



**Serum Uric Acid Level in Chronic Liver Disease and Its Relation to Child-Turcotte-Pugh (CTP) Score**

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**Abstract**

**Introduction:** Cirrhosis can be the final stage chronic liver disease (CLD). Hyperuricemia is a risk factor for the development of cirrhosis. Proposed mechanisms include induction of endothelial dysfunction, insulin resistance, oxidative stress, and systemic inflammation which are now known to be important risk factors for the development or progression of liver diseases.

**Aims and Objectives:** To assess the level of serum uric acid in patients with chronic liver disease and calculate the Child-Turcotte-Pugh (CTP) score. To compare and study the correlation between serum uric acid levels and Child-Turcotte-Pugh (CTP) score in patients with chronic liver disease.

**Materials and Methods:** Hospital based cross sectional observational study done in a single tertiary care center with a sample size 140 with inclusion criteria aged above 12 years fulfilling the Garcia-Tsao criteria for cirrhosis of liver. Patients with gout, Lymph proliferative/myeloproliferative disorders, receiving

chemotherapy, renal dysfunction, malignancy, taking drugs that may interfere with uric acid metabolism, not giving an informed written consent were excluded. We took detailed history and thorough physical examination was done. Serum uric acid was measured by reflectance spectrophotometry, liver function test and other appropriate investigations were done. CTP score calculated and statistical analysis were done.

**Result:** Amongst 140 study subjects, 80 % were males (n = 112) and 20 % (n = 28) were females. Most of the patients belonged to CTP class C (50.71%) followed by CTP class B (40%) and then CTP class A (9.29%). In CTP class A, the mean serum uric acid level was  $4.57 \pm 0.88$  mg/dL. In class B and class C, the mean serum uric acid levels were higher:  $6.42 \pm 1.78$  mg/dL and  $7.97 \pm 2.31$  mg/dL respectively. There was a statistically significant difference between the three classes. (P-value <0.001).

The mean serum uric acid level in alcohol related CLD was  $7.22 \pm 2.11$  mg/dL, in NAFLD related CLD  $7.05 \pm$

2.82 mg/dL, in Chronic hepatitis B  $5.95 \pm 1.43$  mg/dL, in autoimmune hepatitis  $5.28 \pm 1.31$  mg/dL, in Wilsons disease  $5.61 \pm 1.29$  mg/dL, in cryptogenic cirrhosis  $4.02 \pm 1.40$  mg/dL. There was a statistically significant positive correlation between serum uric acid and CTP score (r value: 0.3860; p-value <0.001).

**Conclusion:** This study established a statistically significant positive correlation between serum uric acid levels and CTP score]

**Keywords:** Serum Uric Acid, Chronic Liver Disease, Child-Turcotte-Pugh (CTP) Score, Cirrhosis of Liver.

### **Introduction**

Cirrhosis of liver is a morphological change characterized by conversion of normal architecture to structurally abnormal regenerative nodules surrounded by fibrous tissue. Chronic liver disease (CLD) refers to disease of the liver which persists for more than six months.

The main pathogenic feature underlying liver fibrosis and cirrhosis is activation of hepatic stellate cells, also known as Ito cells or perisinusoidal cells. They are located in the space of Disse between hepatocytes and sinusoidal endothelial cells. Ito cells become activated and secrete extracellular matrix (collagen types 1 and 3, sulphated proteoglycans, and glycoproteins) in response to injury, thus, leading to fibrosis<sup>[1]</sup>.

Liver disease accounts for roughly 2 million deaths per year worldwide, 1 million due to complications of cirrhosis and 1 million due to viral hepatitis and hepatocellular carcinoma. Cirrhosis, at present, is the 11th most common cause of death globally and liver cancer is the 16th leading cause of death; combined, they account for 3.5% of all deaths worldwide. About 2 billion people consume alcohol worldwide and more than 75 million are diagnosed with alcohol-use disorders and are at risk of alcohol-associated liver

disease. Approximately 2 billion adults are obese or overweight and over 400 million have diabetes; both of which are risk factors for non-alcoholic fatty liver disease (NAFLD) and hepatocellular carcinoma (HCC)<sup>[2]</sup>.

