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Original Research Article

Study of serum uric acid level in chronic liver disease and its association with hepatic encephalopathy and LFT parameters

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ABSTRACT

Background: Chronic liver disease (CLD) is a progressive condition associated with complications such as hepatic encephalopathy (HE), a neuropsychiatric manifestation linked to altered purine metabolism and serum uric acid (SUA) levels. While liver function tests (LFTs) evaluate liver health, the role of SUA in CLD, particularly its correlation with HE severity and LFT parameters, remains underexplored. To investigate serum uric acid levels in CLD patients and examine their correlation with HE severity and LFT parameters.
Methods: This cross-sectional study included 54 CLD patients aged 18-85 years from GSVM Medical college Kanpur, selected via random sampling. Clinical and biochemical data, including SUA levels and LFTs, were collected and analysed. Statistical analyses using ANOVA and Pearson correlation assessed associations between SUA, HE grades, and LFT parameters.
Results: Serum uric acid levels significantly correlated with HE severity (ANOVA: $F=6.93$, $p<0.05$), with mean SUA levels rising from 6.28 mg/dL in Grade 0 to 10.41 mg/dl in Grade 2 HE. SUA demonstrated significant negative correlation with serum albumin ($r = -0.36$, $p<0.05$) and positive correlations with PT-INR ($r = 0.33$, $p<0.05$) and creatinine ($r = 0.55$, $p<0.05$). No significant correlation was observed with bilirubin, SGOT or SGPT.
Conclusions: Elevated SUA levels are significantly associated with the severity of hepatic encephalopathy and key LFT parameters. SUA may serve as a valuable biomarker for assessing CLD progression and predicting complications like HE.

Keywords: Chronic liver disease, Serum uric acid, Hepatic encephalopathy, Liver cirrhosis, Liver function tests

INTRODUCTION

Chronic liver disease (CLD) is a global health concern, characterized by the progressive deterioration of liver function due to various etiologies, such as chronic viral hepatitis, alcohol abuse, and non-alcoholic fatty liver disease (NAFLD). The progression of CLD often leads to cirrhosis, a condition where liver architecture is extensively damaged, resulting in complications such as portal hypertension, ascites, and hepatic encephalopathy (HE). Hepatic encephalopathy, in particular, is a significant neuropsychiatric complication associated with liver failure, manifesting as a spectrum of cognitive dysfunction ranging from subtle changes in mental state to deep coma.[1]

While hepatic encephalopathy is traditionally linked to elevated ammonia levels, recent studies suggest that metabolic abnormalities, including altered purine metabolism and changes in serum uric acid (SUA) levels, may also play a role in its pathophysiology. Uric acid is the final breakdown product of purine metabolism, and its

serum levels are regulated by the liver and kidneys. In the context of liver dysfunction, impaired hepatic metabolism and renal insufficiency often lead to hyperuricemia. However, the exact role of serum uric acid in the progression of CLD and its potential association with hepatic encephalopathy remain areas of ongoing research.[2,3]

Liver function tests (LFTs) are routinely used to evaluate the functional state of the liver, providing insights into the degree of liver damage and synthetic failure. Parameters such as serum bilirubin, liver enzymes (ALT, AST, ALP), albumin, and the international normalized ratio (INR) offer valuable information about liver health. However, the relationship between serum uric acid and these conventional LFT parameters in patients with CLD has not been thoroughly explored. Understanding the connection between serum uric acid levels and liver function may offer new insights into the metabolic changes occurring in CLD and provide additional tools for assessing the severity of liver disease and the risk of complications like hepatic encephalopathy.[4,5] In this study, we aim to investigate the serum uric acid levels in patients with chronic liver disease and assess their correlation with the presence and severity of hepatic encephalopathy. Additionally, we will explore the relationship between serum uric acid levels and various LFT parameters to better understand its potential role as a marker of disease severity.[6-8]

METHODS

Study design

This research was conducted as a cross-sectional study over a period of 16 months, from January 2023 to April 2024. The objective was to assess serum uric acid levels in patients with CLD, examining their correlation with the presence and severity of hepatic encephalopathy, as well as their relationship with various LFT parameters.

Study setting

The study was conducted at Ganesh Shankar Vidyarthi Memorial Medical College, Kanpur, Uttar Pradesh, India. Data were collected from both outpatient department and inpatients wards of department of medicine.

Participants

The study included adult patients aged 18 years and above, of either sex, who were diagnosed with chronic liver disease. while exclusion criteria eliminated pregnant patients, those with gout, diabetes mellitus, recent surgery, trauma, chronic kidney disease, hypothyroidism, malignancies, or those on certain medications (e.g., allopurinol, febuxostat, thiazides, furosemide). Informed consent was obtained from all participants before enrolment.

