



## Original Article

# Study of serum uric acid level in chronic liver disease and its correlation with Child-Turcotte-pugh score and platelet indices

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## Abstract

**Background:** Increased blood uric acid levels in chronic liver disease (CLD) promote endothelial dysfunction, insulin resistance, oxidative stress, and systemic inflammation, all of which are key risk factors for liver disease development.

**Objective:** The purpose of this study was to see correlation between blood uric acid levels with Child-Turcotte-Pugh (CTP) score and platelet indices.

**Methods:** A hospital-based cross-sectional research was conducted on individuals with CLD who were above the age of 18. A total of 54 people were included in the study. The levels of uric acid in the blood, as well as the CTP score and platelet indices, were assessed.

**Results:** Among 54 patients most patients belonged to CTP class C (51.85%) followed by CTP class B (40.74%) CTP class A (7.4%). The most prevalent cause of CLD (59.25%) is alcoholic liver disease. The average blood uric acid level in the CTP class A, B, C were  $3.75 \pm 1.5$ ,  $4.2 \pm 2.29$  and  $6.26 \pm 2.92$  respectively and clinically important, showing positive correlation uric acid and CTP score ( $r$  value: 0.347,  $P$ -value 0.001). It was also found that platelet distribution width increases with increasing serum uric acid level.

**Conclusion:** A rise in serum uric acid level coincides with an increase in Child Pugh score, implying that uric acid estimation can be a viable and cost-effective diagnostic marker for assessing the severity of liver cirrhosis.

**Keywords:** CLD, Serum Uric acid, Child Pugh score, cirrhosis.

## Introduction

Chronic liver disease (CLD) is a condition in which the liver parenchyma gradually deteriorates, resulting in fibrosis and cirrhosis.<sup>1</sup> Cirrhosis is currently the 11th leading cause of mortality worldwide.<sup>1</sup> Various etiological variables, such as

alcoholic liver disease, Hepatitis B and C infection, and non-alcoholic fatty liver disease (NAFLD/NASH), can all contribute to the development of chronic liver disease., autoimmune hepatitis and hepatocellular carcinoma.<sup>2</sup> Cirrhosis is defined clinically as

compensated or decompensated. Ascites, variceal haemorrhage, encephalopathy, or jaundice are symptoms of decompensated cirrhosis, which are complications of the major effects of cirrhosis: portal hypertension and liver insufficiency. Other decompensation issues includes hepatorenal syndrome (HRS), spontaneous bacterial peritonitis (SBP), and hepatopulmonary syndrome (HPS)

Compensated cirrhotic patients have a 50% 10-year survival rate, compared to 50% at 18 months for decompensated patients. Decompensation occurs at a rate of about 10% each year in cirrhotic patients.<sup>3,4</sup> In cirrhotic individuals, decompensation develops at a rate of roughly 10% each year.<sup>3,4</sup> such individuals require frequent medical attention as well as an increasing amount of medicine as the condition progresses. The quality of life suffers, and repeated hospitalizations (admissions and stays) are necessary. As the condition advances, the patient may require a liver transplant, which is a costly option for patients and health-care systems. and resulting in out of pocket expenditure of the patient.<sup>5</sup>

It is known fact that uric acid is the last byproduct of purine breakdown. Increased blood uric acid levels induce endothelial dysfunction, insulin resistance, oxidative stress, and systemic inflammation, all of which are significant concerns for the advancement of liver disease, ending in hepatic decompensation.<sup>6</sup> normal serum uric acid level (Male =3.4 – 7.0) (Female =2.4 – 5.7) PDW = (11.5 – 14.5) and MPV = (7.4 – 11.4). Hyperuricemia has also been linked to hypertension, metabolic syndrome, cardiovascular disease, and renal disease.<sup>6</sup> Uric acid is created in situations that cause cellular death and nuclear material deterioration.<sup>7</sup> Uric acid in tissues stimulates inflammation and causes tissue damage.<sup>7</sup> Because high uric acid levels are a recognised side effect of alcohol metabolism, hyperuricemia may be detected in alcoholic liver disease.<sup>8,9</sup>

Platelet indices were dramatically changed in cirrhosis compared to the normal population.<sup>10</sup>

PDW were substantially greater in cirrhotic patients compared to the normal population.<sup>11</sup> The Child-Pugh score has long been used to predict the prognosis of cirrhotic individuals with end-stage liver disease.<sup>11</sup> As a result, this study was conducted to examine the level of blood uric acid in patients with chronic liver disease and to determine the relationship between serum uric acid level and Child-Turcotte-Pugh score. We may be able to determine if it can be utilised as a substitute for the CTP score as a measure of severity and prognosis in individuals with chronic liver disease by doing so.

### Objectives of the Study

- 1) To determine the level of serum uric acid in individuals with chronic liver disease.
- 2) To compute the Child-Turcotte-Pugh (CTP) score of patients presenting with chronic liver disease.
- 3) To compare and investigate the relationship between serum uric acid levels and the Child-Turcotte-Pugh (CTP) score and platelet indices.

