Original Article

Study of Serum Uric Acid Level with Severity of Chronic Liver Disease

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Received: 06-07-2024; **Revised:** 28-09-2024; **Accepted:** 10-10-2024; **Published on:** 15-10-2024.

ABSTRACT

Background: Chronic liver disease (CLD) is increasingly prevalent, with hyperuricemia contributing to its progression by promoting inflammation, oxidative stress, and insulin resistance. High uric acid levels are linked to more severe CLD and poorer outcomes. This study aims to evaluate serum uric acid levels and their significance in patients with chronic liver disease.

Materials and Methods: Following IEC approval, 120 patients with chronic liver disease (CLD) from various causes (excluding factors affecting uric acid levels) were included. Patient symptoms, physical exams, serum uric acid, and liver function tests were documented, and the Child-Turcotte-Pugh (CTP) score was calculated. Statistical analysis assessed associations between uric acid levels, CLD causes, and disease severity.

Results: Of the 120 patients, 70% were male with an average age of 46.22 years. Alcoholic liver disease was the leading cause (52.5%), followed by chronic hepatitis B (22.5%). Serum uric acid levels showed a significant correlation with the Child-Turcotte-Pugh (CTP) score ($p = 0.010$), with higher levels in hepatitis B patients and those in CTP class C. Significant associations were also noted between uric acid and albumin, bilirubin, INR, SGOT, and SGPT levels. ($P<0.05$)

Conclusions: The study indicates that elevated serum uric acid levels correlate with higher Child-Pugh scores, suggesting it as a reliable, cost-effective marker for assessing liver cirrhosis severity. This non-invasive marker can aid in early intervention and monitoring of chronic liver disease.

Keywords: Uric acid, Child Pugh score, Chronic liver disease, NAFLD, Hepatitis B, Alcohol.

INTRODUCTION

Chronic liver disease is one of the frequent causes of death, affecting millions of people worldwide, especially in the developing world. The increasing prevalence of chronic liver disease has been noted in recent times. [1] Chronic liver disease (CLD) in the clinical context is a disease process of the liver that involves a process of progressive destruction and regeneration of liver parenchyma leading to fibrosis and cirrhosis.[2] It is the 11th leading cause of death and the 15th leading cause of morbidity, accounting for 2.2% of deaths and 1.5% of disability-adjusted life years worldwide in 2016.[3]

Chronic liver disease leads to progressive destruction and regeneration of liver parenchyma and finally leads to fibrosis and cirrhosis, common symptoms include fatigue, jaundice, poor appetite, nausea, abdominal distension and intestinal bleeding. common etiologies for CLD include Alcoholism, Portal hypertension, Autoimmune, Hepatitis B, C and others. [4,5]

In CLD, high uric acid (UA) levels are independently associated with severe disease and poor prognosis.[6] UA is not only a by-product of cell death and purine metabolism, but recent research has discovered that it is a mediator of inflammation and tissue damage.[7] In CLD, there is progressive liver damage eventually leading to loss of function.[8] In CLD of different etiologies, UA levels are found to be high.[9]

High UA levels have been considered independent etiological risk factors in patients with nonalcoholic fatty liver disease (NAFLD). [8,10] Hyperuricemia results in endothelial dysfunction, insulin resistance, oxidative stress and adipose tissue inflammation, which leads to development of fatty liver, progression of NAFLD to NASH, and progression of viral and alcoholic liver disease all of which direct towards Chronic liver disease. In different studies, UA levels have been found to correlate directly with the level of tissue damage.[11,12]

The availability of liver transplant has stressed on the need for accurate prognosis so that the patient can be referred at appropriate time.[13] Child-Turcotte Pugh (CTP) or Child Pugh (CP) score is one such universally accepted prognostic score, owing to its simplicity and ease of use. Based on the CP score, CLD patients can be categorised according to the severity of disease.8 On this background, the study is done to measure the serum UA level and to correlate with the disease severity among chronic liver disease patients. [14,15]

In Chronic liver disease, High serum uric acid is independently associated with severe disease and poor prognosis. However, studies regarding the relationship of UA levels with different parameters of liver dysfunction are rare in India. [16] We, therefore, undertook this cross-sectional study to find the level of UA in patients of CLD and its correlation, if any, with the severity of CLD presented as a Child–Pugh score.