Variables

The primary variables examined were biochemical markers, including complete blood count (CBC), liver function tests (LFT), kidney function tests (KFT), serum electrolytes (SE), prothrombin time-international normalized ratio (PT-INR), serum thyroid-stimulating hormone (TSH), glycated hemoglobin (HbA1c), and serum uric acid levels. Clinical parameters included age, sex, body mass index (BMI) and waist circumference.

Data sources/measurement

Data were collected through structured patient interviews, medical records review, and laboratory tests. Biochemical parameters were measured from blood samples, while clinical evaluations were supported by imaging (ultrasonography) and endoscopic investigations. Standardized protocols were followed to ensure the accuracy and consistency of data collection across participants.

Bias

Selection bias was minimized through the use of random sampling, ensuring each eligible patient had an equal chance of being selected. Confounding variables were controlled by adhering to strict inclusion and exclusion criteria. The use of standardized measurement protocols further reduced measurement bias.

Study size

The sample size of 54 patients was calculated based on the prevalence of chronic liver disease in India. With a 95% confidence interval and a 5% margin of error, the sample size was determined using the formula for prevalence studies.

Quantitative variables

Quantitative variables included biochemical markers such as serum uric acid levels, liver function tests, and kidney function tests, among others. Categorical variables such as sex, severity of ascites, and hepatic encephalopathy grades were analysed alongside continuous variables like age and BMI.

Statistical analysis

Data were analysed using SPSS v29.0. ANOVA test was used to assess associations between serum uric acid with Hepatic encephalopathy and LFT parameters. The Pearson correlation analysis was conducted to explore the relationship between serum uric acid levels and various liver function test (LFT) parameters among patients with chronic liver disease (CLD). P-values of less than 0.05 were considered statistically significant.

RESULTS

The distribution of age of the patient is from 18 to 85 years with maximum belongs to age group 41-50 years (31.5%). The mean age is 45.52 years with SD of 14.54 years. (Table 1).

Table 1: Distribution of CLD patients according to age and etiology.

Age group (in years)	Number of patients	Percent
18-30	9	16.7
31-40	11	20.4
41-50	17	31.5
51-60	10	18.5
61-70	5	9.3
> 70 yr	2	3.7
Mean±SD	45.52 ± 14.54 years	
Etiology		
HCV related	6	11.1
HBV related	9	16.7
Alcoholic	39	72.2

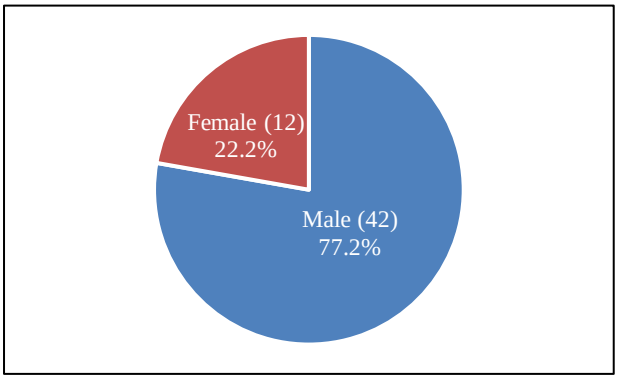

Figure 1: Gender distribution among CLD patients.

Out of 54 patients 42 were males (77.8%) and 12 were females (22.2%) (Figure 1).

Etiological data reveals that 39 cases (72.2%) were alcohol related, 9 cases (16.7%) were HBV related and 6 cases (11.1%) were HCV related (Table 1).

Severity of ascites was also graded in the patients and maximum had moderate ascites (64.8%) followed by severe and mild, 22.2% and 13.0% respectively. Distribution of hepatic encephalopathy (HE) among cases revealed that max cases (36) were not in HE (grade-0) followed by 8 cases in HE grade-2, 7 patients in grade-3, 2 patients in grade-1 and only 1 patient in grade-4 (Table 2).

For hepatic encephalopathy, the mean S. Uric Acid levels were 6.28±2.21 for Grade 0, 7.55±2.90 for Grade 1, 10.41±2.18 for Grade 2, 9.23±2.49 for Grade 3, and 7.80 for Grade 4. The ANOVA results showed an F-value of 6.93 and a p-value of less than 0.05, indicating a significant difference in S. Uric Acid levels among the different grades of hepatic encephalopathy (Table 3). These results suggest that there is a significant difference based on the grades of hepatic encephalopathy.

Table 2: Distribution of patients according to severity of ascites and hepatic encephalopathy.

