

Original Research Article

Study of serum uric acid in liver cirrhosis and its correlation with Child Turcotte Pugh, MELD and UKELD score

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ABSTRACT

Background: Liver cirrhosis is one of the most common causes of morbidity and mortality. The availability of liver transplant has stressed on the need for accurate prognostication. Various scoring systems have been developed for the same and studies have been conducted to find the correlation of various biochemical parameters with these.

Methods: This is a cross sectional study conducted on 100 patients with stigmata of liver cell failure on clinical examination and substantiated by imaging. Serum Uric acid and other biochemical parameters were determined. Child Turcotte Pugh Score, Model for End Stage Liver Disease (MELD) score, United Kingdom Model for End Stage Liver Disease (UKELD) score was calculated and the correlation obtained.

Results: The study showed significant, positive correlation between uric acid level and CTP, MELD and UKELD score. The study also showed the positive correlation of serum uric acid with various biochemical parameters such as total bilirubin, Prothrombin time/ International Normalized Ratio (PT/INR) and serum creatinine and negative correlation with serum albumin, with a significant p value. The mean serum uric acid was found to be 4.79(4.79± 2.0)

Conclusions: The study showed a correlation between serum uric acid and the various available scoring systems such as CTP score, MELD and UKELD score. Hence serum uric acid can be used as an alternative prognostic parameter in predicting the severity and prognosis of cirrhosis of liver.

Keywords: Child Turcotte Pugh score, Liver cirrhosis, Model for end stage liver disease, Prothrombin time/ International normalized ratio, United Kingdom model for end stage liver disease

INTRODUCTION

Liver diseases affect millions of people worldwide.¹The Global Burden of Disease (GBD) reported that over 1 million people died due to cirrhosis in 2010.² Cirrhosis is defined as a diffuse process affecting the liver characterized by fibrosis and nodule formation.

It is the end result of fibrogenesis that occurs with chronic liver injury.³ The common causes include excess alcohol intake, viral hepatitis, Non-Alcoholic Steatohepatitis (NASH) and autoimmune diseases. Alcoholism accounts for >50% of cases and Viral 30-70%.⁴

Uric acid is the end product of purine metabolism.⁵ It is produced in conditions of nuclear destruction. Recent research has shown that it is a mediator of inflammation and tissue damage.⁶

In chronic liver disease, there is progressive damage to liver parenchyma. Alcohol metabolism also causes a rise in uric acid level. In CLD of different etiologies, Uric acid levels were found to be high.⁷ A correlation of uric acid directly with the level of tissue damage has been found in a number of studies. As compared to the serum levels, the tissue levels of uric acid may be even better predictors.⁸ The availability of liver transplant has stressed on the need for accurate prognosis so that the

patient can be referred at appropriate time.³ The most widely used clinical tool to determine prognosis in patients with alcoholic cirrhosis is the Child-Turcotte-Pugh (CTP) score (Child-Pugh class). This is because of its simplicity and ease of use, although, it has its limitations.⁹ The model for end-stage liver disease (MELD) score was developed to determine prognosis in patients undergoing TIPS. It is calculated from serum creatinine, serum bilirubin and prothrombin time (PT/INR). A similar scoring system was developed in UK called United Kingdom Model for End Stage Liver Disease (UKELD).³

The present study is undertaken to find the correlation of serum uric acid with the various scoring systems available to predict prognosis such as Child Turcot Pugh, MELD and UKELD score.

Aims and objectives of the study were to study the serum uric acid level in patients of liver cirrhosis. To determine the correlation between serum uric acid level and CTP, MELD and UKELD score.

METHODS

This is a cross sectional study conducted on 100 patients of Liver cirrhosis treated at Victoria Hospital attached to BMCRI between April 2019 to September 2019. Ethical clearance obtained from the Institutional Ethics Committee. A written informed consent was obtained for the patients willing to participate in the study.

Inclusion criteria

- Patients of liver cirrhosis, above the age of 18 years, with stigmata of chronic liver cell failure on clinical examination and substantiated by imaging studies

Exclusion criteria

- 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, hypothyroidism, diabetes mellitus, hepatorenal syndrome
- Patients with known malignancies on chemotherapy.
- Pregnancy

Cirrhosis of liver was confirmed by ultrasound and biochemical reports. Serum uric acid level was determined.

MELD score was calculated as follows

MELD SCORE = $9.57 \times \log_e(\text{creatinine [mg/dl]}) + 3.78 \times \log_e(\text{total bilirubin [mg/dl]}) + 11.20 \times \log_e(\text{INR}) + 0.643$

MELD Na = MELD score - Na - $0.025 \times \text{MELD} \times (140 - \text{Na}) + 140$.

Sodium is limited in a range of 125-140 and if outside of these bounds, is set to the nearest limit.¹⁰

MELD Score was grouped as follows: Group 1: score= 9 or less, Group 2: score= 10-19, Group 3: score= 20-29, Group 4: score=30-39, Group 5: score= >40.¹¹

UKELD score was calculated as follows¹²

UKELD score = $[(5.395 \times \ln(\text{INR})) + (1.485 \times \ln(\text{creatinine, micromole/L}) + (3.13 \times \ln(\text{bilirubin, micromole/L})) - (81.565 \times \ln(\text{Na mmol/L}))] + 435$.

