



# Study of Association of Uric Acid, LFT and Abdominal USG Parameters in CLD Patients to Assess the Severity of Liver Disease

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## ABSTRACT

### BACKGROUND:

Chronic liver disease (CLD) is a progressive deterioration of liver functions for more than six months, which includes synthesis of clotting factors, other proteins, detoxification of harmful products of metabolism, and excretion of bile. CLD is a continuous process of inflammation, destruction, and regeneration of liver parenchyma, which leads to fibrosis and cirrhosis. For predicting prognosis of end-stage liver disease and severity, various prognostic models are recommended. Child Pugh (CP) score is one such universally accepted prognostic score. High uric acid (UA) levels are independently associated with severe disease and poor prognosis in patients with CLD accompanied by progressive liver damage leading to loss of function eventually. Several studies have established that UA levels have been found to correlate directly with the level of tissue damage. In view of this, the present study was undertaken to evaluate the correlation between serum uric acid and CTP score in patients with CLD.

**AIMS AND OBJECTIVES:** To determine the level of serum uric acid, CTP score and the relationship between serum uric acid levels and the Child-Turcotte-Pugh (CTP) score in assessing severity of the disease in individuals with chronic liver disease.

**MATERIALS AND METHODS:** This study was conducted to correlate serum uric acid levels with child Pugh score in chronic liver disease patients to assess the severity of the disease which included 100 patients. Subjects fulfilling inclusion criteria selected for the study. Each subject admitted as inpatient/outpatient to the study will be evaluated with detail medical history, physical examination, systemic examinations, relevant investigations and Abdominal ultrasound done to look for signs of cirrhosis of the liver and evidence of ascites, then patients are categorized into A, B, C according to CTP score.

**RESULTS:** The mean age of study participants was found to be  $49.55 \pm 12.549$  years. 57% of the study participants belongs to age group of 41-60

years. 79% of the study participants were males and 21% of the study participants were females. The etiology for liver disease was found to be alcohol in 76% of the study participants. 70% of the study participants belong to B and C category of Child Pugh score. 72% of the subjects were having cirrhosis with ascites. 81% of the subjects are having serum uric acid levels  $>6$  in our study. The association was found to be statistically significant between severity of CLD and serum uric acid levels and also found to be statistically significant between child-Pugh score of CLD and serum uric acid levels.

**CONCLUSION:** In the present study, the mean serum uric acid levels were found to be increasing with increase in the child-Pugh score of CLD and it was seen highest in class C and this association was found to be statistically significant between child-Pugh score of CLD and serum uric acid levels. Serum uric acid level is proinflammatory marker which increases with severity of liver disease. Serum uric acid is simple, easily available, cost-effective blood test and routinely done, hence can be considered as a novel marker for inflammation and assess severity and prognosis in patients with chronic liver disease.

## I. INTRODUCTION :

Liver diseases affect millions of people worldwide. The Global Burden of Disease (GBD) reported that over 1 million people died due to cirrhosis in 2010. Chronic liver diseases (CLD) cause significant morbidity and mortality worldwide. Chronic liver disease (CLD) is a disorder in which progressive destruction and regeneration of liver parenchyma leads to fibrosis and further cirrhosis. Cirrhosis is currently the 11th leading cause of mortality worldwide. It is manifested with common symptoms of jaundice, fatigue, nausea, poor appetite, abdominal distension and intestinal bleeding. Several etiological factors can lead to development of CLD. These include alcoholism, portal hypertension, Autoimmune, Hepatitis B, C and others. A range of different radiological and blood investigations