MATERIALS AND METHODS

After approval from institutional ethical committee, this cross-sectional study was carried out for 18 months duration from Sep 2022 to Feb 2024 and 120 adult patients aged >18 years of either gender who were diagnosed with Chronic liver disease on the basis of clinical, radiological and biochemical investigation presenting to the OPD of Department of General Medicine, SAMC & PG Institute, Indore were included. Informed written consent was obtained from all patients satisfying the inclusion criteria after explaining the study protocol in detail.

Inclusion Criteria

- Patients diagnosed with Chronic liver disease on the basis of clinical, radiological and biochemical investigation
- Patients more than 18 years of age

Exclusion Criteria

- Non-consenting patients
- Patients having conditions which significantly alter uric acid level [e.g. patient of known malignancy (leukemias and lymphomas), gout, chronic kidney disease, on chemotherapy, patient on drugs affecting level of uric acid and with recent surgery and trauma] were excluded.

Methodology

All patients coming to the emergency department and general medicine outpatient department were screened, and those fulfilling inclusion and exclusion criteria were enrolled in the study. Patients who left against medical advice were excluded from the study. All the patients and attendants were explained regarding this study, and those consenting were enrolled in the study. All patients were thoroughly investigated and all relevant personal and family history was recorded and detailed clinical examination was done.

Blood samples were collected for all enrolled subjects and evaluated for hemoglobin, total leukocyte count, platelet count, prothrombin time, serum concentration of bilirubin (total and conjugated), serum albumin, serum aspartate aminotransferase (AST/SGOT), and alanine transaminase (ALT/SGPT), and a modified Child–Pugh Score was be calculated.

Data was collected on a prestructured proforma and appropriate analysis was done

Calculation of Child–Turcotte–Pugh (CTP) score

a. CTP score

The score employs five clinical measures of liver disease. Each measure is scored from 1 to 3, with 3 indicating the most severe derangement [Table 1].

Table 1: Child–Turcotte–Pugh (CTP) Score

Measure	1 point	2 points	3 points
Total bilirubin, (mg/dl)	<2	2–3	>3
Serum albumin (g/dl)	>3.5	2.8–3.5	<2.8
PT prolongation (in secs)	<4.0	4.0–6.0	>6.0
INR	<1.7	1.7–2.3	>2.3
Ascites	None	Mild (or suppressed with medication)	Moderate to severe (or refractory)
Hepatic encephalopathy	None	Grades I–II	Grades III–IV

b. Classification of Child–Pugh Score

CLD is classified into Child–Pugh classes A to C, employing the added score from above [Table 2].

Table 2: Classification of Child–Pugh Score

Points	Class	One-year survival	Two-year survival
5–6	A	100%	85%
7–9	B	81%	57%
10–15	C	45%	35%

Statistical Analysis

The collected data were entered into a Microsoft Excel Sheet. Tables were generated using Microsoft Word and Microsoft Excel version 2010. The data were analyzed using the Statistical Package for the Social Sciences (SPSS) IBM version 18.0. The categorical variables were expressed as percentages, frequency, and proportions and compared using Pearson's Chi-square test or Fisher's exact test, as appropriate. A $p \leq 0.05$ was considered statistically significant.

RESULTS

The present study was conducted on 120 patients. The age distribution was between 20 and 80 years. The mean age of the patients was 46.22 ±11.10. In the present study, out of the 120 patients, 84 (70%) were males and 36 (30%) were females with Chronic liver disease of various causes, diagnosed clinically and substantiated by imaging studies.