Child Turcotte Pugh score was calculated as follows³

Table 1: Child Turcotte Pugh Score.

Parameter	1 Point	2 Point	3 Point
Total bilirubin (mg/dl)	<2	2-3	>3
Serum albumin (g/L)	>3.5	2.8-3.5	<2.8
INR	<1.7	1.7-2.3	>2.3
Ascites	None	Mild (or controlled by diuretics)	Moderate to severe (or refractory to diuretics)
Hepatic Encephalopathy	None	Grade 1-2	Grade 3-4

Class A=5-6, Class B=7-9, Class C=10-15

Statistical analysis

Data was tabulated in Microsoft Excel and statistical analysis was done using SPSS for windows (version 20.0) Pearson correlation analysis was used for relationship between quantitative variables such as serum uric acid and CTP, MELD and UKELD score. A p value <0.05 was considered statistically significant.

RESULTS

The present study was conducted on 100 patients. The age distribution was between 22 and 80 years. The mean age of the patients was 48.09 with a standard deviation of 11.14(48.09±11.14). In the present study, out of the 100 patients, 94 were male and 6 were female (Figure 1) with liver cirrhosis of various causes, diagnosed clinically and substantiated by imaging studies.

One of the complications of liver cirrhosis is ascites. It was divided into 3 categories as follows: 1) No ascites 2) Mild or controlled by diuretics 3) Moderate to severe or refractory to diuretics (Table 1) Among the 100 patients, 6 patients had no ascites, 36 had mild ascites controlled with diuretics, and 58 patients had refractory ascites.

(Figure 2) The same classification is used in Child Turcotte Pugh scoring system.

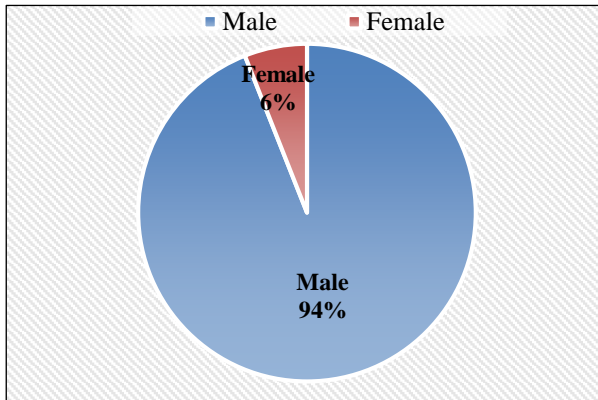


Figure 1: Histopathology picture of sex ratio neurocysticercosis.

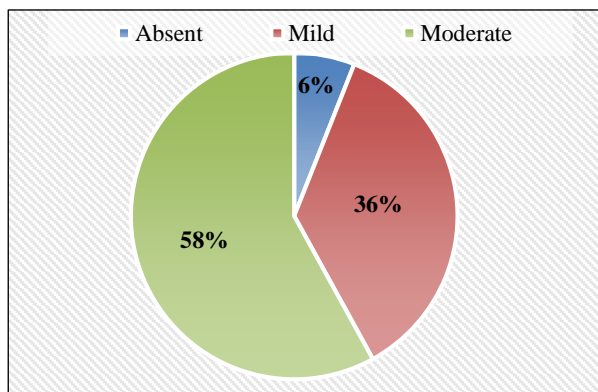


Figure 2: classification of ascites.

Another complication of liver cirrhosis is Hepatic encephalopathy. It was divided into 3 categories as A) No B) Grade 1-2 C) Grade 3-4 (Table 1).

Out of the 100 patients studied, 32 patients had no encephalopathy, 56 patients had grade 1 or 2 encephalopathy and 12 patients had grade 3 or 4 encephalopathy (Figure 3).

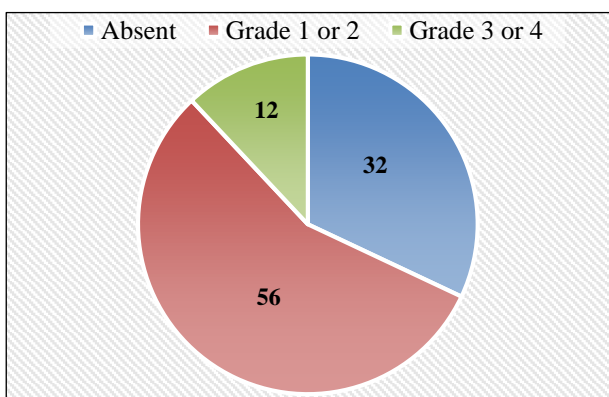


Figure 3: Classification of encephalopathy.

Child Turcotte Pugh score was calculated for each patient and were classified into the respective class. 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).

