Journal of Current and Advance Medical Research
January 2023, Vol. 10, No. 1, pp. 41-46
http://www.banglajol.info/index.php/JCAMR
ISSN (Print) 2313-447X
ISSN (Online) 2413-323X
NLM Catalog ID 101673828
DOI: https://doi.org/10.3329/jcamr.v10i1.69970

ORIGINAL ARTICLE

Association between Serum Electrolyte Level and Outcomes among Hospitalized Liver Cirrhosis Patients Presented with Hepatic Encephalopathy Admitted at a Tertiary Care Hospital

Mostofa Monwar Kowshik[1], Nashid Islam[2], Faysal Ahmed[3], Monira Parveen Konica[4], Partha Pratim Das[5]

[1]Registrar, Dhaka Medical College, Dhaka, Bangladesh; [2]Consultant (Palliative Medicine), Bangladesh Cancer Society and Welfare Homes, Dhaka, Bangladesh; [3]Medical Officer, Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh; [4]Lecturer, Department of General and Dental Pharmacology, Dhaka Dental College, Dhaka, Bangladesh; [5]Associate Professor, Department of Medicine, Dhaka Medical College, Dhaka, Bangladesh

Abstract

Background: Hepatic encephalopathy is the most common and debilitating complication among the patients with cirrhosis. Electrolyte derangement is greatly related to recurrence and outcome of patients hospitalized with hepatic encephalopathy. **Objective:** This study was aimed to find out the association between these two variables in our setting. **Methodology:** The study was a cross-sectional study and conducted among 100 patients admitted with hepatic encephalopathy. Diagnosis and staging of hepatic encephalopathy were done based on West Haven staging, and severity of liver cirrhosis by the MELD (Model for End-Stage Liver Disease) scoring, and the outcomes were determined by the condition of the patients during discharge. Baseline serum electrolyte level was done for all the study participants. **Results**: Among 100 patients, male-female ratio was 7:3 with an average (standard deviation) age 56.25(±14.8) years. Most common causes of hepatic encephalopathy were infection (40.0%), gastrointestinal bleeding (30.0%), electrolyte abnormality (30.0%). Outcomes of hepatic encephalopathy were complete recovery (75.0%), needed ICU admission (15.0%) and death (10.0%). This study found no co-relation between baseline electrolyte and complete recovery of these patients and no association with the outcome of the patients. **Conclusion:** Baseline serum electrolyte have no significant influence on recovery of the patients with hepatic encephalopathy with liver cirrhosis. [*Journal of Current and Advance Medical Research, January 2023;10(1):41-46*]

Keywords: Electrolyte; hepatic encephalopathy; cirrhosis

Correspondence: Dr. Faysal Ahmed, Medical Officer, Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh; **Email:** faysalmmc@yahoo.com; Cell No: +8801717563091; **ORCID:** https://orcid.org/0009-0003-3147-5797

Introduction

Liver cirrhosis is the seventh most common cause of death in both the developed and developing countries[1]. In the last two decades, there is rapid increase in the incidence of hepatitis in the world as well as cirrhosis. Various etiologies of cirrhosis of liver have been identified. Among them, chronic

viral hepatitis (hepatitis B and C) and non-alcoholic steatohepatitis (NASH) are the commonest causes of cirrhosis in Asia and Africa[2].

One of the most common and debilitating complications of cirrhosis of liver is hepatic encephalopathy. The exact worldwide prevalence of hepatic encephalopathy remains unknown, possibly due to differences in the etiological factors, severity of the disease, and challenges in diagnosing minimal or sub-clinical hepatic encephalopathy. In several studies, it has been found that almost 30-45% of cirrhotic patients present with overt hepatic encephalopathy. If rigorously tested; up to two thirds have some degree of mild or subclinical hepatic encephalopathy[3,4]. Studies also reveal that minimal hepatic encephalopathy reduce the quality of life of patients with liver cirrhosis[5].

