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Original Research Article

SERUM SODIUM LEVELS AS A PROGNOSTIC MARKER IN PATIENTS OF HEPATIC ENCEPHALOPATHY

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Abstract

Background: Hepatic encephalopathy is defined as a spectrum of neuropsychiatric abnormalities in patients with liver dysfunction after exclusion of other brain diseases. Hyponatremia is a common finding in patients of hepatic encephalopathy.

Aim: The purpose of present study was to measure serum sodium levels in patients admitted with hepatic encephalopathy and assess its value as prognostic marker.

Material and methods: Serum sodium levels were measured in hundred patients with hepatic encephalopathy admitted in medicine wards of Rajindra Hospital, Patiala. Presence of other complications like coagulopathy, spontaneous bacterial peritonitis, hepatorenal syndrome were also recorded.

Observations: Out of 100 patients of hepatic encephalopathy, hyponatremia was found in 79% of patients. The decrease of serum sodium levels strongly correlated with other complications of decompensated cirrhosis like ascites, spontaneous bacterial peritonitis, hepatorenal syndrome and coagulopathy.

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Conclusion: Hence, we could conclude from our study that hyponatremia, especially with serum sodium levels <125 mEq/L, was associated with severe complications like ascites, coagulopathy, spontaneous bacterial peritonitis and hepatorenal syndrome.
Keywords: hyponatremia, bacterial peritonitis, encephalopathy

INTRODUCTION

The term Hepatic Encephalopathy (HE) encompasses a wide array of transient and subtle reversible neurological and psychiatric manifestations usually found in patients with chronic liver disease and portal hypertension, but also seen in patients with acute liver failure. HE develops in 50% to 70% of patients with cirrhosis, and its occurrence is a poor prognostic indicator, with projected 1-and 3-year survival rates of 42% and 23%, respectively, without liver transplantation.[1]

Hepatic encephalopathy occurs due to the effect of neurotoxic substances like ammonia, mercaptans, octopamine, gamma amino butyric acid (GABA), reaching the central nervous system in the patients with cirrhosis and portal hypertension. [2]

Hyponatremia is defined as a decrease in serum sodium concentration (Na^+) to less than 135 mEq/l.[3] It is a common finding in patients with advanced cirrhosis.[4] Two types of hyponatremia are described in liver cirrhosis; the most important type is hypervolemic hyponatremia (dilutional hyponatremia), which is associated with large ascites (frequently refractory ascites) and edema.[5] Several mechanisms are implicated in the impairment of solute-free water excretion in cirrhosis and in the subsequent development of hyponatremia, including reduced filtrate delivery to distal nephrons and hypersecretion of arginine vasopressin. Of these, reduced effective circulating volume owing to arterial splanchnic vasodilatation is considered the most important afferent factor in baroreceptor-mediated nonosmotic stimulation of vasopressin release from the neurohypophysis in cirrhosis.[6]

There is a possible relationship between hyponatremia and the presence of hepatic encephalopathy.[7]. Encephalopathy that develops after bridging procedures like trans thoracic jugular portosystemic shunts are also associated with increased chances of development of hepatic encephalopathy with lower serum sodium values.[8]

Cirrhotic patients with hyponatremia have poor survival compared with cirrhotic normonatremic patients. There is an association between the presence of hyponatremia and the presence of certain liver cirrhosis complications such as hepatic encephalopathy, hepatorenal syndrome, and refractory ascites.[9]

Various studies have assessed the role of hyponatremia as an independent risk factor for complications of cirrhosis and its possible implications in prevention. The aim of present study is to prognostigate the role of hyponatremia in hepatic encephalopathy.

MATERIAL AND METHODS

A hospital based observational study was conducted on 100 patients admitted with hepatic encephalopathy in medicine wards of Rajindra Hospital, GMC Patiala. The study proposal and

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ethical procedure was approved by the Ethics Committee of Government Medical College, Patiala.

INCLUSION CRITERIA

1. Patients with age more than 18 years irrespective of sex.
2. Patients with clinical symptoms and signs of hepatic encephalopathy.

