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# Association of serum uric acid levels with chronic liver diseases: A cross sectional observational study

[1]Manisha Khande, Assistant Professor Department of Medicine, Pt. JNM Medical College, Raipur, Chhattisgarh.
[2]Uttam Kumar Singh, PG Resident, Department of Medicine, Pt. JNM Medical College, Raipur, Chhattisgarh.
[3]D.P. Lakra, Professor Department of Medicine, Pt. JNM Medical College, Raipur, Chhattisgarh, India.
[4]R.K. Patel, Associate Professor Department of Medicine, Pt. JNM Medical College, Raipur, Chhattisgarh.
[5]C.S. Sharma, Assistant Professor Department of Medicine, Pt. JNM Medical College, Raipur, Chhattisgarh.

**Corresponding Author:** Uttam Kumar Singh, PG Resident, Department of Medicine, Pt. JNM Medical College, Raipur, Chhattisgarh.

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## Abstract

**Background**: Clinically CLD is a disease process of the liver that involves progressive destruction and regeneration of hepatic parenchyma leading to fibrosis and cirrhosis. Liver cirrhosis is a one of major cause of mortality worldwide. The study aims to assess the association of serum uric acid level with severity of chronic liver disease

**Methods**: The study was conducted as a cross sectional study on patients with chronic liver disease presenting at our institute during the study period of one year. The Child -Turcotte-Pugh (CTP) score was used to assess the severity of liver disease. Uric acid levels were then compared with individual CTP scores and various parameters of CTP score.

**Results:** The commonest cause of chronic liver disease among them was alcoholic liver disease [73.3%] followed by Hepatitis B [18.7%] and Hepatitis C [8.0%]. Study showed that the mean (SD) Uric Acid value was 4.42 (1.42) mg/dl in Class A, 5.92 (1.51) mg/dl in Class B and 8.26 (1.73) mg/dl in Class C. The mean uric acid level increased significantly from Class A to Class C as error bar of mean (± Standard Error) of each group did not confined to the margin of each other.

**Conclusion:** The serum uric acid levels increases with increasing severity of Chronic Liver Disease as assessed by Child Pugh Scoring. Maximum mean Uric acid levels were present in CTP Class C patients (8.26) and maximum mean uric acid levels (6.97mg/dl) were noted in Alcoholic Liver Disease. Various parameters like serum Total Bilirubin, INR, and Albumin were significantly associated with serum uric acid Levels in Chronic Liver Disease patients.

Serum uric acid level is an important part of spectrum of Chronic Liver Disease.

**Keywords:** CLD, AST, INR, ALD, URIC ACID

## Introduction

Clinically CLD is a disease process of the liver that involves progressive destruction and regeneration of

hepatic parenchyma leading to fibrosis and cirrhosis. Liver cirrhosis is a one of major cause of mortality worldwide. Liver diseases have high prevalence all over world (prevalence= 4%-18%) as well as in India. Uric acid is the end product of purine metabolism, it is produced in conditions where there is cellular destructions and thus degradation of nuclear materials[1].

Uric acid is not only a byproduct of cell death, but recent research projects have discovered that it's a mediator of inflammation and tissue damage. Uric acid in tissue may be major activator of inflammation and thus it promotes damage to surrounding tissues. In chronic liver diseases, there is progressive damage to liver parenchyma and subsequent loss of functions. Here in CLD of different etiologies uric acid levels are found to be high[2].

In cases of NAFLD, high level of uric acid is considered as independent etiological risk factor. Also, a high uric acid level is known effect of alcohol metabolism and thus hyperuricemia may be found in alcoholic liver diseases. In different biological studies, UA levels have found to be correlate directly with level of tissue damage. Compared to serum level tissue levels UA may be even better predictor of tissue damage. Thus UA may be considered as a marker of tissue damage[3].

Addition to this, hyperuricemia involved in progressive development of hepatitis C virus related disease and liver diseases due to excessive consumption of alcohol. This strongly suggests that increased UA level strongly reflects and even causes an increased oxidative stress and inflammation in systemic circulation. This becomes one of main risk factor for future development of cirrhosis of liver or hepatic inflammation due to necrosis both in alcoholic and non-alcoholic[4].

Recent cross sectional studies showed that increased serum UA levels are reasonably increased in NAFLD and also the prevalence rate of NAFLD increases as the serum UA level increases[5]. These results concluded that elevated serum level of UA may be associated with development of NAFLD. However whether this association of serum uric acid and liver diseases is casual, a by stander, or a consequence of NAFLD still remains under debate[6].

The Child Pugh score is used to assess the prognosis of chronic liver disease mainly cirrhosis. E.G. Child Pugh class A has one year survival 100% and two year survival around 85%. Child Pugh score is now used to determine the prognosis, as well as the required strength of treatment and the necessity of liver transplantation. Five components of CP score are; Total bilirubin, Serum albumin, Prothrombin time, Ascites, Hepatic encephalopathy[7].