Hepatic encephalopathy is defined as ‘‘brain dysfunction caused by liver insufficiency and/or Porto-systemic shunting manifesting as a wide spectrum of neurological or psychiatric abnormalities ranging from subclinical alterations to coma”[6]. Though the actual pathophysiology of hepatic encephalopathy has not been still not clearly understood, but several predisposing factors have been identified. Most common predisposing factors for hepatic encephalopathy are dehydration, hypokalemia, acute kidney injury, non-adherence to medications, constipation, and infections[7-9].

The treatment options for hepatic encephalopathy focus on mainly correction and reversing the predisposing factors. Early identification of the predisposing factors and treatment improves the outcome of the patients. It has been observed in a study that there were increased rates of hepatic encephalopathy, prolonged hospital stays, higher rates of morbidity and mortality in cirrhotic subjects with hypokalemia, hence correction of hypokalemia improves the health of patients, decreases hospital stay, mortality and morbidity[10]. In multiple studies, it has been found that hyponatremia and hypokalemia are often associated with worse prognosis with the patients with hepatic encephalopathy. Guevara, et al reported an association between the occurrence of hepatic encephalopathy and hyponatremia in 70 patients[11].

Qureshi, et al found that a serum sodium concentration of less than 135 mmol/L was associated with a greater frequency of encephalopathy in cirrhotic patients compared to patients whose serum sodium was more than 135 mmol/L., although another cohort study found no association between serum electrolyte levels with the outcome of hepatic encephalopathy[12,13].

However, there is no study in Bangladesh on the association between serum electrolytes and the outcome of hepatic encephalopathy. Early identification and reversal of the predisposing factors will help to decrease morbidity and mortality due to hepatic encephalopathy. This study was aimed to find out the association between these two variables in our setting.

Methodology

Study Design and Settings: This cross-sectional observational study was carried out among the hospitalized patients with cirrhosis of liver and hepatic encephalopathy in the Department of Medicine, Gastroenterology, Hepatology and Critical Care Medicine of Dhaka Medical College, Dhaka, Bangladesh from March 2019 to August 2019 for a period of six months. Both male and female individuals diagnosed with hepatic encephalopathy at any stage of West Haven staging due to cirrhosis of the liver were included. Patients displaying abnormal serum creatinine and bilirubin levels were excluded from the study.

Study Procedure: Data was collected by the investigators using a semi-structured questionnaire sheet during admission. Socio-demographic data and predisposing factors as presence of infection, history of gastro-intestinal bleeding, hemoglobin (Hb), white blood cell (WBC) count, Platelets, Albumin, Blood Urea nitrogen (BUN), Causes of liver cirrhosis, international normalized ratio (INR), serum creatinine, total bilirubin data were collected from the hospital case sheets. Physical examination and higher psychic function test was performed by the attending physicians to grade the hepatic encephalopathy and observe any clinical sign of portal hypertension. Diagnosis and staging of hepatic encephalopathy were done based on West Haven staging, and severity of liver cirrhosis by the MELD (Model for End-Stage Liver Disease) scoring, and the outcomes were determined by the condition of the patients during discharge.

Serum Electrolytes Measurement: Ten ml blood was collected in separate heparinized sterile vials by an expert medical technologist for measuring serum electrolytes. Then the samples were sent to the hospital laboratory in proper precaution within 1 hour of collection. Serum electrolytes are measured by the indirect ion-sensing method using auto-analyzers located in the central laboratories of

hospitals. All patients were given conservative treatment for hepatic encephalopathy and required supportive treatments for the underlying predisposing causes. Next follow up was given during discharge or death of the patient to obtain the outcome.