Cirrhosis can be clinically classified by its status as compensated or decompensated. Decompensated cirrhosis is defined by the presence of ascites, variceal bleeding, encephalopathy, or jaundice, which are complications that result from the main consequences of cirrhosis: portal hypertension and liver insufficiency. Spontaneous bacterial peritonitis (SBP), hepatorenal syndrome (HRS) and hepatopulmonary syndrome (HPS) are other complications of decompensation. In compensated cirrhosis these features are absent. Clinical distinction like this has significant role in prognosis and treatment.<sup>[3]</sup>

Prognosis has a significant role in baseline assessment of all diseases. The outcome of cirrhosis depends on the patient's stage. Compensated cirrhotic patients have a 50% 10-year survival as compared to 50% survival at 18 months for decompensated patients. Cirrhotic patients become decompensated at the rate of approximately 10% per year<sup>[4]</sup>.

### **Child-Turcotte-Pugh (CTP) Score**

Child-Pugh score has been widely used to assess the prognosis of cirrhotic patients in end-stage liver disease. Even though there are certain limitations, Child-Pugh score continues to be one of the robust predictors of prognosis of cirrhosis. Child and Turcotte<sup>[5]</sup> introduced their scoring system in 1964 as a means of predicting the operative mortality associated with portocaval shunt surgery for variceal bleeding. Pugh's<sup>[6]</sup> revised system in 1973 substituted prothrombin time for the less specific variable of

nutritional status. A CTP score of 10 or greater is associated with a 50% chance of death within 1 year.

### **Uric Acid**

Uric acid is the final end product of purine degradation in humans. Hyperuricemia is a known cause of gouty arthritis and kidney stones. In recent times, hyperuricemia has also been implicated in the development of hypertension, metabolic syndrome, cardiovascular disease and kidney disease.

While hyperuricemia has conventionally been considered as a result of these conditions, mechanisms have been proposed by which hyperuricemia could actually cause them. These include induction of endothelial dysfunction, insulin resistance, oxidative stress, and systemic inflammation<sup>[7,8]</sup>, which are now known to be important risk factors for the development or progression of liver diseases. For example, these mechanisms are considered pivotal in the pathogenesis of NAFLD and Non-alcoholic steatohepatitis (NASH)<sup>[9]</sup>. In addition, they help in the progression of hepatitis C virus (HCV) related and alcoholic liver diseases<sup>[10]</sup>. Therefore, it is hypothesized that hyperuricemia is a risk factor for the development of cirrhosis or the presence of hepatic necroinflammation.

Uric acid is produced in conditions leading to cellular destruction and degradation of nuclear material. Uric acid in tissues activates inflammasomes and damages surrounding tissues<sup>[11]</sup>. Elevated uric acid level is an independent etiological risk factor in NAFLD<sup>[12]</sup>. High uric acid level is a known sequel of alcohol metabolism and therefore hyperuricemia may be found in alcoholic liver disease<sup>[13,14]</sup>. In various studies, uric acid levels have been found to correlate with the level of tissue damage<sup>[15]</sup>.

There is a paucity of data regarding relation of uric acid with the severity of chronic liver disease especially in

the Indian context. Hence this study was undertaken to assess the level of serum uric acid in patients presenting with chronic liver disease and to find out the correlation between serum uric acid level and Child-Turcotte-Pugh score. By doing so, we may be able to find out if it can be used as a substitute to CTP score, as a marker of severity and prognosis in patients with chronic liver disease.

### **Aims And Objectives**

1. To assess the level of serum uric acid in patients presenting with chronic liver disease.
2. To calculate the Child-Turcotte-Pugh (CTP) score of patients presenting with chronic liver disease.
3. To compare and study the correlation between serum uric acid levels and Child-Turcotte-Pugh (CTP) score in patients presenting with chronic liver disease.

### **Materials And Methods**

This hospital based cross sectional observational study was done in the Department of Medicine, Assam Medical College and Hospital, Dibrugarh for duration of one year (June 2018 to May 2019). All hepatic cirrhosis patients who attended medicine outpatient department and those admitted in the department of medicine during the study period were taken for study. Ethical clearance was taken from the Institutional Ethics Committee of Assam Medical College and Hospital before start of the study. Informed written consent was taken from the patients or their attendants after explaining about the purpose of the study.

All patients aged above 12 years of age fulfilling the Garcia-Tsao<sup>[15]</sup> criteria for cirrhosis of liver were included. Patients with gout, lymphoproliferative / myeloproliferative disorders, receiving chemotherapy, renal dysfunction, malignancy, taking drugs that may interfere with uric acid metabolism, not giving an informed written consent were excluded from the study.

Considering 95% confidence interval, and taking the findings of study by Paul et al [16] as reference, the sample size for present study was calculated and rounded out to be 140.

