

A Study of Association between Serum Sodium Level and Severity of Liver Cirrhosis Complications at SMS Medical College, Jaipur

Dr. Ziya Ul Haq¹, Dr. Mahendra Kumar Agarwal², Dr. Tarun Khan³

^{1,3}Postgraduate Resident, Department of General Medicine, S.M.S. Medical College & Attached Group of Hospital, Jaipur, India

²Associate Professor, Department of General Medicine, S.M.S. Medical College & Attached Group of Hospital, Jaipur, India

Corresponding Author: Dr. Tarun Khan, Postgraduate Resident, Department of General Medicine, S.M.S. Medical College & Attached Group of Hospital, Jaipur, India

Abstract: Introduction: Chronic liver diseases (CLD) cause significant morbidity and mortality worldwide. Multiple etiological factors lead to a similar clinico-pathological syndrome in CLDs although the rates of progression and clinical course may be different. Globally there had been a 46% increase in CLD mortality in the world between 1980 to 2013. India is one of the focal point of this change. Aim and Objective: To evaluate the prevalence of hyponatremia, to examine whether serum sodium levels correlate with the presence and severity of cirrhotic complications. Material and Methods: This was a Cross sectional Observational Study conducted from May 2019 to August 2020 or till sample size is reached, whichever is earlier at Department of General Medicine of SMS Medical College and associated Hospital, Jaipur. The study included the sample size of 110 patients. Result: In this study we included 110 patients. Most of the patients were aged 50-60 years (46.4%) followed by 60-70 years (38.2%). Only 17 (15.4%) subjects were aged below 50 years. Mean age of subjects was 57.29 years. In our study there were male (80%) and only 22 (20%) were females. We found that Alcohol was the most common cause of cirrhosis among study subjects (92.7%), followed by Hepatitis B (6.4%). Hepatitis C was found in 1 (0.9%) patient as a cause of cirrhosis. In our study most of the patients had Child pugh class B (44.5%) followed by Child Pugh class C (37.3%) and only 20 (18.2%) subjects had Child pugh class A. Conclusion: Dilutional hyponatremia is frequent in cirrhotic patients, found in almost half of the patients. Severe hyponatremia was seen in 27% of cirrhotic patients. Low serum sodium levels in cirrhosis are associated with severe complications of liver cirrhosis like hepatic encephalopathy, hepato-renal syndrome, ascitis, sub-acute bacterial peritonitis, portal hypertension, hepatic hydrothorax and even higher mortality. Hyponatremia can be used as important simple prognostic marker liver cirrhosis and mortality.

Keywords: Chronic liver diseases, clinico-pathological syndrome, Serum Sodium

1. Introduction

Chronic liver diseases (CLD) cause significant morbidity and mortality worldwide. Multiple etiological factors lead to a similar clinico-pathological syndrome in CLDs although the rates of progression and clinical course may be different.^{1,2} Globally there had been a 46% increase in CLD mortality in the world between 1980 to 2013. India is one of the focal point of this change.³⁻⁵ Alcohol was the most common cause of cirrhosis and one fifth of the patients of all etiologies were current alcohol consumers while 12% patients had diabetes.

In cirrhosis Hyponatremia is defined as a reduction in serum sodium below 130 mmol/L.⁶ Though the lower limit of normal of serum sodium concentration is 135 mmol/L, but the patients with serum sodium concentration above 130 mmol/l show pathogenic and clinical features similar to those of patients with serum sodium below 130 mmol/L in cirrhosis.⁷

Hyponatremia results from the inability of the kidney to excrete a water load or excess water intake. Water intake depends upon thirst mechanism. Thirst is stimulated by increase in osmolality. Cirrhotic patients may develop two types of hyponatremia i.e. **hypovolemic hyponatremia and hypervolemic or dilutional hyponatremia.** Neurological manifestations of hyponatremia related to the existence of

brain edema, such as headache, disorientation, confusion, focal neurological deficits, seizures, and, in some cases, death due to cerebral herniation.⁸