Similarly, MELD score calculated for each patient and were grouped into 5 classes based on the scores. As per analysis, 2 patients belonged to MELD Group 1(score= 9 or less), 36 to group 2(score= 10-19), 40 to group 3(score= 20-29), 21 to group 4(score=30-39), 1 to group 5(score= >40) (Figure 4). UKELD scores were also calculated.

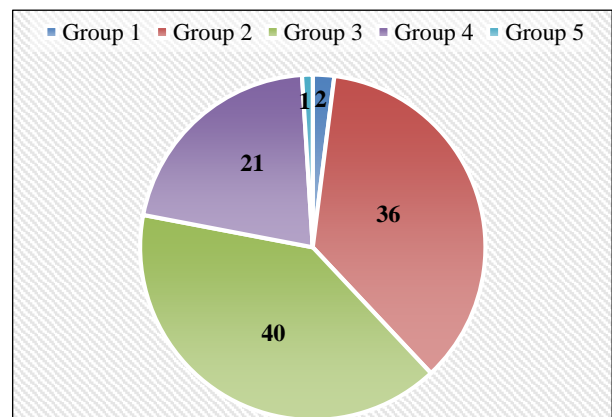


Figure 4: Meld group.

The mean Serum uric acid was 4.79 with a standard deviation of 2(4.79±2). The distribution was between 1.8 mg/dl (minimum) and 9.9 mg/dl (maximum). The mean total bilirubin was found to be 5.84 with a standard deviation of 6.57(5.84±6.57). Serum albumin was found to have a distribution between 1.2 to 5.2 g/dl with a mean of 2.34(2.34±0.63). INR was found to have a mean of 1.86(1.86±0.67) Serum creatinine was found to have a distribution between 0.3 mg/dl to 5.9mg/dl with a mean of 1.16(1.16±0.78).

The mean serum sodium level was found to be 132.86 mEq/L (132.86±4.98). Serum uric acid showed a statistically significant positive correlation with total bilirubin, serum creatinine and PT/INR with a p value of 0.003, <0.001, 0.030 respectively and negative correlation with serum albumin with a P value of <0.001 (Table 2). A p value <0.05 was considered statistically significant. Serum uric acid showed no statistically significant correlation with age (p=0.98) and serum sodium (p=0.70).

The mean CTP score was 10.79 with a standard deviation of 2.32(10.79±2.32). The mean MELD score was 22.75 with a standard deviation of 7.72(22.75±7.72) the mean UKELD score was 58.49. Serum uric acid was found to have a positive, statistically significant correlation (p<0.05) with MELD score, Child Turcot Pugh score and UKELD score with a p value of <0.001, <0.001, 0.01 respectively (Table 3).

Table 2: Correlation of Serum uric acid with various parameters.

	Age (years)	Total bilirubin (mg/dl)	Albumin (g/dl)	INR	Serum creatinine (mg/dl)	Serum Sodium (mEq/L)
Mean	48.09	5.84	2.34	1.86	1.16	132.86
Standard Deviation	11.14	6.57	0.63	0.67	0.78	4.98
Pearson Correlation	0.003	0.292	-0.344	0.207	0.424	-0.039
P value	0.98	0.003	p<0.001	0.03	p<0.001	0.70

Table 3: Correlation of serum uric acid with CTP, MELD and UKELD score for prognosis of liver cirrhosis.

	CTP Score	MELD Score	UKELD Score
Mean	10.79	22.75	58.49
Standard deviation	2.32	7.72	6.86
Pearson correlation	0.472	0.405	0.242
p value	p<0.001	p<0.001	0.01

DISCUSSION

Cirrhosis of liver is associated with significant morbidity and mortality. Several biochemical and radiological markers are used for assessing the extent of liver injury. Using these parameters various scoring systems have been developed for prognostication. Since uric acid is a product of purine metabolism, it is produced during nuclear destruction following cell injury in chronic liver disease leading to cirrhosis. In this cross-sectional study, serum uric acid level was found to be higher in patients with increased MELD score, UKELD score and a higher CTP class. A study from West Bengal, India found a similar correlation. Also, a study from the United States found that the patients with a higher level of serum uric acid had a higher risk of cirrhosis related hospitalization or death.¹³ In this study author also found a significant correlation of serum uric acid with other parameters such as total bilirubin, serum albumin, serum creatinine and INR. A study conducted in Korea showed a significant correlation of uric acid levels with the degree of hepatic histologic change.¹⁴ But whether decreasing uric acid can halt the progression of the disease or prevent future hepatic or cardiac morbidity is yet unknown.¹⁵

This study is limited by a small sample size and lack of histological data. Since it is a cross sectional study, serum uric acid was measured only once. Even with these limitations, the study still shows significant correlation of serum uric acid with various established scoring system for prognostication of liver cirrhosis.

CONCLUSION

The study showed positive correlation between serum uric acid and CTP, MELD and UKELD score. It also

showed correlation between serum uric acid and total bilirubin, serum albumin, serum creatinine and INR. Hence it may act as a surrogate marker for prognosis of liver cirrhosis. However, larger prospective case-control studies are required to ascertain the exact role of serum uric acid in liver cirrhosis.

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