



RELATION BETWEEN SERUM URIC ACID AND FIBROSCAN LIVER FINDINGS IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE: A CROSS-SECTIONAL STUDY FROM NORTH-EAST INDIA

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ABSTRACT **Background:** Non-Alcoholic Fatty Liver Disease (NAFLD) is one of the most common chronic liver diseases worldwide and is strongly associated with obesity, insulin resistance, metabolic syndrome, and type 2 diabetes mellitus. Liver fibrosis is the most important predictor of long-term morbidity and mortality in NAFLD. FibroScan has emerged as a reliable non-invasive modality for assessment of hepatic fibrosis and steatosis. Serum uric acid (SUA), traditionally associated with gout and renal disease, is increasingly recognized as an important metabolic biomarker linked to NAFLD progression. Hyperuricemia contributes to oxidative stress, inflammation, endothelial dysfunction, and hepatic lipogenesis, thereby playing a potential role in fibrosis progression. **Aim:** To study the relation between serum uric acid levels and FibroScan liver findings in patients with Non-Alcoholic Fatty Liver Disease. **Materials and Methods:** This hospital-based cross-sectional observational study was conducted among 190 patients diagnosed with NAFLD attending Assam Medical College and Hospital, Dibrugarh. Detailed clinical assessment, anthropometric measurements, biochemical investigations, ultrasonography, and Point Shear Wave Elastography/FibroScan assessment were performed. Serum uric acid levels were measured and correlated with steatosis and fibrosis severity. **Results:** Higher serum uric acid levels were significantly associated with increasing grades of hepatic steatosis and fibrosis. Patients with advanced fibrosis demonstrated markedly elevated serum uric acid levels compared to patients with mild fibrosis. Liver stiffness measurements showed positive correlation with serum uric acid levels. **Conclusion:** Serum uric acid levels correlate significantly with FibroScan findings in NAFLD patients. Hyperuricemia may serve as a simple, inexpensive, and useful non-invasive biomarker for identifying patients at risk of advanced fibrosis.

KEYWORDS : NAFLD; Serum Uric Acid; FibroScan; Liver Fibrosis; Hyperuricemia; Elastography.

INTRODUCTION

Non-Alcoholic Fatty Liver Disease (NAFLD) has become one of the most important chronic liver diseases worldwide and currently represents a major global public health challenge.¹ It encompasses a spectrum of liver disorders ranging from simple hepatic steatosis to non-alcoholic steatohepatitis (NASH), fibrosis, cirrhosis, and hepatocellular carcinoma.² The increasing prevalence of obesity, insulin resistance, sedentary lifestyle, and unhealthy dietary habits has contributed significantly to the rising burden of NAFLD across the world.

NAFLD is considered the hepatic manifestation of metabolic syndrome and is strongly associated with obesity, type 2 diabetes mellitus, hypertension, dyslipidemia, and cardiovascular disease.³ The global prevalence of NAFLD is estimated to be approximately 25–30% among adults.¹ In India, prevalence ranges from 9% to 32% depending on population characteristics and diagnostic methods used.⁴

South Asian populations are particularly vulnerable to metabolic dysfunction and NAFLD because of higher visceral adiposity and insulin resistance at relatively lower body mass indices.⁵ This has resulted in increasing recognition of “lean NAFLD” in Asian populations.

Although simple steatosis may remain relatively benign, a significant proportion of patients progress to NASH and hepatic fibrosis. Fibrosis stage is considered the most important predictor of long-term liver-related complications and mortality in NAFLD.⁶ Therefore, early identification of patients with advanced fibrosis is clinically important.

Liver biopsy remains the gold standard for diagnosis and staging of fibrosis in NAFLD. However, it is invasive, expensive, associated with sampling variability, and carries risk of complications.⁷ Consequently, non-invasive methods for fibrosis assessment have gained increasing importance.

FibroScan and Point Shear Wave Elastography are ultrasound-based elastographic techniques that assess liver stiffness by measuring propagation velocity of shear waves through hepatic tissue. Increased liver stiffness correlates with increasing fibrosis severity.⁸ These techniques are non-invasive, reproducible, rapid, and widely accepted for fibrosis assessment in chronic liver disease.

