

Association of Hyponatremia and Encephalopathy in Patients with Chronic Liver Disease

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Abstract

Objective: To determine the association of hyponatremia in chronic liver disease patients with presentation of hepatic encephalopathy (HE) at Isra university Hospital Hyderabad.

Methods: This study was cross sectional and carried out at medicine and gastroenterology department of Isra university Hospital Hyderabad and MMC Mirpurkhas. Study duration was from September 2015 to March 2016. All the cases with age more than 25 years, both genders after diagnosis of chronic liver disease with sign and symptoms of Hepatic Encephalopathy were selected in this study. Blood sample for serum sodium level, was send to diagnostic laboratory of the hospital. Hyponatremia was classified as: 130–135 mEq/L (mild), 125–130 mEq/L (moderate) and < 125 mEq/L (severe). Hepatic encephalopathy was categorized according to the West Haven classification (4 grades)

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Results: Total number of cases was 80. Mean age was 48 + 8.5 years. 55 (68.5%) patients were male. Majority of cases, 55 (68.5%) patients were infected with HCV. 40% patients had normal level of sodium, 25% had mild, 20% had moderate while 15% patients had severe hyponatremia. On the grading of encephalopathy, 30 (37.5%) patients had grade 1 encephalopathy while 25/(31.2%) patients had grade 2, 15/(18.8%) had grade 3 while 10 (12.5%) patients had grade 4. The serum sodium levels significantly decreased with increasing severity of hepatic encephalopathy ($P = 0.001$).

Conclusion: We concluded that the hyponatremia is significantly linked with Hepatic Encephalopathy (HE) in patients having chronic liver disease (CLD).

Key Words: CLD, hyponatremia, hepatic encephalopathy.

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Introduction

Chronic liver diseases (CLD) and its complications are the major health problem, due to big burden of Hepatitis C virus and Hepatitis B virus in the community¹ and it is also the commonest reason of death in Pakistani population. It is very common reason of admission to our hospitals.² In the decompensation condition, cases having CLD generally present with ascites, jaundice, portal hypertension, gastrointestinal hemorrhage, spontaneous bacterial peritonitis and hepatic encephalopathy.³ About 30% of patients with CLD usually die due to Porto systemic encephalopathy.⁴ The clinical course of patients with CLD is frequently complicated due to increase in the renal function abnormalities and imbalance of electrolytes.⁵

In the body disturbance of the water is the main sign of advance cirrhosis,⁶ This phenomena of distur-

bance of water is linked to the existence of ascites and is characterized by the development of dilutional hyponatremia, which is a frequent complication and sequel of chronic liver disease.^{5,7} Recent study indicates that hyponatremia is a key prognostic factor in patients with CLD.⁸ The prevalence of hyponatremia [serum Na < 130 mEq/L] in patients with cirrhosis with ascites is approximately 30%.⁹ The relationship between hyponatremia and severity of cirrhosis is associated with the development of complications. hepatic encephalopathy, hepatorenal syndrome and spontaneous bacterial peritonitis are more presented in cases having serum concentration < 130 mEq.¹⁰ Furthermore in cases having ascites, those having hyponatremia have a lower diuretics response, higher frequency of refractory ascites, and frequent requirement of the therapeutic paracentesis.¹¹ A study from Pakistan demonstrated 51.6% of CLD cases had serum sodium concentration below than the normal level.⁵ Borroni et al,¹² reported that hyponatremia was in 30% of CLD cases. Hyponatremia can induce or aggravate Hepatic encephalopathy, leading to disease progression like seizures, coma and even brain death. The aim of this study was to evaluate the association of hyponatremia in chronic liver disease patients with presentation of hepatic encephalopathy.