Evidence support the existence of a relationship between hepatic encephalopathy and low serum sodium concentration. First, serum sodium levels and serum ammonia levels are major factors determining electroencephalographic abnormalities in cirrhosis.⁹

Treatment with vaptans may prevent the reduction in serum sodium levels commonly seen in patients under diuretic therapy. This improve the response to therapy in patients with difficult-to-treat as cites. The improvement of serum sodium concentration may reduce the risk of this complication. According to several studies it can be observed that, hyponatremia occurring as a result of a reduced solute-free water clearance was a key prognostic factor in patients with liver cirrhosis when hyponatremia was incorporated into the MELD score.¹⁰ and there are potential benefits of treating the condition early in Cirrhosis so need is there for further studies regarding this relationship, and there lies rationale of the present study which is conducted to evaluate the prevalence of hyponatremia, to examine whether serum sodium levels correlate with the presence and severity of cirrhotic complications.

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2. Material and Methods

This was an Cross sectional Observational Study. This study was conducted in department of General Medicine of SMS Medical College and associated Hospital, Jaipur. This study was conducted from May 2019 to August 2020.

Inclusion Criteria

- 1) Patients were included in the study on the basis of diagnosis of cirrhosis confirmed by clinical, biochemical, and ultrasonographic findings.
- 2) Age > 18 years and either gender.

Exclusion Criteria:-

- 1) Patients with hepatocellular carcinoma present at admission.
- 2) Patients using diuretics within a 1-month period before admission.
- 3) Patient taking SSRI, TCA, MAO inhibitors, cytotoxic drugs etc.
- 4) Chronic Kidney Disease, Cardiac failure.

3. Observations

In this study we included 110 patients. Most of the patients were aged 50-60 years (46.4%) followed by 60-70 years (38.2%). Only 17 (15.4%) subjects were aged below 50 years. Mean age of subjects was 57.29 years. In our study there were male (80%) and only 22 (20%) were females. We found that Alcohol was the most common cause of cirrhosis among study subjects (927%), followed by Hepatitis B (6.4%). Hepatitis C was found in 1 (0.9%) patient as a cause of cirrhosis. In our study most of the patients had Child pugh class B (44.5%) followed by Child Pugh class C (37.3%) and only 20 (18.2%) subjects had Child pugh class A. In our study normal serum sodium level (>135 mmol/l) was seen in 57 (51.8%) subjects. Hyponatremia was seen in 48.2% subjects of which 23 (20.9%) subjects had sodium level 131 – 135 mmol/l and 30 (27.3%) had sodium level ≤130 mmol/l.

Table 1: Child pugh class in relation to serum sodium level

Child pugh class	≤130 mmol/l		131-135 mmol/l		>135 mmol/l	
	N	%	N	%	N	%
A	1	3.3	1	4.3	18	31.6
B	12	40	10	43.5	27	47.4
C	17	56.7	12	52.2	12	21
Total	30	100	23	100	57	100

Chi-square = 20.354 with 4 degrees of freedom; P < 0.001 (S)

In table 1, the difference in Child pugh class in Hyponatremic patients as compared to normal sodium level was found to be statistically significant (p<0.001). We found that mean Child pugh score was significantly less in patients with sodium level ≤130 mmol/l (10.4) and 131-135 mmol/l (10.3) as compared to patients with sodium level >135 mmol/l (8.16) and this difference was found to be statistically significant (p<0.001).

We found that ascites was more common in patients with sodium level ≤130 mmol/l (90%) and 131-135 mmol/l (87%) as compared to patients with sodium level >135 mmol/l (70.2%), this difference was however not found to

be statistically significant (p>0.05). Grade 2 & 3 ascites was more common in patients with sodium level ≤130 mmol/l (53.3%) and 131-135 mmol/l (26.1%) as compared to patients with sodium level >135 mmol/l (8.8%), and this difference was found to be statistically significant (p<0.001).