are helpful in detection and diagnosis of various hepatobiliary abnormalities. These investigations also help in identifying the basis of clinically suspected disease of liver and to figure out the severity of liver disease.<sup>3</sup>For predicting prognosis of end-stage liver disease and severity, various prognostic models are recommended. Child Pugh (CP) score is one such universally accepted prognostic score. Based on the CP score, CLD patients can be categorised according to the severity of disease. CP score is calculated by the five factors including ascites, encephalopathy, serum bilirubin, albumin and prothrombin time. The score can range from the 5 to 15 points and is classified into three classes Class A, B and C, Class A (5-6 points), Class B (7-9 points) and Class C (10 or above points) correspond to the severity of disease.<sup>4</sup>Uric acid is the final oxidation product of purine metabolism in humans and higher primates and it is excreted in urine.<sup>5</sup> It is generated by the activation of enzyme xanthine oxidase (XO) which catalyses the last two steps of uric acid conversion i.e. hypoxanthine to xanthine and from xanthine to uric acid.<sup>6</sup> It is primarily produced in conditions where there is cellular destruction and thus, degradation of the nuclear material. Uric acid is not only a byproduct of cell death, but recent research has discovered that it is a mediator of inflammation and tissue damage.<sup>7</sup>In tissues, it may be a major activator of inflammasomes and thus, it promotes damage to surrounding tissue.<sup>8</sup>The prevalence of hyperuricemia has progressively increased and has gained recognition as a reliable marker of inflammation as well as cardio vascular risk.<sup>8-10</sup> Studies have shown that uric acid estimation can be a reliable and cost-effective marker for evaluation of severity of liver cirrhosis in Chronic liver disease. Its significance in CLD has not been explored much. The present study was planned to study the association of uric acid with CP scores in patients with CLD.

## II. MATERIALS AND METHODS:

**SOURCE OF DATA-** Patients with newly diagnosed and known case of chronic liver disease who attended the outpatient department and IPD of general medicine department of Raja Rajeswari Medical College and Hospital, Bengaluru .

This present Cross-sectional study, Observational study includes 100 patients after considering inclusion criteria of Age  $\geq$  18 years old, Individuals who are attending medicine OPD /IPD with symptoms suggestive of CLD and Patients willing to give informed consent and Exclusion criteria of Patient on drugs which cause alterations in uric acid levels such as Allopurinol, Febuxostat, Thiazides, Furosemide etc, Patients with known infections, recent surgery, trauma, chronic kidney disease, hepatorenal syndrome, Patients with known malignancies on chemotherapy, Pregnancy.

### SAMPLING METHOD-

- Purposive sampling
- Hospital based study
- Sample size- 100, was determined for the present study using the formula

$$n = \frac{N \cdot e}{1 + e}$$

Where N = Population Size.

e = Margin of error.

(For 95% confidence level, Margin error = 0.05)

### Method of Collection of Data:

After ethical committee approval and obtaining written informed consent from the patients, the study undertaken.

### Study Protocol:

Subjects fulfilling inclusion criteria selected for the study. Each subject admitted as inpatient/outpatient to the study will be evaluated with detail medical history, physical examination, systemic examinations, relevant investigations and Abdominal ultrasound done to look for signs of cirrhosis of the liver and evidence of ascites, then patients are categorized into A, B, C according to CTP score.



TABLE: CHILD PUGH SCORE

Clinical and Lab Criteria	Points*		
	1	2	3
Encephalopathy	None	Mild to moderate (grade 1 or 2)	Severe (grade 3 or 4)
Ascites	None	Mild to moderate (diuretic responsive)	Severe (diuretic refractory)
Bilirubin (mg/dL)	< 2	2-3	>3
Albumin (g/dL)	> 3.5	2.8-3.5	<2.8
Prothrombin time			
Seconds prolonged	<4	4-6	>6
International normalized ratio	<1.7	1.7-2.3	>2.3
<b>Child-Turcotte-Pugh Class obtained by adding score for each parameter (total points)</b>			
Class A = 5 to 6 points (least severe liver disease)			
Class B = 7 to 9 points (moderately severe liver disease)			
Class C = 10 to 15 points (most severe liver disease)			

Investigations including RBS,CBC,Liver function tests, Renal function Tests (Blood urea, Sr. creatinine, Uric acid), PT, APTT, INR, Ultrasound Abdomen and pelvis (done with SAMSUNG RS 80, Multifrequency 3.5 to 5 MHZ ), Special investigations whenever indicated.