Grades of ascitis	Number of patients	Percent
Mild	7	13.0
Moderate	35	64.8
Severe	12	22.2
Hepatic encephalopathy		
Grade 0	36	66.7
Grade 1	2	3.7
Grade 2	8	14.8
Grade 3	7	13.0
Grade 4	1	1.9

Table 3: Association of Etiology, Ascites and Hepatic Encephalopathy with S. uric acid levels among CLD patients.

Variable		S. uric acid	
		Mean	**SD**
Hepatic encephalopathy	Grade 0	6.28	2.21
	Grade 1	7.55	2.90
	Grade 2	10.41	2.18
	Grade 3	9.23	2.49
	Grade 4	7.80	
	ANOVA	F=6.93, p<0.05	

Table 4: Correlation of S. uric acid with LFT and other parameters among CLD patients.

Pearson correlation	S. uric acid	
	r-value	**P value**
S.Bilirubin	-0.01	0.916
S.albumin	-0.36	<0.05
PT-INR	0.33	<0.05
S.Creatnine	0.55	<0.05
SGOT	-0.22	0.105
SGPT	-0.21	0.135

The Pearson correlation analysis was conducted to explore the relationship between serum uric acid levels and various liver function test (LFT) parameters among patients with chronic liver disease (CLD). The results indicated that serum uric acid levels had a very weak negative correlation with serum bilirubin (r = -0.01, p = 0.916), suggesting no significant relationship. A significant negative correlation was found with serum albumin (r = -0.36, p = 0.007),

indicating that lower albumin levels were associated with higher uric acid levels (Table 4).

There was a significant positive correlation with PT-INR ($r = 0.33$, $p<0.05$), showing that higher PT-INR values were related to higher uric acid levels. The strongest correlation was with serum creatinine ($r = 0.55$, $p<0.05$), indicating a substantial positive relationship. Conversely, correlations with SGOT ($r = -0.22$, $p = 0.105$) and SGPT ($r = -0.21$, $p = 0.135$) were negative but not statistically significant. These findings suggest that serum uric acid levels are particularly associated with serum albumin, PT-INR, and creatinine levels in CLD patients.

DISCUSSION

The results of this study, which show a significant association between serum uric acid (SUA) levels and the severity of hepatic encephalopathy (HE) in chronic liver disease (CLD), are well-supported by existing literature. Hyperuricemia, resulting from impaired purine metabolism and renal dysfunction, has been implicated in the pathophysiology of CLD, particularly HE. Studies have demonstrated that toxins such as ammonia and uric acid, which accumulate in liver dysfunction, play critical roles in HE development.

Our findings corroborate earlier research, such as Wang et al which identified that elevated SUA levels correlate with worsening liver function, particularly low albumin levels and increased prothrombin time-international normalized ratio (PT-INR).[9] These studies emphasize that SUA levels reflect systemic and synthetic liver function rather than hepatocellular damage alone. The absence of significant correlations between SUA and liver enzymes (SGOT, SGPT) in our study also echoes findings from prior literature, including Frelikh et al where SUA was more closely linked to systemic inflammation and renal dysfunction.[10]

Moreover, the strong correlation between SUA and serum creatinine found in this study highlights the combined effect of liver and renal impairment in advanced CLD. Elevated SUA levels in such patients are reflective of decreased renal clearance, an important factor in disease progression. This aligns with Shastry et al who noted the potential of SUA as a biomarker for systemic complications like coagulopathy and renal dysfunction in CLD.[11]

The clinical implications are notable. Given its affordability and ease of measurement, SUA could be integrated into routine monitoring for CLD patients. Its role as a potential predictor for HE severity and systemic complications makes it a valuable tool in guiding treatment strategies.[12,13] However, further longitudinal studies are required to confirm whether reducing SUA levels can mitigate the risk of HE or improve patient outcomes.

This study is limited by its sample size and single-centre setting may limit external validity. Exclusion of patients with comorbidities such as diabetes, chronic kidney disease, and malignancies may introduce selection bias. Additionally, the lack of longitudinal data restricts insights into the impact of interventions targeting serum uric acid on clinical outcomes.

CONCLUSION

In conclusion, this study highlights the significant association between serum uric acid levels and the progression of hepatic encephalopathy in patients with chronic liver disease (CLD). The findings suggest that elevated serum uric acid levels correlate with more severe grades of hepatic encephalopathy, indicating its potential role in the pathophysiology of the condition. Moreover, the study reveals significant relationships between serum uric acid and other key liver function parameters, such as serum albumin, PT-INR, and serum creatinine, which could help in assessing the severity of liver dysfunction. These results emphasize the importance of considering serum uric acid as a valuable biomarker in the clinical evaluation of CLD patients, especially in monitoring disease progression and the risk of complications like hepatic encephalopathy. Further research may be required to establish a causal relationship and explore therapeutic implications.

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