**Method of data collection**

Data was collected from all CLD patients attending medicine outpatient department or admitted in the medicine wards. Patients were selected according to inclusion and exclusion criteria mentioned above. We used Garcia – Tsao criteria [15], a non-histopathological diagnostic criterion for cirrhosis of liver to define cirrhosis having the clinical signs of hepatocellular dysfunction, signs of portal hypertension, USG finding suggestive of cirrhosis of liver. Clinical signs of hepatocellular dysfunction were Jaundice, Neurological changes (Hepatic encephalopathy), Skin changes (spider angiomas, palmar erythema), Endocrine changes (breast atrophy, gynaecomastia, testicular atrophy).

Signs of portal hypertension were hematemesis, melena or gastroesophageal varices by UGI endoscopy, splenomegaly, ascites.

Findings in USG abdomen suggestive of cirrhosis of liver are coarse echotexture, nodular surface, increased caudate to right lobe (C/RL) ratio and portal hypertension (ascites, splenomegaly, varices, portal venous flow rate <16 cm/sec).

All patients underwent detailed history and thorough clinical examination, Complete blood count (CBC) with ESR, renal function test (RFT), liver function test (LFT) and PT, INR, random blood sugar (RBS), serum electrolytes (Na+, K+) were done in all patients. Serum Uric acid, ascitic Fluid Analysis (for determining Physical, Chemical, cytological properties and ADA), USG whole abdomen were done in all cases to look for presence of features suggestive of Cirrhosis of

liver and Portal hypertension. In those where diagnostic dilemmas was present even after USG, fibro scan was done. Serological tests for detection of infection with hepatitis B and C virus (HBsAg and Anti HCV antibody) were done in all cases. Esophagogastroduodenoscopy was done for presence and grading of gastroesophageal varices.

Aetiology Specific tests like anti-nuclear antibody (ANA), anti-mitochondrial antibody (AMA), anti-smooth muscle antibody (ASMA), anti-Liver Kidney Microsomal 1 antibody (Anti LKM 1), serum ceruloplasmin, 24 hr urinary copper, serum ferritin, transferrin saturation, HbA1c, lipid profile were done only when indicated.

**Uric acid**

Uric acid is oxidised in the presence of uricase to form allantoin and hydrogen peroxide. Hydrogen peroxide oxidises a leuco dye in the presence of peroxidase to generate a coloured dye. The reflection density of the dye is measured by reflectance spectrophotometry. Normal reference levels: 3.5-8.5 mg/dl (males) and 2.5-6.2 mg/dl (females)

**CTP Score calculation**

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)

Parameter	Points		
	1 Point	2 Points	3 Points
Hepatic encephalopathy	None	Grade 1-2	Grade 3-4
Ascites	None	Mild	Moderate to severe
Bilirubin(mg/dL)	<2	2-3	>3
Bilirubin in PBC	<4	4-10	>10

Albumin(g/dL)	>3.5	2.8-3.5	<2.8
Prothrombin time prolongation (secs prolonged) or INR	< 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 classified into CTP class A, B and C depending on the points scored. A= 5-6 points; B= 7-9 points C= 10-15 points.

Hepatic encephalopathy grading was done as per West Haven criteria. Number connection test (NCT) was used as and when appropriate.

Ascites was classified into None, Mild, Moderate and Severe as per the consensus guidelines of the International Ascites club<sup>[17]</sup>. (Mild/Grade 1: ascites detectable only by ultrasound examination, Moderate/ Grade 2: ascites is manifest by moderate symmetrical distension of abdomen and Severe/ Grade 3: Large or gross ascites with marked abdominal distension).

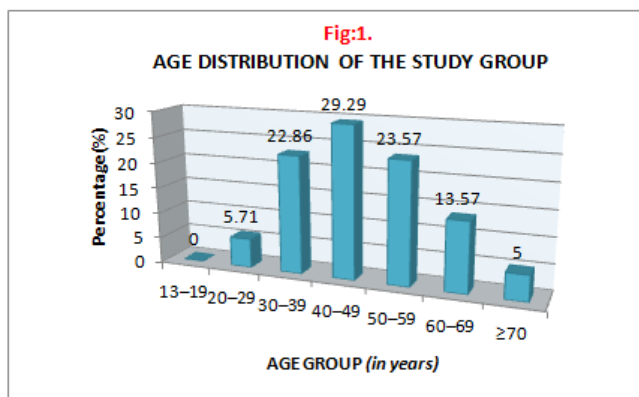
**Statistical Analysis**

The data collected was tabulated in Microsoft Excel Worksheet 2010 and computer-based analysis was performed using the Statistical product and service solutions (SPSS) 20.0 software (SPSS, Chicago, Illinois, USA). Results on continuous measurements are presented as mean ± standard deviation and are compared using Analysis of Variance (ANOVA). Where the p-value was found significant (p<0.05) among 3 groups, post hoc analysis was done to find out the significance between 2 individual groups. Discrete data are expressed as number (%) and analysed using

Chi square test and Fischer’s exact test. Pearson’s correlation coefficient (r) was used to measure the associations among continuous variables. For all analyses, statistical significance was fixed at 5% level (p value < 0.05).

