Original Article

A Study on Association Between Serum Uric Acid and Non-alcoholic Fatty Liver Disease

Varun A[1], Kirubhakaran K[2], Pravin Selvam S[3], Ranga Bashyam S R[2]

Abstract

Background : Non-alcoholic Fatty Liver Disease (NAFLD) is a prevalent liver condition linked with metabolic syndrome, characterized by fat accumulation in the liver without significant alcohol intake. Elevated Serum Uric Acid (SUA) levels are proposed as a potential marker for metabolic disorders, including NAFLD.

Materials and Methods : This cross-sectional study aims to investigate the association between SUA levels and NAFLD in a cohort of 1021 patients from a single center in India. Patients were assessed for demographic, clinical, and biochemical parameters. NAFLD was diagnosed using hepatic ultrasound.

Results : The study found a 32.9% prevalence of NAFLD among 336 patients. Mean SUA levels were significantly higher in the NAFLD group (6.5 ± 1.9 mg/dL) than in the non-NAFLD group (5.6 ± 1.7 mg/dL, $p < 0.001$). Each 1 mg/dL increase in SUA was linked to a 25% higher odds of NAFLD (OR 1.25, 95% CI 1.18 - 1.33, $p < 0.001$). Other significant predictors included age (OR 1.02 per year, $p < 0.001$), male gender (OR 1.35, $p = 0.008$), BMI (OR 1.10 per kg/m², $p < 0.001$), hypertension (OR 1.45, $p < 0.001$), and diabetes mellitus (OR 1.30, $p = 0.021$).

Conclusion : Elevated Serum Uric Acid (SUA) levels are significantly associated with non-alcoholic fatty liver disease (NAFLD), with a 25% increase in odds for each 1 mg/dL rise in SUA. SUA could be a useful biomarker for early NAFLD detection, aiding preventive and therapeutic strategies.

Key words : Non-alcoholic Fatty Liver Disease, Serum Uric Acid, Metabolic Syndrome, Obesity.

Non-alcoholic Fatty Liver Disease (NAFLD) encompasses a range of liver conditions from simple steatosis to non-alcoholic steatohepatitis (NASH), fibrosis, and cirrhosis, strongly associated with metabolic syndrome, obesity, type 2 diabetes, and dyslipidemia[1,2]. NAFLD poses significant public health challenges due to its potential progression to severe liver disease and its link to cardiovascular diseases. Insulin resistance is central to NAFLD, leading to hepatic steatosis, while progression to NASH involves oxidative stress and inflammation[3,4]. Diagnosis typically relies on imaging techniques like ultrasound. Elevated Serum Uric Acid (SUA) levels, common in metabolic disorders, are associated with an increased risk of NAFLD through mechanisms such as oxidative stress and inflammation, making SUA a potential biomarker for early identification and management of NAFLD[5,6].

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Editor's Comment :

- Elevated Serum Uric Acid (SUA) levels are strongly associated with NAFLD, with each 1 mg/dL increase raising the odds by 25%.
- Monitoring SUA levels could aid in early NAFLD detection, allowing for timely intervention and risk reduction strategies. Integrating SUA assessment into routine metabolic screening may enhance preventive care for NAFLD.

Prevalence :

NAFLD affects approximately 25-30% of the global population, with higher prevalence rates reported in individuals with obesity and type 2 diabetes. The condition is particularly prevalent in developed countries due to lifestyle factors such as poor diet and sedentary behavior[7].

Rationale :

Previous studies have suggested a link between SUA levels and the severity of liver disease. Elevated SUA has been associated with various metabolic abnormalities, including insulin resistance, hypertension, and dyslipidemia, which are common in NAFLD[8,9]. However, the relationship between SUA and NAFLD in broader populations remains under-explored. This study aims to explore this relationship

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and assess whether elevated SUA levels can serve as a biomarker for NAFLD.

Materials and Methods

Study Design and Population :

This cross-sectional study was conducted at a single center in India and included a total of 1021 patients. Data were collected from medical records, focusing on patients who had available Serum Uric Acid (SUA) measurements and hepatic ultrasound data confirming the presence or absence of Non-alcoholic Fatty Liver Disease (NAFLD). The study population comprised adults aged 18 years and older who met the inclusion criteria and provided informed consent. The detailed collection of demographic, clinical and biochemical parameters allowed for a comprehensive analysis of the association between SUA levels and NAFLD.

Inclusion and Exclusion Criteria :

The study included adults aged 18 and older with available Serum Uric Acid (SUA) measurements and hepatic ultrasound data confirming or excluding NAFLD, who provided informed consent. Exclusion criteria were significant alcohol consumption (over 20g/day for women, 30g/day for men), other chronic liver diseases, medications affecting liver fat or SUA levels, pregnancy, breastfeeding, malignancy, severe renal impairment (eGFR < 30 mL/min/1.73 m^2), acute or chronic inflammatory conditions, bariatric or obesity surgeries, incomplete medical records and those unwilling to consent.

