

Correlation of Serum Sodium Level with Severity of Hepatic Encephalopathy

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ABSTRACT

Objective: To determine correlation of serum sodium levels with severity of hepatic encephalopathy (HE).

Study Design: A Cross-sectional study.

Place and Duration of the Study: Department of Medicine, Mardan Medical Complex, Mardan from 1st October 2020 to 30th April 2021.

Methodology: A total of 170 patients of both genders with liver cirrhosis presenting with HE aged 35-65 years were included. Under aseptic conditions, blood was taken dispatched to institutional laboratory for serum sodium levels. Severity of hyponatremia was compared with study variables along with grades of HE. Post stratification chi square test was applied and $p < 0.05$ was considered statistically significant.

Results: Out of a total of 170 patients, 140 (82.4%) were male. Overall, mean age was 55.0 ± 3.87 years while 130 (76.5%) patients were aged between 51 to 65 years. Grading of HE revealed most of the patients, 73 (42.9%) to be having grade-III. Grading of hyponatremia revealed that 101 (59.4%) patients had mild hyponatremia, 50 (29.4%) moderate hyponatremia while 19 (11.2%) had profound hyponatremia. Age distribution was found to have significant association with severity of hyponatremia ($p < 0.0001$). Significant correlation between grades of HE and severity of hyponatremia was noted as 15 (78.9%) out of 19 profound hyponatremia cases belonged to HE grade-III whereas all 50 patients of moderate hyponatremia belong to HE grade III and IV ($p < 0.0001$).

Conclusion: Hyponatremia was observed to be a very common abnormality among patients of liver cirrhosis presenting with hepatic encephalopathy. Significant correlation of hyponatremia was found with respect to HE grades as severity of hyponatremia increased with severity of HE grades. Higher age groups had significant association with higher degree of hyponatremia.

Keywords: Hepatic encephalopathy, hyponatremia, liver cirrhosis, serum sodium.

INTRODUCTION

The global prevalence of HCV is estimated to be around 2.5%. HCV is known to be the most common etiology behind liver cirrhosis.¹ Hepatic encephalopathy (HE) is considered to be a major complication of severe acute or chronic liver insufficiency.² The HE is described as alterations in the personality, conscious level, cognitive behavior and motor functioning.³ Infections, gastrointestinal bleeding, electrolyte abnormalities, constipation and dehydration are some of the main precipitation factors for HE.^{4,5} Yearly rates of HE among patients of liver cirrhosis are estimated rise 8%.⁶

Evaluation of sodium levels among patients of HE has been a topic of interest in the recent decades. Shawcross DL et al revealed mean sodium levels among patients of HE to be 123 ± 0.2 mEq/L.⁷ Some researchers have pointed out relatively lower serum sodium levels with higher rates of HE.⁸ Patidar KR et al noted 73.2% of HE cases to have hyponatremia.⁹ Researchers found prevalence of hyponatremia to be 46% among HE cases and 90.9% cases of HE who expired had hyponatremia ($p = 0.002$).¹⁰

Not many studies have tried to evaluate the impact of severity of hyponatremia in HE cases while there is absence of local data this so this study was planned. Result of this study are expected to help clinicians in better evaluation and management approach toward hyponatremia among HE cases so that related morbidity and mortality can be reduced. Aim of this study was to determine correlation of serum sodium levels with severity of hepatic encephalopathy.

METHODOLOGY

This cross sectional study was done at the department of Medicine, "Mardan Medical Complex, Mardan" from 1st October 2020 to 30th April 2021. Approval from "Institutional Ethical Committee" was acquired. Written and verbal consents were sought from caregivers of all patients. Considering anticipated frequency of hyponatremia as 46%⁶ with 95% confidence level and 7.5% margin of errors, the sample size was calculated to be 170 patients.