**Result**

Fig.1. shows that majority of the study subjects (29.29 %) were in the age group of 40-49 years followed by 23.57 % in the age group of 50-59 years. The least number of study subjects were in the age groups, 20-29 years and above 70 years. The mean age of the whole study group was 47.31 ± 12.52 years. Mean age of male patients was 47.06 ± 11.82 years and mean age of females was 48.32 ± 15.21 years.



Majority of the study subjects were males constituting 80% (n = 112). 20 % were females (n = 28) (Fig.2).

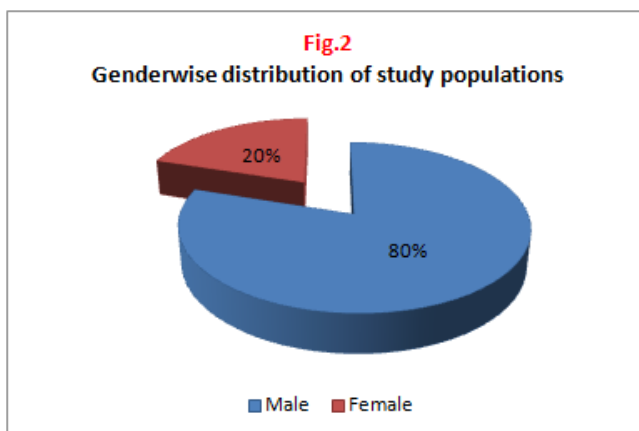


Table.1.shows that the most common cause of cirrhosis was alcohol (70%)followed by NAFLD

(21.43%),Chronic Hepatitis B (4.29%) and Autoimmune hepatitis, Wilson’s disease and Cryptogenic cirrhosis, each accounted for 1.43%. We did not encountered any patient who had HCV related cirrhosis.

Table 1: Aetiology of chronic liver disease in the study group

Aetiology	Number (N)	Percentage (%)
Alcohol	98	70.00
NAFLD	30	21.43
Chronic Hepatitis B	6	4.29
Chronic Hepatitis C	0	0
Autoimmune Hepatitis	2	1.43
Wilson's Disease	2	1.43
Cryptogenic	2	1.43
TOTAL	140	100.00

Table.2. shows gender wise aetiologies of CLD. In males, the most common cause of CLD was alcohol related (77.68%) followed by NAFLD related cirrhosis (15.18%),chronic hepatitis B (4.46%). No male had autoimmune hepatitis. In females, NAFLD related cirrhosis was the leading cause (46.43%) followed by alcohol related cirrhosis (39.29%), autoimmune hepatitis (7.14%). One female patient had chronic hepatitis B. There was one case of Wilsons disease each in male and female. Both the cases of cryptogenic cirrhosis were males.

Table 2: Comparison of aetiology of chronic liver disease in males and females

Aetiology	Male		Female	
	n	%	n	%
Alcohol	87	77.68	11	39.29
NAFLD	17	15.18	13	46.43
Chronic Hepatitis B	5	4.46	1	3.57
Chronic Hepatitis C	0	0.00	0	0.00
Autoimmune Hepatitis	0	0.00	2	7.14
Wilson's Disease	1	0.89	1	3.57
Cryptogenic	2	1.79	0	0.00
TOTAL	112	100.00	28	100.00

Fig.3. shows that most of the patients belonged to CTP class C (50.71%) followed by CTP class B (40%) and then CTP class A (9.29%). Among males 50.89% belonged to Class C, 37.50% were in Class B and 11.61% were in Class A. Among females, 50 % belonged to Class B and 50 % belonged to Class C.