Diagnosis of NAFLD :

NAFLD was diagnosed based on hepatic ultrasound findings, which detect hepatic steatosis. Patients were classified into NAFLD and non-NAFLD groups.

Data Collection :

Data were collected on demographic, clinical, and biochemical parameters, including age, gender, BMI, blood pressure, fasting glucose levels, lipid profiles, and SUA levels. Hypertension was defined as blood pressure ≥140/90 mmHg or current use of antihypertensive medication. Diabetes mellitus was defined as fasting glucose ≥126 mg/dL or use of antidiabetic medication.

Statistical Analysis :

Descriptive statistics were used to summarize the data. Continuous variables were expressed as mean ± Standard Deviation (SD), and categorical variables as percentages. Comparisons between NAFLD and non-NAFLD groups were made using t-tests for continuous variables and chi-square tests for categorical variables. Logistic regression analysis was used to evaluate the association between SUA levels and NAFLD, adjusting for potential confounders such as age, gender, BMI, hypertension, and diabetes mellitus. Statistical significance was set at $p < 0.05$.

Results

Baseline Characteristics of the Study Population :

A total of 1021 patients were included in the study, with 336 patients diagnosed with NAFLD and 685 patients without NAFLD. The baseline characteristics of the study population are summarized in Table 1.

The NAFLD group had significantly higher mean age, BMI and SUA levels compared to the non-NAFLD group.

Distribution of Serum Uric Acid Levels :

Fig 1 shows the distribution of serum uric acid levels in NAFLD and non-NAFLD patients. The median SUA levels were significantly higher in the NAFLD group compared to the non-NAFLD group.

Association between SUA Levels and NAFLD :

Logistic regression analysis was conducted to determine the association between SUA levels and NAFLD, adjusting for potential confounders such as age, gender, BMI, hypertension and diabetes mellitus. Table 2 shows the Logistic Regression Analysis for Association between SUA and NAFLD.

Table 1 — *Baseline Characteristics of the Study Population (n=1021)*

Characteristic	Total (n=1021)	NAFLD (n=336)	Non-NAFLD (n=685)	p-value
Age (years)	45.8 ± 12.3	48.2 ± 11.5	44.4 ± 12.6	<0.001
Gender (M/F)	580/441	210/126	370/315	0.032
BMI (kg/m^2)	27.5 ± 4.8	29.1 ± 5.1	26.7 ± 4.5	<0.001
SUA (mg/dL)	5.9 ± 1.8	6.5 ± 1.9	5.6 ± 1.7	<0.001
Hypertension (%)	35.2	47.6	28.2	<0.001
Diabetes Mellitus (%)	24.1	31.8	19.7	<0.001

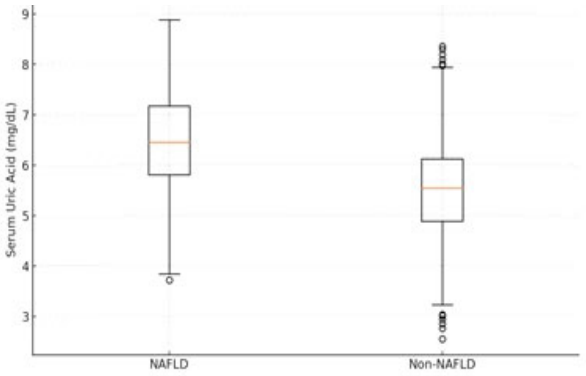

Fig 1 — Distribution of Serum Uric Acid Levels in NAFLD *versus* Non-NAFLD Patients

Table 2 — *Logistic Regression showing Association between SUA and NAFLD*

Variable	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
SUA (per mg/dL)	1.25	1.18 - 1.33	<0.001
Age (per year)	1.02	1.01 - 1.03	<0.001
Gender (Male)	1.35	1.08 - 1.68	0.008
BMI (per kg/m²)	1.10	1.07 - 1.13	<0.001
Hypertension	1.45	1.20 - 1.75	<0.001
Diabetes Mellitus	1.30	1.04 - 1.62	0.021

Correlation between SUA Levels and BMI :

Fig 2 illustrates the scatter plot of Serum Uric Acid levels and BMI in NAFLD *versus* non-NAFLD patients. There is a positive correlation between SUA levels and BMI in both groups, with higher SUA levels observed in the NAFLD group.

Discussion

This study demonstrates a significant association between elevated serum uric acid (SUA) levels and the presence of Non-alcoholic Fatty Liver Disease (NAFLD). SUA remained an independent risk factor for NAFLD after adjusting for potential confounders such as age, gender, Body Mass Index (BMI), hypertension, and diabetes mellitus. The positive correlation between SUA and BMI underscores the critical role of metabolic factors in the pathogenesis of NAFLD. Our findings align with previous research suggesting that metabolic syndrome components are intricately linked with NAFLD, reinforcing the idea that elevated SUA levels are not merely coincidental but may actively contribute to disease pathology[10,11].