We found that that subacute bacterial peritonitis was more common in patients with sodium level ≤130 mmol/l (40%) and 131-135 mmol/l (30.4%) as compared to patients with sodium level >135 mmol/l (15.8%), and this difference was found to be statistically significant (p=0.040). Hepato-renal syndrome was more common in patients with sodium level ≤130 mmol/l (16.7%) and 131-135 mmol/l (13%) as compared to patients with sodium level >135 mmol/l (0%). Hepatic encephalopathy was more common in patients with sodium level ≤130 mmol/l (46.7%) and 131-135 mmol/l (39.1%) as compared to patients with sodium level >135 mmol/l (12.3%), and this difference was found to be statistically significant (p=0.001).

We found that Variceal bleed was more common in patients with sodium level ≤130 mmol/l (33.3%) and 131-135 mmol/l (21.7%) as compared to patients with sodium level >135 mmol/l (17.5%), and this difference was however not found to be statistically significant (p>0.05).

Table 2: Grade of oesophageal Varices in relation to serum sodium level

Oesophageal Varices grade	≤130 mmol/l		131-135 mmol/l		>135 mmol/l	
	N	%	N	%	N	%
Absent	5	16.7	4	17.4	10	17.5
Grade 1	4	13.3	11	47.8	33	57.9
Grade 2	13	43.3	5	21.7	13	22.8
Grade 3	8	26.7	3	13	1	1.8
Total	30	100	23	100	57	100

Chi-square = 23.740 with 6 degrees of freedom; P<0.001 (S)

Table 2 depicts that grade 2 & 3 oesophageal grade was more common in patients with sodium level ≤130 mmol/l (70%) and 131-135 mmol/l (34.7%) as compared to patients with sodium level >135 mmol/l (24.6%), this difference was however not found to be statistically significant (p<0.001).

Figure 1 shows that Gastric varices was less common in patients with sodium level ≤130 mmol/l (16.7%) and 131-135 mmol/l (17.4%) as compared to patients with sodium level >135 mmol/l (29.8%), this difference was however not found to be statistically significant (p>0.05).

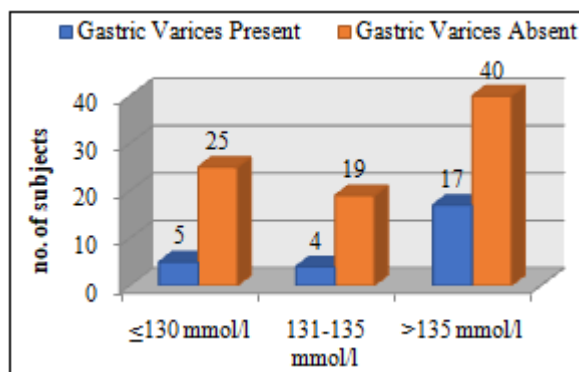


Figure 1: Gastric Varices in relation to serum sodium level

We found that portal hypertension was more common in patients with sodium level ≤ 130 mmol/l (100%) and 131-135 mmol/l (91.3%) as compared to patients with sodium level >135 mmol/l (78.9%), and this difference was found to be statistically significant ($p=0.016$).

Table 3: Mortality in relation to serum sodium level

Mortality	≤ 130 mmol/l		131-135 mmol/l		>135 mmol/l	
	N	%	N	%	N	%
Mortality	6	20	3	13	0	0
Survived	24	80	20	87	57	100
Total	30	100	23	100	57	100

Chi-square = 11.380 with 2 degrees of freedom; P = 0.003 (S)

Table 3 shows that mortality was more common in patients with sodium level ≤ 130 mmol/l (20%) and 131-135 mmol/l (13%) as compared to patients with sodium level >135 mmol/l (0%), and this difference was found to be statistically significant ($p=0.003$).

4. Discussion

Hyponatremia or low serum sodium level is an electrolyte imbalance that commonly occurs in hospitalized patients. Majority are dilutional hyponatremia caused by the impairment of solute-free water clearance. In recent years, hyponatremia has attracted interest as a possible prognostic factor for liver cirrhosis. The present study adds on to the existing research on hyponatremia in cirrhotic patients.