Statistical Analysis: It was purposively recruited 100 participants for this study, aiming to align with a calculated sample size based on a 95% confidence interval, a 10% margin of error, and an assumed 30% prevalence of hepatic encephalopathy in liver cirrhosis. The initial estimation using the formula suggested a sample size of 81; however, considering potential missing data and data cleaning, we increased recruitment to 100 participants. Following data entry and logical validation, statistical analysis was conducted using SPSS 26.0 (Armonk, NY, USA). For continuous variables, mean values along with their respective standard deviations (SD) were utilized for summarization. Categorical variables were summarized by indicating the count and percentage of patients falling into each category. The investigation into the associations between serum electrolyte parameters (Na, K, Cl, HCO3) and discharge outcomes was carried out using multinomial logistic regression models, employing 95% confidence intervals for analysis. Results with a P-value of less than 0.05 were considered statistically significant.

Ethical consideration Ethical clearance was obtained from the Ethical Review Committee. Of Dhaka Medical College, Dhaka (Approval no: MEU-DMC/ECC/2019/134 date: 05/05/2019). Informed written consent was obtained from the eligible patients eligible or their legal guardians if they were unable to give consent. Confidentiality was maintained strictly.

Results

Mean (±SD) age of the participants were 56.25 (±14.8) years among them majority (70.0%) of the respondents were men. Almost half (51.0%) of the respondents belonged to the age group of 45 to 65 years. Mean (±SD) MELD score was 25.5 (±17.0), with 30.0% of the patients having the score within 8.5 to 25.5. The majority of the causes of cirrhosis of liver remained unknown (74.0%). Half (50.0%) of the causes of cirrhosis are known. Among the known causes, the common were HBV (45.0%), HCV (15.0%), followed by NASH (10.0%), rest of the causes remain unknown (cryptogenic). Most common predisposing factor of hepatic encephalopathy was infection (40.0%). The majority (82.0%) of participants had grade II to grade III hepatic encephalopathy during admission (Table 1).

Table 1: Baseline Characteristics of the Patients (n=100)

Variables	Percent
Age (Mean±SD)	56.3±14.8 Years
Age Group	
• Less Than 45 Years	25.0%
• 45 to 65 Years	51.0%
• More Than 65 Years	23.0%
Gender	
• Men	70.0%
• Women	30.0%
MELD score, Mean (±SD)	**25.5±17.0**
• Less Than 8.5	21.0%
• 8.5 to 25.5	30.0%
• More Than 25.5	49.0%
Evidence of portal hypertension at admission	
• Yes	49.0%
• No	51.0%
Causes of liver cirrhosis	
• HBV	45.0%
• HCV	15.0%
• NASH	10.0%
• Unknown	30.0%
Precipitators of hepatic encephalopathy	
• Infection	40.0%
• GIT bleed	30.0%
• Electrolyte Abnormalities	30.0%
Grades of hepatic encephalopathy	
• Grade I	15.0%
• Grade II	39.0%
• Grade III	43.0%
• Grade IV	3.0%

Almost 70.0% of the patients had mild to moderate hyponatremia (serum Na less than 120 mmol/L), with the mean (±SD) Na level 125 (±10.5) mmol/L. Only 25.0% of the patients had severe hypokalemia (serum K level less than 2.5 mmol/L). Half (50.0%) of the patients had serum K level within the range of 2.5 to 3.5 mmol/L, with the mean (±SD) 3.0 (±2.5) mmol/L. Most of the patients had serum HCO_3 and serum Cl level within normal limit. Only 36% of patients had severe anemia (Hb level less than 6.1 gm/dl). Mean (±SD) Hb level was 9.0 (±2.5) g/dL. All patients had leukocytosis (WBC count more than 15000/cumm), and 78.0% cases had thrombocytopenia (platelet count up to 1,50,000/cumm). The majority (70.0%) of patients had hypoalbuminemia (serum albumin level less than 2.8 g/dL) (Table 2).

