

Original Research Article

HYPONATREMIA AS A PREDICTOR OF HEPATIC ENCEPHALOPATHY AND MORTALITY IN CIRRHOSIS OF LIVER

Chandrakala¹, Krutika Rani², Chetan Hallad³, Saarah Farheen⁴, Shailesh Salunke⁵

¹Professor and HOD, Department of General Medicine, FOMS, KBNU, India.

²⁻⁵Junior Resident, Department of General Medicine, FOMS, KBNU, India.

Received : 27/02/2025
Received in revised form : 17/04/2025
Accepted : 04/05/2025

Corresponding Author:

Dr. Chetan Hallad,
Junior Resident, Department of
General Medicine, FOMS, KBNU,
India.
Email: drchetanhallad@gmail.com

DOI: 10.70034/ijmedph.2025.2.195

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2025; 15 (2); 1085-1088

ABSTRACT

Background: Hyponatremia develops in approximately 20-30% of cirrhotic patients with ascites. It causes cerebral oedema, thereby precipitating Hepatic Encephalopathy (HE). Hyponatremia is directly related to deterioration in terms of grades of HE and Mortality rate. **Objectives:** To study the prevalence of hyponatremia and to correlate it with severity of HE and mortality in cirrhosis of liver.

Materials and Methods: This was a prospective study conducted on 82 patients more than 18 years of age diagnosed with cirrhosis of liver. Patients with malignancy, chronic kidney disease, cardiac disease, cerebrovascular accidents and drugs causing hyponatremia were excluded. HE was graded according to West Haven classification. The results were considered significant if p value <0.05.

Results: Out of 82 cirrhosis of liver patients, 68 (83.0%) were males and 14 (17.0%) were females. The mean age was 50.4 ± 10.41 years. Hyponatremia was present in 38 (46.0%) patients with mean 126.34 ± 5.9 mEq/L. HE was present in 46 (56.0%) patients. HE grade I was present in 12 (26.0%), grade II in 15 (33.0%), grade III in 11 (24.0%), grade IV in 8 (17.0%) patients. Out of 38 hyponatremia patients, 29 (76.0%) had HE and out of 44 normonatremic, 17 had HE which was highly significant ($P < 0.001$). Hyponatremia with HE had higher mortality rate (20.0%) than normonatremic with HE (9.0%) which was significant ($P < 0.001$).

Conclusion: As cirrhosis with hyponatremia is associated with higher grades of HE and higher mortality rate, it could be reduced by timely recognition and treating hyponatremia.

Keywords: Hepatic encephalopathy, hyponatremia.

INTRODUCTION

Hepatic cirrhosis is a major contributor to global morbidity and mortality,^[1] with a particularly pronounced impact in developing nations, exerting considerable strain on healthcare resources and professionals. Hyponatremia is defined when serum sodium level is below 130 mEq/L, a frequent complication with ascites, affecting 20-30% of these individuals.^[2] This form of hyponatremia is usually dilutional (hypervolemic), meaning the sodium imbalance results from an excess of water, rather than a deficit in sodium.

Hyponatremia serves as an indicator of advancing liver disease, and studies suggest that its presence

notably heightens the likelihood of developing HE. Moreover, the severity of hyponatremia correlates directly with the severity of HE, with more pronounced hyponatremia linked to higher grades of encephalopathy. Although the exact mechanism linking hyponatremia to HE is still not fully understood, it is believed that the osmotic imbalance caused by sodium fluctuations results in swelling of brain astrocytes, which contributes to neurological dysfunction.

The annual incidence of HE in cirrhosis patients is approximately 8%, with various underlying conditions—such as constipation, esophageal variceal bleeding, and infections like spontaneous

bacterial peritonitis—potentially triggering the onset of HE. Hyponatremia is a key factor in the progression and onset of HE, as it increases the risk of encephalopathy and associated electroencephalographic changes. Recent studies have emphasized the importance of hyponatremia as a significant prognostic marker in patients with chronic liver disease. Cirrhotic individuals with hyponatremia generally have worse survival outcomes compared to those without it. As such, comprehending the relationship between hyponatremia and the frequency and severity of HE is crucial for optimizing patient management. Our study aims to investigate the frequency of hyponatremia in cirrhotic patients and its correlation with the incidence and severity of HE.