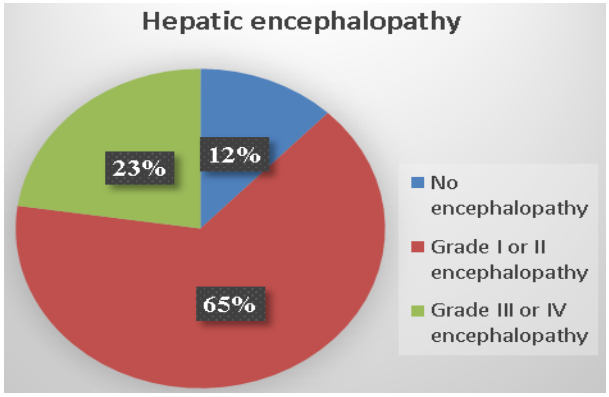
In more than half of the patients i.e. in 63 (52.5%) patients, alcohol was identified as a major cause of chronic liver disease followed by Hepatitis B in 27 (22.5%) patients, and other causes were responsible for chronic liver disease in 28 (23.3%) of patients, and had one case each of Wilson's disease and autoimmune as a cause of chronic liver disease. (Table 3)

Table 3: Distribution of the participants according to the cause of chronic liver cirrhosis

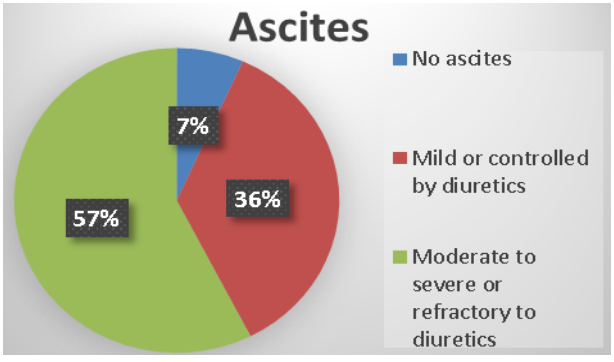
Causes of Chronic liver disease	No. of patients (N=120)
Alcohol	63 (52.5%)
Hepatitis B	27 (22.5%)
Autoimmune	01 (8.3%)
Wilson's	01 (8.3%)
Others	28 (23.3%)
Total	120 (100%)

One of the complications of Chronic liver disease and liver cirrhosis is ascites. It was divided into 3 categories as follows: 1) No ascites 2) Mild or controlled by diuretics 3) Moderate to severe or refractory to diuretics (Table 1) Among the 120 patients, 8 (6.7%) patients had no ascites, 43 (35.8%) had mild ascites controlled with diuretics, and 69 (57.5%) patients had refractory ascites. (Figure 2) The same classification is used in Child Turcotte Pugh scoring system.

Another complication of liver cirrhosis is Hepatic encephalopathy. It was divided into 3 categories as A) No B) Grade I-II C) Grade III-IV (Table 1). Out of the 120 patients studied, 38 (31.7%) patients had no encephalopathy, 67 (55.8%) patients had grade I or II encephalopathy and 15 (12.5%) patients had grade III or IV encephalopathy (Graph 3).



Graph 1: Distribution of patients of CLD depending upon presence of hepatic encephalopathy



Graph 2: Distribution of patients of CLD depending upon presence of Ascites

Child Turcotte Pugh score was calculated for each patient and were classified into the respective class. Out of 120 patients, 12 belonged to Class A (score=5-6), 50 belonged to Class B (score=7-9) and 68 belonged to Class C (score=10-15). (Table 4)

Table 4: Distribution of the participants based on Child Pugh Score

Child Pugh Score	No. of patients (N=120)
5-6 Class A	12 (10%)
7-9 Class B	48 (40%)
≥ 10 Class C	60 (50%)
Total	120 (100%)

Table 5: Correlation of Serum Uric acid level with Child Pugh Score

Serum Uric acid level (N=120)	Child Pugh Score			P value
	Class A (5-6)	Class B (7-9)	Class C (≥10)	
< 4 mg/dl	4 (33.3%)	8 (16.6%)	7 (11.7%)	0.010* Sig
4-7 md/dl	7 (58.4%)	26 (54.2%)	12 (20%)	
>7 mg/dl	1 (8.3%)	14 (29.2%)	41 (68.3%)	
Total	12 (10%)	48 (40%)	60 (120%)	

