Print ISSN: 2321-6379
Online ISSN: 2321-595X

Original Article

Study of Correlation between Serum Sodium and Severity in Chronic Liver Disease

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Abstract

Introduction: The normal range of serum sodium is 135–145 mEq/L. Its homeostasis is vital to the functioning of the cell. An imbalance in the regulation of total body water can lead to abnormal sodium levels. Chronic liver disease (CLD) is associated with disturbance in water homeostasis leading to dysnatremias.

Aims and Objectives: This study aims to study the prevalence of hyponatremia in CLD patients and to correlate the serum sodium levels and severity in CLD patients assessed by Child-Pugh score and MELD score.

Materials and Methods: The study is conducted on consecutive patients admitted with CLD in medical wards (male and female) in Government General Hospital during the study period September 2018 to Febraury 2020.

Results: Alcohol is the most common etiology of CLD in this study followed by hepatitis B.

Conclusion: CLD is associated with abnormal serum sodium concentration. Hyponatremia is the most common abnormality in this study.

Key words: Ascites, Cirrhosis, Hyponatremia

INTRODUCTION

The normal range of serum sodium is 135–145 mEq/L. Its homeostasis is vital to the functioning of the cell. An imbalance in the regulation of total body water can lead to abnormal sodium levels. Chronic liver disease (CLD) is associated with disturbance in water homeostasis leading to dysnatremias.[1-5]

Hyponatremia is defined as concentration of sodium <135 mEq/L. It occurs when there is excess of water in relation to sodium. It is the most common electrolyte disorder in hospitalized patients and more so in CLD patients. A disturbance in total body water regulation leading to decreased clearance of solute free water and the consequent inability to match the urine output to the amount of water ingested leads to dilutional hyponatremia.

Hypernatremia is defined as concentration of sodium more than 145 mEq/L. It is associated with high mortality rate. Hypernatremia, though uncommon compared to hyponatremia in CLD patients, occurs due to use of osmotic cathartics and upper gastro intestinal bleeding. If present, it is associated with increased mortality.

Recent studies have reported that lower serum sodium levels were associated with increased complications and mortality leading to incorporation of sodium in the MELD score. Therefore, we undertook this study in our tertiary hospital to study serum sodium levels in patients admitted with CLD and to establish its significance.

Aims and Objectives

The aims of the study were as follows:

1. To study the prevalence of hyponatremia in CLD patients

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www.ijss-sn.com

Month of Submission : 05-2020
Month of Peer Review : 06-2020
Month of Acceptance : 07-2020
Month of Publishing : 07-2020

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2. To correlate the serum sodium levels and severity in CLD patients assessed by Child-Pugh score and MELD score.

MATERIALS AND METHODS

The study is conducted on consecutive patients admitted with CLD in medical wards (male and female) in Government General Hospital, during September 2018 to Febraury 2020.

Study Design

This study is a cross-sectional observational study.

Method of Collection of Data

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 pro forma. The pro forma contains patient's demographic profile with detailed history, clinical examination that will be carried out at the time of admission, investigations that were done to aid the diagnosis, and the serum sodium level. Patients were selected based on history, examination, laboratory investigations, and radioimaging suggestive of the diagnosis of CLD. 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 into three grades: Grade I – presence on examination not clear, but observed in imaging; Grade II – easily made out examination and palpation; and Grade III – severe abdominal distension requiring large-volume paracentesis. Hepatic encephalopathy was graded using West Haven criteria.

Inclusion Criteria

All patients with CLD diagnosed by examination, laboratory investigations, and radiological imaging were included in the study.

Exclusion Criteria

The following criteria were excluded from the study:

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

Statistics

The collected data were entered into a Microsoft Excel sheet. Graphs and tables were generated using Microsoft Word and Microsoft Excel. Statistical analysis was done using IBM, SPSS. Quantitative data were analyzed using mean, median, mode, and standard deviation. Qualitative data were analyzed using Chi-square test, one-way ANOVA, and Fisher's test. Difference between two variables is considered significant when $P < 0.05$ was obtained.

