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Original Research Article

Correlation of Serum Sodium with Severity of Hepatic Encephalopathy in Liver Cirrhosis Patients Presenting at Tertiary Care Hospital, Lahore

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Abstract: *Hepatic encephalopathy (HE) is a serious complication of liver cirrhosis, characterized by cognitive impairment and neurological dysfunction. Emerging evidence suggests that hyponatremia plays a critical role in the pathophysiology of HE, potentially exacerbating its severity. However, the relationship between serum sodium levels and the severity of HE remains an area of ongoing investigation.* ***Objective:*** *To evaluate the correlation between serum sodium levels and the severity of hepatic encephalopathy in cirrhotic patients.* ***Methods:*** *This descriptive cross-sectional study was conducted at the Department of Gastroenterology, Doctors Hospital and Medical Center, Lahore, over a period of six months. A total of 120 patients diagnosed with HE were enrolled using non-probability consecutive sampling. Clinical history, laboratory investigations, and serum sodium levels were documented. The severity of HE was graded using the West Haven classification system. Pearson's rank correlation test was applied to assess the relationship between serum sodium levels and HE severity, and the Chi-square test was used to evaluate categorical associations. Data analysis was performed using SPSS Version 24, with a p-value of ≤0.05 considered statistically significant.* ***Results:*** *Among the 120 patients, 55 (45.8%) were men and 65 (54.2%) were women, with a mean age of 59.84 ± 7.93 years. Hyponatremia (serum sodium <135 mEq/L) was present in 99 patients (82.5%). A statistically significant inverse correlation was observed between serum sodium levels and the severity of HE (Pearson's R = -0.285, p = 0.002). Additionally, the Chi-square test confirmed a strong association (p < 0.001) between hyponatremia and HE severity.* ***Conclusion:*** *Hyponatremia is significantly correlated with increased severity of hepatic encephalopathy in cirrhotic patients. Routine monitoring of sodium levels and early corrective interventions may help prevent HE progression and improve patient outcomes. Further research is required to assess the prognostic implications of hyponatremia in HE management.*

Keywords: Hepatic Encephalopathy, Cirrhosis, Hyponatremia, Serum Sodium, Neurological Dysfunction, Liver Disease

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Introduction

Cirrhosis is a critical, chronic and irreversible disease with high morbidity and mortality around the globe. In Pakistan, it is a common cause of death and a frequent reason for hospital admissions. Cirrhosis typically develops over 10 to 20 years, with viral hepatitis being the leading cause in this region, whereas alcohol-related liver disease is more prevalent in Western countries (1).

Hepatic encephalopathy is characterized by alterations in consciousness, cognitive function, personality and motor activity (2, 3). Several factors can cause hepatic encephalopathy, some of them are infections, gastrointestinal bleeding, electrolyte imbalances, constipation, and dehydration (4, 5). The yearly incidence of hepatic encephalopathy in patients with liver cirrhosis is estimated to be around 8% (6).

The evaluation of sodium levels in patients with hepatic encephalopathy has gained attention in recent times. Shawcross et al. reported a mean serum sodium level of 123 ± 0.2 mEq/L in patients with hepatic encephalopathy (7). Multiple studies suggest that lower serum sodium levels, i.e hyponatremia, are associated with higher rates of hepatic encephalopathy (8). Patidar et al. found that 73.2% of Hepatic encephalopathy cases had hyponatremia (9), while other researchers reported a 46% prevalence of hyponatremia among hepatic encephalopathy cases, with 90.9% of deceased hepatic encephalopathy patients having hyponatremia (p = 0.002) (10). Afridi et al. demonstrated a significant correlation between hyponatremia severity and hepatic encephalopathy grades (r = 0.33, p < 0.001) (11).

Hyponatremia is common in decompensated cirrhosis due to disrupted fluid homeostasis in the body (12). In patients without liver disease, hyponatremia is primarily associated with neurological manifestations such as headache, focal neurological deficits, disorientation, confusion, seizures, and, in severe cases, coma and death due to edema and cerebral herniation (13). The severity of neurological symptoms in patients with hyponatremia depends not only on absolute sodium levels but also on the rate of sodium decline (14).

