



“TO STUDY THE CLINICAL PROFILE OF PATIENT WITH HYPONATREMIA IN CIRRHOSIS OF LIVER.”

Medicine

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ABSTRACT

BACKGROUND: Dilutional hyponatremia in liver cirrhosis is caused by impaired free water clearance. Serum sodium levels correlate with survival in cirrhotic patients. Low serum sodium concentration is an independent predictor of mortality in patients with cirrhosis, but its relationship between the degree of dilutional hyponatremia and development of cirrhotic complications is unclear. **METHOD:** This prospective study was conducted on 60 patients of cirrhosis of liver admitted in the medicine wards at Sir Takhtasinhji General Hospital, Bhavnagar, during study period of 2 year, after taking consent of patients. All patients were subjected to detailed history and clinical examination. Severity of cirrhosis were assessed by Child-Pugh score. A total score from 5-6, 7-9 and 10-15 was classified as class A, B, C respectively. Presence of complications like ascites, portal hypertension, hepatic encephalopathy, hepatorenal syndrome, gastrointestinal bleeding, coagulopathy are checked. The patients are followed at intervals at 3 and 6 month. **RESULT:** The serum sodium level was strongly associated with the severity of liver cirrhosis as assessed by Child-Pugh and MELD scores (p value 0.0298, 0.0250 respectively). Sodium levels <130 meq/L indicated the existence of grade III or higher hepatic encephalopathy (p value 0.0112) and Hepatorenal syndrome (p value 0.0433) and greater frequency of portal hypertension (p value <0.0001) but not gastrointestinal bleeding, ascites, coagulopathy. **CONCLUSION:** Dilutional hyponatremia is frequent in cirrhotic patients and low serum sodium level are associated with severe complications like hepatic encephalopathy, hepatorenal syndrome, portal hypertension. Early diagnosis and treatment of hyponatremia is important to prevent complications of liver cirrhosis.

KEYWORDS

Hyponatremia In Cirrhosis Of Liver, Child Pugh And MELD Score, Hepatic Encephalopathy, Hepatorenal Syndrome, Portal Hypertension.

INTRODUCTION

Hyponatremia is serum sodium less than 135 meq/L. Hyponatremia is the most common electrolyte disorder.^[1] Its homeostasis is vital to the normal physiologic function of cells. A disturbance in body water homeostasis is a common feature of advanced cirrhosis. This is characterized by a higher rate of renal retention of water in relation to sodium due to a reduction in solute-free water clearance. The consequent inability to adjust the amount of water excreted in the urine to the amount of water ingested leads to dilutional hyponatremia. Hyponatremia, an excess of water in relation to the sodium in the extracellular fluid, is the most common electrolyte disorder in hospitalized patients and particularly so in patients with cirrhosis.^[2]

In recent years, great advances have been made in the knowledge of the pathogenesis of reduced solute-free water clearance in patients with advanced cirrhosis. The inability to excrete an adequate amount of solute-free water in the urine is related to several factors, the most important of which is increased vasopressin release. A reduction of effective circulating volume due to arterial splanchnic vasodilation is considered the afferent factor leading to a baroreceptor mediated non osmotic stimulation of vasopressin release in cirrhosis.

Clinically significant hyponatremia is relatively uncommon and is nonspecific in its presentation; therefore, the physician must consider the diagnosis in patients presenting with vague constitutional symptoms or with altered level of consciousness. Identifying the etiology and risk factors for hyponatremia will help in reducing its incidence and minimize the complications associated with hyponatremia and improve the overall cost of health care. Patients with hyponatremia have a poor survival compared with that of patients without hyponatremia.^[3] According to several recent studies; hyponatremia occurring as a result of a reduced solute-free water clearance was a key prognostic factor in patients with liver cirrhosis when hyponatremia was incorporated into the MELD score.^[3]

There is a lack of Indian data on clinical spectrum of hyponatremia in cirrhosis and treatment strategies to be adapted in various clinical studies; therefore, we planned to undertake this prospective follow up study in patients with cirrhosis at our tertiary care center.

AIMS AND OBJECTIVES

AIM

- To study the clinical profile of patient with hyponatremia in cirrhosis of liver.

