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HYPONATREMIA AS A PREDICTOR OF PROGNOSIS AND COMPLICATIONS IN CIRRHOSIS OF LIVER - A WESTERN INDIA STUDY

Medicine

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ABSTRACT

Background Cirrhosis is an expanding problem with multiple etiologies and most of its morbidity is because of complications like ascites, portal hypertension, spontaneous bacterial peritonitis, esophageal varices, hepatorenal syndrome and hepatic encephalopathy which can also progress to death. According to several recent studies hyponatremia occurring as a result of reduced solute-free water clearance is a key prognostic factor in patients with liver cirrhosis. There is a lack of Indian data on clinical spectrum of hyponatremia in cirrhosis and treatment strategies to be adopted, therefore, we planned to undertake this prospective study in patients with cirrhosis at our tertiary care centre. **Methodology** A total of 120 patients of cirrhosis of liver fulfilling inclusion and exclusion criteria were enrolled in a cross-sectional observational study over a period of 10 months at a tertiary care centre in western India. They were grouped into 3 groups depending on their serum sodium level as >136 meq/l , 131 -135 meq/l and less than 130 meq/l and these groups were compared with each other in terms of their MELD score, Child-Pugh class and complications of cirrhosis such as ascites, portal hypertension, hepatic encephalopathy, hepatorenal syndrome and GI bleeding using appropriate statistical tests.

Results & Conclusions

- Cirrhosis was more common in middle age group.
- Cirrhosis was more common in males than females.
- Hyponatremia was frequent in cirrhotic patients which is dilutional hyponatremia.
- Hyponatremia in cirrhotic patients was significantly associated with severe complications of liver cirrhosis like hepatic encephalopathy, GI bleeding, and hepatorenal syndrome.
- Treatment of hyponatremia is important to prevent possible complications of cirrhosis of liver.

KEYWORDS

Hyponatremia, Cirrhosis of liver, MELD score, Child-Pugh class, Complications of cirrhosis

INTRODUCTION

Chronic liver disease is an expanding problem and has multiple etiologies. It is among the leading causes of death especially in low income countries. Most of the morbidity & mortality of chronic liver disease is due to its progression to cirrhosis & complications of cirrhosis. Ascites, portal hypertension, spontaneous bacterial peritonitis, esophageal varices, hepatorenal syndrome are complications of cirrhosis and in severe cases hepatic encephalopathy & death may occur.[6,7,8-16]

The clinical course of patients with cirrhosis is frequently complicated by the development of abnormality in renal function & electrolyte levels, and hyponatremia is the most common disorder seen in these patient. The prevalence of hyponatremia as defined by serum sodium level of 130 meq/L is 21.6% and if cut off level of 135 meq/L is used, the prevalence increases up to 49.4% .

Hyponatremia associated with cirrhosis is dilutional hyponatremia and is caused by impairment in the renal capacity to eliminate solute free water that causes retention of water that is disproportionate to the retentions of sodium, thus causing a reduction in serum sodium concentration. [1-7]

Recent studies indicate that hyponatremia in patients with cirrhosis predicts poor survival compared with that of patients without hyponatremia. [11] There is a lack of Indian data on clinical spectrum of hyponatremia in cirrhosis and treatment strategies to be adopted in various clinical scenarios therefore, we planned to undertake this prospective study in patients with cirrhosis at our tertiary care centre.

AIMS AND OBJECTIVES

1. To study the prevalence of hyponatremia in patients of liver cirrhosis
2. To evaluate the association between hyponatremia and complications of liver cirrhosis

MATERIALS AND METHODS

After taking due clearance of institutional ethical committee, a cross sectional observational study was carried out among the in-patients of Medicine department of the SSG Hospital Vadodara for a period of 10 months in which 120 patients fulfilling the inclusion and exclusion criteria were enrolled.

Inclusion Criteria:

All patients with cirrhosis of liver coming to SSG hospital in medical OPD or admitted in medical ward as diagnosed from history, biochemical testing and abdominal ultrasound.

Exclusion Criteria:

1) Patients with cardiac failure.
2) Patients on diuretic therapy.
3) Patients with renal disease.

After taking written and informed consent about enrolment in the study and maintaining adequate privacy and confidentiality all patients was subjected to a standardised interview.

Complete medical history was obtained and complete general and systemic examination was done. Patients at the time of inclusion were assessed according to Child-Pugh Score and MELD SCORE and divided according to serum sodium level.

Child- Pugh Score

The score employs five clinical measures of liver disease. Each measure is scored 1-3 with 3 indicating most severe derangement.

