

A Study on Correlation of serum sodium levels with severity of the chronic liver disease

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Abstract

Introduction: A progressive decline in liver function lasting longer than six months, including the production of clotting factors and other proteins, the detoxification of hazardous metabolic waste products, and the excretion of bile, is known as chronic liver disease (CLD). The normal range of serum sodium is about 135-145 mEq/L. Its homeostasis is essential for cell function. Abnormal sodium levels can result from an imbalance in the body's overall water balance management. Patients having chronic liver disease often experience the complication of hyponatremia. Although hyponatremia is often described as having sodium level in those patients less than 135 mEq/L, in people with hepatic disease, the threshold is 130 mEq/L.

Material and Methods: This is a Prospective Cohort Study was done in the department of General Medicine at Rajshree Medical college, Bareilly Uttar Pradesh. The study population comprised of all patients attending OPD /IPD of medicine department at Rajshree Medical college and Hospital with diagnosis of Chronic Liver Disease fulfilling the inclusion criteria were enrolled for this study. Child Pugh and MELD scores was computed for each patient to determine the severity of cirrhosis. The West Haven criteria was used to make a clinical diagnosis of hepatic encephalopathy.

Results: Out of 132 patients, studied most of the patient comes in the 30-50 year age group i.e. 82(62.1%). The mean age of patients was 50.17 ± 10.58 , with a range of 30-80 years. Out of 132 patients, 56.8% subjects were do not had hepatic encephalopathy, 15.9% had grade I, 15.2% had grade II, 7.6% subjects had grade III encephalopathy, 4.5% subject had Grade 4. Association between Coagulopathy and serum sodium level, out of 109 study subjects 27 study subjects had serum sodium ≤ 130 meq/L, out of 23 study subjects with coagulopathy 13 study subjects had serum sodium ≤ 130 meq/L, on comparing there is significant difference with p value 0.011. Mean MELD score were significantly higher in patients with less serum concentration. In addition Child Pugh class C was significantly more in patients with serum sodium levels ≤ 130 meq/L as compared to other patients. Hepatic encephalopathy, hepatorenal syndrome, coagulopathy, variceal bleeding were found significantly more common in patients with serum sodium levels less than 130 meq/l.

Conclusion: In our study, advanced cirrhosis frequently has low serum sodium levels. Patients with low sodium levels are more likely to experience ascites, variceal haemorrhage, hepatic encephalopathy, and hepatorenal syndrome than those with normal serum sodium levels. They correlate well with serum sodium and the CPS and MELD score. These findings suggest that cirrhotic patients should have close monitoring of their serum sodium levels throughout their treatment.

Keywords: Serum sodium, Chronic liver disease, Hepatic encephalopathy

Introduction

A progressive decline in liver function lasting longer than six months, including the production of clotting factors and other proteins, the detoxification of hazardous metabolic waste products, and the excretion of bile, is known as chronic liver disease (CLD). It is a process where there is ongoing inflammation, destruction and regeneration of liver tissue which ultimately leads to fibrosis and cirrhosis.¹

Histologically, Cirrhosis is described as a widespread hepatic process that transforms healthy liver architecture into structurally aberrant nodules and is characterised by fibrosis. From liver damage to cirrhosis, the development might take weeks to years. A preclinical phase followed by clinical phase make up the course of cirrhosis. Once clinical manifestations such as ascites, encephalopathy, and variceal haemorrhage appear, the disease's remaining course is significantly shorter and typically deadly. GI bleeding, ascites, encephalopathy, SBP and hepatorenal syndrome, are the most frequent complications of CLD.²

Refractory ascites, hyponatremia, and decreased arterial blood pressure are some of the clinical indicators of advanced cirrhosis. These conditions are caused by portal hypertension, which elevates serum levels of renin/aldosterone, a reduced response to drugs which are vasoactive, and a reduced clearance of water. In several recent investigations, hyponatremia caused by a reduced water clearance which is solute free was revealed to be a significant prognostic factor in patients with liver cirrhosis when it was taken into account when calculating the MELD score.³

The sodium levels normally is about 135-145 mEq/L. Its homeostasis is essential for cell function. Abnormal sodium levels can result from an imbalance in the body's overall water balance management. Dysnatremias caused by a disruption in water homeostasis are a symptom of CLD.⁴

Patients having chronic liver disease often experience the complication of hyponatremia. Although hyponatremia is often described as having sodium level in those patients <135 mEq/L, in people with hepatic disease, the threshold is 130 mEq/L. The lower limit of normal for sodium levels, 135mEq/L, has been demonstrated to have substantial prognostic significance.⁵