Material and Methods

This study was cross sectional and carried out at medicine and gastroenterology department of Isra university Hospital Hyderabad and MMC Mirpur Khas. Study duration was 7 months from September 2015 to March 2016. All the cases with age more than 25 years, both genders, after diagnosis of chronic liver disease with sign and symptoms of hepatic encephalopathy were selected in this study. All the cases on diuretic therapy, with hepatocellular carcinoma, with diabetes, hypertension (HTN), heart failure and chronic kidney disease (CKD) were excluded from the study. Detailed history, clinical examination and various routine and necessary investigations were done in all cases. After that blood sample for serum sodium level, was sent to diagnostic laboratory of the hospital. The demographic profile of the patients was noted. The severity of decrease sodium concentration was assessed as normal serum sodium [Na⁺] level is 135-145mmol/L and the value < 135 was labeled as low or hyponatremia. The severity of hyponatremia was categorized as: 130–135 mEq/L (mild), 125–130 mEq/L (moderate) and < 125 mEq/L (severe). The hepatic

encephalopathy was graded according to the West Haven classification (4 grades). Grades I-II were taken as mild to moderate encephalopathy, while grades III-IV were taken as severe encephalopathy. All the data regarding age, gender, serum sodium concentration, presence of hepatic encephalopathy were recorded. All the data were entered into SPSS 16.0 version and were analyzed by using the same software.

Results

Total number of cases was 80. Mean age was 48 + 8.5 years. Males were found in the majority as compared to females. Regarding virology status of cases, HCV patients were most common, 10 patients had HBV while 15 patients were infected by both HCV and HBV (Table 1).

Table 1: Basic characteristic of cases (n = 80).

Variables	No. of Patients/(%)
AGE (mean ± SD)	48.4 ± 8.5 years
Gender	
Male	55 (68.5%)
Female	25 (31.5%)
Virology	
HCV	55 (68.5%)
HBV	10 (31.5%)
HCV + HBV	15 (31.5%)

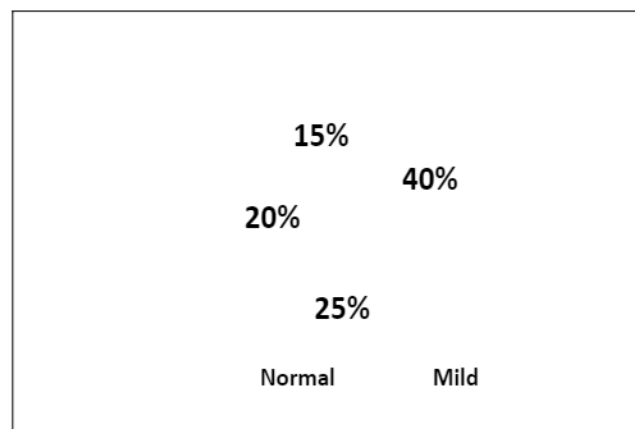


Fig. 1: Hyponatremia Classification n = 80.

According to classification of hyponatremia, majority of the patients had normal level of sodium, 25% had mild, 20% had moderate while 15% patients had severe hyponatremia (**Fig. 1**).

On the grading of encephalopathy, mostly patients were found with grade 1 encephalopathy while 25 patients had grade 2, 15 patients had grade 3 while 10 patients had grade 4 encephalopathy (**Fig. 2**).

In the results of this study serum sodium level significantly decreased with increasing the severity of hepatic encephalopathy $p = \text{value } 0.001$ (**Table 3**).

Discussion

Hepatic encephalopathy (HE) is commonest and serious complications of cirrhosis and is also the main reason of mortality.¹³ Hyponatremia can induce or aggravate HE, leading to disease progression and even death.^{14,15} In this study total number of cases was 80. Mean age was 48 ± 8.5 years. 55 (68.5%) patients were male while 25 (31.5%) patients were female. Similarly Qureshi MA et al.¹⁶ reported that of 202 patients, 90 (44.6%) were males and 112 (55.4%) females. Eighty-one (40.1%) patients were of the age greater than 60 years. Sulehria SB et al.¹⁷ reported that common age was recorded 44.56 ± 3.63 years, 172 (68.8%) were male and 78 (31.2%) were female.