Apart from imaging modalities, there has been increasing interest in metabolic biomarkers associated with NAFLD severity. Serum uric acid (SUA) is emerging as one such important biomarker.

Uric acid is the final product of purine metabolism in humans due to absence of the enzyme uricase. Traditionally, elevated serum uric acid levels were primarily associated with gout and renal disease. However, recent evidence suggests that hyperuricemia is closely associated with obesity, insulin resistance, hypertension, cardiovascular disease, metabolic syndrome, and NAFLD.⁹

Experimental studies have demonstrated that uric acid may directly contribute to hepatic steatosis and fibrosis.¹⁰ Uric acid inhibits adenosine monophosphate-activated protein kinase (AMPK), thereby stimulating hepatic lipogenesis and suppressing fatty acid oxidation.¹⁰ It also induces oxidative stress through activation of nicotinamide adenine dinucleotide phosphate (NADPH) oxidase and increased production of reactive oxygen species.¹¹

Oxidative stress promotes lipid peroxidation, mitochondrial dysfunction, hepatocyte injury, and activation of inflammatory pathways. Uric acid additionally activates the NLRP3 inflammasome, leading to release of pro-inflammatory cytokines such as IL-1 β , IL-6, and TNF- α .¹² These mechanisms may contribute to progression from simple steatosis to steatohepatitis and fibrosis.

Multiple epidemiological studies have demonstrated association

between hyperuricemia and NAFLD. Elevated serum uric acid levels have been correlated with obesity, hepatic steatosis, fibrosis severity, and metabolic syndrome components.¹³ Recent studies have also shown significant correlation between serum uric acid and FibroScan findings in NAFLD patients.¹⁴

Despite increasing evidence globally, limited data are available from India, particularly North-East India where metabolic diseases are rising because of changing lifestyle patterns and dietary transition.

The present study was therefore undertaken to evaluate the relation between serum uric acid levels and FibroScan liver findings in patients with NAFLD attending Assam Medical College and Hospital, Dibrugarh.

MATERIALS AND METHODS

Study Design

This was a hospital-based cross-sectional observational study.

Study Setting

The study was conducted in the Department of Medicine in collaboration with the Department of Radiodiagnosis and Department of Biochemistry, Assam Medical College and Hospital, Dibrugarh, Assam.

Study Population

Patients diagnosed with Non-Alcoholic Fatty Liver Disease attending outpatient and inpatient departments were included in the study.

Sample Size

A total of 190 patients diagnosed with NAFLD were included.

Inclusion Criteria

- Patients aged more than 18 years.
- Ultrasonographic evidence of fatty liver.
- Patients willing to participate in the study.

Exclusion Criteria

- Significant alcohol consumption.
- Viral hepatitis. Autoimmune liver disease.
- Drug-induced liver disease.
- Chronic kidney disease.
- Pregnancy.
- Malignancy.
- Congestive cardiac failure.

Clinical Assessment

Detailed history and clinical examination were performed in all patients. Anthropometric measurements including height, weight, and Body Mass Index (BMI) were recorded.

Biochemical Investigations

Blood investigations included:

- Liver function tests.
- Fasting blood glucose.
- Lipid profile.
- Serum uric acid.
- Serum creatinine.

Serum uric acid estimation was performed using standard laboratory methods.

Hyperuricemia was defined as:

- SUA > 7 mg/dL in males.
- SUA > 6 mg/dL in females.

Ultrasonographic Assessment

Conventional ultrasonography was performed for diagnosis and grading of fatty liver.

Steatosis grading was categorized into:

- Grade I
- Grade II
- Grade III

based on hepatic echogenicity and visualization of vascular structures.

FibroScan / Point Shear Wave Elastography

Fibrosis assessment was performed using Point Shear Wave Elastography/FibroScan with Samsung RS80A and GE Versana Premier ultrasound systems.

Liver stiffness measurements were recorded under standardized conditions.

Fibrosis staging was categorized as:

- F0–F1 : Mild fibrosis
- F2 : Significant fibrosis
- F3 : Advanced fibrosis
- F4 : Cirrhosis

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using appropriate statistical software.