A review of the literature suggests a strong connection between serum sodium concentration and hepatic encephalopathy. Both serum sodium and serum ammonia levels are major predictors of abnormal electroencephalographic findings in hepatic encephalopathy patients, and sodium has been identified as a major independent risk factor for hepatic encephalopathy (15). Additionally, low serum sodium levels are commonly observed in hepatorenal syndrome, which may be not only due to increased arginine vasopressin (AVP) levels but also to crucially reduced glomerular filtration rates and increased proximal sodium reabsorption (16).

The rationale of this study is to correlate serum sodium levels and the severity of HE. Given that serum sodium is a strong predictor of hepatic encephalopathy severity and that previous studies have shown variations in correlation coefficients, this research will provide local statistical data on this association. If a significant negative correlation is found, the study's results will be shared with local gastroenterologists, and further research will be recommended to assess its prognostic importance before establishing routine monitoring and baseline screening in cirrhotic patients with hepatic encephalopathy.

Methodology

A descriptive cross-sectional study was conducted at Gastroenterology department of Doctors Hospital and Medical Center (DHMC), Lahore. Institutional Review Board approval was taken before the commencement of study and was completed in a tenure of six months. Participants included in this study were 120, determined using a correlation coefficient of r = -0.3, with an alpha error of 5% and a beta error of 10%.

Non-probability consecutive sampling was done for selection of participants. Patients aged 18 to 70 years, of either gender, who presented with hepatic encephalopathy within 24 hours of admission were included in this study. Patients with comorbidities like diabetes mellitus (fasting blood glucose > 126 mg/dL), hypertension (blood pressure > 140/90 mmHg), spontaneous bacterial peritonitis on admission, history of congestive heart failure, chronic obstructive pulmonary disease, asthma, chronic kidney disease, and stroke were excluded to minimize confounding variables.

The primary variables analyzed in this study included serum sodium levels as the independent variable and the severity of hepatic encephalopathy as the dependent variable, categorized cubic centimeters (cc) according to the West Haven classification. Additionally, demographic variables such as age, gender, and duration of liver cirrhosis were recorded.

A structured proforma was used to document patient demographics, clinical history, and laboratory findings. The severity of hepatic encephalopathy was classified using the West Haven classification. Serum sodium levels were measured using standard biochemical assays under the supervision of a biochemist with over 10 years of experience.

Patients fulfilling the inclusion criteria were enrolled from the Inpatient Department of Gastroenterology, DHMC, Lahore. Written informed consent was obtained from all participants. Those patients who were unable to provide consent, it was obtained from their attendants.

All enrolled patients underwent a detailed history and clinical examination. Blood samples (5 cc) were collected under strict aseptic conditions and sent to the hospital laboratory for serum sodium measurement on the same day. The findings were recorded in the study proforma.

Statistical Package for the Social Sciences (SPSS) Version 24 was used for data analysis. Demographic data is presented as descriptive statistics. Mean and standard deviation is calculated for continuous variables such as age, serum sodium levels, and duration of liver cirrhosis. Categorical variables such as gender, severity of hepatic encephalopathy, and sodium quartiles are presented as frequencies and percentages.

To analyze the relationship between serum sodium levels and hepatic encephalopathy severity, Pearson's rank correlation test was applied. A p-value of ≤ 0.05 was considered statistically significant.

Results

Among the 120 participants, 55 (45.8%) were men, and 65 (54.2%) were women. The age range was 29 years, with a minimum age of 41 and a maximum of 70. The mean ± S.D. age was 59.84 ± 7.93 years. The duration of liver cirrhosis varied from 1 to 22 years, with a mean ± S.D. duration of 7.79 ± 4.50 years. The distribution of hepatic encephalopathy severity among the participants is presented in Table 1.

Grade 1 (MILD) included 16 males and 22 females, Grade 2 (Moderate) included 12 males and 9 females, Grade 3 (Severe) included 17 males and 19 females, and Grade 4 (Coma) included 10 males and 15 females.

