

HYPONATREMIA IN CIRRHOSIS OF LIVER AND ITS PROGNOSTIC VALUE- AN OBSERVATIONAL STUDY

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Abstract

Introduction: Hyponatremia is a prevalent electrolyte disturbance observed in individuals diagnosed with liver cirrhosis. This condition is closely linked to unfavorable prognostic outcomes and the development of complications such as hepatorenal syndrome and ascites.

Methods: The selection of patients was based on a comprehensive evaluation that included clinical examination, biochemical tests, and ultrasound examination of the abdomen. Upon admission to the hospital, all patients underwent a comprehensive examination, which included the assessment of their serum sodium levels. Throughout their hospitalization, the patients were closely monitored and their progress was observed. The assessment of the severity of cirrhosis was conducted based on the Child-Pugh score. The MELD score and MELD-Na score were computed upon admission.

Results: A study was conducted on a cohort of 150 patients diagnosed with cirrhosis, revealing that the predominant cause of cirrhosis in this particular investigation was attributed to alcohol consumption. A total of 53% of the participants exhibited hyponatremia, defined as a serum sodium concentration below 136 meq/l. The incidence of complications associated with cirrhosis was found to be higher among patients with hyponatremia. Statistically significant findings indicate that complications such as portal hypertension (57%), hepatic encephalopathy (89.28%), hepatorenal syndrome (42.8%), and hyponatremia are prevalent among patients with cirrhosis. The scores for Child-Pugh, Model for End-Stage Liver Disease (MELD), and MELD-Na are elevated in cases of hyponatremia. Mortality is also observed to be more prevalent in cases of severe hyponatremia.

Conclusion: Dilutional hyponatremia is a common occurrence among individuals with cirrhosis, and it is often linked to the development of serious complications associated with liver cirrhosis, such as hepatic encephalopathy and hepatorenal syndrome. The presence of hyponatremia in individuals with cirrhosis is also linked to increased morbidity and mortality rates.

Keywords: Cirrhosis, Hyponatremia, Child Pugh Turcot score, MELD, MELD-Na,

INTRODUCTION

Hyponatremia is a medical condition characterised by a serum sodium level below 136 mEq/L. In the context of cirrhosis, it has traditionally been regarded as significant only when the serum sodium level falls below 130 mEq/L.[1] In general, hyponatremia can be classified into three distinct clinical types: hypovolemic, euvoletic, and hypervolemic. It is worth noting that certain patients may exhibit a combination of symptoms from all three types. Hyponatremia is a common occurrence in individuals with liver cirrhosis, specifically in the presence of a hypo-osmolar serum and an elevated extracellular fluid volume, commonly referred to as "dilutional hyponatremia." In this particular case, there is a notable deficiency in the ability to eliminate free water due to an excessive amount of anti-diuretic hormone (ADH). The diseases that are commonly linked to this form of hyponatremia include cirrhosis, congestive heart failure, specific forms of renal failure, and nephritic syndrome.[2] Hyponatremia commonly manifests in individuals with cirrhosis, primarily in conjunction with an increased volume of fluid outside the body's cells. There are instances of significance where a patient may exhibit hypovolemic hyponatremia due to the utilisation of diuretics or gastrointestinal losses. In the assessment of a patient with cirrhosis and hyponatremia, it is crucial to systematically rule out and address potential etiological factors that may be solely or predominantly responsible for this condition.[3,4] Hyponatremia is prevalent among patients with early or moderately advanced cirrhosis who fall within classes A and B of the Child-Pugh classification. However, it is predominantly observed in cases of advanced disease, specifically those classified as Child-Pugh class C.[5] The close association between hyponatremia and the severity of cirrhosis is further supported by its correlation with the occurrence of complications such as hepatic encephalopathy, hepatorenal syndrome, and spontaneous bacterial peritonitis.[6] The occurrence of severe hyponatremia, necessitating prompt and targeted intervention, is relatively infrequent in individuals with cirrhosis. Hence, the presence of mild to moderate hyponatremia must primarily be evaluated for its clinical significance. Indeed, the presence of hyponatremia is an autonomous prognostic factor for the emergence of hepatorenal syndrome, hepatic encephalopathy, and overall survival.[7,8] The significant predictive capability of serum sodium concentration has resulted in its incorporation into the prognostic model for end-stage liver disease (MELD).[9] This model is extensively utilised to determine the necessity for liver transplantation and to prioritise patients on the waitlist. The objective is to enhance the prognostic capacity of the model, particularly in individuals with cirrhosis and ascites.

