liver disorder worldwide and encompasses a spectrum ranging from simple steatosis to non-alcoholic steatohepatitis and advanced fibrosis. Its global prevalence is estimated between 20–30 % and parallels the rising incidence of obesity and metabolic syndrome [1,2]. NAFLD is strongly associated with type 2 diabetes mellitus (T2DM), hypertension and dyslipidaemia, and patients frequently exhibit elevated hepatic transaminases and features of insulin resistance.

Serum uric acid (sUA) is the final product of purine metabolism and its concentration is influenced both by hepatic production and renal excretion [3]. Elevated sUA levels have been linked to metabolic syndrome, insulin resistance and cardiovascular disease [4,5]. However, isolated sUA measurements may lack specificity in patients with reduced renal function. The ratio of sUA to serum creatinine (sUA/sCr) has therefore been proposed as a renal function-adjusted marker that may better reflect systemic metabolic status. Several recent studies have demonstrated associations between elevated sUA/sCr ratio and NAFLD severity assessed by imaging [6–8]. In this context, the present study aimed to evaluate the relationship between sUA/sCr ratio and NAFLD severity in a cohort of patients undergoing ultrasonography and FibroScan, and to compare the diagnostic performance of sUA, sCr and their ratio in identifying significant hepatic fibrosis.

MATERIAL & METHODS

This hospital-based cross-sectional study was conducted in a tertiary care centre. One hundred adult patients diagnosed with NAFLD on abdominal ultrasonography were consecutively recruited after obtaining informed consent. Patients with excessive alcohol intake (>20 g/day), viral hepatitis, chronic kidney disease, autoimmune liver disease, or medications affecting uric acid metabolism were excluded.

Baseline demographic information and medical history were recorded. Anthropometric measurements included body mass index (BMI) and blood pressure. Comorbid conditions such as hypertension, diabetes mellitus and dyslipidaemia were documented. Fasting blood samples were collected to measure serum uric acid and serum creatinine using standard enzymatic assays; the sUA/sCr ratio was calculated by dividing sUA by sCr.

Assessment of NAFLD severity: Hepatic steatosis severity was graded as mild, moderate–to–severe fatty liver or cirrhosis based on ultrasonography findings. Liver stiffness measurement (LSM) and controlled attenuation parameter (CAP) were obtained using FibroScan (Echosens, Paris, France) to stage fibrosis (F0–F1: no or mild; F2: moderate; F3: severe; F4: cirrhosis).

Continuous variables were summarised as mean±standard deviation (SD) and categorical variables as number (%). Comparisons across NAFLD severity groups were performed using analysis of variance (ANOVA) with post hoc tests. Relationships between markers and fibrosis stage were assessed similarly. Diagnostic performance for predicting significant fibrosis (≥F2) was evaluated by receiver operating characteristic (ROC) analysis and area under the curve (AUC). A p value <0.05 was considered statistically significant. Statistical analyses were conducted using SPSS version 21.

RESULTS

Table 1. Baseline Characteristics of Study Population

Variable	Category	Mean	SD
Age	<40 years	45	45.0%
	41–60 years	51	51.0%
	61–80 years	4	4.0%
Gender	Male	54	54.0%
	Female	46	46.0%
BMI	Normal	18	18.0%
	Overweight	36	36.0%
	Obese	46	46.0%
Comorbidities	Hypertension	67	67.0%
	Diabetes	30	30.0%
	Dyslipidaemia	96	96.0%

The study included 100 participants with a mean age of 41.0±12.1 years; 54 % were male.

Table 2. Distribution of Serum Markers and CAP/ LSM Values

Marker	Category	n (%)/ Mean ±SD
Uric acid (mg/dL)	<4.0	2 (2.0%)
	4.0–5.9	54 (54.0%)
	6.0–6.9	27 (27.0%)
	≥7.0	17 (17.0%)
Creatinine (mg/dL)	<0.8	8 (8.0%)
	0.8–0.99	61 (61.0%)
	1.0–1.19	31 (31.0%)
	≥1.2	0 (0.0%)
sUA/sCr ratio	<5.9	30 (30.0%)
	5.9–6.7	37 (37.0%)
	≥6.8	33 (33.0%)
CAP (dB/m)	Mean±SD	277.59 ± 28.05
LSM (kPa)	Mean±SD	8.38 ± 3.09

More than one-third were overweight and almost half were obese. Hypertension, dyslipidaemia and low physical activity were highly

prevalent. The mean serum uric acid concentration was 5.90±1.01 mg/dL and serum creatinine 0.93±0.10 mg/dL. The mean sUA/sCr ratio was 6.35±1.00. Distribution of these markers and CAP/LSM values are shown in Table 2.