In this study 40% patients had normal level of sodium, 25% had mild, 20% had moderate while 15% patients had severe hyponatremia. As well as Sulehria SB et al.¹⁷ reported that 129 (51.6%) patients had hyponatremia due to chronic liver disease, while 121 (48.4%) had no hyponatremia. In a Korean study¹⁸ prevalence of hyponatremia (less than serum sodium ≤ 135 mmol/L) was 47.9% in hospitalized patients.

The hyponatremia sodium (≤ 130 mmol/L was 27). 1%. In this series on the grading of encephalopathy, 30 (37.5%) patients had grade 1 encephalopathy while 25 (31.2%) patients had grade 2, 15 (18.8%) had grade 3 while 10 (12.5%) patients had grade 4 encephalopathy. Sulehria SB et al.¹⁷ reported that out of 129 patients with hyponatraemia, 16 (12.4%) were having grade I, 24 (18.6%) had grade II, 38 (9.46%) had grade III and 51 (39.54%) had grade IV hepatic encephalopathy.

In the results of this study decreases of serum sodium level is very important in CLD and its severity

Table 2: Grading of Hepatic Encephalopathy ($n = 80$).

Variables	No. of patients	%
Grade: I	30	37.5%
Grade: II	25	12.5%
Grade: III	15	18.8%
Grade: IV	10	31.2%

Table 3: Hyponatremia According to Severity of Hepatic Encephalopathy ($n = 80$).

Encephalopathy	Severity of Hyponatremia			
	Normal N = 32	Mild N = 20	Moderate N = 16	Severe N = 12
Grade: I	20	07	03	00
Grade: II	11	08	05	01
Grade: III	01	04	05	05
Grade: IV	00	01	03	06

$P = \text{value } 0.001$ by applying the chi-square test

is significantly associated with severity of hepatic encephalopathy $p = \text{value } 0.001$. Similarly Samiullah Shaikh et al.¹⁹ stated that the greater frequency of hyponatremia was seen in patients having hepatic encephalopathy. In another study, the severity of hyponatremia, particularly at sodium level ≤ 130 mmol/L, corresponded to increase the risks of ascites, hepatic encephalopathy and other complications of cirrhosis, as compared those with the serum sodium level ≤ 136 mmol/L.^{15,20}

Association between HE and serum sodium levels may be described as; severe liver failure in cases with level of serum sodium < 130 meq/l, and these both events may be pathophysiologically associated.²¹ Decreased sodium level in cases having CLD, is associated with are mark able reduction of organic osmolytes in the cerebral concentration, that probably reflect compensatory osmo regulatory mechanisms against cell swelling.^{22,23}

Conclusion

We concluded that the hyponatremia is significantly associated with hepatic encephalopathy in patients having chronic liver disease. Therefore it is recom-

mended that every patient who presents with chronic liver disease should be investigated for hyponatremia to identify patients at high risk of complications including hepatic encephalopathy.