Table 2: Baseline Laboratory Values of the Patients During Admission (n=100)

Characteristics	Values
Serum Na in mmol/L, Mean (±SD)	125.0 (±10.5)
• Less than 110 mmol/L	30.0%
• 110 to 120 mmol/L	40.0%
• 120 to 135 mmol/L	30.0%
Serum K in mmol/L, Mean (±SD)	3.0 (±2.5)
• Less than 2.5 mmol/L	25.0%
• 2.5 to 3.5 mmol/L	50.0%
• 3.5-5 mmol/L	25.0%
Serum Cl in mmol/L, Mean (±SD)	110.0 (±8.2)
• Less than 78 mmol/L	40.0%
• 78 to 110 mmol/L	30.0%
• 110 to 130 mmol/L	70.0%
Serum HCO3 in mmol/L, Mean (±SD)	24.0 (±4.5)
• Less than 24 mmol/L	21.0%
• More than 24 mmol/L	79.0%
Hemoglobin in g/dL, Mean (±SD)	9.0 (±2.5)
• Less than 6.1 g/dL	36.0%
• 6.1 to 9.0 g/dL	53.0%
• More than 9.0 g/dL	11.0%
WBC	
• Less than 15000 /cumm	49.0%
• More than 15000 /cumm	51.0%
Platelets	
• Less than 50000 /cumm	38.0%
• 50000 to 1,50,000 /cumm	40.0%
• More than 1,50,000 /cumm	10.0%
Serum Albumin in g/dL, Mean (±SD)	2.8 (±1.3)
• Less than 2.8 g/dL	70.0%
• 2.8 to 3.0 g/dL	30.0%

Most used drugs in the patients hospitalized with hepatic encephalopathy were Lactulose and Rifaximin (74%). All the patients were given antibiotics (100%). Other used drugs were Propranolol (75%) and Frusemide (15%). The duration of hospital stay of the patients was 4.5 (2) days. More than half (68%) of the patients had hospital stay <3 days. The rest of the patients had hospital stay from 3 to 10 days. Most (75%) of the patients had complete recovery during discharge from the hospital. Only 10% died, and 15% needed intensive care unit admission (Table 3).

Table 3: Treatment and Outcome of the Patients (n=100)

Variables	Values
Duration of hospital stay in days, mean (±SD)	**4.5±2.0**
• Less than 3 days	68.0%
• 3 to 5 days	25.0%
• More than 5 days	7.0%
Drugs used during hospital stay	
• Frusemide	15.0%
• Rifaximin and lactulose	74.0%
• Propranolol	75.0%
• Antibiotics	100.0%
Outcomes	
• Complete recovery	75.0%
• ICU admission	15.0%
• Death	10.0%

After adjustment of confounding variables, the binary regression model showed no significant ($p<0.05$) association between complete recovery and serum electrolyte level at admission. There was no significant association ($p<0.05$) between other baseline serum electrolyte level and outcome of the patients during discharge (Table 4).

Table 4: Relationship between Serum Electrolyte and Outcome (n=100)

Variables	Standardized Coefficient β (95% CI)	P value
Association with Complete Recovery		
• Serum Na	0.93 (0.73 to 1.20)	0.36
• Serum K	- 0.95 (0.78 to 1.80)	0.48
• Serum Cl	0.85 (0.67 to 1.60)	0.51
• Serum HCO3	1.70 (0.90 to 1.80)	0.33
Association with death		
• Serum Na	1.50 (1.05 to 2.33)	0.85
• Serum K	0.99 (0.73 to 1.33)	0.19
• Serum Cl	1.30 (0.90 to 1.88)	0.47
• Serum HCO3	0.81 (0.62 to 1.07)	0.48
Association with ICU admission		
• Serum Na	0.66 (0.43 to 1.26)	0.78
• Serum K	0.95 (0.67 to 1.70)	0.58
• Serum Cl	0.97 (0.33 to 1.30)	0.63
• Serum HCO3	0.89 (0.67 to 1.24)	0.94

binary regression analysis (adjusted) was computed, and all the precisions were estimated at 95% confidence interval. *The standardized coefficient β was statistically significant at a threshold of $p < 0.05$; CI= confidence interval

Discussion

Hepatic encephalopathy is one of the common complications among the study participants with chronic liver disease. There are multiple factors influencing the outcome of hepatic encephalopathy, but serum electrolyte level shows less significance in determining the outcome of the patients with hepatic encephalopathy.