Table 3. Association of Serum Markers with USG Based Severity of NAFLD

USG severity	Uric acid (mg/dL) Mean±SD	Creatinine (mg/dL) Mean±SD	sUA/sCr ratio Mean±SD
Mild fatty liver	5.32 ± 0.76	0.92 ± 0.09	5.83 ± 0.86
Moderate–to–severe	6.28 ± 0.82	0.93 ± 0.12	6.78 ± 0.86
Cirrhosis	7.22 ± 0.85	1.00 ± 0.06	7.21 ± 0.85
p-value	<0.01	0.0625	<0.01

As NAFLD severity increased on ultrasound from mild fatty liver to cirrhosis, mean sUA, sCr and sUA/sCr ratio all increased, with statistically significant differences for uric acid and sUA/sCr ratio ($p<0.01$) but not for creatinine (Table 3).

Table 4. Association of Serum Markers with Severity of Fibrosis

Fibrosis stage	Uric acid (mg/dL) Mean±SD	Creatinine (mg/dL) Mean±SD	sUA/sCr ratio Mean±SD
F0–F1	5.26 ± 0.74	0.92 ± 0.10	5.74 ± 0.80
F2	6.48 ± 0.51	0.94 ± 0.12	6.93 ± 0.76
F3	6.30 ± 1.07	0.92 ± 0.12	6.88 ± 0.89
F4	7.07 ± 0.84	1.00 ± 0.06	7.11 ± 0.83
p-value	<0.01	0.165	<0.01

Similarly, sUA and sUA/sCr ratio increased progressively across FibroScan stages F0–F1 to F4 ($p<0.01$), whereas creatinine remained non-significant (Table 4).

Table 5. ROC Analysis of Serum Markers for Detecting Significant Fibrosis

Marker	AUC (95% CI)	Best cut-off	Sensitivity (%)	Specificity (%)
Uric acid (mg/dL)	0.855 (0.796–0.921)	>5.85	84.0	70
Creatinine (mg/dL)	0.582 (0.466–0.690)	>0.90	74.0	46
sUA/sCr ratio	0.888 (0.816–0.949)	>6.23	84.0	80

In Table 5, ROC analysis demonstrated that the sUA/sCr ratio had the highest discriminative ability for detecting significant fibrosis (AUC 0.888; best cut-off >6.23) with sensitivity 84 % and specificity 80 %. Serum uric acid alone yielded AUC 0.855, while serum creatinine showed poor discrimination (AUC 0.582).

DISCUSSION

The present study found that both serum uric acid and the serum uric acid-to-creatinine ratio (sUA/sCr) were positively associated with increasing NAFLD severity on ultrasonography and with worsening fibrosis stage on FibroScan. Among the biochemical markers evaluated, the sUA/sCr ratio showed better diagnostic performance than serum uric acid alone for identifying significant fibrosis. This suggests that adjusting uric acid values for renal function may provide a more reliable estimate of the metabolic and hepatic disease burden in patients with NAFLD. This observation is particularly relevant because serum uric acid alone may be influenced by renal handling and therefore may not consistently reflect the true extent of metabolic dysfunction across individuals. By incorporating serum creatinine into the denominator, the sUA/sCr ratio reduces the confounding effect of renal clearance and may therefore serve as a more stable and clinically useful biomarker [6-9].

Our findings are in agreement with previous studies that have demonstrated significant associations between higher sUA/sCr ratios and the presence of NAFLD in different populations diagnosed using FibroScan, computed tomography, ultrasonography, and other imaging modalities [6-9].

The biological basis for this relationship is plausible and supported by prior evidence. Uric acid is no longer regarded only as a by-product of purine metabolism; it is increasingly recognized as a metabolically active molecule that may contribute to insulin resistance, oxidative stress, inflammation, and hepatic fat accumulation [3,5]. Experimental work has shown that uric acid can induce hepatic steatosis by promoting oxidative stress and activating inflammatory pathways, particularly through the NLRP3 inflammasome [5]. These mechanisms are highly relevant to NAFLD, which is itself a disorder of metabolic dysfunction characterized by insulin resistance, lipotoxicity, chronic low-grade inflammation, and progression from simple steatosis to fibrosis in a subset of patients [2,10]. Thus, the observed association between higher sUA/sCr ratio and greater NAFLD severity is not merely statistical, but is also supported by known pathogenic pathways.

Another important explanation is the close interrelationship between hyperuricaemia, insulin resistance, and lipid metabolism. Elevated uric acid levels are commonly associated with obesity, dyslipidaemia, hypertension, and type 2 diabetes mellitus, all of which are major risk factors for NAFLD [8,9]. Uric acid may aggravate hepatic steatosis by enhancing lipogenesis and contributing to mitochondrial dysfunction, while insulin resistance increases the delivery of free fatty acids to the liver and promotes intrahepatic triglyceride accumulation [10]. At the same time, renal excretion is the major route of uric acid elimination, and even subtle differences in renal function may significantly alter circulating uric acid levels [3]. Therefore, use of the sUA/sCr ratio instead of isolated serum uric acid may better reflect the net metabolic burden by partially correcting for inter-individual differences in renal clearance [3,4,6-9].