METHODS

The selection of patients was conducted through a comprehensive evaluation that included clinical examination, biochemical tests, and ultrasound examination of the abdomen. All patients who were enrolled in the study provided informed consent. The pertinent clinical history, examination findings, and laboratory investigations of the patients were documented in a standardized proforma sheet. All study participants underwent an initial examination upon admission to the hospital, during which their serum sodium levels were assessed. Subsequently, the patients were monitored throughout their hospitalization period. The assessment of cirrhosis severity was conducted using the Child-Pugh score. The MELD score and MELD-Na score were computed upon admission.

Inclusion Criteria

All the patients with cirrhosis of liver.

Exclusion Criteria

Patients with cardiac failure,
Patients with chronic kidney disease
Patients on diuretic therapy

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean±SD (Min-Max) and results on categorical measurements are presented in Numbers (%). Significance is assessed at 5% level of significance.

RESULTS

The present study was conducted on a sample of 150 individuals diagnosed with cirrhosis, consisting of 135 males (90%) and 15 females (10%). The average age of the patients was 46.10 ± 10.55 years. Liver cirrhosis is a pathological condition that can be attributed to various causative factors. Among the patients diagnosed with liver cirrhosis, alcoholism was found to be the primary cause in approximately 90% of cases. Additionally, hepatitis B was identified as a contributing factor in approximately 9% of patients, while hepatitis C was observed in approximately 6% of the affected individuals. The present study found that alcohol was the predominant cause, observed in 90% of the patients. The patients were categorised based on their serum sodium levels. Out of the total sample, 37 patients (25%) had serum sodium levels of ≤ 130 meq/L, 42 patients (28%) had serum sodium levels ranging from 131-135 meq/L, and 71 patients (47%) had serum sodium levels of ≥ 136 meq/L.

The average Model for End-Stage Liver Disease (MELD) score among patients with a serum sodium concentration of 130 meq/L or lower was found to be 21.4 ± 8.35 . The mean value of 16.32 ± 6.68 was observed in the group characterised by serum sodium levels ranging from 131 to 135 meq/L. The mean value in the group with serum sodium concentration ≤ 130 meq/L was 13.28 ± 5.84 . There was a notable disparity observed in the MELD score among the three groups, with a p-value of less than 0.0001.

Table: 1 Comparison of the mean meld score of the three groups

SR. NO.	COMPLICATIONS	≤ 130 meq/L n=37	131-135 meq/L n=42	≥ 136 meq/L n=71	Pvalue
1	MELD Score (Mean \pm SD)	21.4 ± 8.35	16.32 ± 6.68	13.28 ± 5.84	< 0.0001

Using ANOVA test $p < 0.05$ statistically significant

The average Child-Pugh score in the subgroup with serum sodium levels of 130 meq/L or lower was found to be 11.6 ± 2 . The average score in the group with serum sodium levels ranging from 131 to 135 meq/L was 10.3 ± 1.85 . The average score observed in individuals with serum sodium levels greater than or equal to 136 meq/L was 9.4 ± 1.53 . There was a notable disparity observed among the three groups in relation to the Child-Pugh score (p value = < 0.0001).

There was a significant association between low serum sodium levels and a higher Child-Pugh class, as compared to individuals with normal serum sodium levels. Out of a cohort of 37 individuals, it was observed that 30 patients fell under the classification of Child-Pugh class C, while the remaining 7 patients were categorised as Child-Pugh class B, all of whom exhibited serum sodium levels equal to or less than 130 meq/L. Out of a cohort of 42 individuals, it was observed that 27 patients fell into class C while 15 patients were categorised as class B, based on their serum sodium levels ranging from 131 to 135 meq/L. A notable statistical distinction exists among the three groups in relation to Child-Pugh class, as indicated by a p-value of 0.005.