RESULTS

Data were collected from 100 patients admitted in our hospital [Table 1]. The mean age of the patients was 46.39 years with a range of 33–80 years [Table 2]. Out of the 100 patients, 85 were male and 15 were female [Table 3].

Alcoholic liver disease was the most common cause of CLD in this study accounting for 88% while chronic hepatitis B was found to be the causative factor in 6%, HBV and alcohol were seen in 5% of patients. One patient had HCV and alcohol as etiology for CLD. The mean concentration of sodium of all patients was 134.03 meq/L with a range of 118–144 meq/L.

Table 1: Clinical presentation of patients at time of admission

Clinical presentation	Number of patients	% of patients
Abdominal distension	100	100
Lower limb swelling	100	100
Altered sensorium	18	18
Gastrointestinal bleeding	19	19

Table 2: The demographic details and causes of CLD

Parameters	Number of patients	% of patients	Mean	Standard deviation
Age	100		46.39	10.227
Gender				
Male	85	85		
Female	15	15		
Cause of CLD				
Alcohol	88	88		
HBV	6	6		
HCV	0	0		
ALC and HBV	5	5		
ALC and HCV	1	1		
Meld score			16.39	6.998
Serum NA			134.03	5.321
≤130 meq/L	26	26		
131–135 meq/L	31	31		
≥136 meq/L	43	43		

Table 3: Frequency of complications

Complications	Number of patients	% of patients
Ascites	100	100
Hepatic encephalopathy	18	18
GI bleeding	19	19
Coagulopathy	12	12
HRS	11	11
SBP	12	12

Based on the serum sodium levels, 26% of patients had serum sodium levels ≤130 meq/L. About 31% of patients had serum sodium levels between 131 and 135 meq/L, while 43% of patients had serum sodium levels ≥136 meq/L. No patients presented with serum sodium >145. The mean MELD score was found to be 16.39 with a range of 7–34.

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 ≤130 meq/L formed one group while those with serum sodium levels between 131 and 135 meq/L and those with ≥136 meq/L were the other two groups. Mean age of patients with sodium levels ≤130 meq/L was 47.23 ± 10.045 years while in those with serum sodium levels 131–135 meq/L and ≥136 meq/L were 46 ± 9.349 years and 46.16 ± 11.11 years, respectively. No statistical difference was found among the three groups ($P = 0.888$).

Serum sodium levels had a strong association with severity of disease as calculated by Child-Pugh class. Among those with serum sodium levels ≤130 meq/L, 13 belonged to Class B and 13 belonged to Class C. Among patients with serum sodium levels between 131 and 135 meq/L, 2 belonged to Class A, 23 belonged to Class B, and 6 belonged to Class C. Among patients with serum sodium levels ≥136 meq/L, 9 belonged to Class A, 30 belonged to Class B, and 4 belonged to Class C ($P = 0.0001$). Patients with serum sodium levels ≤130 meq/L had a mean MELD score of 25.12 ± 5.317, while those with levels between 131–135 meq/L and ≥136 meq/L had mean scores of 16.16 ± 4.390 and 11.28 ± 3.30, respectively. The difference in MELD scores among the three groups was statistically significant ($P = 0.001$). No statistical difference was found among the three groups with respect to age, gender, and causative factor.

All patients presented with abdominal distension and lower limb swelling at the time of admission. Around 19% of patients presented with GI bleeding while 18% of patients presented with a history of altered sensorium.

Among the 100 patients, ascites was present in all the patients present. Hepatic encephalopathy was present in 18% while GI bleeding was found in 19% of patients. Coagulopathy and SBP were found in 12% of patients, while hepatorenal syndrome was found in 11%.

Table 4, there was a significant difference in the occurrence of complications of CLD such as ascites ($P = 0.0001$), hepatic encephalopathy ($P = 0.001$), GI bleeding ($P = 0.005$), coagulopathy ($P = 0.025$), hepatorenal syndrome ($P = 0.0001$), and SBP ($P = 0.001$) among the three groups [Table 5].