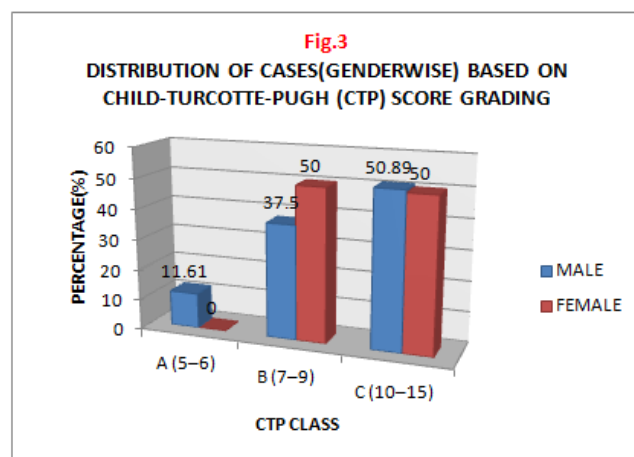


Table.3 .shows in CTP class A, the mean serum uric acid level was  $4.57 \pm 0.88$  mg/dL. In class B and class C, the mean serum uric acid level was  $6.42 \pm 1.78$

mg/dL and  $7.97 \pm 2.31$  mg/dL respectively (p value:  $<0.001$ ).

Table.3: Comparison of mean serum uric acid level between the CTP classes

CTP GRADE (Class)	NUMBER (n)	URIC ACID (mg/dl)		p value
		Mean $\pm$ S.D.	Range	
A (5-6)	13	$4.57 \pm 0.88$	3.03—5.80	$<0.001$
B (7-9)	56	$6.42 \pm 1.78$	2.60—12.50	
C (10-15)	71	$7.97 \pm 2.31$	2.20—16.21	

A vs B: Diff=1.8500, 95%CI=0.3791 to 3.3209, p=0.0095  
 A vs C: Diff=3.4000, 95%CI=1.9587 to 4.8413, p=0.0000  
 B vs C: Diff=1.5500, 95%CI=0.6961 to 2.4039, p=0.0001

Table.4. shows that the mean serum uric acid level in males of CTP class A is  $4.57 \pm 0.88$  mg/dL; in class B it is  $6.64 \pm 1.76$  mg/dL; in class C, it is  $8.17 \pm 2.47$  mg/dL.(p value: $<0.01$ ) The mean serum uric acid level in females of CTP class B is  $5.77 \pm 1.74$  mg/dL; in class C it is  $7.16 \pm 1.23$  mg/dL.(p value: 0.022).

Table.4: Comparison of mean serum uric acid level between CTP classes - gender wise

CTP CLASS	URIC ACID (mg/dL)			
	Number (n)	Male (Mean $\pm$ S.D.)	Number (n)	Female (Mean $\pm$ S.D.)
A (5-6)	13	$4.57 \pm 0.88$	0	—

B (7-9)	42	$6.64 \pm 1.76$	14	$5.77 \pm 1.74$
C (10-15)	57	$8.17 \pm 2.47$	14	$7.16 \pm 1.23$
p-value	0.000*		0.022	

A vs B: Diff=2.0700, 95%CI=0.4908 to 3.6492, p=0.0066  
 A vs C: Diff=3.6000, 95%CI=2.0707 to 5.1293, p=0.0000  
 B vs C: Diff=1.5300, 95%CI=0.5182 to 2.5418, p=0.0014

Table.5. shows that the mean serum uric acid level in alcohol related CLD was  $7.22 \pm 2.11$  mg/dL, in NAFLD related CLD  $7.05 \pm 2.82$  mg/dL, in Chronic hepatitis B  $5.95 \pm 1.43$  mg/dL, in autoimmune hepatitis  $5.28 \pm 1.31$  mg/dL, in Wilsons disease  $5.61 \pm 1.29$  mg/dL, in cryptogenic cirrhosis  $4.02 \pm 1.40$  mg/dL.

Table.5. Comparison of mean serum uric acid level in various aetiologies of chronic liver disease

Aetiologies Of Chronic Liver Disease Aetiology	Number (N)	Uric Acid (Mg/Dl) (Mean $\pm$ Sd)	P Value
Alcohol	98	$7.22 \pm 2.11$	0.1832
NAFLD	30	$7.05 \pm 2.82$	
Chronic Hepatitis B	6	$5.95 \pm 1.43$	—
Autoimmune Hepatitis	2	$5.28 \pm 1.31$	
Wilson's Disease	2	$5.61 \pm 1.29$	—
Cryptogenic	2	$4.02 \pm 1.40$	

Table.6. shows that in alcohol related CLD, the mean serum uric acid level in CTP Class A was  $4.59 \pm 0.71$ mg/dL; in class B  $6.65 \pm 1.80$  mg/dL; in class C was  $8.02 \pm 2.02$  mg/dL. (p value <0.01).

In NAFLD related CLD, the mean serum uric acid level in CTP class A was  $4.91 \pm 0.97$  mg/dL; in Class B was  $6.10 \pm 1.93$  mg/dL; in class C was  $8.87 \pm 3.14$  mg/dL(p value <0.007) .