No	Measure	1 point	2 point	3 point
1	Total bilirubin mmol/l(mg/dl)	<34 (<2)	34-50 (<2-3)	>50 (>3)
2	Serum albumin mg/dl	>3.5	2.8-3.5	<2.8
3	PT INR	<1.7	1.7-2.30	>2.30
4	Ascites	None	Mild	Mod
5	Hepatic encephalopathy	Non	Grade 1-2	Grade 3-4

Meld Score

Calculated by:

$3.78\times\ln(\text{sr.bilirubin(mg/dl)}) + 11.2\times\ln(\text{INR}) +$

$.57\times\ln(\text{sr.creatinin}) + 6.43\times\text{etiology(0-cholestatic,1-others)}$

Following investigations were carried out:

CBC, Urine analysis, RFT, LFT, Total protein, albumin, RBS, Electrolytes, PT Inr, Ascitic fluid analysis, CXR, USG Abdomen, 2D Echo.

All data was analysed using appropriate statistical tests(Chi-square/Fisher Exact test). A p value of <0.05 will be considered statistically significant. Data will be entered in excel sheet and analysed by EPI INFO software.

These patients were grouped on the basis of serum sodium concentration.

1. Serum sodium <130 meq/l
2. Serum sodium 131-135 meq/l
3. Serum sodium >136 meq/l.

These groups were compared with each other for the severity of complications like ascities, portal hypertension, hepatic encephalopathy, GI bleeding, hepatorenal syndrome.

RESULTS

Mean age of study population was 38.10 +11.97. In the present study males accounted for (94.17%) (113 out of 120) & females accounted for 5.83% (7 out of 120) of total patients.

Alcohol was the most common etiology in present study seen in 113 (94%) of patients.

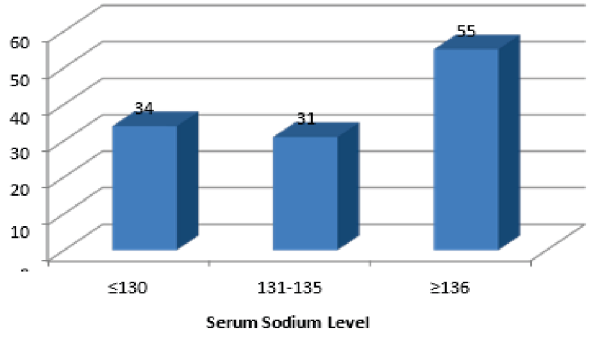

Figure 1

In the present study 34 (28.34%) patients belong to group of serum sodium concentration <130 meq/l. While 31 (25.83%) & 55 (48.83%) belong to serum sodium concentration of 131 – 135 meq/l & >136 meq/l respectively.

Table 1: Distribution of all the patients by Serum Sodium Concentration and MELD score.

Serum Sodium (meq/l)	MELD score(Mean+ SD)
<130	25.77 + 8.69
131-135	21.06 + 7.66
>136	19.12 + 7.4

In the present study low serum sodium was associated with higher MELD score. This was statistically significant.

Table 2: Child Pugh score class according to Serum Sodium level

CP Class	Serum Sodium level		
	<130	131-136	>136
A	1	3	11
B	10	15	21
C	24	17	18

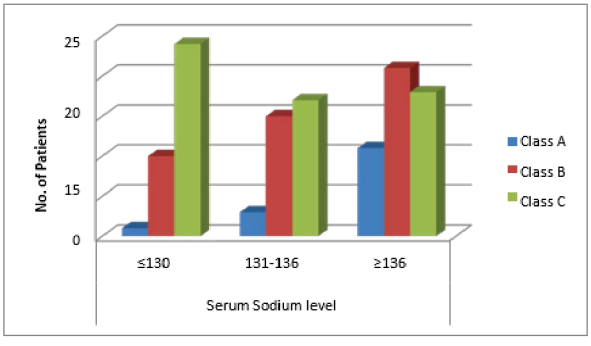

Figure 2

Patient group with lower serum sodium had higher Child Pugh class. This was also statistically significant.

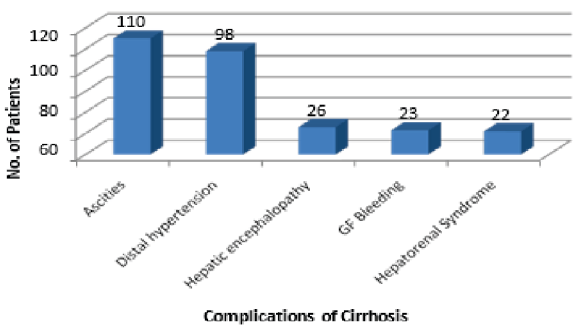

Figure 3

In the present study ascites was seen in 110(91.66%) patients, portal hypertension in 98(81.66%), hepatic encephalopathy in26 (26.66%), gastrointestinal bleeding in 23(23.16%) and Hepatorenal syndrome in 22 (17.5%) patients.