Table 4: Frequencies of complications by serum sodium concentration

Complications	≤130 meq/L	131–135 meq/L	≥136 meq/L	*P*-value
Ascites	26	31	43	0.0001
HE	15	3	0	0.001
GI bleeding	10	6	3	0.005
Coagulopathy	7	2	3	0.025
HRS	11	0	0	0.0001
SBP	8	4	0	0.001

Table 5: Mortality according to serum sodium concentration

Mortality	≤130 meq/L	131–135 meq/L	≥136 meq/L	*P*-value
	8 (30.77%)	1 (3.34%)	0 (0%)	0.0001

Eight patients of the deaths have serum sodium concentration <130 meq/L, one death occurred in patients with serum sodium concentration between 131 and 135 meq/L, and no deaths in group with serum sodium concentration >136 meq/L. The difference in mortality among three groups is statistically significant ($P = 0.0001$).

DISCUSSION

A significant proportion of patients with CLD have abnormal serum sodium concentration. Hyponatremia is the most common occurrence in our study. No patients presented with serum sodium levels >145 meq/L. About 57% of patients had serum sodium levels <135 meq/L, while 26% of patients had serum sodium levels than 130 meq/L [Table 6].

Angeli *et al.* collected data of 997 cirrhosis patients from 28 hepatology departments across Europe, Asia, North America, and South America. Her study revealed that 50.6% of patients had normal serum sodium levels, 27.8% of patients had sodium levels between 131 and 135 mEq/L, and 21.6% of patients had serum sodium levels ≤130 mEq/L.

Kim *et al.* analyzed 188 patients admitted in Ilsan Paik Hospital, Korea, with complications of cirrhosis and found that 52.1% of patients had normal serum sodium levels, while 20.8% of patients had serum sodium levels between 131 and 135. About 27.1% of patients had serum sodium levels ≤130 [Table 7].

Raj *et al.* studied 100 patients with cirrhosis and found that 48% of patients had serum sodium levels more than 136 mEq/L, while 21% of patients had serum sodium

levels between 131 and 135 mEq/L. About 31% of patients had serum sodium levels ≤130 mEq/L.

Borroni *et al.* studied 156 patients admitted with cirrhosis and found that 29.8% of patients had serum sodium levels ≤130 mEq/L [Table 8].

The results of the present study extend the observations made by the above-mentioned studies that decompensated liver disease is associated with abnormal serum sodium concentration. It also shows that hyponatremia is the common abnormality with more than half of the patients having serum sodium levels <135 mEq/L.

Various studies have established that lower sodium levels were associated with ascites that is difficult to manage with diuretics and requiring frequent large-volume paracentesis. Arroyo *et al.* noted that patients having serum sodium less than 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.

Table 6: Comparison of various studies showing distribution of patients according to serum sodium concentration

Studies	≤130 meq/L (%)	131–135 meq/L (%)	≥136 meq/L (%)
Present study	26	31	43
Angeli *et al.* (2006)	21.6	27.8	50.6
Kim *et al.* (2009)	27.1	20.8	52.1
Raja *et al.* (2016)	31	21	48

Table 7: Comparison of studies showing association between serum sodium concentration and hepatic encephalopathy

Studies	≤130 meq/L (%)	131–135 meq/L (%)	≥136 meq/L (%)
Present study	57.7	10.7	0
Angeli *et al.*	38	24	15
Kim *et al.*	43.1	35.8	24.4
Raja *et al.*	60.6	30.3	9

Table 8: Comparison of studies showing association between serum sodium concentration and hepato renal syndrome

Studies	≤130 meq/L (%)	131–135 meq/L (%)	≥136 meq/L (%)
Present study	42.3	0	0
Angeli *et al.*	17	10	6
Kim *et al.*	3.9	2.5	3
Raja *et al.*	77.7	22.2	0

Angeli *et al.* and Bernardi *et al.* 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.

Angeli *et al.* found that 38% of patients who had serum sodium levels ≤130 mEq/L had hepatic encephalopathy compared to 24% with serum sodium levels between 131 and 135 mEq/L.

Kim *et al.* found that 43.1% of patients with serum sodium levels ≤130 mEq/L developed hepatic encephalopathy compared to 35.8% with serum sodium levels between 131 and 135 mEq/L.

Raja *et al.* found that 60.6% of patients had hepatic encephalopathy with serum sodium concentration ≤130 meq/L.