**Statistical Analysis Method:** Data analysed by using descriptive statistics. A suitable statistics test conducted.

### III. RESULTS:

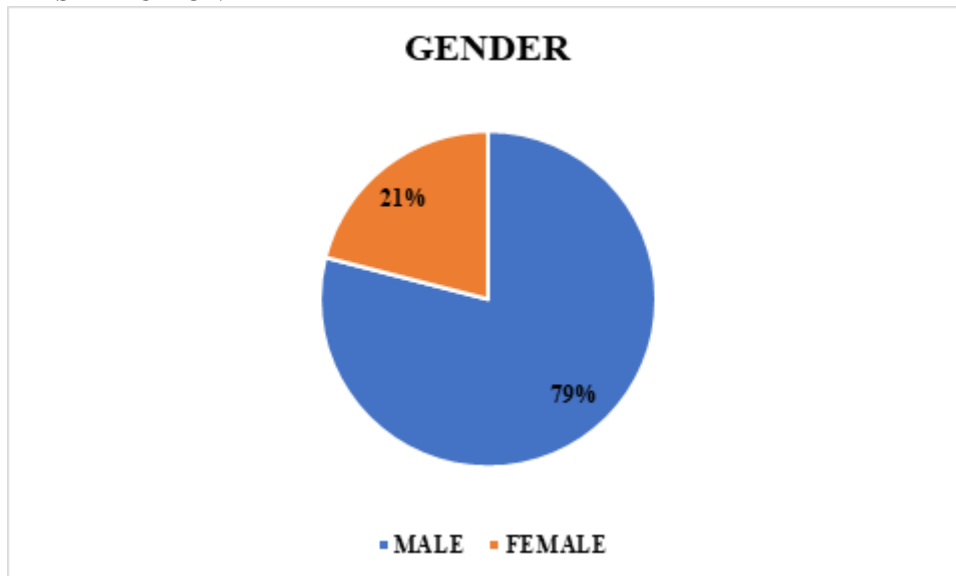
#### 1.DISTRIBUTION OF SUBJECTS ACCORDING TO THEIR AGE GROUPS

AGE	No. Of subjects	Percent
21-30 years	7	7.0
31-40 years	18	18.0
41-50 years	29	29.0
51-60 years	28	28.0
61-70 years	14	14.0
71-80 years	4	4.0
MEAN±SD 49.55±12.549	100	

The mean age of study participants was found to be 49.55±12.549 years.57% of the study participants belongs to age group of 41-60 years.

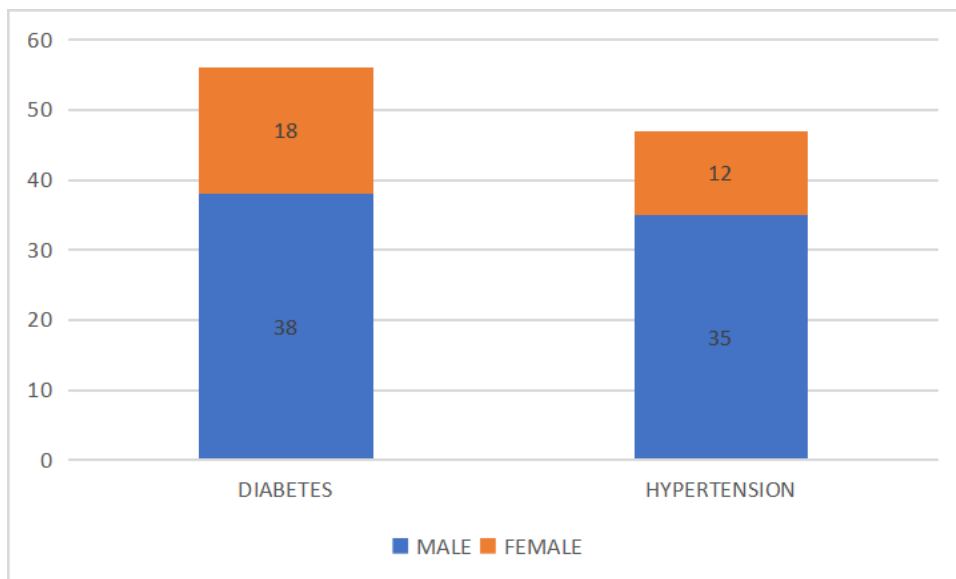


## 2.GENDER DISTRIBUTION



79% of the study participants were males and 21% of the study participants were females.

