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Original Research Article.

Serum Uric Acid Level and Its Association with Child Pugh Score in Chronic Liver Disease

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ABSTRACT

Introduction: Chronic liver disease is a disorder in which progressive destruction of liver parenchyma leads to fibrosis and lead to cirrhosis. Increased level of serum uric acid may be cause insulin resistance, metabolic syndrome and oxidative stress which are the risk factors for progression of liver disease.

Objective: To estimate the levels of uric acid and evaluate its association with the severity of liver disease.

Methods: One hundred fifty patients diagnosed with Chronic liver disease, age between 20 to 65 years, either gender, were enrolled in the study. Patients were grouped as classes A, B and C on the basis of Child Pugh score. Serum uric acid was estimated and compared among the three groups.

Result: Analysis of Variance (ANOVA) was applied and it was observed that there was a significant elevation of serum uric acid level with the progression of disease (P = <0.001). A positive association of uric acid on applying Spearman's correlation, with progression of Child Pugh score was also observed (r = 0.293; P = <0.001)

Conclusion: Increased serum uric acid level with increasing Child Pugh score suggests that uric acid estimation can be a reliable and cost effective marker for evaluation of severity of liver cirrhosis in Chronic liver disease.

Keywords: Hyperuricemia, Child Pugh Score, Cirrhosis, Inflammation, Liver Disease.

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INTRODUCTION

Chronic liver disease (CLD) is a disorder in which progressive destruction and regeneration of liver parenchyma leads to fibrosis and further cirrhosis. It is manifested with common symptoms of jaundice, fatigue, nausea, poor appetite, abdominal distension and intestinal bleeding.[1] Several etiological factors can lead to development of CLD. These include alcoholism, portal hypertension, Autoimmune, Hepatitis B, C and others.[2]

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.[3]

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.[4]

Uric acid is the final oxidation product of purine metabolism in humans and higher primates and it is excreted in urine.[5] 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.[6] 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.[7] In tissues, it may be a major activator of inflammosomes and thus, it promotes damage to surrounding tissue.[8] The prevalence of hyperuricemia has progressively increased and has gained recognition as a reliable marker of inflammation as well as cardio vascular risk.[8-10] 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.

METHODOLOGY

Study Design

This prospective study was conducted in the Department of Biochemistry in collaboration with Department of Gastroenterology at Mahatma Gandhi Medical College and Hospital, Jaipur after seeking approval from the Institutional Ethics Committee (IEC). One hundred fifty diagnosed patients of CLD, age 20 to 65 years, either gender, were enrolled for the study. Pregnant and lactating females and patients with acute liver disease and malignancies were excluded. Blood samples were collected for all enrolled subjects and evaluated for serum Uric acid, Bilirubin and Albumin levels by uricase method, Azobilirubin and Bromocresol green dye binding method respectively using dry chemistry on VITROS 5600 analyzer. Prothrombin time was estimated using Nephromatic method.

CP score was calculated based on the chart below:

Factor	1 point	2 point	3 point
Serum bilirubin (mg/dL)	<2.0	2.0-3.0	>3.0
Serum albumin (g/dL)	>3.5	3.0-3.5	<3.0
Prothrombin time (Seconds Prolonged INR)	<1.7	1.7-2.3	>2.3
Ascites	None	Slight	Moderate
Hepatic encephalopathy	None	Grade 1-2	Grade 3-4

CP Class A: 5-6 points; Class B: 7-9 points; Class C: 10-15 points[4]

Patients were grouped as class A, B & C. Uric acid levels among the three groups were presented as mean ± SD and evaluated statistically by applying one way ANOVA using SPSS software. To further confirm the association of increased serum uric acid levels with CP score, Spearman's correlation was also applied.

Table 1: S. Uric acid level in groups based on CP score

	Class A (n=8)	Class B (n=75)	Class C (n=67)	F Value	P Value
Uric acid (mg/dL)	5.33 ± 1.62	6.24 ± 2.61	7.69 ± 2.33	7.81	<.001