OBJECTIVES

- To study severity of hyponatremia in cirrhosis of liver.
- To evaluate association between hyponatremia and complications in cirrhosis and its prognostic significance.

MATERIALS AND METHOD

Study was carried out on patients diagnosed as cirrhosis of liver on the basis of USG findings with hyponatremia and admitted to Medicine wards of Sir T. General Hospital, Bhavnagar after taking permission from Institutional review board and scientific committee, government medical college, Bhavnagar.

- Study Design:** Prospective study
- Sample Size:** 60 Patients
- Study Duration:** September-2018 to September-2020

INCLUSION CRITERIA

- Patients 12 years and above.
- All the indoor patients presenting with hyponatremia <135meq/L in liver cirrhosis.
- Diagnosis of having liver cirrhosis by clinically and ultrasonographical findings.

EXCLUSION CRITERIA

- Patient's age <12 years.
- Patient having hyponatremia without liver cirrhosis.
- Patient with cardiac failure.
- Patient on diuretic therapy.
- Patient with chronic kidney disease.
- Patient on drugs like SSRI, TCA, MAO inhibitors, cytotoxic drugs etc.

METHOD OF COLLECTION OF DATA

The patients are selected based on clinical examinations, biochemical tests and ultrasound abdomen. Informed consent will be obtained from all patients to be enrolled for the study. The data of the patients was collected and recorded in case record form (CRF). The patient's demographics and the status of the patients at the time of inclusion (inpatient or outpatient) as well as severity of cirrhosis were assessed according to Child-Pugh score. A total score from 5-6, 7-9 and 10-15 was classified as class A, B and C respectively. Presence of complications like ascites, portal hypertension, hepatic encephalopathy, hepatorenal syndrome, gastrointestinal bleeding, coagulopathy are checked in every patients. The patients are followed over a period of 6 month with serum sodium levels measured at regular

intervals at 3 month and 6 month.

STATISTICAL METHODS

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean $\pm$ SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. P value of less than 0.05 was considered as significant. Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups Fisher Exact test has been used to find significance of study parameters on categorical scale between two or more groups.

Statistical software: The Statistical software namely SPSS 15.0, Stata 8.0, Med Calc 9.0.1 and Systat 11.0, Instat were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

RESULT

This study is conducted in 60 cirrhotic patients out of which 50 (84%) are males and 10 (16%) are females. The mean age of the patients was 44.55 ± 9.44 years. Causative factors for liver cirrhosis included alcoholism in 87% of patients, hepatitis B in 13% of patients and hepatitis C in 0% of the patients. Alcohol was the most common etiology in present study, seen in 87% patients.

Patients were classified according to serum sodium level, 40 (67%) belong to serum sodium level ≤ 130 meq/L and 20 (33%) belong to serum sodium level 131-135 meq/L.

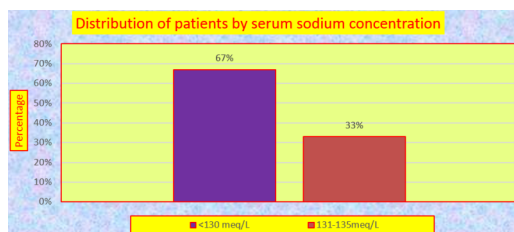


FIGURE -1

The mean MELD score of patients with serum sodium concentration ≤ 130 meq/L was 21.55 ± 7.30 . It was 17.5 ± 4.07 in group with serum sodium levels between 131-135 meq/L. There was significant difference with respect to MELD score in these two groups (p value = 0.025).