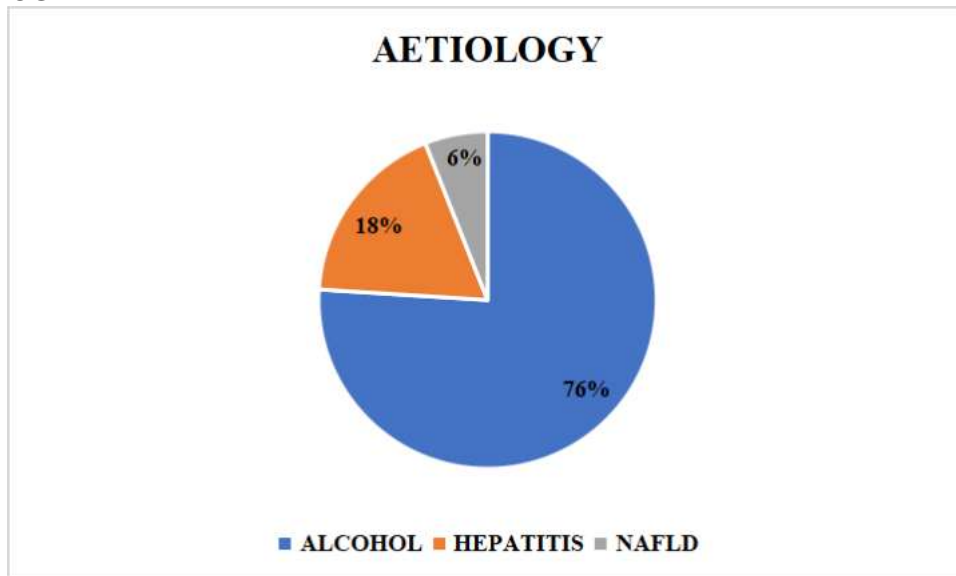
## 3.ASSOCIATION OF COMORBIDITIES AND GENDER:



56% of the study subjects are diabetics and 47% of the study subjects are hypertensives. Both are significant risk factors for METABOLIC SYNDROME and NAFLD

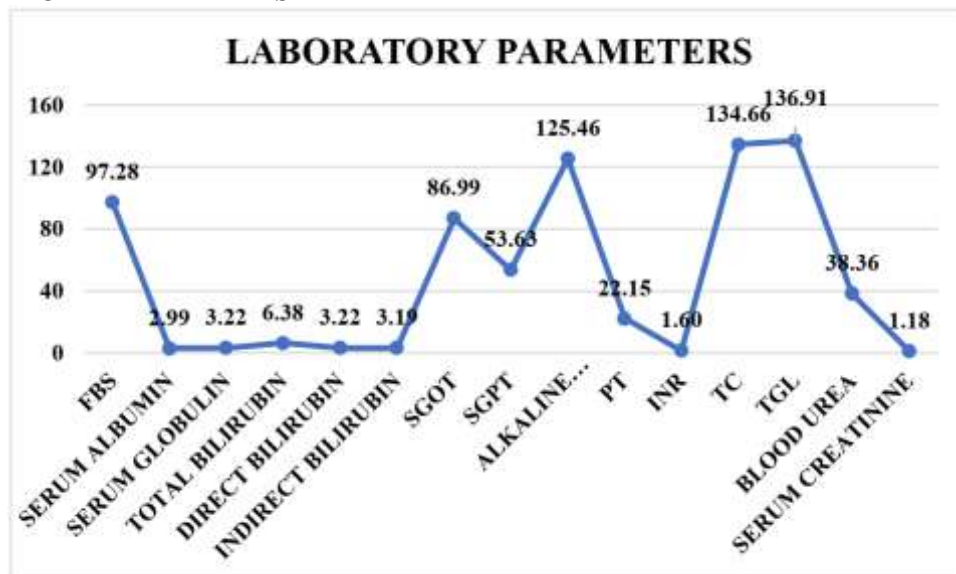


#### 4.AETIOLOGY



The etiology for liver disease was found to be alcohol in 76% of the study participants, hepatitis in 18%, NAFLD in 6%.