Table 6: Comparison of mean serum uric acid level between CTP classes (aetiology wise)

Aetiolo gy	CTP Grade (Class)									p value
	A (5-6)			B (7-9)			C (10-15)			
	n	Mea n	±S. D.	n	Mea n	±S. D.	n	Mea n	±S. D.	
Alcohol	8	4.59	0.71	3 7	6.65	1.80	5 3	8.02	2.02	0.000 0
NAFL D	4	4.91	0.97	1 4	6.10	1.93	1 2	8.87	3.14	0.007 1

Alcohol:  
 A vs B: Diff=2.0600, 95%CI=0.3236 to 3.7964, p=0.0158  
 A vs C: Diff=3.4300, 95%CI=1.7408 to 5.1192, p=0.0000  
 B vs C: Diff=1.3700, 95%CI=0.4159 to 2.3241, p=0.0026  
 NAFLD:  
 A vs B: Diff=1.1900, 95%CI=-2.2287 to 4.6087, p=0.6677  
 A vs C: Diff=3.9600, 95%CI=0.4785 to 7.4415, p=0.0234  
 B vs C: Diff=2.7700, 95%CI=0.3978 to 5.1422, p=0.0196

**Discussion**

**Age distribution in the study group:** Our study showed that majority of the study subjects (29.29 %) were in the age group of 40-49 years followed by 23.57 % in the age group of 50-59 years followed by 22.86% in age group of 30 – 39 years. i.e., Most of the patients (52.86%) belonged to the 40-59-year-old age group. The least number of cases were in the age groups, 20-29 years and above 70 years of age. The mean age for whole study group was  $47.31 \pm 12.52$  years. Mean age for Male was  $47.06 \pm 11.82$  years and mean age for female was  $48.32 \pm 15.21$ years. The youngest cirrhotic was 21 years of age whereas the oldest one was 78 years.

In a large multicentric study by Mukherjee et al<sup>[18]</sup> the mean age of cirrhotic patients was found out to be  $47.7 \pm 13.4$  years. In the north eastern region, they found out that the mean age of patients with CLD was  $44.4 \pm 11.6$  years.

A study by Ahmed et al<sup>[19]</sup> found that the youngest cirrhotic was 25 years, the oldest being 72 years, with 61.25% in the age group 40-59 years.

The findings of our study were consistent with those of above studies which showed maximum prevalence of cirrhosis in the age group of 40-49 years with the mean age being in late 5th decade.

**Gender distribution in the study group:** In our study amongst 140 patients, majority of them were male constituting 80 % (n = 112). Females were 20 % (n = 28).

A study conducted by Mukherjee et al<sup>[18]</sup> showed that 78.6% of study population of liver cirrhotic patients were males and 21.4% were females.

In a study of 160 liver cirrhosis patients by Ahmed et al<sup>[19]</sup>, 15 % of the study subjects were females and 85% were males.

In a hospital based cross-sectional observational study of serum uric acid in chronic liver disease conducted by Paul et al<sup>[16]</sup>, 69.2% of CLD patients were males and 30.8% were females.

The findings of our study were comparable with that of the above-mentioned studies.

**Aetiology of liver cirrhosis in study group**

The present study showed that the most common cause of cirrhosis among the study subjects was alcohol comprising of 98 cases (70%). NAFLD emerged as the second most common cause in 30 cases (21.43%). Chronic Hepatitis B accounted for 6 cases (4.29%). Autoimmune Hepatitis in 2 patients (1.43%), Wilson’s

disease in 2 patients (1.43%), and Cryptogenic cirrhosis in 2 patients (1.43%) were the other causes.

In a study published in 2015 by Ahmed *et al*<sup>[19]</sup>, among 160 patients (136 males and 24 females) of cirrhosis, 110 cases (69%) were alcohol related, 18 each (11% each) were related to hepatitis B and hepatitis C, 2 (1%) autoimmune related, and 12 (8%) cryptogenic.

Mukherjee *et al*<sup>[18]</sup> showed that overall alcohol was the predominant cause of cirrhosis in 34.3% of study subjects followed by Chronic hepatitis B (18.1%) and Chronic hepatitis C (17.3%). NAFLD was the cause in 1.7%. Other causes contributed to 29%. The study also concluded that alcohol was commonest cause (31.6%) of CLD in North Eastern parts of India followed closely by HBV and HCV.

