

Original Research Article

STUDY OF HYPONATREMIA IN CIRRHOSIS OF LIVER AND ITS PROGNOSTIC VALUE IN A TERTIARY CARE CENTER

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ABSTRACT

Background: Chronic liver diseases are quite prevalent in India with a substantial number presenting with decompensated cirrhosis. Hyponatremia has been an important prognostic indicator in cirrhosis. Hyponatraemia predicts worse outcomes and is an independent predictor of survival at 3 and 12 months. So this study was done to determine prognostic significance of hyponatremia; child-turcott-pugh, MELD and MELD-sodium score in liver cirrhosis cases.

Materials and Methods: To study the objective, prospective observational study was conducted on 91 patients with cirrhosis of liver. The CTP, MELD and MELD-Na scores were assessed using receiver operating characteristic curve.

Results: Around 27.47% of patients were between age group 51-60 years. Among total respondents, 88% were male. Alcohol was responsible for causing cirrhosis in 65% of patients. Coagulopathy was most common complication which was present in 70.32% patients. Among hyponatremia patients, most of the them (34%) were having severe Hyponatremia. Ascites was most common complication among severe hyponatremia patients. Severe hyponatremia patients had more mortality.

Conclusion: The study find out that There was direct relationship of complication and mortality with severity of hyponatremia. MELD-Na was found to be superior to CTP and MELD scores in predicting mortality.

Keywords: Cirrhosis, Hyponatremia, CTP, MELD, MELD-Na

INTRODUCTION

Cirrhosis is a condition that is defined histopathologically having a variety of clinical manifestations and complications. The pathologic feature in cirrhosis is the development of fibrosis, causing distortion of the architecture of liver with the formation of regenerative nodules, irrespective of the cause of cirrhosis.

A recent prospective, multicentre study involving 20,701,383 patients showed that 1.28% (n = 266,621) of these patients had chronic liver disease. 65,807 (24.68%) were diagnosed for the first time. Alcoholism (34.3% of 4,413) was the most common cause of cirrhosis, while hepatitis B (33.3%) was the predominant cause of chronic liver disease in general as well as of non-cirrhotic chronic liver disease (40.8% out of 8,163). Hepatitis C was the chief cause of chronic liver disease in the north, alcohol in the

northeast. Hepatitis B was the most common in the east and the south, and non-alcoholic fatty liver disease (NAFLD) in the west.^[1]

Hyponatremia prevalence can be useful tool in identifying high risk patient's prognosis who might require liver transplantation and can be allocated health care services accordingly. Hyponatremia in cirrhosis is considered significant as serum sodium level ≤ 130 mEq/L is prevalent in approximately 22% of patients with cirrhosis. Hyponatremia is a frequent finding in patients with decompensated cirrhosis because of abnormal regulation of body fluid homeostasis.^[2]

Hyponatremia in cirrhosis occurs due to impairment of renal solute-free water excretion, resulting in disproportionate renal retention of water with respect to sodium retention. Renal impairment is often seen but not always present in this type of hyponatremia.² Besides hepatic encephalopathy, hyponatremia is

also prevalent in other complications of cirrhosis. Specifically, hyponatremia is a frequent finding in patients with cirrhosis and bacterial infections. In the majority of patients, hyponatremia occurs in close association with renal failure and correlates with a poor prognosis.^[2]

Hyponatremia in patients with cirrhosis indicates a poor prognosis before liver transplantation (LT) even independent of the Model for End-Stage Liver Disease (MELD) score. Overcorrection of hyponatremia before liver transplantation or peri-operatively can lead to the devastating neurologic condition of osmotic de-myelination syndrome, often irreversible and having high fatality rate.^[3]

Child-Turcotte-Pugh (CTP), Model for End-Stage Liver Disease (MELD) and MELD-sodium (MELD-Na) scores are used for predicting disease severity and mortality among patients with end-stage liver disease.^[1]

The Child-Pugh score is a fairly reliable predictor of survival in cirrhosis. It also predicts the likelihood of major complications, such as bleeding from varices and spontaneous bacterial peritonitis. Moreover, child-pugh class B was used to assess prognosis in cirrhosis and for listing a patient as a candidate for liver transplantation.

The Child-Pugh score was replaced with the Model for End-Stage Liver Disease (MELD) score was calculated from three variables: the prothrombin time expressed as the international normalized ratio (INR), the serum bilirubin level, and the serum creatinine concentration.