In our study most of the patients were aged 50-60 years (46.4%) followed by 60-70 years (38.2%). Mean age of subjects was 57.29 years. Most of the study subjects were male (80%). Similarly **Paolo Angeli et al (2006)**¹¹ in their study had the mean age of the patients 58.7 years. **Samiullah Shaikh et al (2010)**¹² also had majority of male subjects. Alcohol was the most common cause of cirrhosis among our study subjects (927%), followed by Hepatitis B (6.4%). That is identical to various studies done like **Mamun AA et al (2013)**¹³ **M.Kumar Raja et al (2017)**¹⁴.

In our study we found that most of the patients had Child pugh class B (44.5%) followed by Child Pugh class C (37.3%) and only 20 (18.2%) subjects had Child pugh class A. **Samiullah Shaikh et al (2010)**¹² however found that majority of patients belonged to child class C. **Mamun AA et al (2013)**¹³ found that On the basis of Child-Pugh score. out of 85 patient 31 were in class B while rest of the patient 54 were in class C. In our study that hyponatremia was seen in 48.2% subjects of which 23 (20.9%) subjects had sodium level 131 – 135 mmol/l and 30 (27.3%) had sodium level ≤ 130 mmol/l. **Samiullah Shaikh et al (2010)**¹² observed that in patients of cirrhosis hyponatremia (sodium <130 meq/l) was found in 26.7% patients and 24.9% had serum sodium from 131-135 meq/l whereas 48.4% patients had serum sodium >135 . **Mamun AA et al (2013)**¹³ found that about 30% of cirrhotic patient had hyponatremia (serum sodium >130 meq/L). **Bushra Javed et al (2018)**¹⁵ found that the mean serum sodium level was 129.79 ± 8.69 mg/dl. Among 84 (70%) patients of hyponatremia, 27 (22.5%) had mild hyponatremia, 38 (31.67%) had moderate hyponatremia while 19 (15.8%) had severe hyponatremia.

Complications of cirrhosis observed to be more common with hyponatremia. In conformance to that **Maria-Carlota Londoño et al (2006)**¹⁶ in a study found that Patients with hyponatremia (serum sodium lower than 130 mEq/L) had a greater incidence of neurologic disorders, renal failure, and infectious complications than patients without hyponatremia. **Khalil et al (2013)**¹⁷ observed statistically significant increase observed in frequencies of some complications including ascites, intractable ascites, hepatic hydrothorax, spontaneous bacterial peritonitis and hepatic encephalopathy, in hyponatremic patients compared to those without hyponatremia.

Grade 2 and above encephalopathy was more common in patients with sodium level ≤ 130 mmol/l (33.4%) and 131-135 mmol/l (30.4%) as compared to patients with sodium level >135 mmol/l (1.8%). **Samiullah Shaikh et al (2010)**¹² found that hepatic encephalopathy was more frequent in patients with serum sodium < 130 meq/l. **Ibrahim M. Boghdady et al (2015)**¹⁸ found hyponatremia commonly associated with hepatic encephalopathy. Mortality was more common in patients with sodium level ≤ 130 mmol/l (20%) and 131-135 mmol/l (13%) as compared to patients with sodium level >135 mmol/l (0%), and this difference was found to be statistically significant. **Visampally Suresh Kumar et al (2020)**¹⁹ also observed similar findings.

5. Conclusion

Dilutional hyponatremia is frequent in cirrhotic patients, found in almost half of the patients. Severe hyponatremia was seen in 27% of cirrhotic patients. Low serum sodium levels in cirrhosis are associated with severe complications of liver cirrhosis like hepatic encephalopathy, hepato-renal syndrome, ascitis, sub-acute bacterial peritonitis, portal hypertension, hepatic hydrothorax and even higher mortality. Hyponatremia can be used as important simple prognostic marker liver cirrhosis and mortality.

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