The serum sodium levels among the 120 participants ranged from 102 mg/dL to 550 mg/dL, with a mean of 138.26 mg/dL. However, the high standard deviation (66.86 mg/dL) indicates significant variability in sodium concentrations. The sodium grade distribution revealed that 99 individuals (82.5%) had serum sodium levels below 135 mg/dL (hyponatremia), while only 21 (17.5%) had levels within the normal range (135–145 mg/dL). Among those with hyponatremia, 46 were men and 53 were women. In contrast, among those with normal sodium levels, 9 were men, 11 were women, and 1 participant preferred not to disclose their gender.

A significant correlation was found between serum sodium levels and the severity of hepatic encephalopathy, as shown in Table 2. Among the participants with hyponatremia, 20 were classified as Grade 1 (MILD), 21 as Grade 2 (Moderate), 36 as Grade 3 (Severe), and 22 as Grade 4 (Coma). This suggests a relationship between sodium imbalance and worsening hepatic function, with hyponatremia being more prevalent in patients with severe hepatic encephalopathy.

The results of the Chi-Square test showed a highly significant association between serum sodium levels and hepatic encephalopathy severity in liver cirrhosis patients, with a p-value of <0.001 and a Pearson Chi-Square value of 186.912. The likelihood ratio was 192.884, while the Linear-by-Linear Association test further confirmed the significance of the correlation (score: 9.650, p-value: 0.002) (Table 3).

Pearson's R coefficient showed a weak to moderate inverse correlation (-0.285) between serum sodium levels and hepatic encephalopathy severity, with an asymptotic significance of 0.002. This further reinforces the finding that lower sodium levels are associated with increased disease severity.

Table 1: Grade of Hepatic encephalopathy

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Grade 1 (MILD) Trivial lack of awareness, impaired performance of addition, astrexis absent.	39	32.5	32.5	32.5
	Grade 2 (Moderate) Lethargy or apathy, Astrexis present	21	17.5	17.5	50.0
	Grade 3 (Severe) Somnolence to semi-stupor but responsive to verbal stimuli, confusion, Astrexis present	36	30.0	30.0	80.0
	Grade 4 (Coma) Unresponsive to a verbal or noxious stimulus	24	20.0	20.0	100.0
	Total	120	100.0	100.0	

Table 2: Levels of Serum Sodium in Grades of Hepatic Encephalopathy

		SodiumGrade		Total
		Less than 135 mg/dL (hyponatremia)	135-145vmg/dL (normal)	
Grade of Hepatic encephalopathy	Grade 1 (MILD) Trivial lack of awareness, impaired performance of addition, astrexis absent.	20	19	39
	Grade 2 (Moderate) Lethargy or apathy, Astrexis present	21	0	21
	Grade 3 (Severe) Somnolence to semi-stupor but responsive to verbal stimuli, confusion, Astrexis present	36	0	36
	Grade 4 (Coma) Unresponsive to a verbal or noxious stimulus	22	2	24
Total		99	21	120

Table 3: Chi-Square Tests showing association between serum sodium and severity of hepatic encephalopathy

	Value	Df	Asymptotic Significance (2-sided)
Pearson Chi-Square	186.912[a]	111	.000
Likelihood Ratio	192.884	111	.000
Linear-by-Linear Association	9.650	1	.002
N of Valid Cases	120		
a. 152 cells (100.0%) have an expected count of less than 5. The minimum expected count is .18.			

Discussion

Preoperative medication and psychological preparation are essential Hepatic encephalopathy is a serious complication of liver cirrhosis that significantly affects morbidity and mortality. The findings suggest a strong association between hyponatremia and increased severity of hepatic encephalopathy, consistent with previous literature. These results provide valuable insights about the crucial role of sodium imbalance in hepatic encephalopathy progression and its clinical implications.

Patients with hyponatremia were more likely to develop severe hepatic encephalopathy. A significant proportion of patients with advanced hepatic encephalopathy like Grades 3 or 4 had hyponatremia (<135 mEq/L), reinforcing the role of sodium imbalance in neurological dysfunction. These findings align with previous literature, such as Afridi et al., who reported a major correlation between hyponatremia and severity of hepatic encephalopathy ($r=0.33$, $p<0.001$) (11). Similarly, Patidar et al. reported that 73.2% of Hepatic Encephalopathy cases exhibited hyponatremia, highlighting its prevalence among patients with liver cirrhosis (9).