It was later modified to include serum sodium concentration as a factor in the model and a reweighting of the MELD components. MELD Na score includes sodium level of the patient; which gives an edge in predicting the mortality. (MELD-Na) –was implemented for liver transplant allocation in 2016, since hyponatraemia is a strong predictor of mortality among liver transplant waitlist patients.^[1]

A comparison of such scores like Child-Turcotte Pugh, MELD, MELD-Na as a mortality predictor is less extensively studied in end stage liver diseases. This study tries to determine the prevalence and prognostic value of serum sodium in patients with cirrhosis, and a comparison of Child-Turcotte Pugh, MELD, MELD-Na score as a three-month mortality predictor having prognostic value in a tertiary care centre.

MATERIALS AND METHODS

This is prospective observational study conducted on patients with cirrhosis of liver, who were admitted in ICU, Medicine and gastroenterology wards in Geetanjali medical college and hospital from January 2019-december 2019.

Considering the prevalence of hyponatremia as 37%, taking confidence level of 95% and allowable error of 10%, the sample size came 90. Samples were collected by Purposive consecutive sampling. So we

collected data from 91 patients during our study period.

Patients with cirrhosis of liver were evaluated with a detailed history and thorough physical examination. Radiological investigations were conducted as needed. Hematological were done including complete blood count, prothrombin time, International normalized ratio, activated partial thromboplastin time.

Liver function tests which included serum alanine amino transferase, aspartate amino transferase, bilirubin (total, conjugate and unconjugated), total protein along with albumin, globulin and albumin: globulin ratio (A:G). Serum alkaline phosphatase levels were also measured. Renal function was evaluated by measuring serum creatinine, urea and electrolytes. Blood glucose levels were measured. Thyroid functioning was evaluated by measuring the serum levels of thyroid stimulating hormone (TSH). Patients were also screened for HIV, hepatitis B antigen and hepatitis C antibody.

Serum sodium levels were measured on the day of admission, on the day of discharge, after 1 month and 2 months. The Child-Pugh (CTP), Model for end stage liver disease (MELD) and Model for end stage liver disease sodium (MELD-Na) were assessed at the time of admission.

Inclusion Criteria

- All patients with cirrhosis of liver.
- Patients with written informed consent.

Exclusion Criteria

- Patients unwilling to participate in the study.

The data was entered in Microsoft Excel for windows and analysed using statistical packages for social sciences. The data was assessed in proportions, mean and frequency tables. P-value of <0.05 will be considered significant. The CTP, MELD and MELD-Na scores were assessed using receiver operating characteristic curve for predicting 3- month mortality.

RESULTS

Total 91 patients were included in this study. Approximately 88% of the study population was male and 12% were females. Most patients belonged to the 51-60 years age group (27.47%), followed by 31-40 (25.27%), 41-50 (24.17%) years age group.

Alcohol was the most common cause for causing cirrhosis of liver in the study population. 13% patients had no specific cause for cirrhosis. Non-alcoholic steato-hepatitis (NASH) caused cirrhosis in eight patients [Table 1]. Hepato-cellular carcinoma was present in three patients associated with hepatitis B infection.

Coagulopathy was the most common complication among patients. Ascites and jaundice were present in 62(68%) patients. [Table 2]

Regarding serum sodium level, 51(56%) Patients had hyponatremia. Among the hyponatremia patients, 31(61%), 3(6%) and 17(33%) had Severe, Moderate

and Mild hyponatremia respectively (N=51). [Table 3]

It was also observed that complications of cirrhosis were most abundant in patients having severe hyponatremia (Na <125 mEq/L). Patients having moderate hyponatremia (Na= 126-130 mEq/L) had less complication. Among Severe hyponatremia group most common complication was Ascites while among mild Hyponatremia group most common complication was coagulopathy. While jaundice was most common among patients having normal serum sodium level [Table 4].

Out of total 91 patients, 13(14%) patients died. Out of those 13 patients, 11(85%) had severe hyponatremia while 2(15%) had moderate hyponatremia. There was no mortality among patients having mild hyponatremia or having normal serum sodium level. [Figure 1]

Out of 91 patients in the study population, 44 belonged to class C of the Child-Pugh (CTP) score, out of which 11 patients died. 43 patients belonged to class B with two deaths in the same group. Only 4

patients had mild severity of cirrhosis belonging to class A of CTP score. [Table 5]

Receiver operating characteristic curve for predictive value of CTP had an area under curve (AUC) of 0.715 for predicting 3-month mortality. [Figure 2]

Highest numbers of patients (37) were classified with MELD score of 10-19, with two deaths reported. 33 patients had a MELD score ranging from 20-29 with 2 deaths in the same group. 7 patients had a MELD score ranging from 30-39 with 2 deaths in the same group. 4 patients had MELD score <9 and no deaths. 10 patients had a MELD score >40 out of which 7 patients died. [Table 6]