EXCLUSION CRITERIA

1. Patients with cardiac failure.
2. Patients with chronic kidney disease.
3. Patients on drugs such as SSRI, TCA.
4. Patients found to have any other form of encephalopathy like septic, hypertensive, hypoxic encephalopathy.
5. Patients with acute intracerebral events- infarct or haemorrhage.

Informed consent from patient's immediate relative when patient was in encephalopathy and later on from patient when patient recovers from encephalopathy was taken. History and physical examination was done and recorded. Presence of other comorbidites and other complications like coagulopathy, spontaneous bacterial peritonitis, hepatorenal syndrome were also recorded. Hepatic Encephalopathy was graded according to West Haven criteria which categorize HE from grade I to grade IV.

Patients were divided into four groups according to serum sodium levels.

Grading of hyponatremia was done according to serum sodium levels as follows:[10]

1. <125 meq/L - severe hyponatremia
2. 125-130 meq/L – moderate hyponatremia
3. 131-135 meq/L – mild hyponatremia
4. >135 meq/L – normal serum sodium levels.

Statistical analysis was done by using mean, median, standard deviation, Fischer's test, Pearson chi square test. Difference between two variables was considered significant when p value was less than 0.05.

OBSERVATIONS AND RESULTS

Data was collected from 100 patients admitted in our hospital with diagnosis of hepatic encephalopathy. The mean age of patients was 49.36 years with the range of 21-91years. Out of 100 patients, 92 were male and 8 were females. This male preponderance can be explained by alcohol consumption which is more common in male population as alcoholic liver disease was the commonest cause of chronic liver disease (CLD) in our study leading to hepatic encephalopathy accounting for 52% of patients, while chronic hepatitis C and hepatitis B was found to be the causative factor in 9% and 3% of patients respectively. Combined alcohol and hepatitis C was causative factor in 27% of patients. Combined hepatitis C and hepatitis B was found in 1% of patients. NAFLD was found to be the causative factor in 8% of patients. The mean concentration of sodium of all patients was 130.36mEq/L with a range of 108-143 meq/L.

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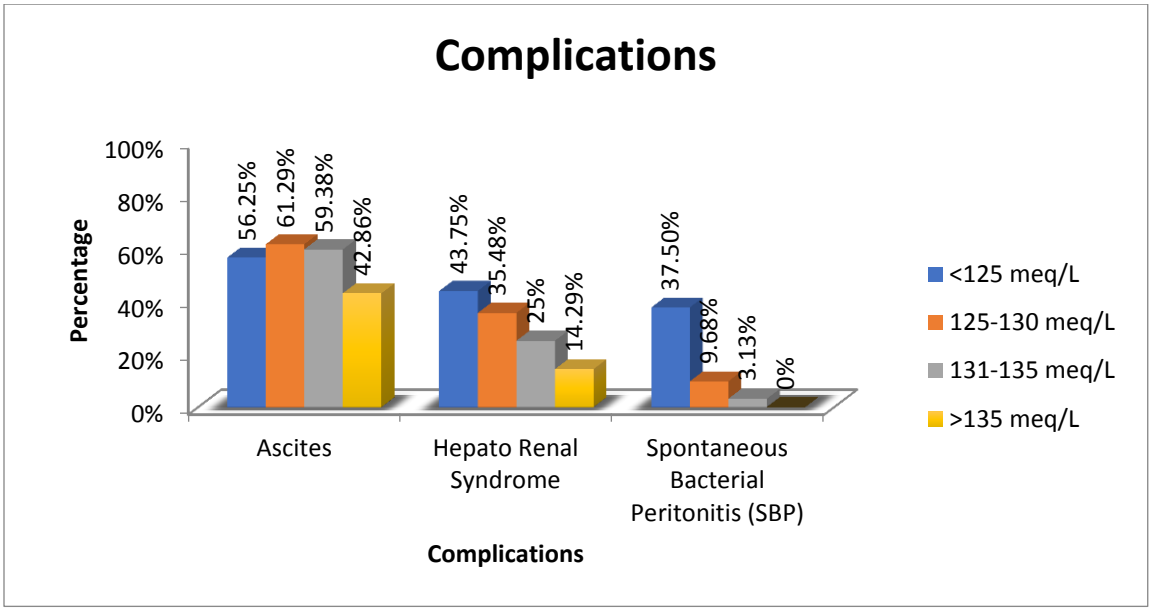
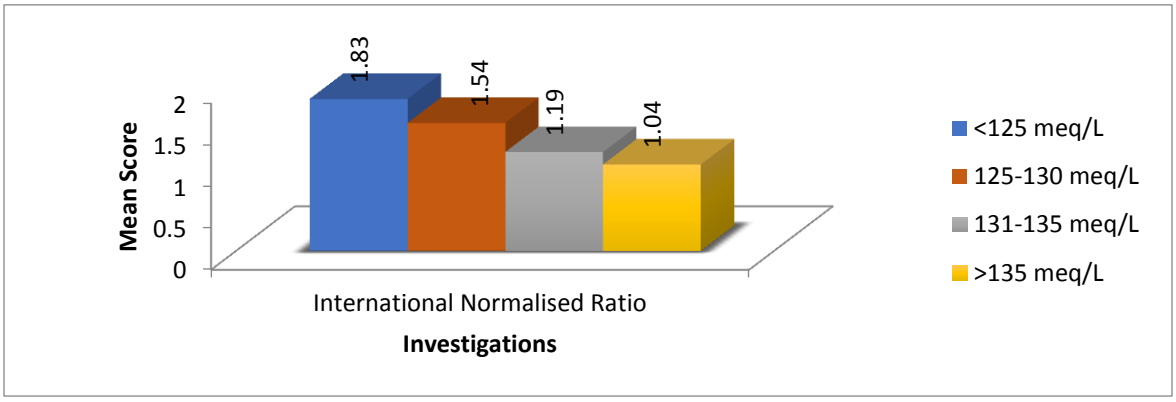
Based on serum sodium levels 16% of patients had serum sodium levels less 125 meq/L, 31% of patients had serum sodium levels between 125-130 meq/L, 32% of patients had serum sodium levels between 131-135 meq/L and 21% of the patients had serum sodium levels more than 135 meq/L.