Inclusion criteria were patients of both genders with liver cirrhosis presenting with HE aged 35-65 years. Exclusion criteria patients of stroke (as per medical history and medical record), or hyperosmolar diabetic coma (known diabetes mellitus and sugar level > 300 mg/dl) or impaired cerebral function (e.g. senile dementia, chronic subdural hematoma). Liver cirrhosis was diagnosed on the basis of sonographic findings of liver as alterations in the shape, parenchymal inhomogeneity and nodularity of the liver. At the time of enrollment, age, gender, duration of HE, previous history of hospitalization for HE were noted. Patients were examined for HE grading as per "West Haven Criteria".¹¹

Under aseptic conditions, blood was taken dispatched to institutional laboratory for serum sodium levels. The normal serum sodium concentration was taken as 135-145 mEq/L or hyponatremia < 135 mmol/L. Hyponatremia was further divided into mild (130-134 mmol/L), moderate (125-129 mmol/L) or profound (< 125 mmol/L).¹² All cases were managed according to local institutional protocols.

For data analysis, SPSS version 26.0 was used. Mean and standard deviation (SD) were representing numerical data while frequency and percentage were shown for categorical variables. Severity of hyponatremia was compared with the grades of HE. Stratification of effect modifier factors like age, gender, grades of hepatic encephalopathy, dehydration status, were done to compare the presence of hyponatremia. Post stratification chi square test was applied and $p < 0.05$ was considered statistically significant.

RESULTS

Out of a total of 170 patients with HE, 140 (82.4%) were male. Overall, mean age was 55.0 ± 3.87 years while 130 (76.5%) patients were aged between 51 to 65 years. Dehydration was observed in 114 (67.1%) cases. There were 110 (64.7%) patients who had past history hospitalization for HE. Grading of HE revealed most of the patients, 73 (42.9%) to be having grade-III HE. Table-1 is showing baseline characteristics of all HE cases.

Table-1: Characteristics of Patients with Hepatic Encephalopathy (n=170)

Characteristics	Number
Gender	Male 140 (82.4%)
	Female 30 (17.6%)
Age (years)	30-40 7 (4.1%)
	41-50 33 (19.4%)
	51-60 66 (38.8%)
	61-65 64 (37.6%)
Dehydration	114 (67.1%)
First admission for Hepatic Encephalopathy	60 (35.3%)
Grades of Hepatic Encephalopathy	I 6 (3.5%)
	II 22 (12.9%)
	III 73 (42.9%)
	IV 69 (40.6%)

All 170 patients of HE were having some kinds of hyponatremia. Grading of hyponatremia revealed that 101(59.4%) patients had mild hyponatremia, 50 (29.4%) moderate hyponatremia while 19 (11.2%) had profound hyponatremia (figure-1).

Table-2 is showing stratification of study variables with regards to severity of hyponatremia. No statistically significant difference was noted in terms of gender (p=0.5452), dehydration (p=0.5091) or past history of hospitalization for HE (p=0.3772) with severity of hyponatremia. Age distribution was found to have significant association with severity of hyponatremia (p<0.0001) as 15 (78.9%) of patients with profound hyponatremia (n=19) were aged between 51-60 years and all 50 (100%) patients of moderate

hyponatremia were aged between 51 to 60 years. Significant correlation between grades of HE and severity of hyponatremia was noted as 15 (78.9%) out of 19 profound hyponatremia cases belonged to HE grade-III whereas all 50 patients of moderate hyponatremia belong to HE grade III and IV (p<0.0001).

Figure-1: Distribution of Grades of Hyponatremia among patients of Hepatic Encephalopathy (n=170)

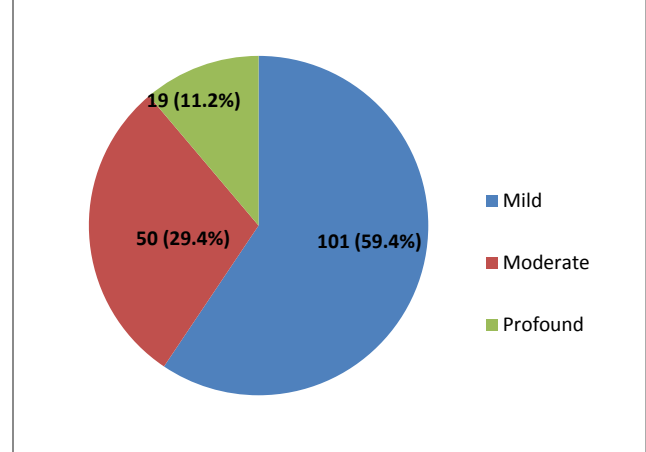


Table-2: Stratification of Study Variables with regards to Severity of hyponatremia

