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Original article

Hyponatremia in patients with chronic liver diseases

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Abstract

Background and Aim: Although many studies have studied the relationship of cirrhosis with various electrolyte imbalances, however there is a scarcity of data correlating disturbances in serum sodium concentration with mortality in patients with decompensated hepatic cirrhosis in terms of survival rates and prognosis of these patients. The objective of the study was to assess the frequency of hyponatremia in patients of chronic liver disease.

Materials and Method: Data were collected from 200 patients admitted in medical wards. Patients were divided into groups based on serum sodium levels and the relevant parameters analyzed among the groups.

Results: Alcohol was the most common cause of DCLD in this study followed by chronic hepatitis B and chronic hepatitis C. 43.3% of patients had serum sodium levels ≥136. 32.99% of patients had serum sodium levels between 131 and 135 while 23.71% of patients had serum sodium levels less than or equal to 130.

Conclusion: Lower serum sodium levels are associated with increased MELD score, increased CPS score and increased mortality indicating the inverse relationship between serum sodium levels and the severity of disease.

Keywords: Hyponatremia, Liver Disease, cirrhosis

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Introduction

Chronic liver disorders (CLD) are a major source of morbidity and death globally. Multiple etiological causes contribute to a similar clinicopathological pathophysiology in Chronic liver disorders, albeit progression rates and clinical course may differ. Hyponatremia is common in patients with advanced stages of liver diseases.[1] Patients with chronic liver disease (CLD) may develop hyponatremia due to either hypovolemia or hypervolemia. Hyponatremia in CLD is currently defined with a level of serum sodium less than 130 meq/L.[2,3]
Electrolyte imbalances are one of the major and well documented consequences of chronic liver disease that develop as a result of third space shifting of body water, decreased effective circulatory volume, poor kidney perfusion, excessive secretion of vasopressin and its altered metabolism, secondary hyperaldosteronism as well as use of diuretics and aldosterone receptor antagonists.[4,5]

Hyponatremia is relatively common in approximately half of the hospitalised patients with chronic liver disease and in nearly 40% of the outpatients with cirrhosis. The coexistence of hyponatremia seems to have several clinical implications in cirrhosis, being associated with increasing Child Pugh Score, massive ascites, hepatorenal syndrome, hepatic encephalopathy and spontaneous bacterial peritonitis. The mortality of patients with hyponatraemia is high in comparison with the patients having normal serum sodium levels.[6,7]

The clinical course of CLD patients is more often complicated due to intensification of abnormalities of renal function and electrolytes imbalance.5 Inside patients' body disturbance of water is main indication of advance stage. This disturbance of water is associated with presence of ascites and is described by progression of dilutional hyponatremia, which is a common complication and consequence of CLD.[8,9] It has been indicated that hyponatremia can be a prognostic factor for CLD patients. In healthy individuals, sodium concentration is sustained properly stable in spite of significant deviations in daily fluid intake, by homeostatic mechanisms which persuade alterations in renal water management.[10,11]
Although many studies have studied the relationship of cirrhosis with various electrolyte imbalances, however there is a scarcity of data correlating disturbances in serum sodium concentration with mortality in patients with decompensated hepatic cirrhosis in terms of survival rates and prognosis of these patients. The objective of the study was to assess the frequency of hyponatremia in patients of chronic liver disease.

Material and Methods

SOURCE OF STUDY:
The study was conducted on consecutive patients admitted with DCLD in Medical Wards in Medical College and Hospital during the study period of one year. Ethical Committee clearance obtained from Institution. Informed consent was obtained from the patients enrolled in the study. The data of the patients were collected using a proforma. The first section of the proforma contains patient's demographic profile with detailed history. The second section contains

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detailed clinical examination that will be carried out at the time of admission. The third section contains investigations that were done to aid the diagnosis and the serum sodium level.

Patients were selected based on history, examination, laboratory investigations and imaging suggestive of the diagnosis of Decompensated Chronic Liver Disease. The presence of various complications and the outcome of the patients were monitored. The severity of the disease was calculated using MELD score and Child Pugh Score. Ascites was classified in to three grades:

Grade I- presence on examination not clear, but observed in imaging;

Grade II - easily made out examination and palpation;

Grade III - severe abdominal distension requiring large volume paracentesis.

Hepatic Encephalopathy was graded using West Haven Criteria. The inclusion and the exclusion criteria of the study are below:

INCLUSION CRITERIA:

All patients with Decompensated Chronic Liver Disease diagnosed by examination, laboratory investigations and radiological imaging.

EXCLUSION CRITERIA:

1. Patients with cardiac failure
2. Patients with chronic kidney disease
3. Patients on drugs such as SSRIs, TCA, MAO inhibitors, cytotoxic drugs etc.

Around 5ml of whole blood, which was free from hemolysis was initially centrifuged at 3000 rates per minute at 10 minutes. The separated serum was analyzed for sodium levels using an automated electrolyte analyzer. Hyponatremia among these patients with chronic liver diseases were defined as a serum sodium level of less than 130meq/L.

The collected data were entered in a Microsoft Excel Sheet and tables were generated using Microsoft Word and Excel. Statistical analysis were done using medcalc 15.8, Minitab 17, IBM SPSS 22. Quantitative data was analysed using Mean, Median, Mode and Standard Deviation(SD). Qualitative data was analysed using Chi Square Test, One way ANOVA and Fisher's test. Difference between two variables is considered significant when 'p' value is less than 0.05.

Results

Data were collected from 200 patients admitted in our hospital. The mean age of the patients was 47.28 years with a range of 25-75 years. Out of the 200 patients, 180 patients were males and 20 patients were females.

