

Study of Serum Uric Acid Level in Liver Cirrhosis and its Correlation with Child Turcotte Pugh Score

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Abstract

Background: Cirrhosis cannot be accurately diagnosed by serologic tests. Even though aberrant biochemical patterns in combination with the clinical picture can point to certain liver illnesses, liver function tests may not always accurately reflect hepatic function. Hyperuricemia has been found to be a risk factor for liver disease. Hence, this study was conducted to determine the serum uric acid level in liver cirrhosis and its correlation with the Child Turcotte Pugh score.

Methods: This was a prospective study among 86 patients with liver cirrhosis conducted in a tertiary care centre using simple random sampling. Their serum uric acid and CTP scores were estimated and analysed using descriptive and inferential statistics in SPSS software.

Results: 36.3% of patients had a Class A score, 31.3% had a Class B score, and 32.5% of them had a Class C score. The mean uric acid value was 5.621 ± 1.861 mg/dL, ranging from 3.4 to 10.9. There was a significant (0.0001) positive correlation (r value 0.642) between serum uric acid and the Child Turcotte Pugh score among patients with liver cirrhosis.

Conclusion: Serum uric acid levels increase with the Child Pugh score, suggesting that uric acid estimation may be a useful and affordable diagnostic marker for assessing the degree of liver cirrhosis.

Keywords: Liver Cirrhosis, Child Pugh Score, Uric Acid, Prospective.

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Introduction

Numerous investigations can help in the identification of liver cirrhosis, including blood investigations, imaging studies and liver biopsy. The Child-Pugh scoring method, often called the Child-Pugh-Turcotte score, was created to forecast mortality in cirrhotic patients. Purine degradation yields uric acid (2, 6, 8 trioxypurine - C₅H₄N₄O₃). Urate, an ionised form of uric acid, circulates at the physiological pH of 7.4, which is normal. Recent studies have shown a strong correlation between the SUA level and the severity of NAFLD-induced liver damage. [1] According to several studies, the increased blood uric acid levels in cirrhotic individuals were mostly due to an increased effective vascular volume, which led to an excessive renal clearance of uric acid. [2]

This study was therefore carried out to determine serum uric acid levels in liver cirrhosis and their correlation with the Child Turcotte Pugh score.

Methods

This was a prospective observational study, conducted over a period of 2 years (October 2021–October 2023) among 86 patients aged eighteen years and older diagnosed with liver cirrhosis at Kilpauk Medical College, Government Royapettah Hospital, and Tamil Nadu Government Dental College-Tertiary Care Centres. Patients with gout, chronic kidney disease, hypothyroidism, recent trauma, surgery, known infections, hepatorenal syndrome, those on drugs that cause alteration in the level of uric acid like febuxostat, allopurinol, thiazides, furosemide, etc.; patients with known

malignancies on chemotherapy and pregnant patients were excluded from the study.

Child Turcotte-Pugh score – scored by numbers and categorized into three classes (Class A, B and C). Serum uric acid levels were estimated in all study subjects. SPSS (Statistical Package of Social Sciences) version 21 was used to analyse the data. Statistics, both descriptive and inferential, were used to analyse the variables. The data of continuous variables obeying normal distribution were represented by “mean ± standard deviation ($x \pm s$)” and the relationship was tested using an unpaired T test. The chi-squared test was used to examine associations between the categorical variables that were expressed as percentages. A two-sided test was used to assess each statistic, with a p-value of 0.05 or lower being considered statistically significant. The setting for all CI (Confidence Intervals) was 95%. Pearson correlation was used to determine the correlation

coefficient between serum uric acid and the Child Turcotte Pugh score or other variables.

Results

The majority (32.5%) of participants were in the age group of 41–50 years. Most, i.e., 82.5%, of the participants were men. The mean duration of cirrhosis was 2.378 ± 2.19 years, ranging from 0 to 7 years.

Child Turcotte Pugh Classification

The mean score of Child Turcotte Pugh was 7.93 ± 2.321 and ranged from 5 to 15. 36.3% of patients had a Class A score, 31.3% had a Class B score and 32.5% of them had a Class C score.

Uric acid

The mean uric acid value was 5.621 ± 1.861 mg/dL ranging from 3.4 to 10.9 (Figure 1).