Study Variables	Severity of Hyponatremia			P-Value
	Mild (n=101)	Moderate (n=50)	Profound (n=19)	
Gender	Male 85 (84.2%)	41 (82.0%)	14 (73.7%)	0.5452
	Female 16 (15.8%)	9 (18.0%)	5 (26.3%)	
Age (years)	30-40 3 (3.0%)	-	4 (21.1%)	<0.0001
	41-50 33 (32.7%)	-	-	
	51-60 25 (24.8%)	26 (52.0%)	15 (78.9%)	
	61-65 40 (39.6%)	24 (48.0%)	-	
Dehydration	64 (63.4%)	36 (72.0%)	14 (73.7%)	0.5091
First admission for Hepatic Encephalopathy	32 (31.7%)	19 (38.0%)	9 (47.4%)	0.3772
Grades of Hepatic Encephalopathy	I 2 (2.0%)	-	4 (21.1%)	<0.0001
	II 22 (21.8%)	-	-	
	III 32 (31.7%)	26 (52.0%)	15 (78.9%)	
	IV 45 (44.6%)	24 (48.0%)	-	

DISCUSSION

In the present study, none of the patients of HE represented with serum sodium level above 135 mEq/L so hyponatremia turned out to be present in all cases. In further division, 59.4%, 29.4% and 11.2% patients were found to have mild, moderate of profound hyponatremia. A significant proportion of patients with CLD are thought to have abnormal serum sodium concentration.¹³ Hyponatremia is the most common occurrence in our study. A multi-central trial accommodating 28 hepatology centers from multiple continents having patients of liver cirrhosis showed that 50.6% cases had normal serum sodium levels while 27.8% cases had mild hyponatremia 21.6% cases had moderate hyponatremia which is showing that hyponatremia is a frequent finding among cases of chronic liver disease.¹⁴ Kim and colleagues analyzing 188 cases presenting with complications of liver cirrhosis, 47.9% patients had hyponatremia.¹⁵ Byung CY and Ray KW from USA hypothesized that hyponatremia and the resultant depletion of the organic osmolytes (like myo-inositol) from the brain cells might be contributing to brain edema which could further be progressing into possible pathogenesis of HE.¹⁶ Additionally, hyponatremia might be posing a 2nd osmotic hit to cerebral edema and astrocyte swelling which might be further precipitating HE.¹⁷ Researchers in the past have shown hyponatremia to be an independent predictor lowering quality of life and might be a contributor to HE in chronic liver disease patients.^{18,19}

Attar B in review study described majority of the cases (90%) of liver cirrhosis to have hyponatremia due to rise in extracellular fluid volume which correlates very well with the present findings.²⁰

A recent local study Younas A et al analyzing correlation of hyponatremia with HE and liver disease revealed that in 96 patients with hyponatremia and chronic liver disease, 84 had HE (p<0.001). Furthermore, in 96 patients with hyponatremia, 25.0% had mild hyponatremia, 58.3% moderate while remaining 16.7% had severe hyponatremia.²¹ Our findings are very consistent with what Younas A et al reported where significant correlation of severity of hyponatremia was observed with regards to grades of HE (p<0.001).²¹

Our findings are consistent with the published literature that hyponatremia is a common finding especially in patients presenting with HE. Researchers in the past have shown that patients of liver cirrhosis with hyponatremia have higher rates of adverse in-hospital outcomes. Moreover, not many studies in the past have analyzed correlation of degree of hyponatremia with HE grading so this was one of the major strengths of this study.

Being a single center study with a relatively small sample size and absence of blinding were some of the limitations of this study. We were unable to correlate outcomes of different grades of hyponatremia with HE grading which would have further given us useful insights.

CONCLUSION

Hyponatremia was observed to be a very common abnormality among patients of liver cirrhosis presenting with hepatic encephalopathy. Significant correlation of hyponatremia was found with respect to HE grades as severity of hyponatremia increased with severity of HE grades. Higher age groups had significant association with higher degree of hyponatremia.

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