Based on these parameters scoring is done and patient is labelled as CP grade A, B, or C. Class A represents least severe chronic liver disease with one to five year survival rate of 95% whereas Class C is most severe liver disease with one to five year survival rate of only 50%. In higher animals and humans the serum uric acid is an end product of purine metabolism, excreted mainly through kidneys. Increased serum uric acid levels was thought to be the main reason for arthritis due to crystal deposition in joints, renal stones and other vascular events[3].

More recently, increased levels of serum uric acid levels also involved in the future development of hypertension, cardiovascular disease, kidney disease and metabolic syndrome[8].

**Methods**

The present study was conducted as an observational cross-sectional study on patients with CLD presenting

at Department of Medicine, Pt. J.N.M. Medical College and Dr. Bhim Rao Ambedkar Memorial Hospital Raipur during the study period of 1 year i.e. from January 1 to December 31. A detailed history was taken from each patient regarding their present complaints, associated symptoms, alcohol intake, smoking, diabetes mellitus, hypertension, hypothyroidism, and drug intake. On admission routine blood investigations like blood glucose, viral markers, CBC, LFT, RFT, prothrombin time and serum uric acid levels and ultrasonography were done. Modified CTP score were calculated for each patients. Haematological and biochemical tests will be performed by the following methods:

a. Haemoglobin, Total Leucocyte Count and Platelet Count by Medonic CA 620/530

b. Serum bilirubin level is calculated by calorimetric assay by Roche/Hitachi 911 analyser: ACN 269.

c. Serum albumin level will be measured by Bromocresol green method.

d. SGOT /SGPT will be measured according to IFCC or with pyridoxal activation by Roche / Hitachi 904 analyser: ACN 111 and 912 analyser: ACN 098.

e. Prothrombin Time by using lyophilized calcified thromboplastin reagent.

Table 1

| 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 |
| INR | <1.7 | 1.7-2.3 | >2.3 |
| Ascites | None | Mild (or suppressed with medication) | Moderate to Severe (or refractory) |
| Hepatic encephalopathy | None | Grade I-II | Grade III-IV |

**Data Analysis:** All collected data were compiled in MS Excel 2013 and checked for consistency and completeness and analysed using SPSS version 16.

Descriptive statistics followed by inferential statistics using non parametric tests like Kruskal-Wallis test and Jonckheere-Terpstra test were conducted as data were not normally distributed (Shaipro wilk test P value 0.001). Spearman's Rho was calculated for identification of correlation between covariates. P value <0.05 was taken as statistically significant.

Table 2

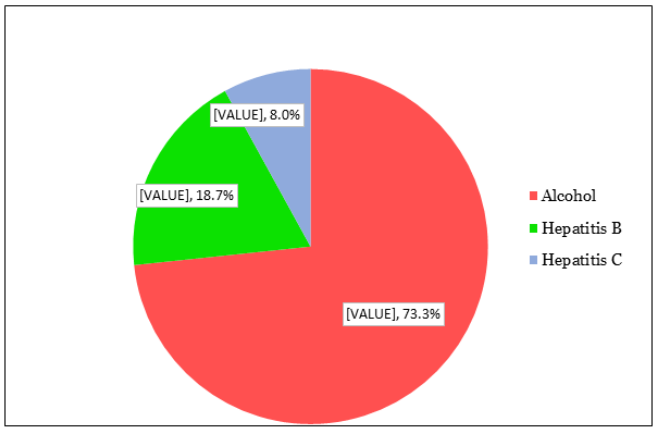
| Points | Class | One Year survival | Two year survival |
|---|---|---|---|
| 5-6 | A | 100% | 85% |
| 7-9 | B | 81% | 57% |
| 10-15 | C | 45% | 35% |

**Results**

Table 3: Distribution of Study Participants According To the Etiology of Liver Disease [N=75]

| Etiology | Number | Percentage |
|---|---|---|
| Alcohol | 55 | 73.3 |
| Hepatitis B | 14 | 18.7 |
| Hepatitis C | 6 | 8.0 |
| Total | 75 | 100.0 |

Graph1: Distribution of patients based on etiology of liver disease




This pie-chart showed that commonest cause of chronic liver disease among them was alcoholic liver disease

[73.3%] followed by Hepatitis B [18.7%] or Hepatitis C [8.0%].

