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To Study the Significance of Serum Uric Acid Level in Chronic Liver Disease

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Abstract

Introduction: Chronic liver disease is one of the frequent causes of death, especially in the developing world. The increasing prevalence of chronic liver disease has been noted in recent times. Hyperuricemia results in endothelial dysfunction, insulin resistance, oxidative stress and adipose tissue inflammation, which leads to development of fatty liver, progression of NAFLD to NASH, and progression of viral and alcoholic liver disease all of which direct towards Chronic liver disease. In Chronic liver disease, High serum uric acid is independently associated with severe disease and poor prognosis. Our aim is to study serum uric acid levels and its significance in patients of chronic liver disease.

Methods: In this study we included 66 patients of chronic liver disease of different etiology; we excluded the patients with factors that influence the level of serum uric acid. After noting patients complaints and conducting thorough physical examination, patient were subjected to various laboratory tests including serum uric acid and liver function tests among others. CTP score was calculated for each patient. Using suitable statistical method, data was analysed to find out any association between serum uric acid level and different causes of chronic liver disease and disease severity using Child Turcotte pugh grading.

Results: We had a total of 66 patients of chronic liver disease, 46 (69.7%) were male, Mean age was found to be 44 ± 12 years. Alcoholic liver disease was the most common cause (52%) of CLD followed by chronic hepatitis B (23%). A higher serum uric acid level was observed among patients with Hepatitis B (7.42 ± 2.8) and patients with CTP class C (7.37 ± 2.8). In our study Correlation between serum uric acid and CTP score (P=0.020), Albumin (P=0.0303), Bilirubin (P=0.0435), INR (P=0.0454), SGOT (P=0.0068), and SGPT (P=0.0397) were found to be statistically significant.

Conclusion: Increased serum uric acid level with increasing child pugh score showed that uric acid can be reliable and cost effective marker for evaluation of severity of liver cirrhosis in chronic liver disease. Serum uric acid, when used as a prognostic marker for liver parenchymal disease is a potential non-invasive and inexpensive method to indicate disease severity, complications and can serve as an early tool for intervention

Keywords: Uric acid; Child pugh score; Chronic liver disease; NAFLD; Hepatitis B; Alcohol

Introduction

Chronic liver disease is one of the frequent causes of death, especially in the developing world. The increasing prevalence of chronic liver disease has been noted in recent times. Chronic liver disease leads to progressive destruction and regeneration of liver parenchyma and finally leads to fibrosis and cirrhosis, common symptoms include fatigue, jaundice, poor appetite, nausea, abdominal distension and intestinal bleeding. Common etiologies for CLD include Alcoholism, Portal hypertension, Autoimmune, Hepatitis B, C and others. Uric acid is the final product of purine metabolism in humans and higher primates and it gets excreted in urine. Hyperuricemia has been recognised as cause of gouty arthritis and kidney stones, recently hyperuricemia also recognised for the development of cardiovascular disease, hypertension and metabolic syndrome. Hyperuricemia results in endothelial dysfunction, insulin resistance, oxidative stress and adipose tissue inflammation, which leads to development of fatty liver, progression of NAFLD to NASH, and progression of viral and alcoholic liver disease all of which direct towards Chronic liver disease. In Chronic liver disease, High serum uric acid is independently associated with severe disease and poor prognosis. Our aim is to study serum uric acid levels in patients of chronic liver disease. To predict the 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. On this background, the study is done to measure the serum UA level and to correlate with the disease severity among chronic liver disease patients [1-8].

Methods

In this study we included 66 patients of chronic liver disease of different etiology; We excluded the patients with factors that influence the level of serum uric acid. A thorough history including pattern of alcohol intake was taken from the patient and their relatives and a thorough clinical physical examination with special attention to abdomen and nervous system was done. Blood sample were sent for all patients for Liver function test including bilirubin, enzymes, protein, albumin, Prothrombin Time (PT). Uric acid (UA) was measured for each patient using Uricase end point method. Radiological imaging with ultrasonography (USG) of abdomen was done to know the degree of ascites. Child Turcotte Pugh score was calculated using various parameters (Bilirubin, Albumin, Prothrombin time, Degree of Hepatic encephalopathy and amount of Ascites) and patients were grouped into 3 CTP Classes of A, B, C. Statistical analysis was done using SPSS software and results were expressed as mean with standard deviation.

