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Observational cross-sectional assessment of dysnatremia in patients with chronic liver disease

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Abstract
Aim: This study was done to study the serum sodium levels in chronic liver disease (CLD) patients and establish its association with the severity of disease in such patients.
Material & Methods: An observational cross-sectional study with 100 cases of chronic liver disease was done in the Department of General Medicine Mamata Medical College, Khammam for 1 year. The study protocol was approved by the Institutional Ethics Committee before commencement and a written informed consent was taken from all patients.
Results: All patients had abdominal distension. It was observed that patients from group A had jaundice ($p<0.05$) and altered sensorium ($p<0.001$) significantly more commonly as compared to those from group B and C. Alcohol consumption was reported by 90% of the patients. Serum sodium levels was not significantly associated with alcohol consumption. Among all examination findings, icterus ($p<0.05$) and clubbing ($p<0.01$) were found to be significantly more common among patients from group A, as compared to patients from group B or C. Pallor, pedal edema, signs of liver cell failure and organomegaly were not significantly associated with serum sodium levels in our study population. hepatic encephalopathy ($p<0.01$), hepatorenal syndrome ($p<0.01$) and coagulopathy ($p<0.01$) were found to occur significantly more common among patients from group A, as compared to those in patients from group B or C. We observed that mean direct bilirubin, alanine transaminase, aspartate transaminase and alkaline phosphatase were significantly higher among group A patients as compared to those from group B or C respectively.
Conclusion: Patients with lower serum salt levels had a substantially higher MELD score and CPS. Low blood sodium levels were linked to more severe liver disease, greater complications, and increased death. As a result, we urge that serum salt levels be checked on a frequent basis in patients with chronic liver disease.

Keywords: Cirrhosis, sodium, hyponatremia, MELD, Prognosis

Introduction

Dysnatremia is an umbrella term to describe hypo or hypernatremia. Hyponatremia (serum sodium concentration <135 meq/L) and hypernatremia (serum sodium concentration >135mEq/L) both primarily are manifestations of imbalance of body water homeostasis which is dependent upon salt and water intake, insensible losses and urinary concentration or dilution (in most circumstances mediated by vasopressin) [1, 2]. Hyponatremia can be divided into euvolemic, hypovolemic and hypervolemic types denoting the presence of decreased, normal or increased total body water. It has been shown that hyponatremia may lead to worse outcomes in a variety of illnesses necessitating admissions to pediatric critical care [3, 4]. Its presence seems to increase the mortality in critical patients [5].

Hyponatremia may be due to chronic organ dysfunctions (that is heart failure or liver dysfunction), diuretic use, syndrome of inappropriate antidiuretic hormone (ADH) secretion, adrenal insufficiency, and cerebral or renal salt wasting syndromes. Hyponatremia is often a marker of severity of underlying disease [6, 7]. In addition to critical illness per se, factors contributing to hyponatremia in ICU include excess use of hypotonic fluids and drugs stimulating antidiuretic hormone secretion [8].

Since thirst and free access to water are the most important mechanisms that prevent hypernatremia, critically ill patients and older patients are at high risk for this disorder [7, 9]. Since hypernatremia is often iatrogenic, hypernatremia acquired in the ICU has been considered as an important index of quality of care [10]. Only a few studies have been conducted to examine the relationship between blood sodium levels and the occurrence and severity of liver cirrhosis complications.

Hypernatremia has multiple adverse effects on physiologic functions, which may explain its association with increased mortality. Hypernatremia aggravates peripheral insulin resistance [11], impairs hepatic gluconeogenesis and lactate clearance [12, 13] and decreases left ventricular contractility [14]. Additionally, hypernatremia is associated with various neuromuscular manifestations, such muscle weakness and cramps [15]. Neurologic impairment remains the most severe consequence of hypernatremia and may prolong the need for mechanical ventilation and delay weaning. Finally, too rapid correction of chronic hypernatremia can cause cerebral edema [16].

Thus, the current study was conducted to investigate blood sodium levels in chronic liver disease patients and determine their relationship with the disease severity in the such individuals.