Table 6: Correlation of Serum Uric acid level with Albumin, Bilirubin, INR, SGOT, and SGPT

		Serum Uric acid level			P value
		≤ 4 mg/dl	4-7 md/dl	≥7 mg/dl	
Albumin	>3.5g/dl	5	16	5	0.0275*
	2.5-3.5g/dl	9	11	37	
	<2.5g/dl	3	18	16	
Bilirubin	<2mg/dl	11	9	28	0.0410*
	2-3 mg/dl	2	28	19	
	>3mg/dl	3	9	11	
INR	<1.7	9	27	34	0.0414*
	1.7-2.3	2	16	18	
	>2.3	7	2	5	
SGOT	<40 u/l	5	33	13	0.0054*
	>40 u/l	13	13	43	
SGPT	<40 u/l	13	27	18	0.0316*
	>40 u/l	5	19	38	

In our study we found there is a strong Correlation between serum uric acid and CTP score in CLD patients, which is statistically significant (p=0.010). A higher serum uric acid

level was observed among patients with Hepatitis B (7.41 ± 2.7) and patients with CTP class C (7.36 ± 2.68) (Table 5).

In our study Correlation between serum uric acid and CTP score (P value 0.010), Albumin (P value 0.0275), Bilirubin (P value 0.041), INR (P value 0.0414), SGOT (P value 0.0054), and SGPT (P value 0.0316) were found to be statistically significant. (Table 6)

DISCUSSION

Chronic liver disease is linked to considerable morbidity and mortality, necessitating the assessment of liver injury through various biochemical and radiological markers. These parameters have facilitated the development of several scoring systems for prognostication. Notably, uric acid, a product of purine metabolism, is generated during nuclear destruction following cell injury in chronic liver disease, particularly in cases leading to cirrhosis.

In our study, the mean age of participants was 46.22 ± 11.10 years, with the majority (54 participants, or 45%) aged between 36-50 years, followed by 32 participants (26.7%) in the 21-35 year age group. These findings are consistent with those of Chandramouli et al.[1] , Zelber-Sagi et al.[17] and Noklang S et al. [18] who reported mean ages of 44 ± 12 years, 43.9 ± 10.2 years, and 44.54 ± 11.22 years,

In the present study, a higher proportion of 84 (70%) were males, while 36 (30%) were females diagnosed with chronic liver disease from various causes, confirmed through clinical assessment and imaging studies. This male predominance is consistent with findings from studies conducted by Chandramouli et al.[1] and Noklang S et al.[18], highlighting potential demographic trends in chronic liver disease prevalence. Understanding this gender distribution is crucial for identifying risk factors and tailoring interventions for those most affected.

In the present study of 120 patients, 63 (52.5%) were identified as alcoholic, establishing it as a major risk factor for chronic liver disease. This finding aligns with several other studies that also highlight alcoholic liver disease as a predominant cause. For example, Chandramouli et al.[1] reported that 34 (51.5%) of their patients in Karnataka, India, had alcoholic liver disease, followed by Hepatitis B in 15 (23%) patients. Similarly, Kumar P et al. [19] found a high prevalence of alcoholic liver disease in India. Paul R et al. [20] noted that among 52 patients in West Bengal, 36.6% had alcoholic liver disease, with non-alcoholic fatty liver disease (NAFLD) following. Additionally, a study by Singh B et al. [21] in Manipur identified alcohol as the most common cause of chronic liver disease (69.7%), followed by chronic hepatitis C (15.2%). Our findings are consistent with these previous reports.