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Inclusion criteria

1. Patients diagnosed with chronic liver disease based on clinically and radiologically

2. Patients willing for and giving consent to participate in the study.

Exclusion criteria

1. Patients not willing to participate in the study.

2. Patients having conditions which significantly alter serum uric acid level.(eg patients of known malignancy, patients on chemotherapy, patients on allopurinol/feboxostat/, patient with known infections and patients of recent surgery).

Results

We had a total of 66 patients of chronic liver disease, 46 (69.7%) were male; Mean age was found to be 44 ± 12 years. In more than half of the patients i.e in 34(52%) patients, alcohol was identified as a major cause of chronic liver disease followed by Hepatitis B in 15(23%) patients, and other causes were responsible for chronic liver disease in 15(23%) of patients, and had one case each of wilson's disease and autoimmune as a cause of chronic liver disease (Table 1). Out of 66 patients, 33(50%) patients belongs to CTP score between ≥ 10 followed by 26(39.4%) patients had CTP score of 7-9, Only 7(10.6%) have CTP score between 5 and 6 (Table 2). In our study we found there is a strong Correlation between serum uric acid and CTP score in CLD patients, which is statistically significant (p=0.020) (Table 3). A higher serum uric acid level was observed among patients with Hepatitis B (7.42 ± 2.8) and patients with CTP class C (7.37 ± 2.8). In our study Correlation between serum uric acid and CTP score (P=0.020), Albumin (P=0.0303), Bilirubin (P=0.0435), INR (P=0.0454), SGOT (P=0.0068), and SGPT (P=0.0397) were found to be statistically significant (Table 4).

Causes of Liver Cirrhosis	Percentage chance of cause
Alcohol	52%
Hepatitis B	23%
Chronic liver disease	23%
Wilson's disease	1.50%
Autoimmune Disease	22.70%

Table 1: Distribution of the participants according to the cause of chronic liver cirrhosis

S.No.	Child Pugh Score	Number of case (n=66)
1	5-6 CLASS A	07 (10.6%)
2	7-9 CLASS B	26 (39.9%)
3	≥ 10 CLASS C	33 (50%)
	Total	66 (100%)

Table 2: Distribution of the participants based on Child Pugh Score

Serum Uric acid le (n=66)	Child Pugh Score		
	CLASS A (5-6)	CLASS B (7-9)	CLASS C(≥10)
<4 mg/dl	2 (28.5%)	4 (15.3%)	4 (12.1%)
4-7 mg/dl	4 (57.1%)	14 (53.8%)	7 (21.2%)
≥ 7 mg/dl	1 (14.2%)	8(30.7%)	22 (66.6%)

Total	7 (100%)	26 (100%)	33 (100%)
P value	0.02		

Table 3: Correlation of Serum Uric acid level with Child Pugh Score

		Serum uric acid level			P value
		≤ 4 mg/dl	4-7 mg/dl	≥ 7 mg/dl	
Albumin	>3.5 g/dl	3	9	3	0.0303
	2.5-3.5 g/dl	5	6	20	
	<2.5 g/dl	2	10	8	
Bilirubin	<2 mg /dl	6	5	15	0.0435
	2-3 mg/dl	1	15	10	
	>3 mg/dl	3	5	6	
INR	<1.7	5	15	18	0.0454
	1.7-2.3	1	9	10	
	>2.3	4	1	3	
SGOT	<40 u/l	3	18	7	0.0068
	>40 u/l	7	7	24	
SGPT	<40 u/l	7	15	10	0.0397
	0 u/l				

Table 4: Correlation of Serum Uric acid level with Albumin, Bilirubin, INR, SGOT, and SGPT

Discussion

In keeping currently, the present study entitled "To Study the Significance of Serum Uric Acid Level in Chronic Liver Disease" was carried out in the Department of General Medicine, Netaji Subash Chandra Bose Medical College and Hospital, and Jabalpur (M.P) after taking ethical clearance from Institutional Ethics Committee. The study duration was of one and half year from 1st March 2020 to 31st August 2021. In our study mean age of the study participants was 44 ± 12 years with maximum study paticipants i.e 30(45.4%) of them were between 36-50 years of age group followed by 18(27.2%) in 21-35 years of age, which similar findings by Zelber-Sagi observed that the mean age of Study participants was 43.9 ± 10.2 years [9]. A similar study of Shyamala, et al. (2017) conducted in