Table: 2 Comparison of mean Child-Pugh score and Child-Pugh class

complication		≤ 130 meq/L n=37	131 - 135 meq/L n=42	≥ 136 meq/L n=71	Pvalue
Child-Pugh score		11.6 ± 2	10.3 ± 1.85	9.4 ± 1.53	< 0.0001
Child-Pugh class	Class A	0	0	2	0.0058
	Class B	7	15	41	
	Class C	30	27	28	

Among a cohort of 150 patients diagnosed with cirrhosis, it was observed that all 150 patients (100%) exhibited ascites, while 133 patients (89%) presented with portal hypertension. Additionally, 45 patients (30%) were found to have hepatic encephalopathy, 27 patients (18%) experienced gastrointestinal bleeding, and 5 patients (3%) displayed coagulopathy. Furthermore, 21 patients (14%) were diagnosed with Hepatorenal syndrome. In the current investigation, it was observed that ascites was observed in all 37 patients who exhibited serum sodium levels below 130 meq/L. Similarly, ascites was also present in all 42 patients with serum sodium levels ranging from 131 to 135 meq/L. Furthermore, ascites was found in all 71 patients who displayed serum sodium levels exceeding 136 meq/L. There is a lack of statistical significance observed among the three groups in relation to the presence of ascites. All 37 patients with a serum sodium level below 130 meq/L (100%) exhibit portal hypertension. A total of 39 out of 42 patients, accounting for 93% of the sample, who exhibited serum sodium levels ranging from 131 to 135, were diagnosed with portal hypertension. A total of 58 out of 71 patients (81%) who exhibited serum sodium levels greater than 136 meq/L were found to have portal hypertension. A statistically significant difference was observed among the three groups in relation to portal hypertension, as indicated by a p-value of 0.0412.

levels >135 meq/L. Levels greater than 136 milliequivalents per litre (meq/L). A statistically significant difference exists between these groups in relation to hepatic encephalopathy, as indicated by a p-value of 0.00001. Gastrointestinal haemorrhage is observed in 12 out of 37 patients exhibiting serum sodium levels below 130 meq/L, in 3 out of 42 patients with serum sodium levels ranging from 131-135 meq/L, and in 13 patients out of a total of 71 patients with serum sodium levels exceeding 136 meq/L. There is a lack of statistical significance observed among the three groups in relation to gastrointestinal bleeding, as indicated by a p-value of 0.057. The occurrence of coagulopathy is observed in 3 out of 37 patients who exhibit serum sodium levels below 130 meq/L, while it is observed in 1 out of 71 patients who exhibit serum sodium levels above 136 meq/L. There is no statistically significant difference observed among these three groups in relation to coagulopathy, as indicated by the p-value of 0.6301. Hepatorenal syndrome is observed in 28% (10/37) of patients with a serum sodium level below 130 meq/L, 14% (6/42) of patients with a serum sodium level between 131-135 meq/L, and 6% (4/71) of patients with a serum sodium level above 136 meq/L. Statistical significance was observed among the three groups in relation to hepatorenal syndrome, as indicated by a p-value of 0.038.

Table: 3 Frequency of complications by serum sodium concentration

Sr. No.	COMPLICATIONS	≤130me q/L n=37	131 - 135meq/ L n=42	≥136meq /L n=71	Pvalue@
1	Ascites	37(100%)	42(100%)	71(100%)	0.93
2	Portal Hypertension	37(100%)	39(93%)	58(81%)	0.0412
3	Hepatic Encephalopathy	22(60%)	16(39%)	6(9%)	0.00001
4	GI Bleeding	12(32%)	3(7%)	12(17%)	0.05755
5	Coagulopathy	3(8%)	0(0%)	1(2%)	0.63011
6	HRS	10(28%)	6(14%)	4(6%)	0.038