MATERIALS AND METHODS

This was a prospective study conducted in the Department of General Medicine from 1st June 2022 to 31st May 2023. A total of 82 patients, aged more than 18 years, diagnosed with cirrhosis of the liver, were included in the study. Patients with malignancy, chronic kidney disease, cardiac diseases, cerebrovascular accidents, or those on medications known to cause hyponatremia were excluded from the study.

A detailed history and clinical examination were performed for all patients. Relevant investigations, including complete hemogram, liver function tests, renal function tests, serum sodium levels, and arterial blood gas analysis, were carried out. The severity of hepatic encephalopathy (HE) was assessed using the West Haven classification, which categorizes HE into grades I to IV.

Serum sodium levels were measured to determine the presence of hyponatremia. Patients were classified as either hyponatremic ($\text{Na}^+ < 135 \text{ mEq/L}$) or normonatremic ($\text{Na}^+ > 135 \text{ mEq/L}$). Hyponatremic patients were classified as mild, moderate and severe if serum sodium levels are 135-130, 129-125 and less than 125 mEq/L respectively. The correlation between hyponatremia, the severity of HE, and mortality rate was assessed. Data were analyzed using appropriate statistical tests, and a p-

value of < 0.05 was considered statistically significant.

Aim of the Study

1. To study the prevalence of hyponatremia in cirrhosis of liver.
2. To correlate hyponatremia with severity of HE and mortality rate in cirrhosis of liver.

RESULTS

This was a prospective study conducted on 82 cirrhosis of liver patients, to co-relate the relationship between the severity of hyponatremia and hepatic encephalopathy (HE). Out of 82 patients, 68 (83.0%) were males and 14 (17.0%) were females. The mean age was 50.4 ± 10.41 years. Out of 82 patients 38(46.0%) had hyponatremia. The mean sodium level was $126.34 \text{ mEq/L} \pm 5.9$. Out of 38 patients 34.2% had sodium levels $\leq 124 \text{ mEq/L}$, 39.5% had levels between 125–129 mEq/L, and 26.3% had levels between 130–134 mEq/L, indicating moderate variability.

Out of 82 patients, 46(56.1%) had HE, among them 26.1% had Grade-I, 32.6% had Grade-II, 23.9% had Grade-III and 17.4% had Grade IV HE. There was a positive co-relation between hyponatremia and HE with 76.3% of hyponatremic patients having HE which was statistically highly significant ($P = 0.0006$). Further analysis revealed a significant correlation between the severity of hyponatremia and the grades of HE. In patients with mild hyponatremia, 50% had no HE, while those with moderate or severe hyponatremia showed higher rates of Grade-III and Grade-IV HE. The chi-square test ($X^2 = 29.17$, $P = 0.001$) and correlation coefficient ($r = 0.437$, $P < 0.01$) highlighted a significant relationship between the two conditions, suggesting that the severity of hyponatremia is strongly associated with the progression of hepatic encephalopathy.

Additionally, the study found that patients with both hyponatremia and HE had a significantly higher mortality rate (20%) compared to those with eunatremia and HE (7%), with this difference being statistically significant ($P < 0.001$). This underscores the increased risk associated with hyponatremia in patients with hepatic encephalopathy.

Table 1: Basic characteristics

Basic characteristics		Details
Age in years(mean)		50.4±10.41
Sex	Males(no)	68
	Females(no)	14
Hyponatremia(meq/L) (mean)		126.34 ± 5.9
Hepatic Encephalopathy(no)		
Grade I		12
Grade II		15
Grade III		11
Grade IV		08
Mortality Rate (%)	Hyponatremia with HE	20
	Eunatremic with HE	7

Table 2: Severity of hyponatremia (n=38)

Hyponatremia	Frequency	Percentage (%)
≤ 124	13	34.2
125—129	15	39.5
130—134	10	26.3
Total	38	100.0
Mean ± SD	126.34 ± 5.9	

