Original Article

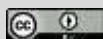# Prognosis of Hepatic Encephalopathy on Discharge in A Tertiary Level Hospital 🔓

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ABSTRACT

Introduction: *Hepatic encephalopathy (HE) is a frequent complication of cirrhosis and a major public health problem. It is assumed that approximately 60-80% of patients with liver cirrhosis develop hepatic encephalopathy. The study aimed to see the prognosis of hepatic encephalopathy on discharge in a tertiary-level hospital.* ***Methods:*** *This prospective observational study was conducted at the Department of Medicine in Combined Military Hospital (CMH), Dhaka, Bangladesh for 6 months. A total of 50 subjects were included in this study.* ***Result:*** *In this study, nearly three- a fifth (58%) of the patients exhibited HBsAg, 20% had Anti HCV antibody, 6% Anti-HBc, and 14% had Non-HBV. Repeated measure ANOVA analysis revealed that the improvement of the patients in terms of these variables was highly significant (p<0.001). USG examination at baseline showed that 10% of the patients had hepatomegaly, 82% splenomegaly and 72% had ascites which reduced to 8%, 78%, and 68% respectively on 3rd day of admission and 6%, 78%, and 66% on the day of discharge. But at discharge, only 2% of the patients were classified as WHC grade-2, 10% as comatose.* ***Conclusion:*** *The majority of the HE of moderate to severe grade in the present study came down to grade 0-1 or to unimpaired state which denotes a good prognosis. The diagnosis and grading of the severity of HE using West Haven Criteria (WHC) is of utmost importance in deciding the treatment options for a favorable outcome.*

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INTRODUCTION

Hepatic encephalopathy is an important complication of cirrhosis with significant morbidity and mortality [1]. It is a frequent complication of cirrhosis and a major public health problem with increasing incidence. It causes a spectrum of neurologic manifestations that develop in association with different liver diseases [2]. It is a medical phenomenon that is described as neuropsychiatric manifestations of chronic or acute liver diseases and is characterized by psychomotor, intellectual, and cognitive abnormalities with emotional/affective and behavioral disturbances. However, HE must be differentiated from neurologic manifestations resulting directly from bilirubin accumulation (kernicterus), cerebral hemorrhage secondary to disorders of coagulation caused by liver disease, or other abnormalities that are not secondary to liver failure. The nomenclature that several authors have used for HE is confusing. For this reason, several efforts have been made to reach a consensus, especially for the design of clinical trials [3]. HE is generally classified according to the underlying liver disease and the evolution of the neurological manifestations. The most frequent liver disease is cirrhosis, usually accompanied by extrahepatic portal-systemic shunts (spontaneous or surgical). HE also can be seen in acute liver failure, where it constitutes the hallmark of the disease. In rare cases, HE develops in the absence of any sign of parenchymal liver disease and is caused by portal-systemic shunting of congenital or surgical origin. However, HE most frequently develops from liver cirrhosis (60%-80%) [4][5][6][7][8]. The most widely used scale to classify the severity of HE is the West Haven Scale (WH) criteria ranging from 0-4 in increasing order of severity [7]. HE is a key reason for readmission among patients hospitalized for complications of cirrhosis. Among patients admitted for HE, 40% of patients previously hospitalized for HE may be readmitted within 1 year for HE-related reasons. Recurrent HE and hospitalization for cirrhotic complications are associated with impaired quality of life. In addition, recurrences (especially those requiring hospitalization) may contribute to persistent cognitive deficits (e.g. impairment in reaction time, attention, and working memory) after the resolution of an acute episode of overt HE [1]. Minimal hepatic encephalopathy (MHE) is a clinically significant disorder that impairs daily functioning, driving performance, work capability, and learning ability. It also predisposes to the development of overt encephalopathy and increases falls and mortality [9]. In a study, the most common precipitant was spontaneous bacterial peritonitis in 83 (20.5%), constipation in 74 (18.3), and urinary tract infection in 62 (15.3%). 140 patients had 2 precipitating factors while no precipitant was noted in 50 (12%) patients. Mean hospital stay 4±3 days. Complete reversal of HE was noted in 366 (91%) patients while the remaining had grade 1 HE on discharge. Nine patients died during their stay in the hospital. Without transplantation severe, HE signifies a poor prognosis (58% at 1 year and 77% at 3-year mortality in one case series) [10]. The study aimed to analyze to see the

prognosis of hepatic encephalopathy on discharge in a tertiary-level hospital.

OBJECTIVES
General Objective
- To determine the severity of HE based on WHC on admission to decide the course of management and at discharge to evaluate the in-hospital outcome of management.

Specific Objectives
- To assess the demographic characteristics of the patients with hepatic encephalopathy.
- To study the clinical and laboratory features of patients with hepatic encephalopathy.
- To categorize the study objects based on WHC.
- To see the changes in liver function status following an intervention.
- To assess the immediate prognosis of hepatic encephalopathy among hospitalized patients.