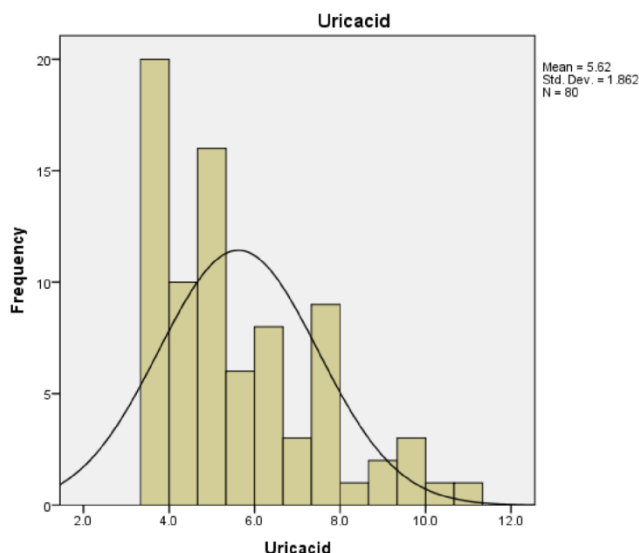


Figure 1: Mean Uric Acid Levels

Association between Child Turcotte Pugh Score and Serum Uric Acid

As shown in Table 1, the mean uric acid levels were higher among patients who had Class C liver cirrhosis. The values were 4.356 ± 0.669 mg/dL, 5.177 ± 1.431 mg/dL and 7.459 ± 1.707 mg/dL among CTP classes A, B and C respectively and this difference was statistically significant.

Table 1: Association of Mean Uric Acid Levels based on Child Turcotte Pugh Score

Sl. No.	Class	Mean	SD	P-Value
1	A	4.356	0.669	0.002
2	B	5.177	1.431	
3	C	7.459	1.707	

Correlation between Child Turcotte Pugh Score and Serum Uric Acid

There was a positive correlation between serum uric acid and the Child Turcotte Pugh score among patients with liver cirrhosis. (Figure 2)

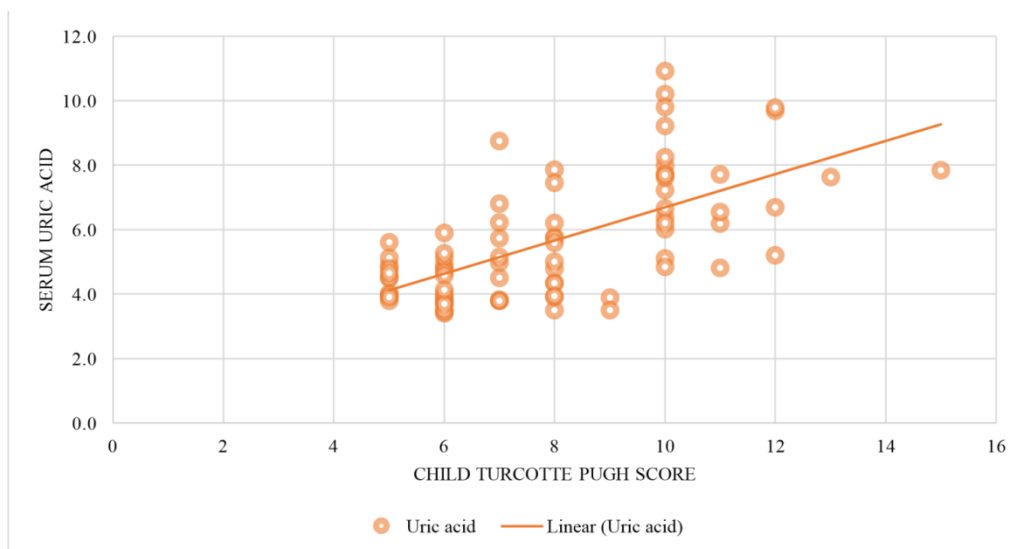


Figure 2: Correlation between Serum Uric Acid and Child Turcotte Pugh Score

Correlation Coefficient of Uric Acid with Variables

Serum uric acid had a significant positive correlation with the Child Turcotte Pugh score, duration in years, prothrombin time, thromboplastin time, alkaline phosphatase, and portal vein diameter. Serum uric acid had a significant negative correlation with hemoglobin, total protein and serum albumin. (Table 2)