Patients having CLD are relatively more likely to experience this electrolyte abnormality than other hospitalized patients. Dilutional hyponatremia results from a disturbance in the control of total body water that causes a decrease in the clearance of solute and the failure to balance the volume of urine produced with the amount of water consumed.⁶

A known consequence of severe chronic liver disease is hyponatremia, which is

thought to be caused by a disturbed balance of bodily water. In severe chronic liver disease, there is splanchnic vasodilatation causing reduction in effective arterial blood volume which serves as a stimulus for the non-osmotic activation of vasopressin release.⁷

Material and Methods

This is a Prospective Cohort Study was done in the department of General Medicine at Rajshree Medical college, Bareilly Uttar Pradesh.

The study population comprised of all patients attending OPD /IPD of medicine department at Rajshree Medical college and Hospital with diagnosis of Chronic Liver Disease fulfilling the inclusion criteria were enrolled for this study.

Inclusion Criteria:

1. All the patients above 18 years with CLD by history, clinical examination, laboratory investigations and Ultrasonography.
2. Both male and female are included in study
3. Those who give consent will be included

Exclusion Criteria:

1. Patients age less than 18 years.
2. cardiac failure patients.
3. CKD patients.
4. Patients on drugs such as MAO inhibitors, TCA, diuretics, SSRIs, cytotoxic drugs.

Data Collection:

1. All the patients with diagnosis of chronic liver disease attending the OPD/IPD of Department of Medicine was enrolled for the study. designed proforma will be taken. Written informed consent was taken from all the individuals.
2. Individuals diagnosed with CLD by history, clinical examinations, laboratory investigations and ultrasonography were taken. detailed history was taken from all patients and was done.
3. Child Pugh and MELD scores was computed for each patient to determine the severity of cirrhosis. The West Haven criteria was used to make a clinical diagnosis of hepatic encephalopathy.

Child-Pugh score

The Child-Pugh score can reasonably predict survival in various liver illnesses and can also indicate the possibility of serious cirrhosis complications such spontaneous bacterial peritonitis and bleeding from varices. It can vary from 5 to 15 and is determined by summing the results of five parameters (serum bilirubin, serum albumin, prothrombin time, ascites, and hepatic encephalopathy).

Class A=5 -6 points

Class B=7 -9 points

Class C= 10 points

Child-Pugh score of seven or more shows decompensation, which implies cirrhosis (Class B)

The MELD score is a method for predicting a patient's prognosis for liver disease that was developed prospectively. This score was initially determined using three non-invasive

measurements: the blood creatinine level, the prothrombin time represented as INR, and the serum bilirubin levels. In 2016, serum sodium, another crucial indicator of survival after liver transplantation, was added to the MELD score.

Statistical Analysis:

Microsoft Excel and SPSS 20.0 were used for statistical analysis. The quantitative data were analysed using the arithmetic mean \pm SD (or median), while qualitative (categorical) data were described using frequencies (%). $P = 0.05$ or lower were regarded as significant and calculated by test of significance formula.

Results

Table 1 showed that Out of 132 patients, studied most of the patient comes in the 30-50 year age group i.e. 82(62.1%). The mean age of patients was 50.17 ± 10.58 , with a range of 30-80 years.

Table 1: Age distribution of Study Population in years

Age	Frequency	Percent
30-50 year	82	62.1
50-70 year	45	34.1
Greater than 70 year	5	3.8
Total	132	100.0

Table 2: Sex distribution of Study Population

Sex	Frequency	Percent
Male	88	66.7
Female	44	33.3
Total	132	100.0

Table 2 showed that Out of 132 patients, studied mostly patients are male 88 (66.7%).

Table 3: Grade of Hepatic encephalopathy distribution of Study Population

Grade of HE	Frequency	Percent
No HE	75	56.8
Grade I	21	15.9

Grade II	20	15.2
Grade III	10	7.6
Grade IV	6	4.5
Total	132	100.0

Table 3 shows that Out of 132 patients, 56.8% subjects were do not had hepatic encephalopathy, 15.9% had grade I, 15.2% had grade II, 7.6% subjects had grade III encephalopathy, 4.5% subject had Grade 4.