Material & Methods

An observational cross-sectional study with 100 cases of chronic liver disease was done in the Department of General Medicine, Mamata Medical College, Khammam for 1 year. The study protocol was approved by the Institutional Ethics Committee before commencement and a written informed consent was taken from all patients.

Inclusion Criteria

Patients in the age group of 18 to 65 years, irrespective of gender, diagnosed with chronic liver disease.

Exclusion Criteria

Patients aged less than 18 years, with comorbid cardiac failure, with comorbid chronic kidney disease and those taking drugs that alter serum sodium levels.

100 cases were divided into 3 groups: - Those with serum sodium levels less than or equal to 130 meq/l were classified as group A, those with serum sodium levels between 131-135 meq/l as group B and those with serum sodium levels greater than or equal to 136 meq/l as group C. In the present study, 100 patients were included. It was observed that 30% were in group A (≤ 130 mEq/l, n=30), 30% were in group B (131 to 135 mEq/l, n=30) and 40% were in group C (≥ 136 mEq/l, n=40).

Demographic information about the patients was obtained from their medical records. A history, physical examination, biochemical markers, ultrasonography, and upper gastrointestinal endoscopy were used to identify cirrhosis. Each patient's venous blood was taken and submitted to the institutional laboratory for analysis of serum electrolytes, liver function tests (LFTs), renal parameters, prothrombin time (PT), activated partial thromboplastin time (aPTT), and international normalised ratio (INR). An automatic biochemical analyzer was used to test the biochemical indicators, while an automated haematology analyzer was used to measure the whole blood cell counts. Complications in the patients included hepatic encephalopathy, varices, hepatorenal syndrome, and infections. In addition, child-Turcotte Pugh score (CPS) and model for end stage liver disease (MELD) score was calculated for all patients [11].

Statistical Analysis

All analysis were done using SPSS software, version 24.0. Descriptive analysis of quantitative parameters was expressed as means and standard deviation. Ordinal data were expressed as absolute number and percentage. Cross tables were generated and chi square test was used for testing of associations. One-way ANOVA was used for comparison of quantitative parameters, along with Bonferroni post-hoc test. A p value of <0.05 is considered statistically significant.

Results

Table 1: Comparison of baseline characteristics between groups based on serum sodium levels

Variables		Group A (≤ 130 mEq/l, n=30)	Group B (131 to 135 mEq/l, n=30)	Group C (≥ 136 mEq/l, n=40)	Total	P value
Age group (Years)						
25 to 40	N	6	10	12	28	
	%	20	33.34	30	28	
41 to 60	N	19	17	24	60	0.40
	%	63.34	56.66	60	60	
61 to 80	N	5	3	4	12	
	%	16.66	10	10	12	
Gender						
Female	N	3	5	12	20	
	%	10	16.66	30	20	0.25
Male	N	27	25	28	80	
	%	90	83.34	70	80	
Clinical presentation						
Abd distension	N	30	30	40	100	NA
	%	100	100	100	100	
GI bleed	N	6	6	6	18	0.15
	%	20	20	15	18	
Jaundice	N	16	10	8	34	<0.05
	%	53.34	33.34	20	34	
Alt sensorium	N	18	6	3	27	<0.001
	%	60	20	7.50	27	
	N	28	28	34	90	0.80
Alcohol	%	93.34	93.34	85	90	
Examination findings						
Pallor	N	6	6	8	20	0.88
	%	20	20	20	20	
Icterus	N	24	15	5	44	<0.05
	%	80	50	12.50	44	
Clubbing	N	12	12	4	28	<0.01
	%	40	40	10	28	
Pedal edema	N	27	24	30	81	0.75
	%	90	80	75	81	
S/o liver cell failure	N	27	29	36	92	0.16
	%	90	96.66	90	92	
Organomegaly	N	3	10	8	21	0.20
	%	10	33.34	20	21	

All patients had abdominal distension. It was observed that patients from group A had jaundice (p<0.05) and altered sensorium (p<0.001) significantly more commonly as compared to those from group B and C. Alcohol consumption was reported by 90% of the patients. Serum sodium levels were not significantly associated with alcohol

consumption. Among all examination findings, icterus ($p<0.05$) and clubbing ($p<0.01$) were found to be significantly more common among patients from group A, as compared to patients from group B or C. Pallor, pedal edema, signs of liver cell failure and organomegaly were not significantly associated with serum sodium levels in our study population.