In the present study, patients with serum sodium levels ≤130 mEq/L had increased frequency of hepatic encephalopathy compared to the other two groups.

Angeli *et al.* found that 17% of patients with serum sodium levels ≤130 mEq/L had hepatorenal syndrome compared to 10% and 6% in patients with serum sodium levels 131–135 mEq/L and more than 135 mEq/L, respectively.

Kim *et al.* reported that 3.9% of patients with serum sodium levels ≤130 mEq/L had hepatorenal syndrome compared to 2.5% and 3% in patients with serum sodium levels 131–135 mEq/L and more than 135 mEq/L, respectively.

Raja *et al.* found that 77.7% of patients had HRS with serum sodium concentration ≤130 meq/L.

In the present study, patients with serum sodium levels ≤130 mEq/L had increased frequency of hepatorenal syndrome compared to other two groups.

Angeli *et al.* found that low sodium level was associated with increased frequency of spontaneous bacterial peritonitis.

Kim *et al.* reported that 33.3% of patients with serum sodium levels ≤130 mEq/L had SBP compared to 30.7% and 16.3% in patients with serum sodium levels 131–135 mEq/L and ≥136 mEq/L, respectively.

The present study also lends support to the above observations. About 30.77% of patients with serum sodium levels ≤130 mEq/L had SBP compared to 13% of patients

Table 9: Comparison of studies showing association between serum sodium concentration and SBP

Studies	≤130 meq/L (%)	131–135 meq/L (%)	≥136 meq/L (%)
Present study	30.77	13	0
Kim *et al*.	33.3	30.7	16.3

with serum sodium levels between 131 and 135 mEq/L [Table 9].

Angeli *et al*., Kim *et al*., and Shaikh *et al*. found no association between GI bleeding and sodium levels. The present study showed increased frequency of GI bleeding in patients with low sodium levels.

Warren *et al*. reported that 15 out of 25 patients with decompensated liver disease had hypernatremia in their study. The present study had no patients with serum sodium levels more than 145 mEq/L.

Kim *et al*. found that lower sodium levels were associated with increased MELD score and Child Pugh score. This indicates that lower serum sodium levels were associated with severe disease.

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.

Summary

The study was conducted on 100 patients admitted with CLD in medical wards in GOVERMENT HOSPITAL/ GOVERNMENT MEDICAL COLLEGE SURYPETA, Telangana. Alcohol is the most common etiology of CLD in this study followed by hepatitis B. Hyponatremia is the most common sodium abnormality (57%). No patients presented with hypernatremia.

Patients were divided into three groups based on serum sodium; those with serum sodium levels ≥136 mEq/L comprised one group while those with 131–135 mEq/L and ≤130 mEq/L formed the other two groups.

Serum sodium level was not associated with age, gender, and etiology of CLD.

Serum sodium ≤130 meq/L indicated the existence of ascites ($P = 0.0001$), hepatic encephalopathy ($P = 0.001$), hepatorenal syndrome ($P = 0.0001$), and spontaneous bacterial peritonitis ($P = 0.001$). Patients with serum sodium <130 mEq/L had increased frequency of complications than those with ≥136 mEq/L.

There was a significant difference in severity scores such as MELD and CPS among the three groups. Patient with serum sodium levels ≤130 meq/L had increased mortality (30.7%; $P = 0.0001$).

CONCLUSION

CLD is associated with abnormal serum sodium concentration. Hyponatremia is the most common abnormality in this study. Age, gender, and cause of CLD did not have any association with serum sodium levels.

Serum sodium levels <135 mEq/L are associated with increased frequency of complications such as ascites, hepatic encephalopathy, hepatorenal syndrome, spontaneous bacterial peritonitis, and GI bleeding when compared to patients with serum sodium levels ≥136 mEq/L.

Patients with serum sodium concentration <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 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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How to cite this article: Kumar VS, Ashok RA. Study of Correlation between Serum Sodium and Severity in Chronic Liver Disease. Int J Sci Stud 2020;8(4):122-126.

Source of Support: Nil, **Conflicts of Interest:** None declared.