TABLE - 1: Comparison of the mean MELD score of two groups

MELD SCORE	< 130 meq /L (%) (n=40)	131-135 meq/L (%) (n=20)	P value
11-15	10 (25%)	07 (35%)	0.025
16-20	11 (27.5%)	10 (50%)	
21-25	08 (20%)	02 (10%)	
26-30	05 (12.5%)	01 (05%)	
31-35	05 (12.5%)	0 (0%)	
36-40	01 (2.5%)	0 (0%)	
Mean MELD	21.55 $\pm$ 7.30	17.5 $\pm$ 4.07	

The mean Child-Pugh score in the group with serum sodium levels ≤ 130 meq/L was 11.1 ± 1.27 . The mean score in the group with serum sodium levels between 131-135 meq/L was 10.3 ± 1.38 . There was significant difference in these two groups with respect to Child-Pugh score (p value = 0.0298). Low serum sodium had significantly high child pugh class compared to normal serum sodium. Among 40 patients with serum sodium ≤ 130 meq/L, 36 patients were in Child-Pugh class C and 4 patients were in Child-Pugh class B. Among 20 patients with serum sodium levels between 131-135 meq/L, 15 patients were in class C and 5 patients were in class B.

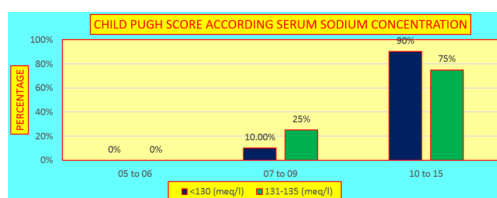


FIGURE-2

Out of 60 patients of cirrhosis, 58 patients (97%) had ascites, 50 patients (83%) had portal hypertension, 23 patients (38%) had hepatic encephalopathy, 14 patients (23%) had gastrointestinal bleeding, 5 patients (8%) had coagulopathy, 13 patients (22%) had Hepatorenal syndrome.

In the present study, ascites is present in all 40 patients with serum sodium levels ≤ 130 meq/L. There is no statistical significant difference in these two groups with respect to ascites.

TABLE-2: Frequency of complications by Serum sodium concentration

COMPLICATIONS	≤ 130 meq/L (n = 40)	131-135 meq/L (n = 20)	P value
Ascites	40 (100%)	18 (90%)	0.1073
Portal hypertension	40 (100%)	10 (50%)	0.0001
Hepatic encephalopathy	20 (50%)	03 (15%)	0.0112
GI bleeding	12 (30%)	02 (10%)	0.1117
Coagulopathy	04 (10%)	01 (5%)	0.6563
Hepatorenal syndrome	12 (30%)	01 (5%)	0.0433

Portal hypertension is present in all 40 patients with serum sodium level ≤ 130 meq/L (100%). 10 out of 20 patients (50%) with serum sodium levels between 131-135 had portal hypertension. There was significant statistical difference in these two groups with respect to portal hypertension (p value 0.0001).

Hepatic encephalopathy was present in 20 patients out of 40 (50%) with serum sodium levels ≤ 130 meq/L. 3 out of 15 patients (15%) with serum sodium levels between 131-135 meq/L had hepatic encephalopathy. There is significant statistical difference in these two groups with respect to hepatic encephalopathy (p value 0.0112).

Gastrointestinal bleeding is present in 12 out of 40 patients with serum sodium levels ≤ 130 meq/L. There is no significant statistical significance in these two groups with respect to gastrointestinal bleeding (p value = 0.1117).

Coagulopathy is present in 4 out of 40 patients with serum sodium levels ≤ 130 meq/L. There is no significant significance in these two groups with respect to coagulopathy (p value = 0.6563).

Hepatorenal syndrome is present in 12 out of 40 patients in patients with serum sodium ≤ 130 meq/L. 1 out of 20 patients (5%) with serum sodium levels between 131-135 meq/L had hepatorenal syndrome. There is statistical significance in these two groups with respect to hepatorenal syndrome (p value = 0.0433).

In the group of serum sodium levels ≤ 130 meq/L, 5 (12.5%) patients died, while 2 (10%) patients died in group of serum sodium levels 131-135 meq/L. Hence statistically significant difference was not found in mortality among these two groups.

DISCUSSION

Hyponatremia is frequent in cirrhosis of liver. This is thought to be due to a higher rate of renal retention of water in relation to sodium due to a reduction in solute free water clearance.

Frequency of causative factors among these two groups were comparable and statistical difference was found in this respect (p value of 0.0431).