Alcohol emerged as the most common aetiology of CLD in our study. This was similar to the findings of the study by Ahmed *et al*<sup>[19]</sup> and Mukherjee *et al*<sup>[18]</sup>. However, NAFLD was the 2nd most common cause in our study. This finding was a deviation from the 2 above mentioned studies. This can be explained by the fact that there is an increasing burden of metabolic syndrome due to recent unhealthy life style practices. NAFLD is considered to be the hepatic manifestation of metabolic syndrome. Another reason for NAFLD superseding chronic hepatitis B could be the increasing awareness about Hepatitis B vaccination among the public and hence a decrease in HBV related cirrhosis.

A study by Paul *et al*<sup>[16]</sup> showed that alcohol was the commonest (36.5%) followed by NAFLD (28.9%) and chronic viral hepatitis (21.1%). Cryptogenic cirrhosis accounted for 7.7%, autoimmune hepatitis 3.8% and Wilson's disease 1.9%. Our findings were in concordance with the observations of this study.

In our study there was a difference in the aetiology of CLD among males and females. In males, the most

common cause of CLD was alcohol related (77.68%) followed by NAFLD related cirrhosis (15.18%). The 3rd most common cause of CLD in males was Chronic hepatitis B (4.46%). In females, NAFLD related cirrhosis was the leading cause (46.43%) followed by Alcohol related cirrhosis (39.29%). The 3rd most common cause of CLD in females was autoimmune hepatitis (7.14%). Both the cases of autoimmune hepatitis were females and both the cases of cryptogenic cirrhosis were males.

#### **Patient distribution according to CTP grade:**

Our study shows that most of the patients belonged to CTP class C (50.71%) followed by CTP class B (40%) and then by CTP class A (9.29%). Among males 50.89% belonged to Class C, 37.50% were in Class B and 11.61% were in Class A. Among females, 50 % belonged to Class B and 50 % belonged to Class C.

In a study by Paul *et al*<sup>[16]</sup> 30.77% of patients belonged to Class A; 55.77% to class B; and 13.46 % to Class C.

Almani *et al*<sup>[20]</sup> observed that 37% of study subjects had Child-Pugh's 'A' grade of prognosis, 37% had Child-Pugh's 'B' grade of prognosis and 26% had Child-Pugh's 'C' grade of prognosis.

Yan *et al*<sup>[21]</sup> had reported that 22.6 % of the patients had cirrhosis of Child-Pugh grade A, 41.5 % of grade B and 35.9% of grade C.

The findings of our study were comparable with that of the above 3 studies as majority of the patients belonged to Class B and Class C. This shows that most patients seek medical care only during the later stages of the cirrhosis as well as due to the difficulty in diagnosing CLD in its early stages.

### Comparison and correlation between serum uric acid level and Child-Turcotte-Pugh (CTP) score

In our study, in CTP class A, the mean serum uric acid level was  $4.57 \pm 0.88$  mg/dL. In class B and class C, the mean serum uric acid levels were higher:  $6.42 \pm 1.78$  mg/dL and  $7.97 \pm 2.31$  mg/dL respectively. We performed an analysis of variance (ANOVA) test and determined that there was a statistically significant difference between the mean serum uric acid levels of these three groups. (P-value  $<0.001$ ). On post hoc analysis, there was a statistically significant difference between individual classes as well. Pearson's correlation coefficient was used to assess the relation between serum uric acid level and CTP score and there was a positive correlation between the two variables (r-value: 0.3860 and p-value  $<0.001$ ).

A study by Paul et al<sup>[16]</sup> found that in CTP class A, the mean serum uric acid level was  $3.98 \pm 1.3$  mg/dL. In class B and class C, the mean serum uric acid level was  $5.74 \pm 2.35$  mg/dL and  $9.38 \pm 2.31$  mg/dL respectively. This was the only study that linked serum uric acid level with CTP classes and uric acid levels were significantly higher in class B and C as compared to class A (p-value  $< 0.0001$ ). Serum uric acid levels also showed positive correlation with CTP score (r value: 0.44; p-value- 0.02). The findings of our study were in concordance with the above-mentioned study.

A study by Afzali et al<sup>[22]</sup> concluded that serum uric acid levels were associated with the development of cirrhosis and presence of elevated liver enzymes. Also, persons with higher serum uric acid had a greater risk of cirrhosis related hospitalization or death. Compared to persons in the lower third of the distribution of serum uric acid ( $<4.8$  mg/dL), those in the top third ( $>6$  mg/dL) had a higher risk of cirrhosis related

hospitalization or death (adjusted hazard ratio = 2.8, 95% confidence interval (CI) 51.3-5.7).

