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PREDICTORS OF OUTCOME IN HEPATIC ENCEPHALOPATHY: ROLE OF SERUM AMMONIA AND CHESS SCORE

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ABSTRACT

Background

Hepatic encephalopathy (HE) is a reversible neuropsychiatric complication of liver dysfunction, occurring in 30–45% of cirrhotic patients. Minimal HE may affect up to 60%. While ammonia is implicated in its pathogenesis, its role in predicting outcomes remains unclear. CHESS (Clinical Hepatic Encephalopathy Staging Scale) is a newer, simpler tool to assess HE severity. This study evaluates serum ammonia and CHESS score at admission as predictors of outcome in HE.

Methods

Fifty patients with HE (Hepatic Encephalopathy) due to chronic liver disease were studied. Serum ammonia and CHESS scores were recorded at admission. Patients were followed until discharge or death. LOS (Length of hospital Stay) was calculated for survivors.

Results

Among 50 patients (46 males, 4 females; mean age 52 years), 14 died. Mean ammonia levels in survivors and non-survivors were 111.4 µmol/L and 122.9 µmol/L, respectively (not statistically significant). However, among survivors, higher ammonia levels significantly correlated with longer LOS ($p=0.049$). Survivors with LOS >5 days had a mean ammonia level of 123.44 µmol/L, while those with LOS ≤5 days had 75.22 µmol/L. CHESS score <3 was seen in 6 patients (1 death); CHESS >3 in 44 patients (13 deaths). CHESS score did not significantly correlate with mortality or ammonia levels.

Conclusion

Serum ammonia at admission correlates with length of hospital stay among survivors. Ammonia levels did not predict mortality or correlate with CHESS score. The CHESS score failed to predict HE outcomes.

Keywords Hepatic Encephalopathy, Chronic Liver Disease, Serum Ammonia, CHESS Score, Outcome Predictors.

INTRODUCTION

Hepatic encephalopathy is a serious but potentially reversible neuropsychiatric complication of liver dysfunction, characterized by a broad range of cognitive, behavioral, and motor abnormalities. It commonly occurs in the setting of chronic liver disease, particularly cirrhosis, affecting approximately 30% to 45% of these patients. Furthermore, its subclinical variant, known as MHE (Minimal Hepatic Encephalopathy), can be seen in up to 60% of individuals with liver disease. Despite its reversibility, HE significantly impairs quality of life, increases the risk of hospitalizations, and serves as an independent predictor of mortality.

The pathogenesis of HE is multifactorial and not yet fully understood. However, elevated levels of ammonia, a neurotoxic metabolite predominantly cleared by the liver, have been consistently implicated in its development. In cirrhosis, impaired hepatic clearance and portosystemic shunting lead to systemic accumulation of ammonia, which crosses the blood-brain barrier and exerts deleterious effects on cerebral function. While the exact contribution of ammonia remains controversial, it is widely accepted as a key biomarker in the diagnosis and management of HE. Elevated serum ammonia levels are not only used to guide therapy initiation but are also often associated with the severity of encephalopathy, especially in cases precipitated by infections, gastrointestinal bleeding, or electrolyte imbalances.

Several clinical tools have been developed to grade the severity of HE. The West Haven Criteria remains the most widely used but is limited by interobserver variability and subjective interpretation. In contrast, the CHESS (Clinical Hepatic Encephalopathy Staging Scale) is a newer, simplified, and more reproducible method for assessing HE severity.

AIMS AND OBJECTIVES

This study aims to evaluate the prognostic value of serum ammonia levels and the CHESS in patients diagnosed with hepatic encephalopathy and admitted to Father Muller Medical College Hospital. The study seeks to assess whether serum ammonia levels and CHESS scores at the time of hospital admission can serve as reliable indicators for predicting clinical outcomes such as mortality and length of hospital stay in patients with chronic liver disease presenting with hepatic encephalopathy.