In the group of serum sodium levels ≤ 130 meq/L, 7 (20%) patients died, while 5(11%) patients died in group of serum sodium levels 131-135 meq/L. No patient died in group of serum sodium levels ≥ 136 meq/L. Hence statistically significant difference was found in mortality among these three groups

Table: 4 Mortality according to serum sodium concentration

	≤130 meq/L n=37	131-135 meq/L n=42	≥136meq/L n=71	Pvalue @
Mortality	7(20%)	5(11%)	0	0.03

@ using Chi Square test; p value <0.05 – statistically significant (95% CI)

DISCUSSION

The occurrence of hyponatremia is common in individuals with cirrhosis of the liver. This phenomenon is believed to be attributable to an elevated ratio of water retention in the kidneys compared to sodium, resulting from a decrease in the clearance of solute-free water.

The current study examines the prevalence of hyponatremia among a cohort of 150 patients diagnosed with liver cirrhosis. Results indicate that over half (53%) of the patients with cirrhosis exhibit hyponatremia, defined as a serum sodium level below 135meq/L. A total of 28% of patients exhibit serum sodium levels below the threshold of 130meq/L. A trial was conducted by Angeli P et al[10]involving a sample size of 997 patients diagnosed with liver cirrhosis. The study conducted by the researchers found that the prevalence of hyponatremia, defined as a serum sodium level below 135meq/L, was 49.4%. Furthermore, when the threshold for hyponatremia was set at ≤130meq/L, the prevalence was found to be 21.6%. A study was conducted by Borroni et al. [11] involving a sample of 156 individuals diagnosed with liver cirrhosis. The study found that the prevalence of hyponatremia was 29.8% when the serum sodium concentration was below 130 meq/L.

Based on the findings of previous studies conducted by Kim JH et al[12], BorroniS et al[11], and Shaikh S et al[13], it has been demonstrated that there is no established correlation between the aetiology of cirrhosis and serum sodium levels. The current study observed a notable disparity among the groups in relation to child-pugh, as indicated by a statistically significant p-value of 0.0001. Among patients diagnosed with hyponatremia, the average Child-Pugh score was found to be higher when compared to patients with normal serum sodium levels. Within a sample size of 25 patients with serum sodium levels equal to or less than 130 meq/L, 20 patients were classified as Child-Pugh class C and 5 patients were classified as Child-Pugh class B. Similarly, among a group of 28 patients with serum sodium levels ranging from 131-135 meq/L, 18 patients were classified as Child-Pugh class C and 10 patients were classified as Child-Pugh class B. Based on the findings of Angeli et al. [10], it was determined that a significant proportion of patients, specifically 55%, who exhibited low levels of serum sodium were classified under child pugh class C.

According to the study conducted by Shaikh et al. [13], there was a higher prevalence of low serum sodium levels observed in patients diagnosed with severe liver failure, specifically those classified under Child-Pugh class C.

This suggests that there is a positive correlation between the severity of hyponatremia and the severity of liver disease.

In the current study, it was observed that there was no discernible variation in ascites among the three groups of patients with hyponatremia. However, among individuals with serum sodium levels equal to or less than 130 meq/L, there is a higher occurrence of significant ascites that necessitates the performance of paracentesis. In the study conducted by Angeli et al. [10], it was observed that a lower level of serum sodium was correlated with a higher prevalence of refractory ascites, increased fluid accumulation, and an increased probability of undergoing paracentesis. Shaikh et al. (year) found that individuals with a serum sodium level below 130 meq/L exhibit a greater prevalence of refractory ascites.

Based on the findings of Angeli P et al, it was observed that hepatic encephalopathy occurred in 38% of patients with serum levels below 130meq/L. Furthermore, the prevalence of hepatic encephalopathy was found to be 24% among patients with serum sodium levels ranging from 131 to 135 meq/L, and 15% among patients with serum sodium levels exceeding 135meq/L. In the current investigation, it was observed that 60% of individuals exhibiting serum sodium levels below 130

meq/L experienced hepatic encephalopathy, whereas 39.2% of patients with serum sodium concentrations ranging from 131 to 135 meq/L displayed hepatic encephalopathy. Among patients whose serum sodium levels exceeded 136 meq/L, it was observed that 8.5% of them experienced hepatic encephalopathy. Therefore, a substantial correlation exists between hepatic encephalopathy and hyponatremia (p value = 0.00001). The findings of this investigation align with the aforementioned studies.