Among 100 patients, ascites was present in 56% of the patients while portal hypertension was present in all the patients. Hepatorenal syndrome was found in 29% patients, while spontaneous bacterial peritonitis was found in 10% patients. There was a statistically significant difference in the occurrence of complications of CLD such as ascites (p value-0.016), hepatorenal syndrome (p value-0.001), spontaneous bacterial peritonitis (p value-0.041) and coagulopathy(p value-0.001) among four groups.(Graph-1,2)

GRAPH 1: Bar diagram showing frequency of complications among four groups according to serum sodium concentration.



GRAPH 2: Bar diagram showing mean INR among four groups.



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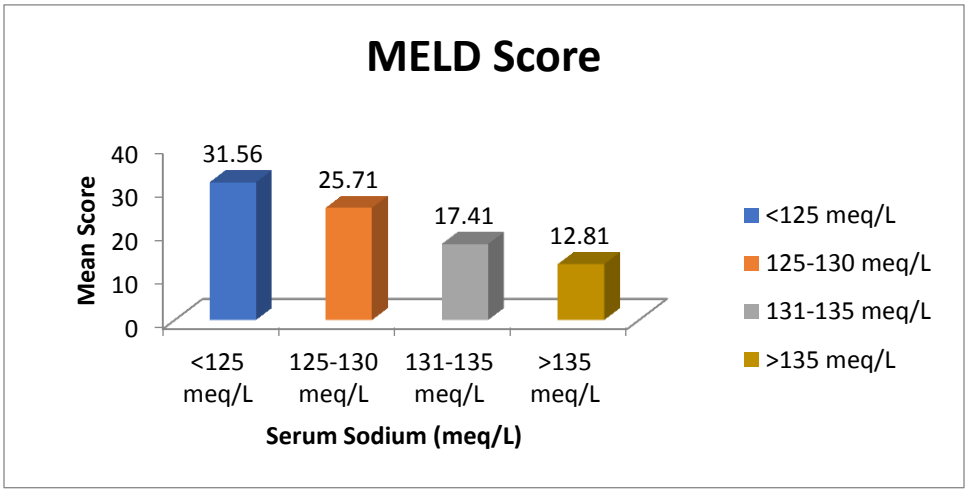
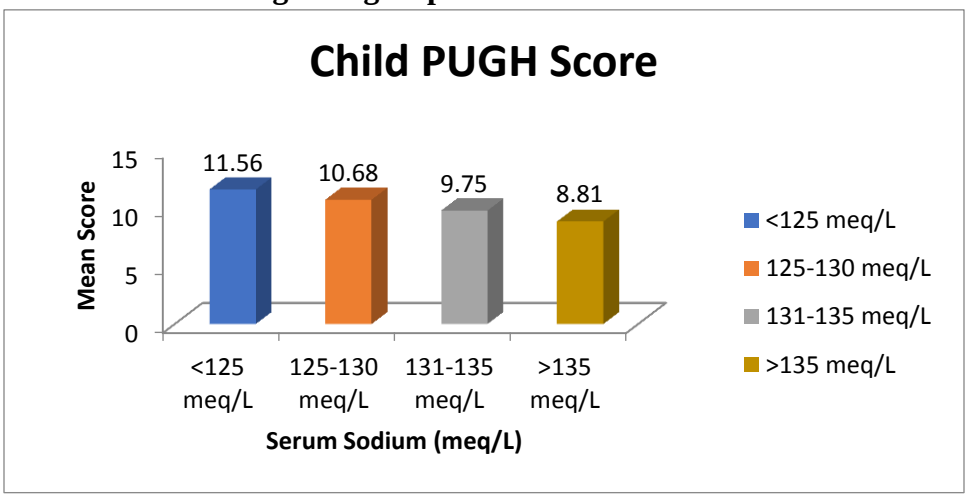
Hyponatremia was also profoundly associated with increase in the MELD-Na scores and Child pugh score among four groups. (Graph 3 and 4)