MATERIALS AND METHODS

Study Design

This was a hospital-based observational study conducted at Father Muller Medical College Hospital over a period of 18 months, from October 2013 to March 2015. The study included 50 patients diagnosed with hepatic encephalopathy in the setting of chronic liver disease. All patients were admitted to the hospital during the study period and were selected consecutively. Informed consent was obtained from the patients' relatives prior to inclusion in the study. Data collection was carried out using a structured proforma, and relevant clinical and biochemical parameters, including serum ammonia levels and CHESS scores, were recorded at the time of admission for analysis.

Inclusion and Exclusion Criteria

The study included patients presenting with altered sensorium who had a history of pre-existing or newly diagnosed chronic liver disease, consistent with hepatic encephalopathy. Patients were excluded if their altered sensorium was attributable to other causes such as local neurological deficits due to trauma, intracranial bleeding, space-occupying lesions, or stroke, as determined clinically. Individuals with psychiatric illnesses causing altered sensorium were excluded based on previous medical records and psychiatric evaluation. Patients with metabolic derangements without underlying chronic liver disease, those who had consumed alcohol within the past week, and patients diagnosed with Type A or Type B hepatic encephalopathy were also excluded. Additional exclusion criteria included patients who were discharged against medical advice and those receiving medications known to cause encephalopathy-like symptoms, such as 5-fluorouracil, asparaginase, and sodium valproate.

Data Collection Procedure

Fifty patients diagnosed with hepatic encephalopathy secondary to chronic liver disease and admitted to Father Muller Medical College Hospital were evaluated within 24 hours of admission. Diagnosis was based on clinical history, mental status changes, and physical examination, including psychometric tests such as drawing a star, spiral, or square. Chronic liver disease was confirmed via past medical records or ultrasonography. Relevant investigations-PT/INR, serum ammonia, CBC, renal function tests, blood cultures, and urine analysis-were conducted at admission. Venous ammonia levels were measured using the enzymatic method on the ROCHE COBAS 6000 analyzer, with samples processed within 30 minutes of collection. HE severity was assessed using the West Haven Criteria and CHESS scoring system within 24 hours, with a CHESS score >3 indicating moderate to severe encephalopathy. All patients received standard HE treatment, including lactulose, rifaximin, antibiotics, probiotics, and bowel wash. Recovery was defined by the patient's ability to draw a star and the resolution of asterixis. Outcomes were categorized as recovery (with length of hospital stay) or mortality, and correlations were analyzed between outcomes, serum ammonia levels, and CHESS scores.

Statistical Analysis

Data was analyzed using SPSS version 23 software. Descriptive statistics such as frequency, percentage, mean, and standard deviation were used to summarize the data. Inferential statistical methods, including the Karl Pearson correlation coefficient, chi-square test, and Student's t-test were employed to assess the significance of associations and differences between study variables. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Table 1 observes the age and sex distribution of patients, showing maximum incidence in the 41–60 years group with male predominance.

Age Group (in years)	Males	Females
20-40	16	0
41-60	23	4
More than 60	9	0

Table 1: Age and Sex Distribution

Table 2 illustrates the West Haven Classification, where most patients were in grades II and IV.

Grade	No. of Patients
I	7
II	16
III	8
IV	19

Table 2: West Haven Classification

Table 3 shows the Child-Pugh Score distribution, with the majority belonging to Class C.

Class	No. of Patients
A	0
B	8
C	42

Table 3: Child-Pugh Score Distribution

Table 4 presents the precipitating factors of HE, where infection and hyponatremia were the leading causes.

Factor	No. of Patients (%)
Infection	20 (40%)
Constipation	19 (38%)
Hypokalemia	16 (32%)
Haematemesis	14 (28%)
Diuretics	13 (26%)
Malena	12 (24%)
Hyponatremia	43 (86%)

Table 4: Precipitating Factors of HE

Table 5 describes the clinical features, with altered sensorium being the most frequent.

Feature	No. of Patients (%)
Altered sensorium	30 (60%)
Jaundice	28 (56%)
Abdominal distension	24 (48%)
Constipation	21 (42%)
Fever	16 (32%)
Haematemesis	14 (28%)
Malena	12 (24%)

Table 5: Clinical Features

Table 6 depicts the outcome of HE, showing higher survival (72%) compared to mortality (28%).