In our knowledge, this is the first study to explore the association between baseline serum electrolyte level and outcome of the patient with hepatic encephalopathy with liver cirrhosis among the Bangladeshi population. This study found no co-relation between baseline electrolyte and complete recovery of these patients, which is contradictory with study conducted in Pakistan where it was evidenced that hypokalemia in cirrhotic patients is associated with increased rate of hepatic encephalopathy, increased economic burden, high rate of morbidity, mortality, and prolonged hospital stay[10]. Again, our study had found no association between other serum electrolyte levels and outcome of the patients during discharge, which is like a Mexican cohort study among same type of patients were there was no association between baseline serum electrolyte level and outcome during discharge was not found[13]. In contrast to a study done by Guevara, et al where negative influence and hyponatremia and outcome of hepatic encephalopathy was reported our study found no association between these two variables[11, 14].

Regarding the causes of hepatic encephalopathy, the most prevalent cause in our study was infection, which is almost 2.5 times of the incidence of hepatic encephalopathy in Egypt (15%)[15]. The incidence of GI bleeding is lower in our study in contrast to another studies[8-10]. Among the causes of liver cirrhosis, the most prevalent cause was found in our study was HBV, and among other known causes, the prevalence of HCV was found lower than the studies done in Chittagong[16].

In this study the most common (75%) outcome of hepatic encephalopathy after admission was complete recovery, which was much higher than other studies where 48% patients died after admission with hepatic encephalopathy. Also, only 15% patients needed ICU admission in our study, while in the same study 35% patients needed ICU referral[16].

Most used drugs for treatment of hepatic encephalopathy on the patients recruited in this study were Lactulose, Rifaximin. Although in another studies Lactulose and Rifaximin were mostly used drugs, usually in single, while in our study these two drugs were mostly used in combination[16].

Conclusion

It can be said that, from our study we found that baseline serum electrolyte had less significance in determining the outcome of the patients with hepatic encephalopathy with liver cirrhosis. Also, the most common precipitating factor of hepatic encephalopathy in cirrhotic patients was infection. But it is hopeful that 75% of patients admitted with hepatic encephalopathy achieved complete recovery. But further research with larger population should be done to supplement our findings, so that the clinicians can use the findings of the study to predict the outcome of the patients with hepatic encephalopathy in early and take measures to correct the cause.

Acknowledgements
The authors gratefully acknowledge the Department of Microbiology and Immunology, Dhaka Medical College and Hospital (DMCH), Dhaka, Bangladesh for all the technical support for this study.

Conflict of Interest
The authors declare no conflicts of interest.

Financial Disclosure and Funding Sources
The author received no funding for this study.

Contributions to authors: Conception and design: MMK, PPD; Acquisition, analysis, and interpretation of data: MMK, NI, FA, MPK, PPD; Manuscript drafting and revising it critically: MMK, NI, FA, MPK, PPD; Approval of the final version of the manuscript: MMK, NI, FA, PPD; Guarantor accuracy and integrity of the work: MMK

Data Availability
Any inquiries regarding supporting data availability of this study should be directed to the corresponding author and are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate
Ethical approval for this study was granted by the Ethical Review Committee of Dhaka Medical College, Dhaka (Approval no: MEU-DMC/ECC/2019/134 date: 05/05/2019). As this was a prospective study the written informed consent was obtained from all study participants. All methods were performed in accordance with the relevant guidelines and regulations.