Alcoholic liver disease was the commonest cause of DCLD in the present study that accounts for 92.5% while chronic hepatitis B and hepatitis C was found to be the causative factor in 6.2% and 1.3% respectively. The mean concentration of sodium of all patients was 138.20 with a range of 120-150.

Based on the serum sodium levels, 23.71% of patients had serum sodium levels less than or equal to 130. 32.99% of patients had serum sodium levels between 131 and 135, while 43.3% of patients had serum sodium levels ≥136. No patients presented with serum sodium greater than 145. The mean MELD score was found to be 13.54 with a range of 7.5- 33.7.

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Alcohol was the most common cause of DCLD in this study followed by chronic hepatitis B and chronic hepatitis C. 43.3% of patients had serum sodium levels ≥136. 32.99% of patients had serum sodium levels between 131 and 135 while 23.71% of patients had serum sodium levels less than or equal to 130.

Patients were classified into three groups based on the serum sodium level to assess the association between serum sodium levels and patient characteristics, complications and severity of disease as calculated by MELD score and CPS. Those with serum sodium levels less than or equal to 130 formed one group while those with serum sodium levels between 131-135 and those with ≥136 were the other two groups. Mean age of patients with sodium levels ≤130 was 53+19.29, while in those with serum sodium levels 131- 135 and ≥136 were 47.38+16.98 and 52.88+17.26 respectively. No statistical difference was found among the three groups. (p value - 0.877).

Serum sodium levels had a strong association with severity of disease as calculated by Child Pugh Class. Among those with serum sodium levels ≤130, 25 belonged to class B and 24 belonged to class C. Among patients with serum sodium levels between 131-135; 4 belonged to class A, 48 belonged to class B and 14 belonged to class C. Among patients with serum sodium levels ≥136, 18 belonged to class A, 58 belonged to class B and 9 belonged to class C. (p value <0.0001)

Patients with serum sodium levels ≤130 had a mean MELD score of 20.45+9.64, while those with levels between 131-135 and ≥136 had mean scores of 18.23+8.35 and 14.0+1.45 respectively. The difference in MELD scores among the three groups was statistically significant. (p value <0.0001)

No statistical difference was found among the three groups with respect to gender and causative factor.(p value – 0.479, 0.376 respectively). All patients presented with abdominal distension and lower limb swelling at the time of admission, while clinically detectable jaundice was found in around 30% of patients. Around 20% of patients presented with GI bleeding while 14 patients presented with history of altered sensorium.

When compared to patients with serum sodium levels ≥136, patients with serum sodium levels ≤130 had a significantly increased risk for complications: 109.29 sodium level was seen in Hepatic Encephalopathy, 8.36 sodium level was seen in for GI bleeding, 5.69 sodium level was seen in for Coagulopathy, 78.2 sodium level was seen in for Hepatorenal syndrome and 46.61 sodium level was seen in for SBP. Ascites and portal hypertension did not have statistical difference and increased risk.

When compared to patients with serum sodium levels ≥136, patients with serum sodium levels between 131 and 135 had a significantly increased risk for complications: 13.42 sodium level was seen in Hepatic Encephalopath; 1.30 sodium level was seen in for SBP. Other complications did not have statistical difference among the two groups.

Among 46 patients with serum sodium levels ≤130, 14 patients died. Among 66 patients with serum sodium levels between 131 and 135, 4 patients died. There were no deaths among patients

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with sodium levels ≥136. The difference in mortality among these three groups was statistically significant.

Table 1: Distribution of Patients according to Complications

Complications	≤130 meq/L	131-135meq/L	≥136 meq/L
Ascites	46	64	84
Hepatic Encephalopathy	26	8	0
Coagulopathy	14	4	6
SBP	16	8	0
Portal Hypertension	46	64	74
GI Bleeding	18	14	6

Discussion

A significant proportion of patients with DCLD have abnormal serum sodium concentration. Hyponatremia is the most common occurrence in our study. No patients presented with serum sodium levels greater than 145. 58.4% of patients had serum sodium levels less than 135, while 25.58% patients had serum sodium levels than 130. Serum sodium levels less than 120 were uncommon.

Angeli P[12] et al collected data of 997 cirrhosis patients from hepatology departments across Europe, Asia, North America and South America. Her study revealed that 50.6% patients had normal serum sodium levels, 27.8% patients had sodium levels between 131-135 mEq/L and 21.6% patients had serum sodium levels less than or equal to 130 mEq/L.

Various studies have established that lower sodium levels were associated with ascites that are difficult to manage with diuretics and requiring frequent large volume paracentesis. Arroyo et al[13] noted that patients having serum sodium less than 130 mEq/L had a relatively low GFR and subsequently decreased free water clearance. These patients responded poorly to diuretics when compared with those who had sodium levels more than 130 mEq/L.

Angeli P et al and Bernardi et al[14] also found that poorer response to diuretics was associated with lower serum sodium concentration compared to patients who showed response to diuretics. The present study also found that patients with lower sodium levels had higher grade of ascites.

The present study also showed that patients with sodium levels ≤130 mEq/L had higher MELD score and Child Pugh Score compared to other two groups. The present study also shows increased mortality among patients with lower sodium levels.

Conclusion

Hyponatremia is the most common abnormality in this study. Patients with serum sodium concentration less than 130 mEq/L are the most affected. Lower serum sodium levels are associated with increased MELD score, increased CPS score and increased mortality indicating the inverse relationship between serum sodium levels and the severity of

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disease. Thus patients with decreased serum sodium levels should be considered a high risk population because of the increased frequency of complications and mortality.

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