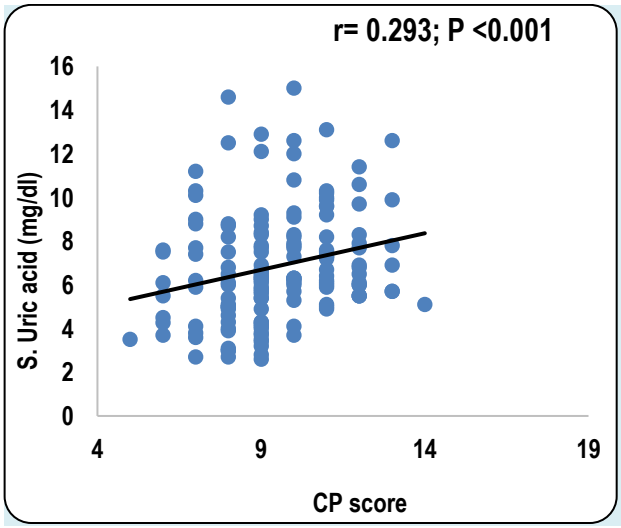

Figure 1: Correlation of S. Uric acid with CP score

RESULTS

All enrolled patients were grouped on the basis of their CP scores. On applying one way ANOVA, it was observed that all there was a significant increase in serum uric acid levels with the progression of disease (P <0.001) (Table 1). A positive association of uric acid on applying Spearman's correlation, with progression of CP score was also observed (r = 0.293; P <0.001) (Figure 1).

DISCUSSION

Progression of liver disease is assessed by the universally accepted score; CP score. Severity of disease is measured by the 5 variables included hepatic encephalopathy, Ascites, serum bilirubin, albumin and INR. These variables are decided the grade of liver disease respectively Class A, B and C. The study reported increased uric acid levels with rise in severity of disease. In a similar study of Paul R et al, 2013 showed in their study that Uric acid may be considered as a marker of severity of CLD and the levels are correlate with the higher CP grades. Serum uric acid acts as a surrogate marker in assessing the prognosis of CLD.[11]

Uric acid is the end product of purine metabolism, which is derived from endogenous and exogenous sources.[12] It is metabolized by the muscles, the intestines and the liver and is catalyzed by XO. Approximately two-third of uric acid is excreted in urine, and the remaining one third is excreted in feces.[13]

Serum uric acid is well known factor for the development of gout but besides this contributing the pathogenesis of chronic nephropathy and arthritis. High levels of uric acid associated with cardio-metabolic disease including the cardiovascular disease and all the metabolic disease associated with metabolic syndrome.[14] Components of metabolic syndrome such as hypertension, hyperinsulinemia, hypertriglyceridemia and diabetes in the hyperuricemic population.[15-17]

Singh Bet al, 2019 observed that serum uric acid level is tempting and potentially useful to speculate whether hyperuricemia is a cause or a marker & higher uric acid level with higher CP grading. High uric acid level in patients with CP class C than class B and class A.[18]

An increased level of uric acid reflects oxidative stress in the tissue and it is a marker of metabolic syndrome also. Respective conditions are associated with the liver injury and severity of CLD.[19] Liver injury is characterised by high blood level of oxidative marker. It considered as a marker of oxidative stress. Uric acid levels have been found to correlate with the increases of CP grade.[18] Hyperuricemia can induce endothelial dysfunction of reduced bioavailability of endothelial nitric oxide in rats.[19] High levels of uric acid induces the oxidative changes in adipocytes and inflammation, this process is crucial for causing metabolic syndrome in the obese mice.[20]

Benerji GV et al, 2013 concluded in their study that significant elevation of serum uric acid is observed in cirrhosis of liver, amoebic liver abscess and viral hepatitis. Hence the elevation of serum uric acid level along with the classical liver enzymes might be a risk factor for incidence of CLD.[21] Similar findings were also reported by Afzali A et al, 2010.[22]

Lombardi R et al, 2016 reported that Serum uric acid has a pathogenic mechanism in particular oxidative stress and insulin resistance and other metabolic features in which obesity and type 2 diabetes mellitus is the most important. Serum uric acid has emerged as a possible predictor of liver damage & hepatic steatosis and it has been reported to play a major role in complications associated with non-alcoholic fatty liver disease (NAFLD).[23] Bansal A et al, 2017 observed in their study that increased serum uric acid concentration is a risk factor in

NAFLD.[24] Hejazi A et al, 2019 reported a strong correlation between the uric acid and the development of inflammatory disease. Early detection of Hyperuricemia can serve as a predictor of inflammation and can help in managing the development of liver tissue damage associated with inflammatory disorders.[25]

CONCLUSION

There is a significant elevation in serum uric acid with the progression of liver disease. Hence increased levels of serum uric acid with the classical liver enzymes might be a risk factor for of chronic liver disease. The levels are found to correlate with higher CP grades. It act as a surrogate marker in the prognosis of chronic liver disease with the different etiological factors as alcoholism, hepatitis, NAFLD, non-alcoholic steatohepatitis autoimmune disorders or due to drug induced where there is increased cellular destruction.

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