### Materials and Methods

The current hospital-based, analytic cross-sectional observational study was conducted by the Department of Medicine at Sri Manakula Vinayagar Medical College and Hospital (SMVMCH), which is located in the rural area of Pondicherry union territory. SMVMCH is located on the Puducherry-Villupuram district boundary and provides complete services to individuals living near the UT-Tamil Nadu border (Villupuram district). After getting ethical approval, the trial lasted six months. The current study has a sample size of 54 people.

Ethical principal was adhered throughout the study. After describing the purpose of the research to the patients or their attendants, informed written consent was obtained. The participants were consecutively selected.

Based on the inclusion criteria, all hepatic cirrhosis patients who attended the medicine

outpatient department and those admitted to the department of medicine throughout the study period who were vocal and willing were chosen for the study: Patients over the age of 18 with liver cirrhosis were included in the study. Exclusion criteria: Patients having a history of chemotherapy, hyperuricemia, gout, using medicines that may interfere with uric acid metabolism, recent surgery, or injuries that may interfere with uric acid metabolism were barred from participating in the research.

All patients underwent complete clinical examination and detailed history was obtained to look for symptoms of hepatic dysfunction such as jaundice. Skin alterations (spider angiomas, palmar erythema), Neurological changes (Hepatic encephalopathy),<sup>9</sup> Endocrine changes (breast atrophy, gynaecomastia, testicular atrophy). All patients had a complete blood count (CBC) with platelet indicators such as MPV, PDW, renal function test (RFT), liver function test (LFT) and PT, INR, random blood sugar (RBS), serum electrolytes (Na<sup>+</sup>, K<sup>+</sup>), and serum uric acid. Analysis of Ascitic Fluid (for determining Physical, Chemical, cytological properties and ADA) In all cases, an ultrasound of the entire abdomen was performed to look for the presence of features suggestive of liver cirrhosis, such as coarse echotexture, nodular surface, increased caudate to right lobe (C/RL) ratio, and portal hypertension (ascites, splenomegaly, varices, portal venous flow rate of 16 cm/sec). CTP score was determined based on the above research. In the presence of uricase, uric acid is oxidised to create allantoin and hydrogen peroxide. In the presence of peroxidase, hydrogen peroxide oxidises a leuco dye to produce a pigmented dye.<sup>7</sup> Reflectance spectrophotometry is used to determine the dye's reflection density.

Normal reference levels: 3.5-8.5 mg/dl (males) and 2.5-6.2 mg/dl (females).<sup>12</sup> The CTP score of each patient was calculated on the basis of 2 qualitative (Ascites and Hepatic Encephalopathy)

and 3 quantitative variables (Albumin, Bilirubin, and INR) as mentioned below.<sup>12</sup>

Parameters	Points		
	1	2	3
Hepatic encephalopathy	Nil	Grade 1-2	Grade 3-4
Ascites	Nil	Mild	Moderate to severe
Serum Bilirubin (mg/dl) <sup>8</sup>	<2	2-3	>3
Serum Bilirubin in PBC. <sup>8</sup>	<4	4-10	>10
Albumin(g/dL) <sup>8,12</sup>	>3.5	2.8-3.5	<2.8
Prothrombin time prolongation (secs prolonged) or INR. <sup>8</sup>	< 4s or INR<1.7	4-6s or INR 1.7-2.3	>6 or INR >2.3

Points ranging from 1 to 3 were given for each parameter, mentioned above, based on clinical evaluation and assessment of laboratory values, following which the CTP score was calculated by adding the sum of the points assigned to each parameter.

Patients were then divided into CTP classes A, B, and C based on the number of points they received. 5-6 points for A; 7-9 points for B C is worth 10-15 points. The West Haven criteria<sup>12</sup> were used to grade the hepatic encephalopathy. When necessary, the number connection test (NCT) was utilised. According to the International Ascites Club's consensus rules, ascites was classed as None, Mild, Moderate, or Severe.<sup>13</sup> (Mild/Grade 1 ascites is only visible by ultrasound examination, Mild/Grade 2 ascites is manifested by moderate symmetrical abdominal distension, and Severe/Grade 3 ascites is manifested by large or gross ascites with notable abdominal distension.)

**Consideration for Ethics:** The SMVMCH - Institutional Ethics Committee (EC CODE NO:08/2020) accepted the study protocol. Throughout the study, voluntarism, privacy, and secrecy were preserved.

## Results

**Sociodemographic profile:** Of the 54 patients participated in the research, 74% were male and 26% were female. The average age of responders was 37.4±10 years. The majority of participants, 59.4 percent, had alcoholic liver disease with a

high CTP score, followed by CTP class B (40.74 percent) and CTP class A (7.4 percent), while just 3.8 percent had autoimmune hepatitis. The mean

blood uric acid level in NAFLD patients was found to be high ( $7.68 \pm 1.31$ ).