GRAPH 3: Bar diagram showing relationship of mean MELD Na score to serum sodium concentration among four groups.



GRAPH 4: Bar diagram showing relationship of mean Child Pugh score to serum sodium concentration among four groups.



Among 100 patients, 59% of patients were discharged and 41% patients were expired. Among 16 patients with severe hyponatremia, 15 patients (93.75%) expired. Among 31 patients with moderate hyponatremia, 13 patients (41.94%) expired. Among 32 patients with mild hyponatremia, 12 patients (37.50%) expired. There was one death among 21 patients (4.76%) with normal serum sodium levels. Hyponatremia was profoundly associated with increase in mortality among different groups. The difference in mortality among these groups was statistically significant (p value – 0.014).(Graph-5)

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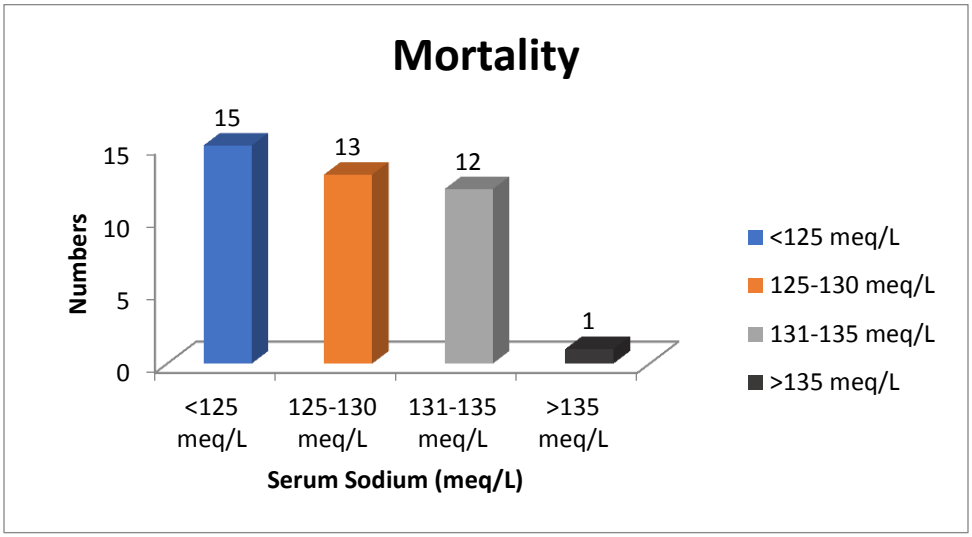
GRAPH 5: Bar diagram showing mortality according to serum sodium concentration among four groups.