Table 2: Correlation Coefficient of Uric Acid with Variables

Test	r value	P-Value
Child Turcotte Pugh score	0.642	0.0001
Age	-0.099	0.383
Duration in years	0.541	0.0001
Hemoglobin	-0.236	0.035
Platelet	-0.041	0.718
Prothrombin time	0.481	0.0001
TB	0.573	0.0001
ALP	0.395	0.0001
TP	-0.266	0.017
Serum albumin	-0.404	0.0001
Portal vein diameter	0.455	0.0001

Diagnostic Accuracy of Serum Uric Acid

The sensitivity was 82.8% and the specificity was too low (0.03%) for serum uric acid in diagnosing liver cirrhosis at the cut-off value of 3.75. But serum uric acid had better sensitivity (80.8%) and

specificity (70.4%) in diagnosing liver cirrhosis at the cut-off value of 5.65 among patients with CTP Class C. (Table 3)

The ROC curves for various cut-off values of serum uric acid are as shown in Figures 3-5.

Table 3: Diagnostic Accuracy of Serum Uric Acid with Standard CTP Score

	CTP A	CTP B	CTP C
Cut off	3.75	4.25	5.65
AUC	0.228	0.481	0.805
P value	<0.0001	0.787	<0.0001
Sensitivity	82.80%	68%	80.80%
Specificity	0.03%	34.50%	70.40%

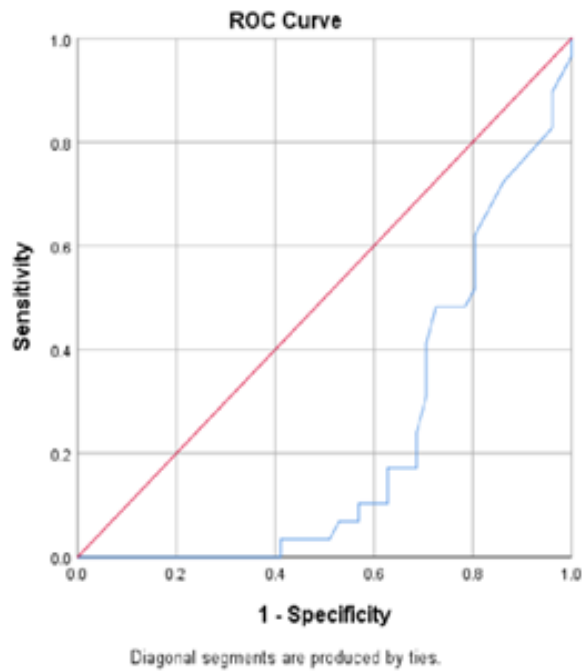


Figure 3: Receiver Operating Curve Analysis for the Serum Uric Acid Cutoff Value of 3.75 g/dL

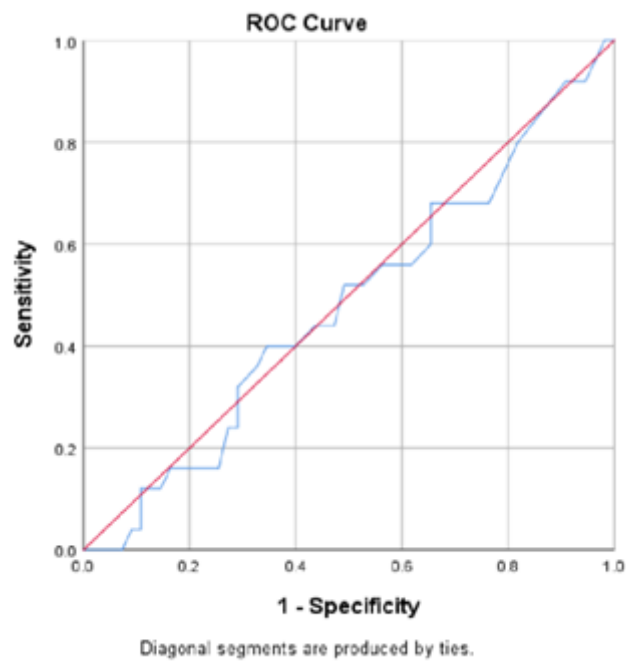


Figure 4: Receiver Operating Curve Analysis for the Serum Uric Acid Cutoff Value of 4.25 g/dL