Table 3: Severity of Hepatic Encephalopathy (n=46)

Grades of HE	Frequency	Percentage (%)
Grade-I	12	26.1
Grade-II	15	32.6
Grade-III	11	23.9
Grade-IV	08	17.4
Total	46	100.0

Table 4: Association between Hyponatremia with Hepatic Encephalopathy

Hyponatremia	Hepatic Encephalopathy		Total	Test value, P-value and Significance
	Yes	No		
Yes	29	9	38	X ² = 11.754, P=0.0006, HS
No	17	27	44	
Total	46	36	82	

NS= not significant, S=significant, HS=highly significant

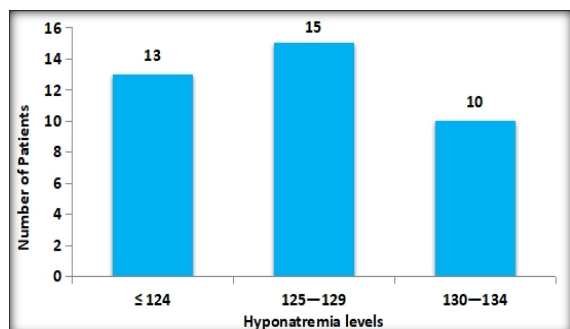
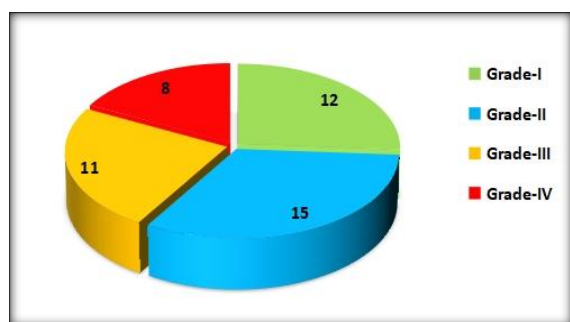
There was statistically highly significant association between Hyponatremia and Hepatic Encephalopathy (P<0.001).

Table 5: Correlation of severity of Hyponatremia with Grades of Hepatic Encephalopathy

Hyponatremia	Grades of HE				None	Total	P-value & significance
	I	II	III	IV			
Mild	2	2	1	0	5	10	Test value=29.17 P= 0.001 HS
Moderate	2	3	5	2	3	15	
Severe	0	1	5	6	1	13	
None	6	5	4	2	27	44	
Total	10	11	15	9	36	82	
Correlation coefficient	r = 0.437, P< 0.01 highly significant correlation						

NS= not significant, S=significant, HS=highly significant

There was statistically highly significant association (correlation) between severity of Hyponatremia with Grades of Hepatic Encephalopathy (P<0.001).

**Figure 1: Bar diagram represents Serum Sodium Levels****Figure 2: Pie diagram represent Severity of Hepatic Encephalopathy**

DISCUSSION

Hyponatremia is a common electrolyte imbalance in patients with cirrhosis, often linked to the development and severity of hepatic encephalopathy. Symptoms can range from mild confusion to severe encephalopathy and coma. The degree of hyponatremia is directly associated with the severity of hepatic encephalopathy, and lower sodium levels are linked to increased mortality. Hyponatremia develops in approximately 20-30% of cirrhotic patients.^[2] (Table 1).

In our study out of 82 patients of cirrhosis, 38(46.0%) patients had hyponatremia. The mean sodium level in this study was 126.34 mEq/L, which falls within the range frequently observed in cirrhotic patients with HE,^[3] (Table 2). The distribution of hyponatremia in this study, with 34.2% having sodium levels ≤ 124 mEq/L, 39.5% between 125–129 mEq/L, and 26.3% between 130–134 mEq/L, reflects the varying severity of sodium imbalances commonly seen in patients with liver dysfunction, as reported by other studies.^[3-4] (Table:2).