Quantitative variables were expressed as mean $\pm$ standard deviation. Qualitative variables were expressed as percentages.

Correlation between serum uric acid levels and FibroScan findings was assessed using Pearson's or Spearman's correlation coefficients as appropriate.

A p-value < 0.05 was considered statistically significant.

RESULTS

Demographic Characteristics

Among the 190 patients included in the study, the majority belonged to middle-aged age groups. Male predominance was observed. Most patients were overweight or obese according to Body Mass Index classification.

Serum Uric Acid Distribution

Elevated serum uric acid levels were observed in a significant proportion of patients. Male patients demonstrated relatively higher SUA levels compared to female patients.

Ultrasonographic Severity

Grade II fatty liver was the most common ultrasonographic finding followed by Grade I and Grade III disease.

Patients with severe steatosis demonstrated higher mean serum uric acid levels compared to patients with mild steatosis.

FibroScan Findings

FibroScan assessment revealed varying degrees of fibrosis among study participants.

Mild fibrosis was most commonly observed, although a substantial proportion demonstrated advanced fibrosis.

Higher liver stiffness measurements were associated with elevated serum uric acid levels.

Relation Between Serum Uric Acid and Fibrosis Severity

Patients with advanced fibrosis demonstrated significantly elevated serum uric acid levels compared to patients with mild fibrosis.

A positive correlation was observed between serum uric acid levels and liver stiffness measurements.

Increasing fibrosis stage was associated with progressive increase in serum uric acid levels.

Relation Between Serum Uric Acid and Steatosis Severity

Serum uric acid levels increased progressively with increasing grades of hepatic steatosis.

Patients with Grade III steatosis had significantly higher mean SUA levels compared to Grade I steatosis.

Association with Metabolic Parameters

Hyperuricemia showed significant association with:

- Increased Body Mass Index.
- Obesity.
- Dyslipidemia.
- Metabolic syndrome features.

Patients with elevated SUA levels demonstrated greater metabolic derangement.

DISCUSSION

NAFLD is increasingly recognized as a multisystem metabolic disorder closely linked with obesity, insulin resistance, dyslipidemia, and cardiovascular disease.³ The present study evaluated the relation between serum uric acid levels and FibroScan liver findings in patients with NAFLD.

The study demonstrated significant positive correlation between serum uric acid levels and severity of hepatic steatosis and fibrosis.

Hyperuricemia and NAFLD

Recent years have witnessed increasing interest in the role of hyperuricemia in metabolic diseases. Serum uric acid is now considered not merely a marker but also a possible mediator of metabolic dysfunction.⁹

Hyperuricemia has been associated with obesity, hypertension, insulin resistance, metabolic syndrome, chronic kidney disease, and cardiovascular disease.¹⁵ The present study also demonstrated association between elevated serum uric acid levels and obesity.

Insulin resistance plays a major role in development of both hyperuricemia and NAFLD. Hyperinsulinemia decreases renal uric acid excretion leading to elevated serum uric acid levels.¹⁶ Simultaneously, insulin resistance promotes hepatic triglyceride accumulation by increasing adipose tissue lipolysis and free fatty acid influx into hepatocytes.

Uric Acid and Hepatic Steatosis

Experimental studies have demonstrated that uric acid contributes directly to hepatic fat accumulation.¹⁰ Uric acid inhibits AMP-activated protein kinase (AMPK), an important regulator of lipid metabolism. AMPK inhibition stimulates de novo lipogenesis while suppressing fatty acid oxidation, resulting in hepatic triglyceride accumulation.

In the present study, serum uric acid levels increased progressively with increasing grades of steatosis. Patients with severe steatosis demonstrated significantly higher SUA levels compared to mild disease.

These findings are consistent with previous studies from Asian and Western populations demonstrating association between hyperuricemia and hepatic steatosis severity.¹³

Oxidative Stress and Inflammation

Oxidative stress is central to progression of NAFLD from simple steatosis to steatohepatitis and fibrosis.¹⁷

Uric acid contributes to oxidative stress by activating NADPH oxidase and increasing production of reactive oxygen species.¹¹ Reactive oxygen species induce lipid peroxidation, mitochondrial dysfunction, hepatocyte injury, and inflammation.