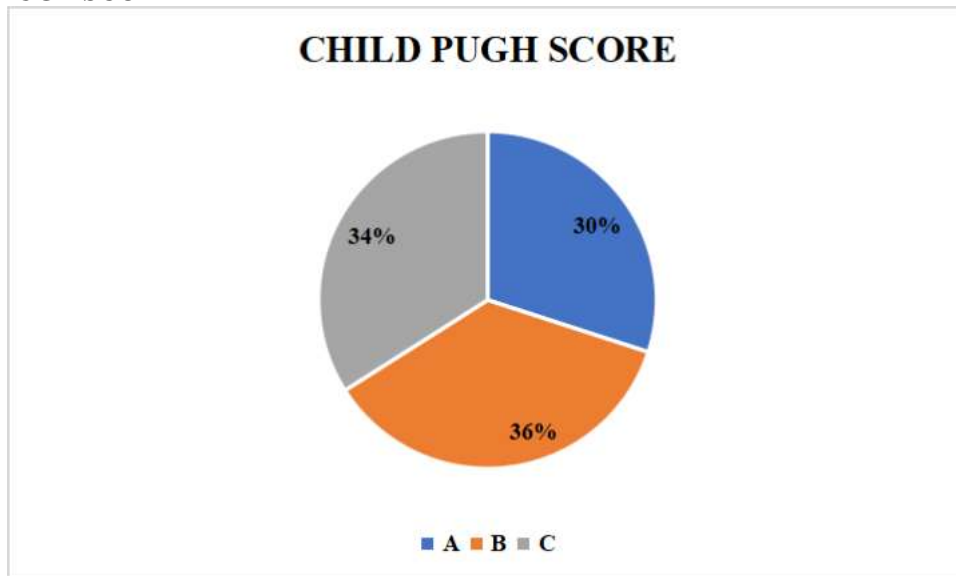
#### 5.LABORATORY PARAMETERS



Mean values of SGOT,SGPT,TB and PT are raised and mean values of serum albumin are decreased, these parameters suggestive of CLD.



### 6.CHILD PUGH SCORE



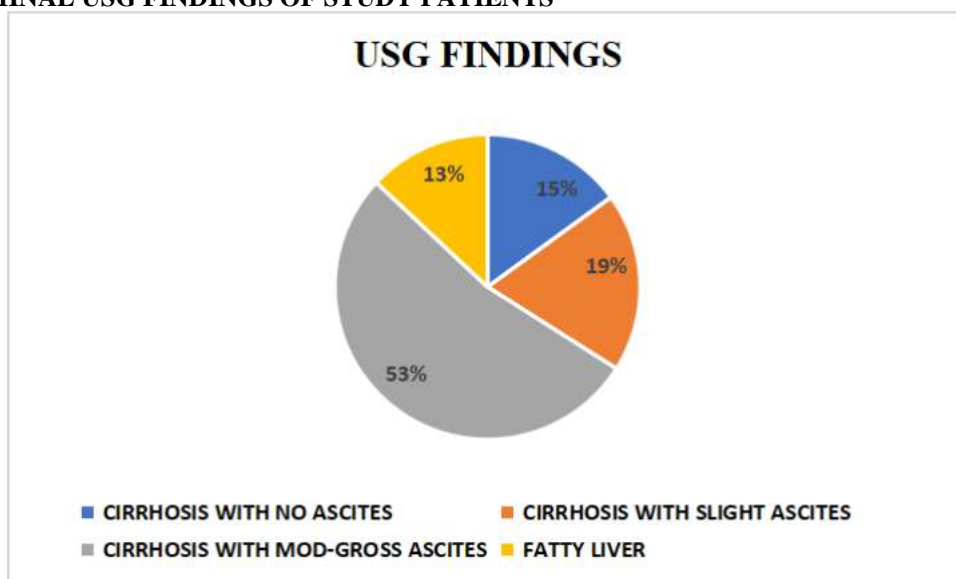
70% of the study participants belong to B and C category of Child Pugh score

### 7.SERUM URIC ACID LEVELS

SERUM URIC ACID LEVELS	No. Of Subjects	PERCENT
<6	19	19.0%
6-8	34	34.0%
8-10	37	37.0%
>10	10	10.0%

81% of the subjects are having serum uric acid levels >6 in our study.