Table 4: Distribution of Child-Pugh score of Study Population

CPS	Frequency	Percent
Class A	6	4.54 %
Class B	42	31.82%
Class C	84	63.64%
Total	132	100.0%

Table 4 shows that Out of 132 patients, studied that most of **Child-Pugh score** are included in class C i.e. 84(63.64%) in patients., 31.82% subjects were having child-Pugh score B and 4.54% subjects had CPS class A

Table 5: Distribution Serum sodium of Study Population

Serum sodium Meq/L	Frequency	Percent
≤ 130	40	30.3%
131-135	28	21.2%
≥ 136	64	48.5%
Total	132	100.0%

Table 5 shows that Out of 132 patients, studied that serum sodium are 64 (48.5%) in the range of above 136 Meq/L.30.3% study subjects were had serum sodium \leq 130, whereas 21.2% study subjects had serum sodium in the range of 131-135.

Table 6: Association between grade of HE and serum sodium level

Variables		Serum sodium			Total	Chi-square statistics (p-value)
		\leq 130 Meq/L	131-135 Meq/L	\geq 136 Meq/L		
Grade of HE						
No HE	Count	9	11	55	75	53.01 (0.000)
	% of Total	6.8%	8.3%	41.7%	56.8%	
Grade I	Count	8	7	6	21	
	% of Total	6.1%	5.3%	4.5%	15.9%	
Grade II	Count	11	6	3	20	
	% of Total	8.3%	4.5%	2.3%	15.2%	
Grade III	Count	8	2	0	10	
	% of Total	6.1%	1.5%	0.0%	7.6%	
Grade IV	Count	4	2	0	6	
	% of Total	3.0%	1.5%	0.0%	4.5%	

Table 6 shows Association between grade of HE and serum sodium level, Out of 6 study subjects 4 had \leq 130 Meq/L, out of 10 grade III study subjects 8 had \leq 130 Meq/L, out of 20 study subjects with grade II, 11 study subjects had \leq 130 Meq/L and out of 75 study with no HE only 9 study subjects had \leq 130 Meq/L, on comparing there is significant association with p value 0.0

Table 7: Association between Coagulopathy and serum sodium level

Variables		Serum sodium			Total	Chi-square statistics (p-value)
		\leq 130.0 Meq/L	131.0-135.0 Meq/L	\geq 136.0 Meq/L		
Coagulopathy						
Absent	Count	27	25	57	109	9.07 (0.011)
	% of Total	20.5%	18.9%	43.2%	82.6%	
Present	Count	13	3	7	23	
	% of Total	9.8%	2.3%	5.3%	17.4%	

Table 7 shows Association between Coagulopathy and serum sodium level, out of 109 study subjects 27 study subjects had serum sodium \leq 130 Meq/L, out of 23 study subjects with coagulopathy 13 study subjects had serum sodium \leq 130 Meq/L, on comparing there is significant difference with p value 0.011.

Table 8: Association between hepatorenal syndrome and serum sodium level

Variables		Serum sodium				Chi-square statistics (p-value)
		≤ 130 eq/L	131.0-135.0 Meq/L	≥ 136.0 Meq/L	Total	
Hepatorenal syndrome						
Absent	Count	32	25	64	121	14.23 (0.000)
	% of Total	24.2%	18.9%	48.5%	91.7%	
Present	Count	8	3	0	11	
	% of Total	6.1%	2.3%	0.0%	8.3%	

Table 8 showed Association of Serum sodium with hepatorenal syndrome of Study Population, out of 11 study subjects with hepatorenal syndrome, 8 study subjects had sodium levels < 130 meq/l, whereas out of 121 subjects without hepatorenal syndrome 32 subjects had sodium levels < 130 meq/l, on comparing there is significant association with p value 0.0

Table 9: Association between child-Pugh score and serum sodium level

Variables		Serum sodium				Chi-square statistics (p-value)
		≤ 130.0 Millieq/L	131.0-135.0 Millieq/L	≥ 136.0 Millieq/L	Total	
Child-Pugh score						
Class A	Count	0	0	6	6	39.53 (0.00)
	% of Total	0.0%	0.0%	4.54%	4.54%	
Class B	Count	2	7	33	42	
	% of Total	1.51%	5.30%	25%	31.82%	
Class C	Count	38	22	24	84	
	% of Total	28.8%	16.67%	18.18%	63.64%	

Table 9 shows Association of Child Pugh score with serum sodium of study subjects, out of 84 study subjects with child-Pugh class C, 38 study subjects had sodium levels <130 me/l, out of 42 subjects with class B, 2 subjects had sodium < 130 meq/l, whereas out 6 study subjects of class A, none of them had sodium < 130 meq/l, on comparing there is significant association with p value 0.0.