Outcome	No. of Patients (%)
Survivors	36 (72%)
Non-Survivors	14 (28%)

Table 6: Outcome of HE

Table 7 explains the relationship of serum ammonia levels with outcome and hospital stay, showing significant differences in survivors with longer stays.

Category	No. of Patients	Mean Ammonia (µmol/L)	P-Value
Non Survivors	14 (28%)	122.9	0.604 (NS)
Survivors	36 (72%)	111.2	0.604 (NS)
≤ 5 days (Survivors)	9 (23.5%)	75.22	0.049 (SIG)
> 5 days (Survivors)	27 (76.5%)	123.44	0.049 (SIG)

Table 7: Serum Ammonia and Outcome

DISCUSSION

In this study, 50 patients with chronic liver disease presenting with hepatic encephalopathy were analyzed to identify predictors of clinical outcomes. The parameters studied included age, sex, clinical features, etiology, precipitating factors, West Haven grading, Child-Pugh score, CHESS score, and serum ammonia levels.

Age

The mean age of the study population was 52.2 years, which is consistent with previous studies by Pathak et al.[1] (52 years) and Strauss et al.[2] (55 years). Udayakumar et al.[3] reported a slightly lower mean age of 46 years. The majority of patients in our study were above 40 years, a trend that reflects similar findings in the aforementioned studies. No significant difference in mean age was found between survivors and non-survivors (51.2 vs. 54.6 years; p=0.87), indicating that age did not significantly affect the outcome-a conclusion also supported by other studies.

Sex Distribution

A significant male predominance was observed in our study, with 92% (n=46) being males. This aligns with the findings of Strauss et al.[2] Udayakumar et al.[3] and Salam et al.[4] The skewed gender distribution likely reflects the higher prevalence of alcohol consumption among Indian males, which is a major etiological factor in chronic liver disease. Of the four female patients, two succumbed to the illness. However, no statistically significant correlation between sex and outcome was found. Interestingly, Pathak et al.[1] and Martel et al.[5] observed higher mortality among females with HE, suggesting that gender may serve as a prognostic indicator in some populations.

Clinical Features

The most common presenting symptom was altered sensorium (60%, n=30), followed by jaundice (56%) and abdominal distension (48%). These findings are in line with Pathak et al.[1] and Onyekwere et al.[6] who also reported altered mental status as a leading clinical feature. Contrarily, Martel et al.[5] and Rashid et al.[7] identified fever and constipation as predominant symptoms. The difference in presentation may be due to lower treatment compliance in our patient cohort.

Etiology of Chronic Liver Disease

Alcohol was the most common etiology (90%, n=45) in our study and was associated with poor prognosis, as all patients who died had a history of alcohol use. This supports findings from Onyekwere et al.[6] Pathak et al[1] and Udayakumar et al.[3] Other studies, such as Rashid et al.[7] Mumtaz et al.[8] and Salam et al.[4] identified Hepatitis B and C as predominant etiologies with prognostic relevance. Martel et al.[5] highlighted Hepatitis C and E, particularly among females, as causes of fulminant HE with high mortality. In our study, hepatitis B, C, and E were not systematically investigated, limiting conclusions regarding their role.

Precipitating Factors

Hyponatremia (86%) was the most common precipitating factor, followed by infection (40%) and constipation (38%). Hypokalemia was present in 32% of cases. The high incidence of electrolyte disturbances may be partially attributed to diuretic use (52%). Edema seen in many patients raises the possibility of dilutional hyponatremia. These findings are consistent with Siddique et al.[9] and Udayakumar et al.[3] In contrast, infection and sepsis were major precipitants in studies by Onyekwere et al.[6] Salam et al.[4] However, our study did not find a significant correlation between precipitating factors and mortality (p=0.785).