Cite this article as: Kowshik MM, Islam N, Ahmed F, Konica MP, Das PP. Association between Serum Electrolyte Level and Outcomes among Hospitalized Liver Cirrhosis Patients Presented with Hepatic Encephalopathy Admitted at a Tertiary Care Hospital. J Curr Adv Med Res 2023;10(1):41-46

ORCID
Mostofa Monwar Kowshik: https://orcid.org/0009-0007-1356-2618
Nashid Islam: https://orcid.org/0000-0002-5059-2441
Faysal Ahmed: https://orcid.org/0009-0003-3147-5797
Monira Parveen: https://orcid.org/0000-0002-8033-2237
Partha Pratim Das: https://orcid.org/0009-0001-8942-5608

Article Info
Received: 27 September 2022
Accepted: 12 October 2022
Published: 1 January 2023

References

1. Hospital Episode Statistics, Admitted Patient Care - England, 2002-03 [Updated on 1 Dec 2003, Accessed on 05 September 2023]. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/hospital-episode-statistics-admitted-patient-care-england-2002-03
2. Schuppan D, Afdhal NH. Liver cirrhosis. The Lancet. 2008;371(9615):838-51
3. Sarker M. Hepatic Encephalopathy, Cleveland clinic [Internet]. Ohio, USA. [Accessed on 05 September 2023]. Available from: https://my.clevelandclinic.org/departments/digestive/medical-professionals/hepatology/hepatic-encephalopathy
4. Hepatic Encephalopathy in Chronic Liver Disease. 2014 practice guideline by the European Association for the Study of the Liver and the American Association for the Study of Liver Diseases. J Hepatol. 2014;61(3):642-59
5. Agrawal S, Umapathy S, Dhiman RK. Minimal hepatic encephalopathy impairs quality of life. Journal of clinical and experimental hepatology. 2015;5: S42-8
6. Jalan R, Damink SW, Hayes PC, Deutz NE, Lee A. Pathogenesis of intracranial hypertension in acute liver failure: inflammation, ammonia and cerebral blood flow. Journal of hepatology. 2004;41(4):613-20
7. Iwasa M, Sugimoto R, Mifuji-Moroka R, Hara N, Yoshikawa K, Tanaka H, Eguchi A, Yamamoto N, Sugimoto K, Kobayashi Y, Hasegawa H. Factors contributing to the development of overt encephalopathy in liver cirrhosis patients. Metabolic brain disease. 2016;31:1151-6
8. Pantham G, Post A, Venkat D, Einstadter D, Mullen KD. A new look at precipitants of overt hepatic encephalopathy in cirrhosis. Digestive Diseases and Sciences. 2017;62:2166-73
9. Wijdicks EF. Hepatic encephalopathy. New England Journal of Medicine. 2016;375(17):1660-70
10. Jamali AA, Jamali GM, Jamali AA, Chandio MH, Tanwani BM. Hypokalemia in cirrhotic patients. Indo American Journal of Pharmaceutical Sciences. 2018;5(3):1831-8
11. Guevara M, Ginès P. Hyponatremia in liver cirrhosis: pathogenesis and treatment. Endocrinologia y Nutricion: Organo de la Sociedad Espanola de Endocrinologia y Nutricion. 2010;57:15-21
12. Qureshi MO, Khokhar N, Saleem A, Niazi TK. Correlation of hyponatremia with hepatic encephalopathy and severity of liver disease. J Coll Physicians Surg Pak. 2014;24(2):135-7
13. Alsaad AA, Stancampiano FF, Palmer WC, Henry AM, Jackson JK, Heckman MG, et al. Serum electrolyte levels and outcomes in patients hospitalized with hepatic encephalopathy. Annals of hepatology. 2018 Sep 13;17(5):836-42
14. 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 International. 2010;30(8):1137-42
15. Gad YZ. Precipitating factors of hepatic encephalopathy: An experience at Mansoura Specialized Medical Hospital, Egypt. Ann Trop Med Public Health 2012;5:330-4
16. Khatun UF, Sayeed A, Hussain SM, Paul S, Kawsar NM, Al-Azad MA. Etiological study of acute on chronic liver failure among patients admitted in medicine ward in Chittagong medical college hospital. Journal of Armed Forces Medical College, Bangladesh. 2013;9(2):77-82