The AUC for MELD was 0.845 for predicting the 3-month mortality in the study population. [Figure 3]

Maximum number of patients (21) had a MELD-Na score <17 with no deaths. Two deaths occurred out of 18 patients in both groups with MELD-Na ranging from 23-26 and 27-31. Highest number of deaths (9 out of 20 patients) were seen with MELD-Na >32. [Table 7]

The AUC for MELD-Na was 0.869 for predicting 3-month mortality in the study population. [Figure 4]

Table 1: Etiology of cirrhosis of liver in the study population (N=91)

Cause of cirrhosis	Number	Percentage
Alcohol	59	65%
Idiopathic	12	13%
Hepatitis B	10	11%
Non-alcoholic steato-hepatitis	8	9%
Hepatitis C	1	1 %
Wilson's disease	1	1 %
Total	91	100%

Table 2: Distribution of complications of cirrhosis among Patients (N=91)

Complications	Number of Patients N = 91	Percentage
Coagulopathy	64	70.32 %
Ascites	62	68.13 %
Jaundice	62	68.13%
PHTN	55	60.44 %
Hepatic encephalopathy	17	18.68 %
HRS	11	12.09 %
GI- Bleeding	11	12.09 %
Seizure	2	2.2 %

Table 3: Prevalence of Hyponitremia (N=91)

Serum sodium levels	Classification of Hyponatremia	Number of Patients	Percentage (N=91)
<125 mEq/L	Severe	31	34
126-130 mEq/L	Moderate	3	3
131-135 mEq/L	Mild	17	19
≥135 mEq/L	No Hyponatremia	40	44
Total		91	100

Table 4: Distribution of complications of cirrhosis among patients with mild, moderate and severe hyponatremia (N=91)

Complication	Serum sodium levels				Total
	<125 mEq/L	126–130 mEq/L	131–134 mEq/L	>135 mEq/L	
Coagulopathy	25	3	13	23	64
Ascites	29	2	7	24	62
Jaundice	18	3	12	29	62
PHTN	20	3	9	23	55
HE	7	1	3	6	17
GI Bleeding	4	1	2	4	11
HRS	9	0	0	2	11
Seizure	2	0	0	0	2

Table 5: Relation of CTP score with mortality

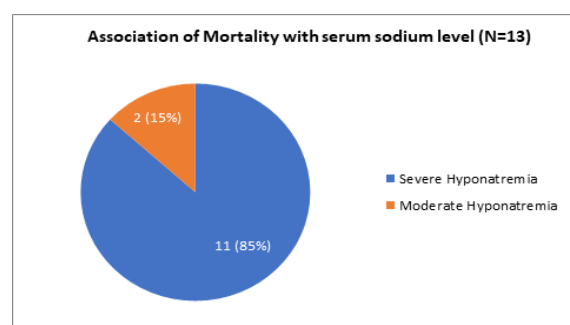
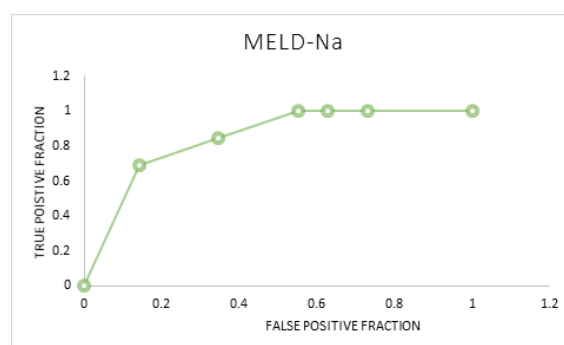
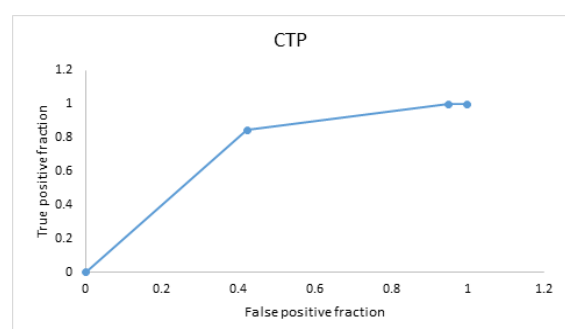
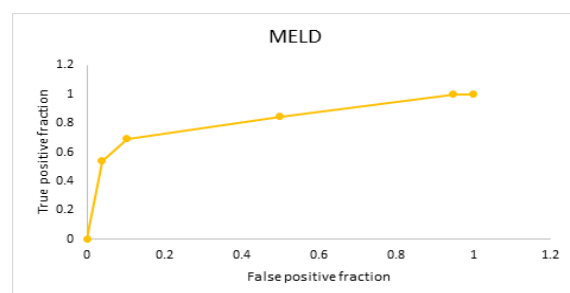
CTP (Score)	Number of Patients	Number of Death
Mild (5-7)	4	0
Moderate (7-9)	43	2
Severe (>10)	44	11
Total	91	13