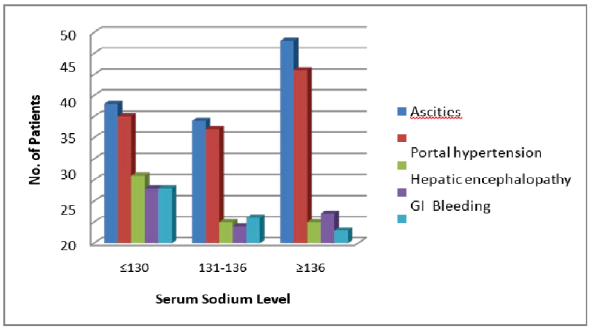

Figure 4

There was a significant difference in three groups of patients with serum sodium < 130 meq/l, 131-135 meq/l and > 136 meq/l with respect to the complications of liver cirrhosis namely hepatic encephalopathy, gastrointestinal bleeding, hepatorenal syndrome.(P value = 0.001,0.007, 0.0005 respectively).However no statistical significant difference was found in three group with respect to ascites and portal hypertension(P value= 0.24, 0.17 respectively).

DISCUSSION

Avgeli P. et al conducted multi center study in overseas countries in which 997 patients with liver cirrhosis and concurrent ascites were assigned to three groups based on serum sodium concentration in a manner similar to that of current study. The prevalence of hyponatremia at a serum sodium < 138 meq/L, < 130 meq, was 49.4% and 21.6% respectively. Jong Hoon Kim et al (2009) showed prevalence of hyponatremia was 27%, 20.8% & 52.1% in patient with serum sodium < 130 meq/L, 131-135 & >135 respectively. Shaikh S. et al (2010)conducted a case control study constituting 217 patients with cirrhosis. hyponatremia (Sodium < 130 meq/L) was present in 58/217 (26.7%) patients and 54/217 (24.9%) patient had serum sodium level 131-135 meq/L while 105/217 (48.4%) patient had serum sodium > 135 meq/L.

The present study also indicates that a large proportion of patients with cirrhosis have abnormal values of serum sodium concentration. In fact more than one half (54%) of patients with cirrhosis had serum sodium level below the normal range (<135 meq/L) and 28% had value < 130 meq/L.

Although it is generally believed that the existence of serum sodium, concentration < 130 meq/L is associated with difficult to treat ascites few studies have been reported that specifically analyze the relationship between serum sodium level and responsiveness of ascites to diuretic therapy. Arroyo et al 3 reported that the presence of serum sodium < 130 meq/L was associated with lower glomerular filtration rate and solute free clearance and a poorer response to diuretics compared with patients with serum sodium >130 meq/L. Sub sequent studies by Bernardi et al[105] and Angeli et al showed that patients who do not respond to diuretic therapy had lower serum sodium concentrations compared with patients who respond to diuretics. The results of the current study confirm and extend these observations by showing that patients with serum sodium concentration < 130 meq/L have higher frequency of refractory ascites.

According to Paolo Angeli hepatic encephalopathy was present in 38% of the patients with serum sodium <130 meq/L , 24% of patient with serum sodium between 131-135 meq/L and 15% of patients had serum sodium level > 135 meq/L. Kim JH et al (2009) showed hepatic encephalopathy was present in 23% of the patients with serum sodium < 130 meq/L compared with 14% of patient with serum sodium between 131-135 meq/L & 24% of patient had serum sodium level >135 meq/L. Shaikh et al (2010) showed hepatic encephalopathy was present in 26/217 (11.9%) patients, of which 15/5 (25.8%) patients were with serum sodium <130 meq/L. In the present study the frequency of hepatic encephalopathy was associated with serum sodium level in such a way that in patients with serum sodium < 130 meq/L, 16/34 patients (47.05%) had hepatic encephalopathy; with serum sodium concentration 131-135 meq/L, 5/31 (16.12%) patients had hepatic encephalopathy & with serum sodium >136 meq/L 5/55 (9.09%) patients were having hepatic encephalopathy.

In the present study the frequency of hepatorenal syndrome was 38.23% (13/34) in patients with serum sodium <130 meq/L compared to 19.35% (6/31) with serum sodium 131/135 meq/L & 5.5%(03/55) in patients with serum sodium > 136 meq/L. Angel P et al showed HRS in 17% patient with serum sodium <130 meq/L compared with 10% in patients with sodium 131-135 only 6% in patients with normal serum sodium >136 meq/L. Kim J H et al (2009) showed HRS in 17% patients with serum sodium<130 meq/L compared with 10% in patients with serum sodium 130-135 meq/L & only 6% in patients with normal serum sodium.

In the present study 38.23%(13/34) of GI bleeding cases were associated with serum sodium <130 meq/l compared to 12.9% (04/31) with serum sodium level 131-135 & 12.72% (7/55) with serum sodium >136. In Kim J H study it was found that >53% of patient had GI bleeding with low serum sodium level <135 meq/L while 32.6% patient had GI bleeding with normal serum sodium level.

CONCLUSION

From our study we conclude that

- Cirrhosis was more common in middle age group.
- Cirrhosis was more common in males than females.
- Hyponatremia was frequent in cirrhotic patients which is dilutional hyponatremia.
- Hyponatremia in cirrhotic patients was significantly associated with severe complications of liver cirrhosis like hepatic encephalopathy, GI bleeding, and hepatorenal syndrome.
- Treatment of hyponatremia is important to prevent possible complications of cirrhosis of liver.

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