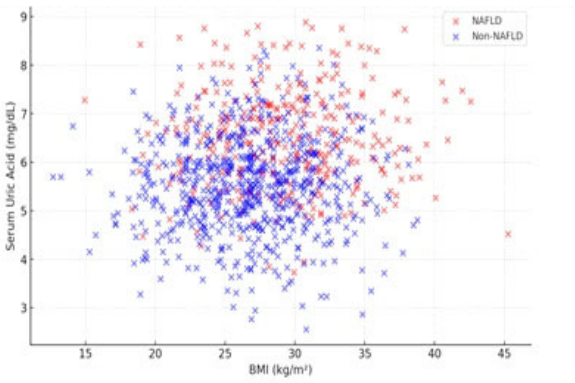

Fig 2 — Scatter Plot of Serum Uric Acid Levels and BMI in NAFLD *versus* Non-NAFLD Patients

The elevated SUA levels observed in NAFLD patients suggest that hyperuricemia may contribute to the development and progression of NAFLD[6,7]. This association is likely mediated by multiple mechanisms, including oxidative stress, inflammation, and endothelial dysfunction, which are known to be influenced by elevated uric acid levels. Hyperuricemia can induce oxidative stress by generating reactive oxygen species, leading to lipid peroxidation and cellular damage in the liver. Additionally, elevated SUA can stimulate the production of pro-inflammatory cytokines, exacerbating hepatic inflammation and promoting the progression from simple steatosis to NASH and fibrosis. Endothelial dysfunction, another consequence of hyperuricemia, can impair hepatic microcirculation, further contributing to liver damage[12,13]. These findings support the hypothesis that SUA is not merely a bystander but an active participant in the pathogenesis of metabolic liver diseases. The interplay between elevated SUA levels and metabolic syndrome components highlights the systemic nature of NAFLD and underscores the importance of a holistic approach to managing this condition[13].

The routine measurement of SUA could be a valuable tool in identifying patients at risk for NAFLD, enabling early intervention and management. Elevated SUA levels, as a potential biomarker for NAFLD, could guide clinicians in stratifying risk and implementing targeted strategies for prevention and treatment. Lifestyle modifications, such as weight loss, dietary changes, and increased physical activity, are cornerstone interventions that can reduce SUA levels and improve metabolic health. Pharmacological treatments aimed at lowering SUA levels, such as xanthine oxidase inhibitors (eg, allopurinol and febuxostat), might also play a role in mitigating NAFLD

progression. However, the long-term benefits and safety of these interventions in the context of NAFLD require further investigation[14-16].

Moreover, incorporating SUA measurement into routine clinical practice could help identify patients who might benefit from more aggressive lifestyle or pharmacological interventions, potentially reducing the burden of NAFLD and its complications. While our study provides valuable insights into the association between SUA and NAFLD, further longitudinal studies are needed to establish causality and determine the effectiveness of interventions aimed at reducing SUA levels in preventing or treating NAFLD. Additionally, research exploring the molecular mechanisms underlying the relationship between SUA and NAFLD could uncover novel therapeutic targets, offering new avenues for managing this increasingly prevalent condition.

The prevalence of NAFLD in our study population was 32.9%, which is consistent with global prevalence estimates. This underscores the high burden of NAFLD in clinical practice and the need for effective screening and management strategies.

Strengths and Limitations :

One of the key strengths of this study is the large sample size, which provides sufficient power to detect significant associations and allows for generalizability of the findings. Additionally, the comprehensive data collection on various metabolic parameters enables a robust adjustment for confounders in the logistic regression analysis. The use of ultrasound for diagnosing NAFLD adds to the reliability of the diagnosis.

This study has several limitations. First, the cross-sectional design limits causal inference between elevated SUA levels and NAFLD; longitudinal studies are needed for temporal relationships. Second, the single-center setting may limit generalizability. Third, NAFLD diagnosis was based on ultrasound, which, though reliable, is less accurate than liver biopsy. Additionally, potential confounders like dietary habits and genetic predispositions were not considered.

Conclusion

In conclusion, this study found a significant association between elevated Serum Uric Acid levels and the presence of Non-alcoholic Fatty Liver Disease. Elevated SUA levels were independently associated with NAFLD after adjusting for age, gender, BMI, hypertension and diabetes mellitus. These findings suggest that SUA could serve as a useful biomarker for early identification of patients at risk for NAFLD. Given the high prevalence of NAFLD and its association with metabolic disorders, routine measurement of SUA in clinical practice could aid in the early detection and management of NAFLD. Further research, particularly longitudinal studies, is needed to confirm these findings and to explore the underlying mechanisms linking SUA and NAFLD. The strengths of this study include its large sample size and comprehensive data collection, while limitations include its cross-sectional design and single-center setting.

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Conflicts of Interest : The authors declare no conflicts of interest

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