### 8.ABDOMINAL USG FINDINGS OF STUDY PATIENTS





53% of the study participants were found to have cirrhosis with moderate-gross ascites on USG. 19% of the study participants were found to

have cirrhosis with mild ascites on USG.72% of the subjects were having cirrhosis with ascites.

9.ASSOCIATION OF SERUM URIC ACID WITH USG FINDINGS

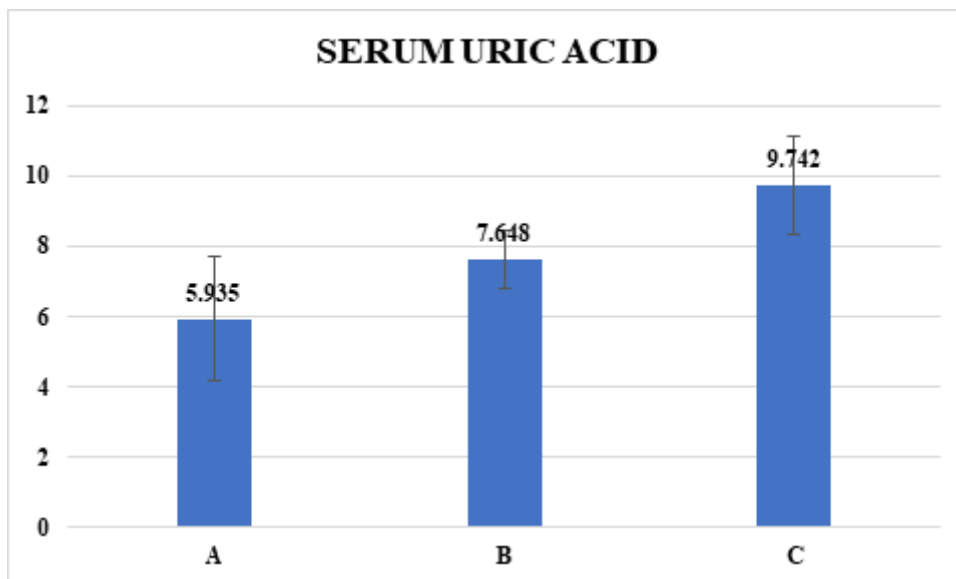
USG FINDINGS	SERUM URIC ACID		P VALUE
	MEAN	SD	
FATTY LIVER	8.757	1.6688	
CIRRHOSIS WITH NO ASCITES	5.235	1.5624	<0.001
CIRRHOSIS WITH SLIGHT ASCITES	7.252	1.6892	
CIRRHOSIS WITH MOD-GROSS ASCITES	8.000	1.3923	

The mean serum uric acid levels were found to be higher fatty liver and with increase in the grading of ascites based on USG. The

association was found to be statistically significant between severity of CLD and serum uric acid levels.

10.ASSOCIATION OF SERUM URIC ACID WITH CHILD PUGH SCORE

CHILD PUGH SCORE	SERUM URIC ACID		P value
	Mean	S. D	
A	5.935	1.7815	<0.001
B	7.648	0.8247	
C	9.742	1.3793	



The mean serum uric acid levels were found to be increasing with increase in the child-Pugh score of CLD. The association was found to

be statistically significant between child-Pugh score of CLD and serum uric acid levels.



#### IV. DISCUSSION

In this study, the mean age of study participants was found to be  $49.55 \pm 12.549$  years. 29% of the study participants belonged to the age group of 41-50 years followed by 28% in 51-60 years. 79% of the study participants were males and 21% were females. Similar to our study, 48% of the study participants were between the ages of 41 and 60, and 79% of them were men in the Yadav et al study. These results were comparable to those of Gupta et al.'s study<sup>88</sup> too. Noklang, et al. observed a male predominance (84%) too and the most of their patients were aged between 41 and 50 years (42%) like our study.

Our study found 86% of the study participants having a personal history of alcohol usage and 31% them as smokers. 53% of the study participants were found to have cirrhosis with moderate-gross ascites on USG. 19% of the study participants were found to have cirrhosis with mild ascites on USG.