**Table 1:** Aetiology of chronic liver disease and comparison of uric acid and CTP in the study group

Cause of cirrhosis	N% (n=54)	Serum Uric acid Mean $\pm$ SD	CTP-A	CTP-B	CTP-C
Alcoholic liver disease	32 (59.3%)	$4.40 \pm 2.11$	2	17	13
Chronic hepatitis B	5 (9.3%)	$4.2 \pm 2.82$	0	2	3
Chronic hepatitis C	3 (5.6%)	$6.3 \pm 1.43$	0	2	1
NASH/NAFLD	6 (11.2%)	<b><math>7.68 \pm 1.31</math></b>	0	2	4
Auto immune hepatitis	2 (3.8%)	$4.93 \pm 1.29$	1	1	0
Hepatocellular carcinoma	6 (11.2%)	$4.73 \pm 1.40$	1	45	1
Total (n=54)	54		4	28	22

**Table 2:** Correlation of child pugh score with various biochemical parameters

Child pugh score	Mean platelet volume (MPV) Mean value	Platelet Distribution Width (PDW) Mean value	Uric acid Mean value (95CI)
A	8.2	14.85	3.75, (1.35-6.34)
B	9.17	17.2	4.27, (3.39- 5.17)
C	8.86	18.01	6.27, (4.96-7.557)
Pearson correlation	0.118	0.192	0.345
P value	0.03	0.05	0.03

(Table 2)When comparing CPS scores A and B, it is obvious that PDW mean value and mean serum uric acid rise in CPS score C. It discovered a statistically significant positive link between blood uric acid levels and CTP score ( $r = 0.347$ ,  $P = 0.03$ ).

## Discussion

Our study showed majority of the study population were 50% in 35 – 45 years age group, which are working age group, which is a point to consider as it affects the over country's economy This is comparable to the study done by Das J et al.<sup>12</sup> In the current study, 74% of the enrolled participants were male and 26% were female, which is consistent with the findings of Mukherjee et al,<sup>13</sup> who found that 78% of the study population of liver cirrhotic patients were males and 24% were females, and Ahmed et al,<sup>14</sup> who found that 15% of the study subjects were females and 85% were males. The current study found that alcohol was the most prevalent cause of cirrhosis among the study individuals, accounting for 59.3 percent. NAFLD and hepatocellular carcinoma (11.2 percent) appeared as the second most

prevalent cause, which is consistent with the findings of a research done by Das J et al.<sup>12</sup> NAFLD, on the other hand, was the second most prevalent cause in our research. This can be explained by the fact that the prevalence of metabolic syndrome is growing as a result of recent bad lifestyle choices. NAFLD is the hepatic manifestation of metabolic syndrome, and it is also an independent predictor of future risk of CVD, Type 2 DM, and so on.<sup>15</sup> As a result, the Government of India has improved NAFLD in the NPCDCS programme, which shares a similar health promotion and prevention strategy.<sup>15</sup> Another cause for NAFLD supplanting chronic hepatitis B might be increased public awareness of Hepatitis B vaccination, resulting in a reduction in HBV-related cirrhosis. According to our findings, the majority of the patients belonged to CTP class B, Which is contrast to study conducted by paul et al<sup>16</sup>, Das J et al.<sup>12</sup>, Mukherjee et al<sup>13</sup>, majority of the patients belonged by class A. Which implies that most patients seek medical care only during the later stages of the cirrhosis as well as due to late diagnosis CLD in its early stages.

In our research, The mean serum uric acid level in CTP class A was 3.75. The mean blood uric acid levels in classes B and C were 4.27 and 6.26, respectively. Pearson's correlation coefficient was utilised to analyse the relationship between blood uric acid level and CTP score, and it was shown to be positive (r-value: 0.370 and p-value: 0.003). This is consistent with the findings of a research done by Das J et al.,<sup>12</sup> who determined that blood uric acid levels were linked to the development of cirrhosis and the presence of increased liver enzymes. PDW was considerably higher among patients with elevated blood uric acid and CP score in our investigation, which is consistent with the findings of Mukker P et al.<sup>13</sup>

**Already known finding:** Alcoholic liver disease is the most frequent cause of cirrhosis; the more severe the illness (CPS 3), the higher the blood uric acid level, which acts as a sign of chronic liver disease; NAFLD is the second most common cause, particularly among male, obese patients who lead sedentary lives.

**New finding of this study:** Platelet distribution width increases with increasing serum uric acid level and CTP Score, while mean platelet volume is not affected.

**Limitation of the study:** hospital-based cross-sectional study conducted at a single health care institution with a limited sample size, the results cannot be generalised. It is unclear if hyperuricemia actually causes liver cirrhosis or if it is simply a measure of the severity of chronic liver disease.

### Conclusion

The increased blood uric acid level with rising Child Pugh score shows that uric acid estimation can be a valid and cost-effective measure for assessing the degree of liver cirrhosis in chronic liver disease.

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