The current investigation reveals that Hepatorenal syndrome is observed in 28% (10 out of 37) of patients exhibiting serum sodium levels below 130meq/L, in contrast to a prevalence of 14.28% (6 out of 42) among patients with serum sodium levels ranging from 131 to 135meq/L. The prevalence of hepatorenal syndrome in patients with serum sodium levels greater than 135meq/L is 6.38% (4 out of 71 individuals). A notable disparity in the occurrence of hepatorenal syndrome is observed among the three groups, as supported by statistical analysis. A statistically significant correlation has been observed between hepatorenal syndrome and hyponatremia, as indicated by a p -value of 0.038. Based on the findings of Kim JH et al⁴, the prevalence of Hepatorenal syndrome is observed to be 17% among patients with a serum sodium level below 130meq/L, in contrast to a prevalence of 10% among patients with a serum sodium level ranging from 130-135meq/L. Based on the findings of Angeli P et al², the prevalence of hepatorenal syndrome is observed to be 17.6% among patients exhibiting a serum sodium level below 130 meq/L, in contrast to a prevalence of 10% among patients with a serum sodium level ranging from 130 to 135 meq/L. Hyponatremia represents a significant riskfactor in the pathogenesis of hepatorenal syndrome among individuals afflicted with ascites. The heightened susceptibility to hepatorenal syndrome could potentially be attributed to a more pronounced impairment of circulatory function in individuals afflicted with hyponatremia.

The current investigation reveals a higher mortality rate among patients exhibiting low serum sodium levels (≤ 135 meq/L) in comparison to individuals with normal sodium concentrations. In the group of patients with low serum sodium concentration, a total of eight fatalities were observed, whereas no deaths were reported among patients with normal serum sodium levels. All of the reported fatalities were observed in individuals with elevated Model for End-Stage Liver Disease (MELD) scores. The average Model for End-Stage Liver Disease (MELD) score in the expired group of the current study was 23 ± 7.76 . The average MELD-Na score in the group of patients who died was 27.37 ± 6.02 . The average MELD and MELD-Na scores among the patients who survived were 15.56 ± 7.18 and 18.75 ± 7.313 , respectively. Sodium is a constituent element within the composition of MELD. Several studies have proposed that the MELD-Na score demonstrates superiority over the MELD score in predicting mortality among patients who are awaiting liver transplantation. In a study conducted by Moini et al. [14], it was found that a serum sodium level below 130 meq/L and an elevated Model for End-Stage Liver Disease (MELD) score are strong indicators of early mortality in individuals who are on the waiting list for liver transplantation.

A decrease in serum sodium levels is considered to be a detrimental prognostic factor in individuals diagnosed with liver cirrhosis. Borroni et al. [11] conducted an inpatient study which demonstrated that the presence of hyponatremia is associated with an unfavourable short-term prognosis in terms of in-hospital mortality. The study conducted by Heuman et al. [15] indicates that the Model for End- Stage Liver Disease (MELD) score, persistent ascites, and low serum sodium levels (<135 meq/L) were identified as autonomous factors that can predict early mortality.

Conclusion

Dilutional hyponatremia is a common occurrence among individuals with cirrhosis, and reduced levels of sodium in the bloodstream have been linked to the development of severe complications associated with liver cirrhosis, such as hepatic encephalopathy and hepatorenal syndrome. Hyponatremia is additionally correlated with elevated morbidity and mortality rates among individuals with cirrhosis. Therefore, hyponatremia serves as a valuable indicator that can be utilised for evaluating the prognosis of individuals diagnosed with liver cirrhosis. The inclusion of sodium levels in the Model for End-Stage Liver Disease (MELD) score proves to be significantly more

advantageous than relying solely on the MELD score in order to evaluate the prognosis and determine the suitability of liver transplantation for a patient.

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