In the present study, 36% of the study participants were categorized as Child-pugh score B, 34% of them were categorized as Child-pugh score C and 30% of the study participants were categorized as Child-pugh score A. In the Yadav et al.<sup>83</sup> research, about 50% of the study subjects were classified as CTP Class C, but the majority of study subjects in the Gupta et al. and Paul et al. research belonged to CTP Class B categorization which was in concordance with our study.

Also, a study done by Anand P<sup>11</sup> showed when RI and Child-Pugh Score were compared, the mean Child-Pugh Score was 6.43 for patients with  $RI < 0.7$  and 13.1 for patients with  $RI > 0.7$ , and the author concluded a very strong link indicated by a correlation coefficient of 0.873 which was statistically significant.

Only 8–20% of chronic heavy drinkers go on to develop cirrhosis, and between 10–35% get alcoholic hepatitis; most, however, end up with fatty liver. Alcoholic hepatitis is a syndrome that can range widely in severity and have different presenting symptoms. The most severe clinical picture could be liver failure, encephalopathy, prolonged prothrombin time, and severe jaundice. NAFLD is among the most prevalent liver conditions that physicians treat. In the general population, its prevalence varies from 3% to 24%, and it increases with age and post menopause<sup>80</sup>.

The aetiology for liver disease in our study was found to be alcohol in 76% of the study participants, hepatitis in 18%, NAFLD in 6%. 72% of the study participants were found to have decompensated liver disease in our study. In the study population of Anand P, alcohol consumption

(52%) was the most common cause of cirrhosis, followed by hepatitis B (26%).

According to studies, Serum uric acid levels have been found to significantly rise as the disease progresses. They have also been proposed as a substitute marker to assess the severity of chronic liver disease, and early identification of hyperuricemia may aid in the management of the inflammatory disorders-related liver tissue damage. Additionally, there was a higher CTP score and serum uric acid, which is thought to be an oxidative marker for liver injury.

The mean serum uric acid levels in our study were  $7.835 \pm 2.02$ mg/dL. Similar to our study, in the Yadav et al study, uric acid levels were raised in around 57% of the individuals, with mean values of  $7.1 \pm 2.7$ mg/dL. In contrast, Gupta et al. found that the mean uric acid (mg/dL) among the study subjects was  $6.69 \pm 2.92$ , with 76% of the subjects reporting higher uric acid levels.

In our study, the mean serum uric acid levels were found to be higher in relation with fatty liver and cirrhosis with increase in the grading of ascites based on USG and this association was found to be statistically significant between severity of CLD and serum uric acid levels.

In the present study, the mean serum uric acid levels were found to be increasing with increase in the child-pugh score of CLD and it was seen highest in class C and this association was found to be statistically significant between child-pugh score of CLD and serum uric acid levels. We compared our findings with several studies as described below.

Similarly, according to the Yadav et al.<sup>13</sup> study, uric acid levels rose as disease severity increased, and the mean uric acid level in CTP Class C was significantly higher than in Class A and B. Our results were consistent with those of Gupta et al.<sup>88</sup>, who also observed that the mean uric acid level in CTP Class C was higher than in Class A and Class B. In agreement with Manomenane et al., Prakash et al. also observed a substantial, positive correlation between the CTP score and the level of uric acid. Maximum serum uric acid levels were found in CTP class C in the Noklang et al<sup>21</sup> investigation, and they were correlated with the development of CLD. The serum UA level rised with increasing CTP class in their study. Serum uric acid levels rose in CLD patients with a high CTP class, as shown by Paul et al.

#### V. CONCLUSION

In the present study, the mean serum uric acid levels were found to be increasing with increase in the child-pugh score of CLD and it was





seen highest in class C and this association was found to be statistically significant between child-pugh score of CLD and serum uric acid levels.

Serum uric acid level is proinflammatory marker which increases with severity of liver disease.

Serum uric acid is simple, easily available, cost effective blood test and routinely done, hence can be considered as a novel marker for inflammation and assess severity and prognosis in patients with chronic liver disease.

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