DISCUSSION

Hyponatremia is commonly encountered problem in patients with end stage liver disease. Severe hyponatremia is associated with increased severity of HE. Infact, the severity of hyponatremia, particularly at serum sodium concentrations ≤130 mmol/L, corresponded to higher risks for developing ascites, hepatic encephalopathy and other complications of cirrhosis, compared with the risks in patients with a serum sodium ≥ 136 mmol/L.[11] In our study it was observed that hepatic encephalopathy is associated with abnormal serum sodium concentration. Patients with severe hyponatremia were associated with increased frequency of complications of chronic liver disease such as Ascites (p value-0.016), Hepatorenal Syndrome (p value-0.001), Coagulopathy (p value-0.001), Spontaneous Bacterial Peritonitis (p value-0.041) when compared to patients with normal serum sodium levels and results obtained are statistically significant (p value<0.05).

Table 1: Comparison of studies showing association between serum sodium concentration and hepatorenal syndrome.

Studies	Frequency of Hepatorenal Syndrome			
	<125meq/L	125-130 meq/L	131-135 meq/L	>135 meq/L
Present Study	43.75%	35.48%	25%	14.29%
Angeli P et al	17%		10%	6%
Kim JH et al	3.9%		2.5%	3%
Gupta GK et al	48.05%		13.63%	2.17%
Reddy DDK et al	28%		14%	6%

In our study, patients with severe hyponatremia have high frequency of hepatorenal syndrome. Angeli P et al[14] , Kim JH et al[15], Gupta GK et al[16] and Reddy DDK et al[17] also found that patients with severe hyponatremia have high frequency of hepatorenal syndrome.

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Table 2: Comparison of studies showing association between serum sodium concentration and SBP.

Studies		Frequency of SBP		
	<125meq/L	125-130 meq/L	131-135 meq/L	>135meq/L
Present Study	37.50%	9.68%	3.13%	0%
Kim JH et al	33.3%		30.7%	16.3%
Gupta GK et al	15.58%		9.09%	3.26%

In our study 37.50% of patients with severe hyponatremia had SBP as compared to 9.68% and 3.13% of patients with moderate and mild hyponatremia respectively. Kim JH et al [15] and Gupta GK et al[16] had found similar findings. Angeli P et al[14] also found that low sodium level was associated with increased frequency of spontaneous bacterial peritonitis.

Table 3: Mortality and serum sodium concentration.

Mortality	<125meq/L (N=16)	125-130 meq/L (N=47)	131-135 meq/L (N=32)	>135meq/L (N=21)	p value
Present Study	15 (93.75%)	13 (41.94%)	12 (37.50%)	1(4.76%)	0.006
Visampally SK et al	8(30.77)%		1(3.34)%	0(0%)	0.001
Reddy DDK et al	5(20%)		3(11.1%)	0(0%)	0.03

In our study percentage of patients with hyponatremia had higher mortality as compared to patients with normal serum sodium levels. Also, percentage of mortality increases as severity of hyponatremia increases. Mortality was significantly higher in severe hyponatremia patients as compared to mild, moderate hyponatremia.

Visampally SK et al[18] and Reddy DDK et al[17] had also found similar findings. Our study is comparable to above studies as mortality was significantly associated with severity of hyponatremia and results are statistically significant (p value<0.05).

CONCLUSION

Hepatic Encephalopathy is associated with abnormal serum sodium concentration. Patients with serum sodium levels less than 125meq/L were associated with increased frequency of complications such as Ascites, Hepatorenal Syndrome, Spontaneous Bacterial Peritonitis, when compared to patients with serum sodium levels more than 135meq/L. Lower serum sodium levels were associated with increased MELD score, increased CPS score indicating the inverse relationship between serum sodium levels and the severity of disease. Percentage of mortality was significantly higher with severity of hyponatremia. Thus, patients with decreased serum

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sodium levels should be considered a high-risk population because of increased frequency of complications and mortality.

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