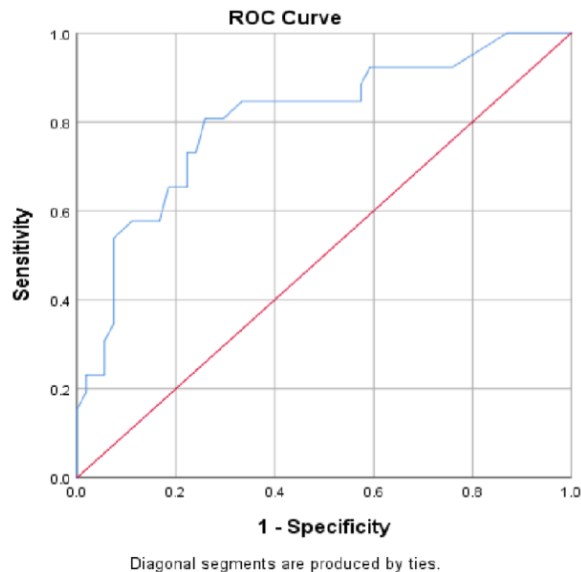


Figure 5 Receiver Operating Curve Analysis for the Serum Uric Acid Cutoff Value of 5.65 g/dL

Discussion

This prospective observational study was carried out to determine the correlation of serum uric acid with the Child Turcotte Pugh score.

Serum Uric Acid Levels

In the present study, the mean uric acid value across the groups was 5.621 ± 1.861 mg/dL ranging from 3.4 to 10.9. The mean uric acid levels were 4.356 ± 0.669 mg/dL, 5.177 ± 1.431 mg/dL and 7.459 ± 1.707 mg/dL among CTP classes A, B and C respectively. CTP class C had higher mean values than classes A and B. Similar to the present study, the mean value of blood uric acid was 6.19 (3.25 mg/dl), and 7.73% of patients had hyperuricemia (>7 mg/dl) in the study by Hasan et al. The mean uric acid level in a study by Prakash BC et al. [3] was 4.79, with a standard deviation of 2 ranging from 1.8 to 9.9 mg/dl.

Gupta J et al. [4] observed that the mean uric acid (mg/dl) was 6.692.92 among 50 chronic liver disease patients older than 18 years. 24 percent of the participants had normal uric acid (3.1-5), while 38 (76 percent) of the subjects had greater uric acid or hyperuricemia.

According to a study by Manonmene et al., [5] blood uric acid levels were 3.75 ± 1.5 , 4.2 ± 2.29 , and 6.26 ± 2.92 in the CTP classes A, B, and C, respectively. In a similar study by Das et al., the mean blood uric acid level in CTP class A was 4.57 (0.88) mg/dL. The mean blood uric acid levels were higher in classes B and C, measuring 6.42 (1.78) mg/dL and 7.97 (2.31) mg/dL, respectively. The mean uric acid levels were 3.98, 5.74 and 9.38 in CTP classes A, B, and C respectively in the study conducted by Paul et al. [6]

In line with the observation of the present study, Manonmene et al., [5] Das et al. [7] and Paul et al. [6] found that CTP class C had higher mean uric acid values compared with other classes.

Child Turcotte Pugh Score

The mean score of Child Turcotte Pugh was 7.93 ± 2.321 and ranged from 5 to 15. 36.3% of patients had a Class A score, 31.3% had a Class B score, and 32.5% of them had a Class C score. The majority of the 220 liver cirrhotic patients studied by Hasan et al. [8] (52.3%) belonged to CTP Class C. A maximum of 46 (75.4%) of the 61 hyperuricemic patients were in CTP class C, followed by 13 (21.3%) and 2 (3.3%), respectively, in CTP classes B and A.

According to a study by Manonmene et al., [5] out of 54 patients with chronic liver disease aged more than eighteen years, the majority (51.85%) belonged to CTP class C, followed by CTP class B (40.74%), and CTP class A (7.4%). Gupta J et al. [4] found that 34%, 56% and 10% of participants had CTP classes A, B, and C respectively. The participants with CTP classes A, B, and C had mean uric acids of 4.03, 5.17, and 8.94, respectively.

The mean CTP score was 10.79 ± 2.32 in a study by Prakash BC et al. [3] Out of 100 patients, only two were classified as Class A (score: 5–6), 50 as Class B (score: 7-9), and 68 as Class C (score: 10–15). Das et al. [7] observed that the majority of the 140 patients with liver cirrhosis belonged to CTP class C (50.71%), followed by CTP class B (40%) and CTP class A (9.29%). The mean blood uric acid level in CTP class A was 4.57 (0.88) mg/dL. The mean blood uric acid levels were higher in classes B and C, measuring 6.42 (1.78) mg/dL and 7.97 (2.31) mg/dL, respectively.