Table 4: Distribution of the Patients According To Uric Acid Levels [N= 75]

| Uric acid level | Number | Percentage | Descriptive statistics |
|---|---|---|---|
| Normal<br>Male [3.4 -7.0 mg/dl]<br>Female [2.4-6.0 mg/dl] | 37 | 49.3 | **Uric acid [mg/dl]**<br>Mean (SD)= 6.7 (2.16)<br>Median (IQR)= 6.9 (4.5, 8.3)<br>Range= 2.4, 11.0 |
| Elevated<br>Male [ > 7 mg/dl]<br>Female [ > 6 mg/dl] | 38 | 50.7 | |
| Total | 75 | 100.0 | |

Table 5: Distribution of The Patients According To Child Pugh (CTP) Score [N= 75]

| CTP Class (score range) | Number | Percentage | Descriptive statistics |
|---|---|---|---|
| Class A (5- 6) | 13 | 17.3 | **CTP Score**<br>Mean (SD): 9.3 (2.5)<br>Median (IQR): 9 (7, 11)<br>Range: 5, 15 |
| Class B (7- 9) | 29 | 38.7 | |
| Class C (10- 15) | 33 | 44.0 | |
| Total | 75 | 100.0 | |

The above table showed that some (17.3%) participants were in Class A whereas mostly participants were in Class B (38.7%) and Class C (44.0%). The mean (SD) CTP score was 9.3 (2.5) ranging from 5 to 15.

**Discussion**

This study was conducted on admitted patients at medicine ward. A detailed history, complete examination, biochemical investigations, haematological study, radioimaging in 75 patients with chronic liver disease was done. Also Serum Uric acid levels were studied in relation to chronic liver disease and various haematological and biochemical parameters of chronic liver disease. 75 patients of chronic liver disease were enrolled in this study with mean age of presentation 49.1 (ranging from 28-70 years). 78.7% of patients (59 patients) were male and 21.3% of patients (16 patients) were female. The study showed that majority of patients were male, 59 (78.7%) and 16 patients (21.3%) were female. Talking about age distribution, most of the cases were in 50-59 years age group and minimum cases in 28-30 years age group. The study reveals that the commonest cause of chronic liver disease among these patients is Alcoholic Liver Disease (73.3%) followed by Hepatitis-B (18.7%) and Hepatitis-C (8%). In India studies, Dhiman and Duseja et al[9] found higher prevalence of ALD.

Our study showed Maximum mean Uric acid levels were present in CTP Class C patients (8.26), followed by Class B(5.92) and Class A(5.92). As the CTP class increases, Serum uric acid level also increases. Rudrajit Paul et al[10] demonstrated that serum uric acid levels increased with high CTP class in CLD patients.

Our study reveals Alcoholic liver disease patients had highest UA levels (mean 6.97 mg/dl) as compared to Hep-C (mean 6.55 mg /dl) and Hep-B (mean 5.54 mg/dl). Raut Sayali E and Pagar Atish B et al[11] demonstrated that consistent and very significant ($p<0.0001$) increase in serum uric acid with increasing quantity of alcohol.

In our study, serum uric acid was significantly correlated with all parameters of CTP, I.E. correlation were moderate for total bilirubin ($\rho= 0.408$), INR ($\rho= 0.445$), hepatic encephalopathy score ($\rho= 0.436$) and albumin ($\rho= - 0.428$) whereas ascites score showed high correlation ($\rho= 0.652$) with uric acid level. Previous study by Siddiqui SA and Ahmad M et al[12] demonstrated coagulation abnormalities were profound in CLD patients.

**Comparison of present study with similar studies**

| | |
|---|---|
| This study Khande M etal (2021) | The present study reveals Alcoholic liver disease patients had highest UA levels (mean 6.97 mg/dl) as compared to Hep-C (mean 6.55 mg /dl) and Hep-B (mean 5.54 mg/dl). In present study, serum uric acid was significantly |

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|---|---|
| | correlated with all parameters of CTP, I.E. correlation were moderate for total bilirubin (ρ= 0.408), INR (ρ= 0.445), hepatic encephalopathy score (ρ= 0.436) and albumin (ρ= - 0.428) whereas ascites score showed high correlation (ρ= 0.652) with uric acid level. |
| Duseja et al[9] | Found higher prevalence of ALD as compared to CLD |
| Rudrajit Paul etal[10] | Demonstrated that serum uric acid levels increased with high CTP class in CLD patients. |
| Raut Sayali E and Pagar Atish B et al[11] | Demonstrated that consistent and very significant (p<0.0001) increase in serum uric acid with increasing quantity of alcohol. |
| Siddiqui SA and Ahmad M etal[12] | Demonstrated coagulation abnormalities were profound in CLD patients. |

**Conclusion**

The serum uric acid levels increases with increasing severity of Chronic Liver Disease as assessed by Child Pugh Scoring. Maximum mean Uric acid levels were present in CTP Class C patients (8.26) and maximum mean uric acid levels (6.97mg/dl) were noted in Alcoholic Liver Disease.

Various parameters like serum Total Bilirubin, INR, and Albumin were significantly associated with serum uric acid Levels in Chronic Liver Disease patients.

Uric acid in tissues may be an activator of inflammasomes and thus, it may promote damage to surrounding tissue. It is a mediator of inflammation and tissue damage. Serum uric acid may thus be considered as a marker of severity of Chronic Liver Disease.

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