Out of 120 patients, 12 were classified as Class A (score 5-6), 50 as Class B (score 7-9), and 68 as Class C (score 10-15). This distribution aligns with the findings of Chandramouli et al.[1], who reported that 33 (50%) had a CTP score of ≥10, 26 (39.9%) were in the 7-9 range, and only 7 (10.6%) fell between 5-6. Similarly, Noklang S et al.[18] noted maximum uric acid levels in CTP Class C patients, consistent with our results. Prakash BC et al.[15] found 8 patients in Class A, 20 in Class B, and 28 in Class C, which aligns with our findings. In contrast, Singh B et al. [21] reported 30 patients in Class B, 20 in Class C, and 16 in Class A, indicating a different distribution. However, Singh B et al.[21] also highlighted that hyperuricemia may serve as a cause or marker of liver disease, with higher uric acid levels correlating with higher CTP grading, particularly in Class C patients compared to Classes B and A.

In our study, we found a strong correlation between serum uric acid levels and CTP scores in chronic liver disease (CLD) patients, with higher CTP scores associated with elevated uric acid levels (p=0.010). A higher serum uric acid level was observed among patients with Hepatitis B (7.41 ± 2.7) and patients with CTP class C (7.36 ± 2.68). This aligns with findings from Singh B et al. [23], who noted hyperuricemia as both a cause and a marker of higher CTP grading, and Paul R et al.[20], who demonstrated increasing uric acid levels with rising CTP classes. Choudhary J et al.[22] reported similar elevations in uric acid with liver disease progression among 150 patients. Chandramouli et al.[1] also highlighted this correlation, while Noklang S et al.[18] found maximum uric acid levels in CTP class C patients, with a mean level of 8.295 mg/dl. These findings collectively underscore the significance of monitoring uric acid as an indicator of CLD progression.

In our study, serum albumin, bilirubin, INR, SGOT, and SGPT were all significantly associated with CTP scores, with p-values of 0.0275, 0.041, 0.0414, 0.0054, and 0.0316, respectively. Chandramouli et al.[1] demonstrated low serum albumin levels in CLD patients, supporting our findings. Additionally, Vinotha T et al.[23] reported hyperbilirubinemia associated with hyperuricemia, with a p-value <0.001, reinforcing our results. Siddiqui SA and Ahmad M et al. [24] noted profound coagulation abnormalities in CLD patients, consistent with our study.

Noklang S et al. [18], Afzali A et al. [25], Noel S. et al.[26] also found high serum SGOT levels linked to elevated serum uric acid levels, while Chen S et al. [27] observed elevated ALT in patients with hyperuricemia. Zelber-Sagi et al.[17] similarly reported a significant association between serum uric acid and elevated ALT. Prakash BC et al. [15] reported that in their cross-sectional study, serum uric acid levels were found to be higher in patients with increased CTP scores. Collectively, these studies align with our findings, suggesting that increased serum uric acid reflects oxidative stress in tissues and serves as a marker of metabolic syndrome, both of which are associated with the progression of chronic liver disease. Most studies indicate that hyperuricemia correlates with higher CTP scores and poor prognosis in CLD patients.

Furthermore, a study conducted by Lee YH et al.[28] in Korea demonstrated a significant correlation between uric acid levels and the degree of hepatic histologic changes. However, whether reducing uric acid can halt disease

progression or prevent future hepatic or cardiac morbidity remains unknown.

This study is limited by a small sample size and the absence of histological data. Additionally, as a cross-sectional study, serum uric acid was measured only once. Despite these limitations, the study demonstrates a significant correlation between serum uric acid levels and Child Pugh scoring system for the prognostication of Chronic liver disease.

CONCLUSION

Chronic liver disease is a significant cause of global morbidity and mortality, necessitating effective diagnostic tools to identify patients at risk for complications. In this study, we measured serum uric acid levels and correlated them with the Child Pugh Score, revealing a strong association. While the Child Pugh Score is a well-established predictor of morbidity, serum uric acid can also serve as an early indicator of patients at high risk for complications and mortality. The increase in serum uric acid levels with higher Child Pugh Scores suggests that uric acid may be a reliable and cost-effective marker for assessing liver cirrhosis severity. Overall, serum uric acid presents a non-invasive and inexpensive method to evaluate disease severity and facilitate early intervention in chronic liver disease**.**

Source of Support: The author(s) received no financial support for the research, authorship, and/or publication of this article

Conflict of Interest: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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