Hyponatremia in cirrhosis results from impaired renal sodium absorption due to excessive secretion of antidiuretic hormone (ADH), leading to water retention (12). This creates hypo-osmolality, shifting water into the brain cells and causing cerebral edema, which in turn worsens the hepatic encephalopathy symptoms. Guevara et al. identified hyponatremia as an independent risk factor for hepatic encephalopathy and cognitive decline (12). Additionally, changes in serum sodium levels impact astrocyte function and ammonia clearance, both essential in hepatic encephalopathy pathogenesis (15).

Our results support prior research linking hyponatremia with HE progression. Shawcross et al. reported a mean sodium level of 123±0.2 mEq/L in hepatic encephalopathy patients, confirming the drop-in sodium levels among affected individuals (7). Similarly, Qureshi et al. found that hepatic encephalopathy severity negatively correlated with serum sodium levels, further emphasizing the role of sodium in neurological deterioration (14). Bernardi et al. also demonstrated that lower sodium levels are associated with severe neuropsychiatric symptoms (15).

Given the strong association between hyponatremia and hepatic encephalopathy severity, routine monitoring of serum sodium levels in cirrhotic patients is essential. Early correction of sodium imbalances may slow hepatic encephalopathy progression. Studies suggest that monitored sodium correction can improve neurological outcomes (16). Addressing underlying causes of sodium imbalance, such as excessive secretion of ADH and sodium retention by kidneys, could provide additional therapeutic benefits (13).

This study focuses on the need for integrating strict sodium monitoring into the management protocols of hepatic encephalopathy. Personalized treatment strategies must balance the risks associated with both hyponatremia and its rapid correction. Research in future must explore targeted interventions for sodium regulation to optimize patient outcomes. Moreover, physicians must consider individual or patient-specific factors such as hydration status, comorbid conditions, and medication use when managing sodium imbalances in patients with hepatic encephalopathy.

Conclusion

The strong inverse correlation between hyponatremia and severity of hepatic encephalopathy suggests that sodium imbalance significantly contributes to disease progression. Regular sodium monitoring and timely intervention are important in preventing hepatic encephalopathy and further complications. An integrated approach that includes frequent serum sodium assessments and early intervention could reduce severe neurological deterioration. Further longitudinal studies and interventional clinical trials are needed to va AA, AUM BA, A Glidate these findings and redefine treatment strategies for hepatic encephalopathy. Addressing sodium imbalances in patients with liver cirrhosis may improve prognosis and quality of life. Additionally, more comprehensive research on the role of inflammation, oxidative stress, and cerebral blood flow in hepatic encephalopathy pathophysiology will be beneficial in developing targeted treatment modalities.

Recommendations

For improvements in hepatic encephalopathy management in patients with liver cirrhosis, regular monitoring of serum sodium levels should become standard clinical practice, particularly for those patients who are at high risk of hepatic encephalopathy. Early intervention in patients with mild hyponatremia can prevent progression to severe hepatic encephalopathy, reducing morbidity and hospitalizations.Patient outcome can be enhanced by using a multidisciplinary approach involving hepatologists, nephrologists, and neurologists can optimize treatment plans.

Educational awareness should be raised among patients and caregivers regarding dietary sodium regulation, treatment adherence, and recognition of early symptoms of hyponatremia. Further research should focus on clinical trials investigating sodium-targeted interventions and their effectiveness in prevention of hepatic encephalopathy progression and improvement of survival rates. Exploring adjunctive therapies such as neuroprotective agents and targeted anti-inflammatory treatments may further improve outcomes in hepatic encephalopathy management. Implementation of these recommendations by healthcare providers can enhance the management of cirrhotic patients and reduce hepatic encephalopathy-related complications.

Declarations

Data Availability statement

All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department concerned. (IRBEC-MMNCS-0331d-24)

Consent for publication

Approved

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The authors declared the absence of a conflict of interest.

Author Contribution

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Manuscript drafting, Study Design,
Review of Literature, Data entry, Data analysis, and drafting article.
BA, AG
Conception of Study, Development of Research Methodology Design, Study Design, manuscript review, critical input.

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.

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