Table 6: MELD score and mortality in the study population

MELD Score	Number of Patients	Number of Death
≤ 9	4	0
10-19	37	2
20-29	33	2
30-39	7	2
> 40	10	7
Total	91	13

Table 7: MELD-Na score and mortality in the study population

MELD-NA score	Total	Mortality
<17	21	0
17-20	8	0
21-22	6	0
23-26	18	2
27-31	18	2
>32	20	9
Total	91	13

**Figure 1: Association of Mortality with serum sodium level (N=13)****Figure 4: Receiver operating characteristic curve for predictive value of MELD-Na score****Figure 2: Receiver operating characteristic curve for predictive value of CTP score****Figure 3: Receiver operating characteristic curve for predictive value of MELD score.**

DISCUSSION

This study was conducted on 91 patients. Male predominance was observed in the study population with 88 % being males. In a study conducted by Mukherjee et al,^[4] 73% were male having cirrhosis. While in study conducted by Solanki et. Al⁵ in 2017, Male Predominance was 71%.

The mean age of the study population is 49.03 ± 11 years with a range from (20-78 years). Our results were similar to a study conducted by Solanki et al,^[5] where the mean age was 50 ± 16 years. A different study done by Acharya et. Al¹ found similar age distribution with the mean age being 48.94 ± 12.63 years. The age distribution in this study correlates with the above studies.

A multicentric study conducted by Mukherjee et al,^[4] also found alcohol to be the most common cause of cirrhosis in their study, followed by hepatitis B. A similar study conducted by Sharma et al,^[6] also found alcohol as the etiological agent for cirrhosis in 62.9% of patients.

Out of the various complications associated with cirrhosis of liver, coagulopathy was the most

common in this study. A study conducted by Trimurkhe et al,^[7] in eastern Madhya Pradesh observed ascites in 84.8 % of patients, followed by jaundice (60%), Splenomegaly (57.6%), upper gastro-intestinal bleed (38.4%), thrombocytopenia (20%), Hepatic encephalopathy (18.4%) and hepatorenal syndrome in 12%. The findings of this study correlate with the results observed in our study. A study conducted by Kim et al,^[8] found hyponatremia, especially serum sodium <130 to be associated with a higher number of complications. A similar study conducted by Kumar et al,^[9] also found low sodium levels to be associated with greater complications in cirrhosis. Low sodium levels were associated with ascites, hepatorenal syndrome, hepatic encephalopathy significantly but not with varices. A similar study done by Ennaifer,^[10] found hyponatremia to be present in 42 % of their subjects with cirrhosis. A study conducted by Kumar raja et al,^[11] found hyponatremia in 52% of patients with cirrhosis.

Out of the 13 deaths that occurred in the study, 11 had severe hyponatremia and was statistically significant. ($P < 0.05$). Ray kim et al,^[12] in 2005 conducted a study and found significant association between serum sodium levels and mortality ($p < 0.001$). A similar study done by Ennaifer et al,^[10] found low serum sodium levels as a negative prognostic marker with increased short-term morbidity and mortality in their study. Hafez et al,^[13] in his study found significant association of mortality with low serum sodium levels ($P < 0.001$). The findings of this study are comparable to these studies and suggest serum sodium level is an independent risk factor for predicting mortality in patients of cirrhosis.

In our study MELD-Na was found to be superior than CTP and MELD scores in predicting 3-month mortality in patients with cirrhosis. A study conducted by Ghannan et al,^[14] found similar results with MELD-Na scores being a better predictor of mortality than the other scores. Lan Wu et al,^[15] also found MELD-Na to be superior in predicting mortality than CTP and MELD score. On the contrary a study conducted a similar study done by Acharya et. All found CTP score to be a better predictor of 3-month mortality than MELD and MELD-Na.

CONCLUSION

Almost in all the studies, cirrhosis is common in male as compare to female. Alcohol is an independent risk factor for cirrhosis of liver which signifies why cirrhosis is more common in male. There was direct relationship of complication and mortality with severity of hyponatremia. MELD-Na was found to be superior to CTP and MELD scores. In other study CTP was found better for predicting mortality. Such

variation in predictive capacity of these scores could be due to sample size, difference in etiology of cirrhosis in different regions of India, geographical variation and complications. A larger multi-centre study is required in India to further evaluate these scores to correctly classify patients who would be benefitted with a timely liver transplant referral using this score.

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