Additionally, uric acid activates inflammatory pathways including NF- κ B and NLRP3 inflammasome pathways leading to increased release of inflammatory cytokines such as IL-1 β and TNF- α .¹² These inflammatory processes contribute to progression of fibrosis.

Relation Between Serum Uric Acid and FibroScan Findings

Fibrosis stage is considered the most important predictor of long-term outcomes in NAFLD.⁶ Therefore, identification of biomarkers associated with fibrosis is clinically important.

The present study demonstrated significant correlation between serum uric acid levels and FibroScan liver stiffness measurements.

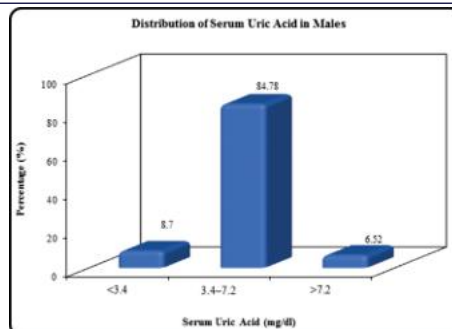
Patients with advanced fibrosis had significantly elevated SUA levels compared to those with mild fibrosis.

These findings support previous studies demonstrating association between serum uric acid levels and fibrosis severity assessed by elastography.¹⁴

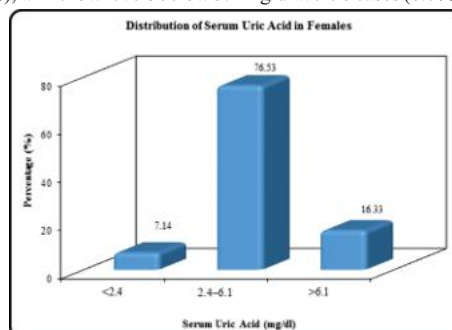
Possible mechanisms linking hyperuricemia and fibrosis include:

- Oxidative stress.
- Endothelial dysfunction.
- Activation of hepatic stellate cells.
- Chronic inflammation.
- Mitochondrial injury.

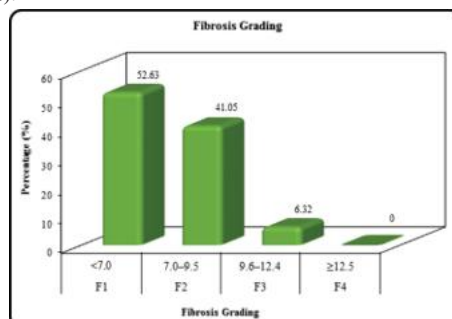
Uric acid-induced oxidative stress activates hepatic stellate cells leading to collagen deposition and extracellular matrix accumulation.¹⁸



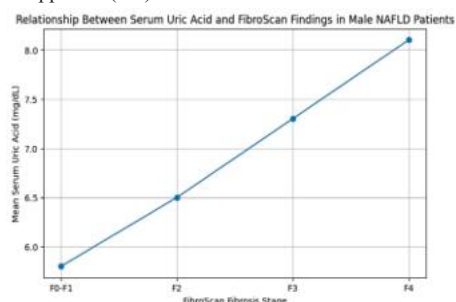
Among 92 males, serum uric acid levels were mostly normal at 3.4–7.2 mg/dl (78 cases, 84.78%). Hyperuricemia above 7.2 mg/dl affected 6 (6.52%), while low levels below 3.4 mg/dl were 8 cases (8.7%).



Among 98 females, serum uric acid levels were predominantly normal at 2.4–6.1 mg/dl (75 cases, 76.53%). Elevated levels above 6.1 mg/dl occurred in 16 (16.33%), while low levels below 2.4 mg/dl 7 cases (7.14%).