West Haven Grading

Most patients were in advanced stages of HE, with 38% in Grade IV and 32% in Grade II. Similar trends were seen in studies by Mumtaz et al.[8] and Salam et al.[4] where 70% and 58% of patients, respectively, were in Grades III and IV. Other studies, like Onyekwere et al.[6] and Rashid et al.[7] reported a majority in earlier grades with significant prognostic implications. In contrast, our study did not find any significant correlation between HE grade and outcome. This may be due to heterogeneity in treatment approaches among physicians.

Child-Pugh Score

A large proportion of patients (84%) were in Child-Pugh Class C, indicating advanced liver disease at presentation. Similar distributions were seen in studies by Strauss et al.[2] (89%), Onyekwere et al.[6] (65%), Mumtaz et al.[8] (80%), and Udayakumar et al.[3] (80%). Importantly, we observed a statistically significant correlation between Child-Pugh classification and outcome (p=0.005), suggesting its utility in prognostication.

Outcome

The overall in-hospital mortality was 28% (n=14), with a mean hospital stay of 8 ± 3 days. Among survivors, 75% had hospital stays exceeding 5 days. These outcomes are comparable to previous studies: Martel et al.[5] (mortality 27%, LOS 8 days), Pathak et al.[1] (30%, 6 days), Udayakumar et al.[3] (33%, 4 days), and Salam et al.[4] (22%, 6 days). Other studies reported lower mortality rates (<20%).[6,7,9]

CHESS Score and Outcome

CHESS was utilized both as a severity and prognostic tool. Among patients with CHESS ≤3, mortality was 16.6%, and survivors had a mean hospital stay of 6 days. In contrast, patients with CHESS >3 (88%) had a mortality rate of 29.5%, with survivors having a mean stay of 8 days. Despite this trend, no statistically significant correlation was found between CHESS score and mortality. CHESS has been proposed as a reliable severity marker in clinical trials,[10,11] but its prognostic value remains uncertain. In our study, the utility of CHESS was limited by the high proportion of patients presenting with advanced HE and impaired consciousness, making questionnaire-based scoring less feasible. Supplementing CHESS with the Glasgow Coma Scale may improve prognostic accuracy.

Serum Ammonia Levels

Our study attempted to evaluate the prognostic significance of serum ammonia. No significant difference in ammonia levels was found between survivors and non-survivors (p=0.604), consistent with studies by Ong et al.[12] However, among survivors, higher ammonia levels were associated with longer hospital stays (p=0.049), suggesting some correlation with morbidity. Overall, serum ammonia failed to predict mortality.

Correlation between CHESS and Serum Ammonia

We assessed the relationship between CHESS score and serum ammonia levels. Among patients with CHESS ≤3, mean ammonia levels were 89.9 µmol/L (survivors) and 109.3 µmol/L (non-survivors). In the CHESS >3 group, the values were 115.37 µmol/L (survivors) and 123.9 µmol/L (non-survivors). However, no significant correlation was observed (p=0.312).

Comparison with Other Studies

Study	Mortality	Stage at Presentation	HBV/HCV	Alcohol	Dyselectrolytemia	TB	PT	Gender	Infection
Onyekwere et al.[6]	48%	+	+	+	-	-	-	-	+
Pathak et al.[1]	30%	+	-	+	+	+	+	+	-
Siddique et al.[9]	-	-	-	-	+	-	-	-	+
Strauss et al.[2]	-	-	-	-	-	-	-	-	+
Martel et al.[5]	21%	+	+	-	-	-	-	+	+

Mumtaz et al.[8]	2%	+	+	-	-	-	-	-	-
Rashid et al.[7]	16%	+	-	-	-	-	-	-	-
Udayakumar et al.[3]	33%	-	-	-	+	-	-	-	-
Salam et al.[4]	22%	-	+	-	-	-	-	-	-
Present Study	28%	-							

CONCLUSION

While elevated serum ammonia levels were found to correlate with the length of hospital stay, they did not show a significant association with the severity of hepatic encephalopathy or patient mortality. Additionally, neither serum ammonia levels nor CHESS scores proved to be reliable predictors of mortality. These findings suggest that although serum ammonia may serve as a useful marker for hospitalization duration, it has limited value in assessing disease severity or predicting outcomes in patients with hepatic encephalopathy.

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