Discussion

Most of the patients in the current study 82, or 62.1% are in the 30–50 age range. The patient's age was 50.17 on average, with a standard deviation of 10.58. The study's authors, Bhandari A et al.¹³ had a mean age of 53.44 7.57 years. According to Kumar V S et al.¹⁰ the patients' age varied from 33 to 80 years old, with average age of 46.39. 85 patients in total were recruited for this study by Mamun A. A. et al.¹¹ with mean (SD) ages of 46 and 47 correspondingly, without any statistically significant mean difference. Total of 95 individuals were taken in the trial, according to Nareddy S. R. et al.¹²

In our study participants 88 (66.7%) of the 132 patients in the study were men. 95 patients in all, including a majority of men (91, 95.8%) were included in the study by Nareddy S. R. et al.¹² 85 patients were recruited for the study by Mamun A. A.¹¹ et al., 61 (75%) of them were men, and 24 (25%) were women. Thirty (63.8%) of the 114 individuals with CLD investigated by Bhandari A et al.¹³ were men, whereas 17 (36.2%) of the patients were women. In the study by Jong Hoon Kim et al.¹⁴ 132 males (70.2%) and 56 women (29.8%) were included.

57 of 132 patients had hepatic encephalopathy. 31 of 57 HE patients had blood sodium levels < 130 mEq/L and 16 in range of 131 to 135 milli Eq/L. According to Angeli et al.¹⁵ 38% of individuals with sodium concentration \leq 130 mEq/L suffer from encephalopathy of hepatic origin. Kim et al.¹⁴ studied that 43.1% of individuals with sodium concentration \leq 130 milliEq/L experienced encephalopathy of hepatic origin. 61% of patients have encephalopathy and sodium levels \leq 130 meq/L.

11 of 132 tested had hepatorenal syndrome, and 8 had sodium concentrations < 130 mEq/L. According to Angeli et al.¹⁵ 10% and 6% of patients with blood sodium concentration between “131.0-135.0” milli Eq/L and more than 135 mEq/L, respectively, developed hepatorenal syndrome. Patients with blood salt levels < 130 mEq/L were 3.9% more likely to have hepatorenal syndrome, according to Kim et al.¹⁴

In the current study, 39 (29.5%) study participants had variceal haemorrhage, compared to 93 (70.5%) who did not. 15 (11.4%) of 39 patients with variceal haemorrhage had sodium < 130 milli eq/l. Nareddy S. et al.⁴⁵ found no increase in variceal bleeding.

Out of 132 patients studied, 84 (63.64%) were Child-Pugh class C, 42 (31.82%) were class B, and 6 (4.54%) were class A. 38 (28.8%) of 84 Class C patients had sodium levels below 130 mEq/L, while 22 (16.67%) had values in range of 131 to 135 mEq/L. Kim et al.¹⁴ found a relationship between CPS and salt levels. Individuals with sodium concentration < 130 mEq/L exhibited higher Child Pugh scores, according Kumar et al.¹⁰

Child-Pugh Class C has a mean serum sodium level of 128.01mEq/L, while Class A has mean sodium levels of 139.50mEq/L. Individuals with sodium concentration < 130.0 milli Eq/L are mostly diseased. Lower blood sodium levels are connected to greater CPS scores and death, suggesting an inverse connection between serum sodium and illness severity. Kim et al.¹⁴ found a relationship between Child Pugh and salt levels. Severe sickness was connected to lower serum sodium levels.

The current study found significant variations between MELD and serum sodium. Individuals with blood sodium conc. < 130 milli Eq/L have a MELD of 31.03 ± 5.09 , those with sodium concentration in range of 131.0 to 135.0 mEq/L had a MELD score of 26.64 ± 5.19 , and those with serum sodium concentration beyond 136 mEq/L had a MELD score of 18.53 ± 5.16 . On comparison there is significant association suggesting there is inverse connection between sodium and illness severity assessed by MELD score with significant p value. Kumar et al.¹⁰ found a large variation in MELD scores between the three groups.

Conclusion

Based on our research, we can say that in current study the majority of the study participants experienced ascites, hypertension, variceal haemorrhage, coagulopathy, and hepatorenal syndrome. In our study, advanced cirrhosis frequently has low serum sodium levels. Patients

with low sodium levels are more likely to experience ascites, variceal haemorrhage, hepatic encephalopathy, and hepatorenal syndrome than those with normal serum sodium levels. They correlate well with serum sodium and the CPS and MELD score. These findings suggest that cirrhotic patients should have close monitoring of their serum sodium levels throughout their treatment.

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