Karnataka, India showed mean age to be 44.54 years. In the present study of 66 patients, 34(51.5%) are alcoholic, as major risk factor for Chronic liver disease, and below listed studies as Alcoholic liver disease as major cause of Chronic liver disease, Shyamala, et al. study conducted in Karnataka, India among 50 patients most of the patients were having Alcoholic Liver Disease (80%) followed by Hepatitis-B (12%) and Hepatitis-C (6%) and Autoimmune Hepatitis (2%). A study conducted in India Dhiman and Duseja, et al. found higher prevalence of Alcoholic liver disease. Rudrajit, et al. study conducted in west bengal, India among 52 patients found Alcoholic (36.6%) as a commonest cause, followed by NAFLD. Bobi singh, et al. study conducted in Manipur, India found Alcohol was the most common cause (69.7%) of CLD followed by chronic hepatitis C (15.2%). Our Observations are consistent with above mentioned authors.

Out of 66 patients,33(50%) patients were classified as chronic liver disease with CTP score ≥ 10 followed by 26(39.9%) patients had CTP score of between 7-9, only 7(10.6%) patients have CTP score between 5-6. Following Shyamala, et al. study conducted in Karnataka, India found

to have Maximum Uric acid levels in CTP Class C patients, as similar to present study, Prakash BC, et al. study. Out of 100 patients, 2 belonged to Class A (score=5-6), 50 belonged to Class B (score=7-9) and 68 belonged to Class C (score=10-15) are in coherence with present study, Bobi singh M, et al. Study conducted in 66 patients, 30 patients belong to CTP class B, 20 patients in CTP Class C, 16 patients in Class A, above study is in contrast to the present study, In coherence to my study Singh Bet, et al. study observed hyperuricemia is a cause or a marker and higher uric acid level with higher CTP grading, High uric acid level in patients with CTP class C than class B and Class A [10-13].

In our study we found there is a strong Correlation between serum uric acid and CTP score in CLD patients, where there is higher CTP score with high serum uric acid levels. In coherence to my study Singh Bet, et al. (2019) study observed hyperuricemia is a cause or a marker and higher uric acid level with higher CTP grading, Rudrajit Paul, et al. demonstrated similar as in the present study that serum uric acid levels increased with high CTP class in CLD patients. Jaishree, et al. study conducted in Rajasthan, India among 150 patients found significant elevation of serum uric acid with progression of liver disease. In the Present Study the above variables serum Albumin, bilirubin, INR, SGOT and SGPT, found to be significant with a P=0.0303, 0.0435, 0.0454, 0.0068 and 0.0397 respectively, A study by Ernst Hasch, et al. demonstrated low serum albumin levels in CLD patients, these study are coherence with above study. According to Vinotha T, et al. hyperbilirubinemia associated with Hyperuricemia with P<0.001, these studies are in Coherence with above study. Siddiqui SA and Ahmad M, et al. demonstrated coagulation abnormalities were profound in CLD patients; the present study is in coherence with the above mentioned study. Anita Afzali, Noel S. Weiss, et al. demonstrated High serum SGOT levels were associated with high serum uric acid level. Shuang chen, et al. also found elevated ALT in patients with Hyperuricemia. According to Zelber-Sagi, et al, serum uric acid has significant association with elevated ALT. The above mentioned studies are in coherence with present study. Increased level of serum uric acid reflects the oxidative stress in tissues and also a marker of metabolic syndrome, both these conditions are associated with progression of chronic liver disease. Majority of studies depicted hyperuricemia patients has high CTP score and poor prognosis [14-16].

Conclusion

As we know Chronic liver disease is one of the leading causes of morbidity and mortality globally, it is necessary to develop various tools or investigations to diagnose it and predict those patients who are likely to develop various complications of CLD. In this study we evaluated CLD by measuring their serum uric acid level and correlated it with Child Pugh Score of the patient. We observed that there was a strong correlation between Child Pugh Score and Serum uric acid level. Though, Child Pugh Scoring system is a predictor of morbidity in CLD patients, Serum uric acid level can also be used as an early indicator for predicting patients at high risk of developing complications and mortality due to CLD. Increased serum uric acid level with increasing child pugh score showed that uric acid can a be reliable and cost effective marker for evaluation of severity of liver cirrhosis in chronic liver disease. Serum uric acid, when used as a prognostic marker for liver parenchymal disease is a potential non-invasive and inexpensive method to indicate disease severity, complications and can serve as an early tool for intervention.

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