The high prevalence of HE in this study (56.1%) supports the well-established link between

hyponatremia and hepatic encephalopathy (Table 3). Previous research, such as a study by Gupta et al. (2017), found that 50-60% of patients with cirrhosis exhibit some degree of HE, and hyponatremia is a key factor in this association.^[5] The present study's finding that 76.3% of hyponatremic patients had HE further strengthens the argument that low sodium levels are strongly associated with the development of HE, a finding corroborated by studies like that of Patidar et al. (2013), which showed that hyponatremia is a significant predictor of HE in cirrhotic patients.^[6]

Further analysis of the correlation between the severity of hyponatremia and HE grades also aligns with previous work. The higher rates of Grade-III and Grade-IV HE in patients with moderate to severe hyponatremia (as compared to those with mild hyponatremia) are consistent with findings from a study by Wong et al. (2014), which showed that more severe hyponatremia correlates with advanced stages of HE,^[7] (Table 5). The statistical significance of the correlation ($r = 0.437$, $P < 0.01$) confirms that the degree of sodium imbalance is closely related to the progression of encephalopathy (Table:4), further validating the results from other studies like those by Bownes et al. (2016), who reported a similar correlation in cirrhotic patients.^[8] Hyponatremia, particularly in its severe form, serves as a strong predictor of mortality in cirrhotic patients. Moreover, the study's finding that patients with both hyponatremia and HE have a significantly higher mortality rate (20%) compared to those with eunatremia and HE (7%) adds important evidence to the growing body of literature linking hyponatremia with worse outcomes in liver disease. This result is in line with research by Malhi et al. (2015), who demonstrated that hyponatremia is an independent predictor of poor prognosis and higher mortality in patients with cirrhosis and HE.^[9-10] The statistical significance of this finding ($P < 0.001$) underscores the critical need for close monitoring and management of sodium levels in patients with hepatic encephalopathy to improve survival outcomes.

CONCLUSION

The study highlights a significant association between hyponatremia and hepatic encephalopathy (HE), with more severe hyponatremia linked to higher grades of HE. Patients with both hyponatremia and HE had a higher mortality rate, emphasizing the negative impact of low sodium levels on outcomes. These findings underline the importance of monitoring and managing sodium levels in HE patients, as hyponatremia worsens both the severity of HE and the overall prognosis.

REFERENCES

1. Scaglione S, Kliethermes S, Cao G, Shoham D, Durazo R, Luke A, et al. The epidemiology of cirrhosis in the United States: A population-based study. *J Clin Gastroenterol*. 2015;49(8):690-6.
2. Dooley JS, Lok AS, Garcia-Tsao G, Pinzani M, editors. *Sherlock's diseases of the liver and biliary system*. 13th ed. Chichester: John Wiley & Sons; 2018. p. 138-40
3. Wu G, Zhang X, Chen H, et al. Sodium imbalances and hepatic encephalopathy: A clinical review. *Hepatology Res*. 2019;49(3):215-222.
4. Yuan S, Xu L, Liu X, et al. Hyponatremia in cirrhosis: Clinical implications and management. *World J Gastroenterol*. 2015;21(1):23-33.
5. Gupta S, Rajender G, Kumar A, et al. Prevalence and management of hepatic encephalopathy in cirrhotic patients. *Liver Int*. 2017;37(9):1335-1342
6. Patidar KR, Shah VH, Gavis M. Role of hyponatremia in the prognosis of hepatic encephalopathy. *Hepatology*. 2013;57(2):616-623.
7. Wong F, Bernardi M, Balk R, et al. Predictors of hepatic encephalopathy in cirrhosis. *Lancet*. 2014;383(9931):1985-1995.
8. Bownes D, Bassendine MF, O'Grady J, et al. Hyponatremia as a predictor of hepatic encephalopathy. *J Hepatol*. 2016;64(3):625-632.
9. Malhi H, Gores GJ, Sowa J, et al. Hyponatremia and its effect on survival in cirrhosis and hepatocellular carcinoma. *J Clin Gastroenterol*. 2015;49(1):24-30.
10. Younas A, Riaz J, Chughtai T, Maqsood H, Saim M, Qazi S, Younus S, Ghaffar U, Khaliq M. Hyponatremia and its correlation with hepatic encephalopathy and severity of liver disease. *Cureus*. 2021 Feb;13(2).