In a comparative study of ALT, AST, GGT and Uric acid levels in Liver diseases by Benerji et al<sup>[23]</sup>, serum uric acid levels were found to be significantly elevated in patients of liver cirrhosis ( $10.6 \pm 2$ mg/dl) when compared to matched controls ( $5.0 \pm 2$  mg/dL). (P-value  $<0.01$ )

A study by Bhandari et al<sup>[24]</sup> concluded that oxidative stress was associated with the development and progression of cirrhosis. There was worsening of oxidative stress with increasing grades of CTP score. Cirrhotic patients showed a significant increase in the levels of pro-oxidant marker malondialdehyde and a significant decrease in levels of antioxidant markers like Superoxide dismutase and Catalase in erythrocytes and Glutathione in the blood when compared to healthy controls. On grading the patients based on Child Pugh score, the patients in class C had lower levels of antioxidant markers.

### Comparison of mean serum uric acid level between CTP classes - gender wise

From our study, we found out that the mean serum uric acid level in males of CTP class A was  $4.57 \pm 0.88$  mg/dL; in class B it was  $6.64 \pm 1.76$  mg/dL; in class C, it was  $8.17 \pm 2.47$  mg/dL. (p-value:  $<0.01$ ). The mean serum uric acid level in females of CTP class B is  $5.77 \pm 1.74$  mg/dL; in class C it is  $7.16 \pm 1.23$  mg/dL. (p-value:0.022). The results were statistically significant. Post hoc analysis also showed statistically significant difference in the mean serum uric acid levels between two individual classes among males. From the above, we can infer that even though there was not a significant difference between the mean serum uric acid level of males and females, the levels between the various CTP classes in both the genders showed a

significant difference. There was progressive increase in mean serum uric acid level from CTP class A to Class C irrespective of the gender.

#### **Comparison of mean serum uric acid level in various aetiologies of CLD**

In our study the mean serum uric acid level in alcohol related CLD was  $7.22 \pm 2.11$  mg/dL, in NAFLD related CLD  $7.05 \pm 2.82$  mg/dL, in chronic hepatitis B  $5.95 \pm 1.43$  mg/dL, in autoimmune hepatitis  $5.28 \pm 1.31$  mg/dL, in Wilsons disease  $5.61 \pm 1.29$  mg/dL, in cryptogenic cirrhosis  $4.02 \pm 1.40$  mg/dL. The findings were not statistically significant. (p-value: 0.1832)

In a study by Paul *et al*<sup>[16]</sup>, the mean serum uric acid level in alcoholic CLD was  $4.62 \pm 1.7$  mg/dL, in NAFLD related CLD  $5.87 \pm 1.74$  mg/dL, in chronic viral hepatitis  $8.51 \pm 2.7$  mg/dL, in autoimmune hepatitis  $8.8 \pm 0.56$  mg/dL, in Wilsons disease  $5.6$  mg/dL, in cryptogenic cirrhosis  $3.85 \pm 0.98$  mg/dL. In this study viral induced hepatitis had significantly higher uric acid levels than alcoholic CLD (p-value <0.0001) but a statistical comparison between other aetiologies could not be done because of small sample size. The differences between the result of this study and ours may have been due to difference in sample size and selection criteria.

A study by Afzali *et al*<sup>[22]</sup> showed little association between serum uric acid level and presence of viral hepatitis B or C.

#### **Comparison of mean serum uric level in various CTP classes – aetiology wise**

Our study showed that in Alcohol related CLD, the mean serum uric acid level in CTP class A was  $4.59 \pm 0.71$  mg/dL; in class B,  $6.65 \pm 1.80$  mg/dL and in class C was  $8.02 \pm 2.02$  mg/dL. This was statistically significant. (p-value < 0.01).

In NAFLD related CLD, the mean serum uric acid level in CTP class A was  $4.91 \pm 0.97$  mg/dL; in Class B was  $6.10 \pm 1.93$  mg/dL; in class C was  $8.87 \pm 3.14$ mg/dL. This was also found out to be statistically significant. (p-value-0.0071). The number of cases in other aetiologies were too small for statistical analysis and comparison.

Thus, there was a statistically significant increase of mean serum uric acid level from CTP class A to class C, irrespective of whether the aetiology of cirrhosis was alcohol or NAFLD. This despite the fact that the mean serum uric acid level in both these aetiologies were similar.

#### **Conclusion**

Our novel study established that there was a statistically significant positive correlation between serum uric acid levels and CTP score. We found higher uric acid levels in patients with higher CTP grades which raises an important possibility as to whether uric acid plays a causative or even a promotive role in hepatocyte inflammation and necrosis or whether it is just a marker of severity of cirrhosis. To delineate this conundrum we need large prospective cohort studies.

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