Correlation of Serum Uric Acid with Child Turcotte Pugh Score

Our study found that the mean uric acid levels were higher among patients who had Class C liver cirrhosis based on the Child Turcotte Pugh score and the difference was statistically significant. There was a significant (0.0001) positive correlation (r -value = 0.642) between serum uric acid and the Child Turcotte Pugh score among patients with liver cirrhosis.

Hasan et al. [8] studied the relationship between serum uric acid and liver enzymes. As cirrhotic patients advanced to higher CTP classes, the mean serum uric acid level gradually increased, and there was a positive association between serum uric acid and liver enzymes.

According to a study by Manonmene et al., [5] there was a significant positive correlation between uric acid and CTP score (r -value = 0.347, p -value 0.001). Prakash BC et al [9] also observed a substantial, positive correlation between the CTP (r -value = 0.472), MELD (r -value = 0.405), and UKELD scores (r value = 0.242) and uric acid levels.

The course of the disease was significantly associated with an increase in blood uric acid level, as determined by Choudhary J et al. [10] among 150 patients with chronic liver disease aged 20 to 64 years (p = 0.001). Additionally, the advancement of the Child Pugh score was found to be positively correlated with uric acid using Spearman's correlation (r = 0.293; p = 0.001).

Gupta J et al. [4] found a substantial positive association between uric acid and total bilirubin (r = 0.59; P = 0.001), SGOT (r = 0.43; p = 0.007), SGPT (r = 0.47; p = 0.004), and CTP score (r = 0.48; p = 0.004) using Pearson correlation analysis. Das et al. [7] found that serum uric acid and CTP score had a statistically significant positive correlation (r = 0.3860; p = 0.001). Paul et al. (80) found that serum bilirubin, SGOT, and mortality were all significantly correlated with UA levels (r = 0.567, r = 0.464, respectively). There was a positive correlation between serum UA and CTP score (r = 0.44; p = 0.02), ALP (r = 0.18; p = 0.12) and a negative correlation with albumin (r = -0.43; p = 0.007).

The present study's results, which showed a substantial positive association between serum uric acid and the CTP score, were consistent with those of the previous studies. Serum uric acid levels were higher in patients with advanced liver cirrhosis.

Zhou et al. [11] research on meta-analysis confirmed that high SUA levels elevated the risk of NAFLD. In a meta-analysis, Liu et al. also discovered that people in the highest SUA category

had a 40% higher chance of developing the condition NAFLD. In a meta-analysis, Wijarnpreecha K et al. [12] observed that the risk of NAFLD was considerably higher in individuals with hyperuricemia than in individuals with normal uric acid levels, with a pooled OR (Odds Ratio) of 1.97 (95% CI, 1.69-2.29). The serum uric acid level was thus found to be a significant independent risk factor for advanced liver disease.

Serum Uric Acid and Other Variables

In this study, serum uric acid had a significant positive correlation with the Child Turcotte Pugh score, duration in years, prothrombin time, thromboplastin time, alkaline phosphatase, and portal vein diameter. Serum uric acid had a significant negative correlation with hemoglobin, total protein and serum albumin.

Prakash BC et al. [9] study also demonstrated a positive correlation between serum uric acid and a number of biochemical variables, including total bilirubin (r value = 0.292), prothrombin time/international normalised ratio (PT/INR) (r value = 0.207), and serum creatinine (r value = 0.424),, as well as a negative correlation between serum albumin and uric acid.

Similarly, Gupta J et al. [4] observed substantial positive associations between uric acid and total bilirubin (r = 0.59; P = 0.001), SGOT (r = 0.43; P = 0.007), SGPT (r = 0.47; P = 0.004), and CTP Score (r = 0.48; P = 0.004) using Pearson correlation analysis.

Paul et al. [6] found that serum bilirubin, SGOT, and mortality were all significantly correlated with UA levels (r = 0.567, r = 0.464, respectively). There was a positive correlation between serum UA and CTP score (r = 0.44; p = 0.02), ALP (r = 0.18; p = 0.12) and a negative correlation with albumin (r = -0.43; p = 0.007).

Conclusion

This study shows that as cirrhotic patients advance to higher CTP classes, the mean serum uric acid level gradually increases, and there is a positive association between serum uric acid and liver enzymes. Further, follow-up trials could be recommended among liver cirrhosis patients to know the exact pathogenesis of uric acid in liver diseases.

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