In the present study, the sUA/sCr ratio increased progressively across ultrasound-defined severity groups, from mild fatty liver to moderate-to-severe fatty liver and cirrhosis. A similar stepwise rise was also seen across FibroScan fibrosis stages, with the highest values observed in patients with advanced fibrosis. This graded relationship suggests that the sUA/sCr ratio may reflect not only the presence of NAFLD but also the severity of hepatic involvement. Previous studies have also shown that higher sUA/sCr values are associated with greater hepatic steatosis and more adverse metabolic profiles [4,6-9]. Wang et al. reported that higher sUA/sCr was independently associated with NAFLD detected by FibroScan in the United States population [4]. Seo et al. demonstrated a significant association between elevated sUA/sCr and CT-defined NAFLD [6]. Wang et al. found a similar association in Chinese non-obese individuals with normal LDL cholesterol [7]. Ma et al. further showed that sUA/sCr remained associated with NAFLD even in persons with normal serum uric acid levels, suggesting that the ratio may reveal risk not captured by serum uric acid alone [8]. Choi et al. also confirmed a positive correlation between NAFLD and the serum uric acid-to-creatinine ratio in a large cross-sectional study [9]. Our results therefore extend these findings by showing that the ratio is associated not only with NAFLD presence but also with fibrosis severity in an Indian hospital-based cohort.

The ROC analysis in our study adds further clinical relevance. The sUA/sCr ratio had the highest area under the curve among the evaluated markers for predicting higher fibrosis (F2 and above), and a cut-off of around 6.2 provided useful sensitivity and specificity. This suggests that the ratio may be clinically helpful in identifying patients who are more likely to have significant fibrosis. Since NAFLD is highly prevalent and liver biopsy is neither feasible nor necessary in most patients, there is an ongoing need for simple and inexpensive non-invasive biomarkers that can help stratify risk [2,10]. In this context, the sUA/sCr ratio appears attractive because it is derived from routinely available laboratory parameters and does not add extra cost to patient evaluation [4,6-9].

The clinical profile of our study population also supports the metabolic context of these findings. Most participants were middle-aged, and the majority were overweight or obese, with high rates of hypertension and dyslipidaemia. This is consistent with the well-established epidemiological association between NAFLD and the broader metabolic syndrome [1,2,10]. Since both NAFLD and hyperuricaemia share common metabolic determinants, the association observed in our study is likely a reflection of this interconnected pathophysiology [1-3,5,10]. At the same time, the better performance of the sUA/sCr ratio compared with serum creatinine alone suggests that the ratio is not simply a surrogate for renal status, but rather a composite marker capturing the interaction between urate metabolism and systemic metabolic dysfunction [3,4,6-9].

Certain limitations of the present study should be considered while interpreting the findings. First, the study was single-centre and cross-

sectional in design, so causality cannot be established. Although higher sUA/sCr ratios were associated with greater NAFLD severity and fibrosis, it cannot be concluded whether the elevated ratio contributes directly to disease progression or is a consequence of the associated metabolic abnormalities [4,6-9]. Second, NAFLD severity was assessed by ultrasonography and FibroScan rather than histopathology. While these are accepted and practical non-invasive modalities, they do not fully replace liver biopsy for precise disease characterization [2,10]. Third, although the sample size was sufficient to detect significant associations, it was relatively modest for detailed subgroup analysis, especially in cirrhotic and advanced fibrosis categories. Larger studies would be useful to improve the precision of cut-off values and to examine performance across different demographic and metabolic subgroups [4,6-9].

In summary, the present study supports the growing evidence that the serum uric acid-to-creatinine ratio is a simple, inexpensive, and clinically meaningful biomarker associated with both steatosis severity and fibrosis burden in NAFLD. Compared with serum uric acid alone, the sUA/sCr ratio appears to offer better utility by accounting for renal function and thereby better reflecting the underlying metabolic disturbance. If validated further in larger prospective studies, this ratio may become a useful adjunctive tool for non-invasive risk stratification and early identification of patients at higher risk of progressive NAFLD.

CONCLUSION

The serum uric acid to creatinine ratio rises in parallel with increasing severity of NAFLD and liver fibrosis. Among the markers evaluated, the sUA/sCr ratio provided the best diagnostic performance for detecting significant fibrosis. Given its simplicity and low cost, the sUA/sCr ratio could serve as a useful adjunctive biomarker for risk stratification and monitoring in patients with NAFLD.

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Conflict of Interest

None declared.

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