References

1. Nadeem MMA, Yousaf M, Zakaria T, Hussain N, Ali 2005. The value of clinical signs in diagnosis of cirrhosis. *Pak. J. Med. Sci.* 2005; 21: 121-4.
2. Almani SAAS, Memon AI, Memon I, Shah Q, Rahpoto R, Solangi, 2008. Cirrhosis of liver: Etiological factors, complications and prognosis. *J. Liaquat Uni Med Health Sci.* 2008; 7: 61-6.
3. Khyalappa R, Bardeskar A. Significance of Hyponatremia in Decompensated Chronic Liver Diseases. *Sch. J. App. Med. Sci.* 2016; 4: 606-608.
4. Hayat AS, Shaikh N, Memon F. Identification of Precipitating Factors in Hepatic Encephalopathy Patients at Liaquat University Hospital Jamshoro. *World Appl. Sci. J.* 2010; 8 (6): 661-66.
5. Qureshi MO, Khokhar N, Saleem A, Niazi TK. Correlation of Hyponatremia with Hepatic Encephalopathy and Severity of Liver Disease. *Journal of the College of Physicians and Surgeons Pakistan.* 2014; 24 (2): 135-37.
6. Ginès P, Berl T, Bernardi M. Hyponatremia in cirrhosis: from pathogenesis to treatment. *Hepatology.* 1998; 28: 851-64.
7. Gaglio, MarfoK, Chiodo J. Hyponatremia in Cirrhosis and End-Stage Liver Disease: Treatment with the Vasopressin V₂-Receptor Antagonist Tolvaptan. *Dig Dis Sci.* 2012; 57 (11): 2774-85.
8. Shaikh S, Mal G, Khalid S, Baloch GH, Akbar Y. Frequency of hyponatremia and its influence on liver cirrhosis-related complications. *J Pak Med Assoc* 2010; 60: 116-20.
9. Cárdenas A, Ginès P. Predicting mortality in cirrhosis-serum sodium helps. *N Engl J Med.* 2008; 359: 1060-6.
10. Shaikh S, Mal G, Khalid SH, Baloch GH, Akbar Y. Frequency of hyponatraemia and its influence on liver cirrhosis – related complications. *J Pak Med Assoc.* 2010; 602: 116-120.
11. Bernardi M, Serena C, Santi L. Hyponatremia in Patients with Cirrhosis of the Liver. *J. Clin. Med.* 2015; 4: 85-101.
12. Borroni G, Maggi A, Sangiovanni A, Cazzaniga M, Salerno F. Clinical relevance of hyponatremia for the hospital outcome of cirrhotic patients. *Dig Liver Dis.* 2000; 32: 605-10.
13. Khokhar N, Niazi SA. Chronic liver disease related mortality pattern in Northern Pakistan. *J Coll Physicians Surg Pak.* 2003; 13: 495-7.
14. Li W, Shaoqi Y, Rui H, Jianguo H. Hyponatremia in patients with cirrhosis with hepatic encephalopathy [Internet]. [updated 2011 Mar 17; cited 2011 Dec 15]. Available from: <http://www.hi128.com>
15. Guevara M, Baccaro ME, Ríos J, Martín-Llahí M, Uriz J, Ruiz del Arbol L, et al. Risk factors for hepatic encephalopathy in patients with cirrhosis and refractory ascites: relevance of serum sodium concentration. *Liver Int.* 2010; 30: 1137-42.
16. Qureshi MO, Khokhar N, Saleem A, Niazi T K. Correlation of Hyponatremia with Hepatic Encephalopathy and Severity of Liver Disease. *Journal of the College of Physicians and Surgeons Pakistan.* 2014; 24 (2): 135-137.
17. Sulehriasb, Zafar MS, Rauf, M, Ghafoor A. Frequency of Hyponatraemia in Hepatic Encephalopathy in Chronic Liver Disease at Mayo Hospital, Lahore. *PJMHS.* 2013; 4: 1204-6.
18. Borroni G, Maggi A, Sangiovanni A, Cazzaniga M, Salerno F. Clinical relevance of hyponatremia for the hospital outcome of cirrhotic patients. *Dig Liver Dis.* 2000; 32: 605-10.
19. Shaikh S, Mal G, Khalid S, Baloch GH, Akbar Y. Frequency of hyponatraemia and its influence on liver cirrhosis-related complications. *J Pak Med Assoc.* 2010; 60 (2): 116-20.
20. Cárdenas A, Ginès P. Predicting mortality in cirrhosis-serum sodium helps. *N Engl J Med.* 2008; 359: 1060-6.
21. Angeli P, Wong F, Watson H, Gines P. Hyponatremia in cirrhosis: results of a patient population survey. *Hepatology.* 2006; 44: 1535-42.
22. Restuccia T, Gomez-Anson B, Guevara M, Alessandria C, Torre A, Alayrach ME. Effects of dilutional hyponatremia on brain organic osmolytes and water content in patients with cirrhosis. *Hepatology.* 2004; 39: 1613-22.
23. Haussinger D. Low grade cerebral edema and the pathogenesis of hepatic encephalopathy in cirrhosis. *Hepatology.* 2006; 43: 1187-90.