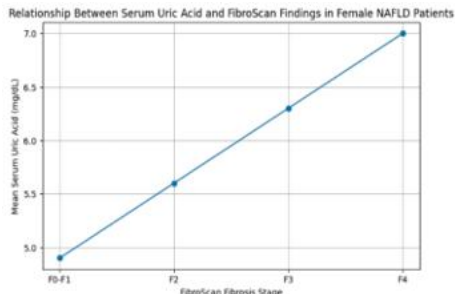


Out of 190 participants assessed for fibrosis by liver stiffness measurement (LSM), most showed mild or no significant fibrosis. F1 (<7.0 kPa) affected 100 cases (52.63%), F2 (7.0–9.5 kPa) had 78 (41.05%), F3 (9.6–12.4 kPa) involved 12 (6.32%), and no F4 (≥ 12.5 kPa) cases appeared (0%).



The graph demonstrates a progressive increase in mean serum uric acid levels with advancing FibroScan fibrosis stages among male patients with Non-Alcoholic Fatty Liver Disease. Male patients with mild fibrosis (F0–F1) had comparatively lower serum uric acid levels, while those with significant fibrosis (F2), advanced fibrosis (F3), and cirrhosis (F4) showed steadily increasing uric acid concentrations. This positive trend suggests a significant association between hyperuricemia and severity of hepatic fibrosis in male NAFLD patients. The findings support the concept that elevated serum uric acid may reflect worsening metabolic dysfunction, oxidative stress, and inflammatory activity contributing to progression of liver fibrosis. The

graph also indicates that serum uric acid may serve as a simple and non-invasive biochemical marker for identifying male NAFLD patients at higher risk of advanced liver disease.



The graph in female NAFLD patients similarly shows a gradual rise in mean serum uric acid levels with increasing FibroScan fibrosis severity. Females with mild fibrosis exhibited lower serum uric acid values, whereas patients with advanced fibrosis and cirrhosis demonstrated progressively higher levels. Although absolute serum uric acid values were comparatively lower in females than males, the overall trend remained similar, indicating a positive correlation between hyperuricemia and hepatic fibrosis severity. This relationship suggests that serum uric acid may also be an important metabolic and inflammatory marker in female NAFLD patients. The observed increase in uric acid levels with worsening fibrosis further supports the role of hyperuricemia in progression of NAFLD and highlights its potential utility as a non-invasive biomarker for disease severity assessment in females.

Role of FibroScan

Liver biopsy remains the gold standard for fibrosis assessment but has significant limitations because of its invasive nature and sampling variability.⁷

FibroScan and elastography techniques provide non-invasive, reproducible, and reliable methods for fibrosis assessment.⁸

The present study demonstrated that liver stiffness measurements correlated positively with serum uric acid levels, suggesting that hyperuricemia may reflect ongoing hepatic injury and fibrosis progression.

Clinical Implications

The findings of the present study have important clinical implications.

Serum uric acid is:

- Simple.
- Inexpensive.
- Easily available.
- Widely reproducible.

Therefore, elevated serum uric acid levels may help identify NAFLD patients at risk of advanced fibrosis.

Early recognition of high-risk patients may facilitate

Lifestyle modification.

- Weight reduction.
- Metabolic control.
- Closer monitoring.
- Prevention of progression to cirrhosis.

In resource-limited settings, serum uric acid may serve as a practical screening biomarker for risk stratification.

Regional Importance

There is limited literature regarding association between serum uric acid and FibroScan findings in NAFLD patients from North-East India.

Rapid urbanization, dietary transition, increasing obesity, and sedentary lifestyle are contributing to rising burden of metabolic diseases in this region.

The present study therefore provides important regional data regarding metabolic biomarkers and fibrosis assessment in NAFLD.

Limitations

Certain limitations should be acknowledged:

- Cross-sectional design limits causal inference.

- Single-center study.
- Liver biopsy was not performed.
- Longitudinal follow-up was not available.

Despite these limitations, the study demonstrates significant association between serum uric acid levels and FibroScan findings in NAFLD patients.

CONCLUSION

Serum uric acid levels correlate significantly with FibroScan liver findings in patients with Non-Alcoholic Fatty Liver Disease.

Elevated serum uric acid levels are associated with increased severity of hepatic steatosis and fibrosis.

Hyperuricemia may serve as a simple, inexpensive, and useful non-invasive biomarker for identifying NAFLD patients at increased risk of advanced fibrosis.

Further prospective multicentric studies are required to validate these findings and evaluate the role of uric acid-lowering strategies in NAFLD management.

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