Table 2: Comparison of complication rate between groups based on serum sodium levels

Complications		Group A (≤ 130 mEq/l, n=30)	Group B (131 to 135 mEq/l, n=30)	Group C (≥ 136 mEq/l, n=40)	Total	P value*
Port hypertension	N	27	27	32	86	0.10
	%	90	90	80	86	
Hepatic	N	15	6	4	25	<0.01
encephalopathy	%	50	20	10	25	
Hepatorenal	N	14	5	5	24	< 0.01
syndrome	%	46.66	16.66	12.50	24	
Spontaneous bacterial	N	3	2	0	5	0.55
peritonitis	%	12	6.66	0	5	
	N	12	5	3	20	<0.01
Coagulopathy	%	40	16.66	7.50	20	

Portal hypertension was observed in 86%, hepatic encephalopathy in 25%, hepatorenal syndrome in 24%, spontaneous bacterial peritonitis in 5% and coagulopathy in 20%. Of these, hepatic encephalopathy ($p<0.01$), hepatorenal syndrome ($p<0.01$) and coagulopathy ($p<0.01$) were found to occur significantly more common among patients from group A, as compared to those in patients from group B or C.

Table 3: Comparison of liver function between groups based on serum sodium levels

Liver function		Mean	SD	Minimum	Maximum	P value*
Total bilirubin (mg/dl)	Group A	3.14	2.34	0.50	9.40	
	Group B	2.90	2.20	0.60	12.18	0.08
	Group C	2.20	1.80	0.61	7.13	
Direct bilirubin (mg/dl)	Group A	2.10	1.80	0.21	6.20	
	Group B	1.60	1.40	0.34	6.70	<0.01
	Group C	1.30	1.20	0.30	4.45	
Alanine transaminase (U/l)	Group A	86.34	84.16	11.19	545.15	
	Group B	55.25	18.40	17.13	95.15	<0.01
	Group C	45.90	16.90	12.15	82.12	
Aspartate transaminase (U/l)	Group A	102.98	95.40	20.14	600.15	
	Group B	66.64	20.80	30.15	149.13	<0.01
	Group C	58.52	22.20	18.12	130.12	
Alkaline phosphatase (U/l)	Group A	140.60	96.06	80.12	624.10	
	Group B	100.80	29.00	70.15	192.19	<0.01
	Group C	92.18	19.21	66.14	140.12	
Total protein (gm/dl)	Group A	6.24	0.90	4.90	7.70	
	Group B	6.20	0.70	4.20	8.56	0.80
	Group C	6.26	0.92	4.20	8.28	
Albumin (gm/dl)	Group A	3.48	0.83	1.80	6.08	
	Group B	3.30	0.72	1.91	5.15	0.09
	Group C	3.60	0.60	2.45	4.96	

We observed that mean direct bilirubin, alanine transaminase, aspartate transaminase and alkaline phosphatase were significantly higher among group A patients as compared to those from group B or C respectively.

Table 4: Comparison of liver cirrhosis severity between groups based on serum sodium levels

Variables	Mean	SD	Minimum	Maximum	P value*
MELD					
Group A	18.82	6.40	6.14	32.04	<0.01
Group B	14.56	5.55	8.13	30.02	
Group C	12.98	4.40	8.12	26.04	
CPS					
Group A	9.90	2.20	6.12	14.06	<0.01
Group B	8.82	1.60	6.12	13.07	
Group C	7.70	1.75	6.12	15.05	

We observed that mean MELD score was significantly higher among group A patients as compared to those with group B and group C. We also observed that mean Child Pugh score was significantly higher among group A patients as compared to those with group B and group C.