In the present study, there was significant difference in these groups with respect to child-pugh (p value = 0.0298). In patients with hyponatremia with serum sodium concentration ≤ 130 meq/L the mean child-pugh score was higher as compared to the mean child-pugh score in group with serum sodium levels between 131-135 meq/L. Among 40 patients with serum sodium levels ≤ 130 meq/L, 36 patients were in child-pugh class C and 4 patients were in class B, among 20 patients with serum sodium levels between 131-135 meq/L, 15 patients were in class C and 5 patients were in class B. According to Angeli P et al^[5], 55% of patients with low serum sodium levels belong to child pugh class C. In Shaikh S et al^[7], low serum sodium levels were more frequent in patients with severe liver failure (child-pugh class C). This indicate that as hyponatremia became more severe, severity of liver disease is also more.

In the present study Mean MELD score in two groups, ≤ 130 meq/L,

131-135 meq/L and was 21.55 ± 7.30 , 17.5 ± 4.07 respectively. There was significant difference with respect to MELD score in two groups (p value of 0.0250). This is correlate with Saibaba Madhavrao Ankushkar study^[4] in which Mean MELD score in two groups, ≤ 130 meq/L, 131-135 meq/L was 25.91 ± 8.092 , 28.00 ± 8.385 , respectively. There was significant difference with respect to MELD score in two groups (p value ≤ 0.0001).

In present study, in patients with hyponatremia there is no difference among the two groups with respect to ascites. But in patients with serum sodium ≤ 130 meq/L, there is increased incidence of gross ascites requiring paracentesis. In Angeli P et al^[5] study also, low serum sodium level was associated with higher prevalence of refractory ascites, greater fluid accumulation, greater likelihood of undergoing paracentesis. According to Shaikh et al,^[7] the patients with serum sodium levels < 130 meq/L have higher frequency of refractory ascites.

According to Angeli P et al^[5], hepatic encephalopathy was present in 38% of the patients with serum sodium < 130 meq/L and is present in 24% of patients with serum sodium between 131-135 meq/L. In the present study, 50 % of patients with serum sodium levels < 130 meq/L had hepatic encephalopathy compared to 15% patients with serum sodium concentration between 131-135 meq/L had hepatic encephalopathy. Hence there is significant association between hepatic encephalopathy and hyponatremia (p value = 0.0112), the results of this study were similar to the above mentioned other studies.

In the present study, Hepatorenal syndrome is present in 30% of patients with serum sodium levels < 130 meq/L compared to 5% of patients with serum sodium concentration between 131-135 meq/L. There is significant statistical difference in frequency of hepatorenal syndrome in the two groups. There is significant association between hepatorenal syndrome and hyponatremia (p value = 0.0433). According to Kim JH et al^[6], Hepatorenal syndrome is present in 17% of patients serum sodium < 130 meq/L compared with 10% in patients with serum sodium 131-135 meq/L. According to Angeli P et al^[5], hepatorenal syndrome present in 17.6% patients with serum sodium < 130 meq/L compared to 10% in patients with serum sodium 131-135 meq/L. Hyponatremia is major risk factor for development of hepatorenal syndrome in patients with ascites.

In present study, portal hypertension present in 100% of patients with serum sodium levels < 130 meq/L compared to 50 % of patients with serum sodium concentration between 131-135 meq/L. There is significant statistical difference in frequency of hepatorenal syndrome in the two groups. (p value = 0.0001) This is correlate with Saibaba Madhavrao Ankushkar study^[4] in which 100% of patients with serum sodium level < 135 meq/L compared to 95% patients with serum sodium concentration between 131-135 meq/L (p value = 0.011).

In the present study, mortality is more in patients with low serum sodium (≤ 130 meq/L). 5 patients died in group with low serum sodium concentration < 130 meq/L. This is correlate with Saibaba Madhavrao Ankushkar study^[4] in which 12 patients died in group had serum sodium < 135 meq/L.

CONCLUSION

Dilutional hyponatremia is frequent in cirrhotic patients and low serum sodium levels in cirrhosis are associated with severe complications of liver cirrhosis like hepatic encephalopathy, hepatorenal syndrome, portal hypertension and high morbidity and mortality. Early diagnosis and treatment of hyponatremia is important to prevent possible complications of liver cirrhosis.

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