Table 5: Comparison of mortality rate between groups based on serum sodium levels

Outcome		Group A (≤ 130 mEq/l, n=30)	Group B (131 to 135 mEq/l, n=30)	Group C (≥ 136 mEq/l, n=40)	Total	P value*
Discharged	N	24	27	40	91	
	%	80	90	100	91	<0.001
Expired	N	6	3	0	9	
	%	20	10	0	9	

Overall, 9 of the patients expired. It was observed that mortality was 20 percentages among group A patients, which was significantly higher than that of group B patients (10%) or group C patients (0%).

Discussion

Dysnatremia is the most common electrolyte disorder in hospitalized patients. It encompasses hyponatremic and hypernatremic conditions. It is a common finding at Intensive Care Unit (ICU) admission [17, 19]. Nearly one third of critically ill patients have dysnatremia at ICU admission.[18] Hyponatremia is a pathologic condition defined as a serum sodium < 135 mmol/L. It is the most common electrolyte disorder in hospitalized patients. Up to 40% of the overall hospitalized patients have a hyponatremia at admission.[20] Presence of severe hyponatremia on hospital admission has been demonstrated to be independently associated with an increased risk for ICU admission and poor prognosis [21]. Hyponatremia affected 60% of the individuals in this research. Kim and colleagues discovered that 27.1% of participants had serum sodium of 130 mmol/l, 20.8% had serum sodium of 131 to 135 mmol/l, and 52.1 percent had serum sodium of 136 mmol/l.[22] Umemura et colleagues studied mortality in cirrhotic patients on conventional diuretics and discovered links between blood sodium levels and clinical features [23].

All patients had abdominal distension. It was observed that patients from group A had jaundice ($p<0.05$) and altered sensorium ($p<0.001$) significantly more commonly as compared to those from group B and C. Alcohol consumption was reported by 90% of the patients. Serum sodium levels were not significantly associated with alcohol consumption. Among all examination findings, icterus ($p<0.05$) and clubbing ($p<0.01$) were found to be significantly more common among patients from group A, as compared to patients from group B or C. Pallor, pedal edema, signs of liver cell failure and organomegaly were not significantly associated with serum sodium levels in our study population. Portal hypertension was observed in 86%, hepatic encephalopathy in 25%, hepatorenal syndrome in 24%, spontaneous bacterial peritonitis in 5% and coagulopathy in 20%. Of these, hepatic encephalopathy ($p<0.01$), hepatorenal syndrome ($p<0.01$) and coagulopathy ($p<0.01$) were found to occur significantly more common among patients from group A, as compared to those in patients from group B or C. Ascites were shown to be considerably less prevalent in individuals with blood sodium levels of 139 mEq/l, according to Umemura et al (45 vs 65%) [23].

We observed that mean direct bilirubin, alanine transaminase, aspartate transaminase and alkaline phosphatase were significantly higher among group A patients as compared to those from group B or C respectively. Umemura et al [23] colleagues discovered that individuals with serum sodium levels of 139 mEq/l had considerably reduced median AST, ALT, GGT, and total bilirubin. We observed that mean MELD score was significantly higher among group A patients as compared to those with group B and group C. We also observed that mean Child Pugh score was significantly higher among group A patients as compared to those with group B and group C. In another study, Umemura et al [23] colleagues found that patients with MELD values of 139 mEq/l had considerably lower median MELD scores. Jenq et al [24] on the other hand, found no significant relationship between MELD score and blood sodium level. It was 32.9±13.9 for patients with sodium levels less than 135 mEq/l and 29.4±13.6 for patients with sodium levels greater than 135 mEq/l, $p=0.158$. CPS was considerably higher in individuals with blood sodium levels less than 135 mEq/l (12.4±2.3) than in those with serum sodium levels greater than 135 mEq/l (11.1±2.1).

Conclusion

In conclusion, individuals with lower serum salt levels had a substantially higher MELD score and CPS. Furthermore, hepatic encephalopathy, hepatorenal syndrome, and coagulopathy were shown to be considerably more prevalent in individuals with blood sodium levels more than 130 mEq/l than in other patients. Our findings show that hyponatremia is common in people with chronic liver disease. Low blood sodium levels were linked to more severe liver disease, greater complications, and increased death. As a result, we urge that serum salt levels be checked on a frequent basis in patients with chronic liver disease. Those suffering from hyponatremia should be prioritised for acute treatment.

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