METHODS & MATERIALS

This prospective observational study was conducted at the Department of Medicine in Combined Military Hospital (CMH), Dhaka, Bangladesh for 6 months. A total of 50 subjects were included in this study. Informed written consent was taken from the study subjects. Data was collected using a pre-formed data sheet. Data processing and analysis were done by using SPSS version 17. The test statistics used to analyze the data were descriptive statistics, the McNemar Chi-square test,

and Repeated Measure ANOVA statistics. To see the changes in liver function test variables (serum bilirubin, serum albumin, and PT). for all analytical tests, the level of significance was set at 0.05 and $p < 0.05$ were considered significant. All information was kept confidential and used only for this study purpose. The ethical Clearance Certificate was obtained from the Director General of Medical Services, Bangladesh Armed Forces.

Inclusion Criteria
- Patients with established hepatic encephalopathy according to West Haven Criteria.
- Patients who had given consent to participate.

Exclusion Criteria
- Other causes of acute confusional state, e.g. patients with focal neurological signs, hypoglycemia, or subdural hematoma.
- Patient with liver disease without having encephalopathy.
- Patient with acute hepatic failure.

RESULTS

Age distribution of the patients showed that 16% of the patients were 40 or less than 40 years old, 38% were 49-45 years old, 22% were 50-60 years old and 24% were more than 60 years old. The mean age was 50 (range: 29-69) years. A male preponderance was observed in the series with male to female ratio being 4:1 [Table I].

Table I: Distribution of patients by their demography (N=50)

Demography	N	%
Age (years)		
≤40	08	16.0
40-50	19	38.0
50-60	11	22.0
>60	12	24.0
Sex		
Male	39	78.0
Female	11	22.0

*Mean age= (50.8±10.2) years; Range= (29-69) years

More than three-quarters (76%) of the patients were urban residents and the rest were rural residents [Figure 1].
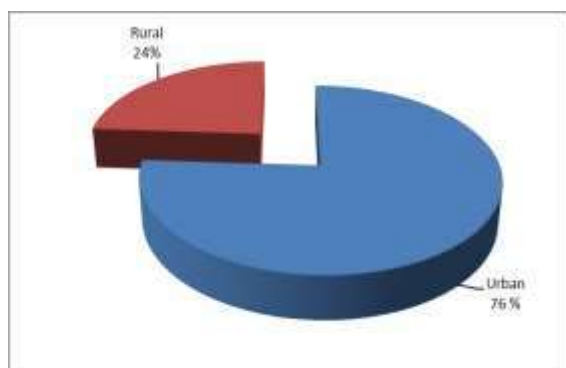

Figure 1: Distribution of Patients by their residents (N=50)

Concerning occupation, service holders comprised 40% followed by business at 26%, household work at 24%, farming at 8%, and laborer at 2% [Figure 2]. Majority (94%) of the patients were Muslim and the rest were Hindu (4%) and of the religions (2%) [Figure 3].
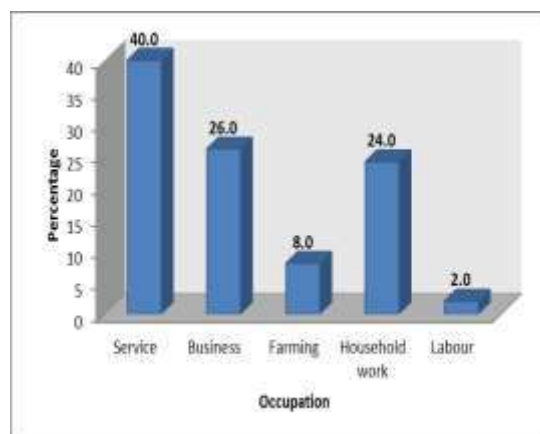

Figure 2: Distribution of patients by their occupation (N=50)
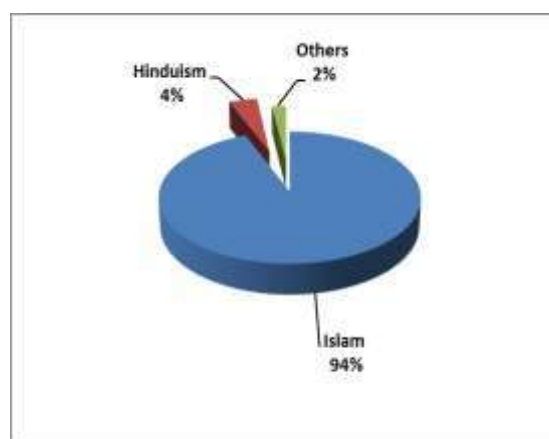

Figure 3: Distribution of patients by their religion (N=50)

16% of the patients were primary level educated, 26% were secondary or SSC level educated, 42% were higher secondary level educated 8% graduated, and 2% were post-graduate level [Figure 4].
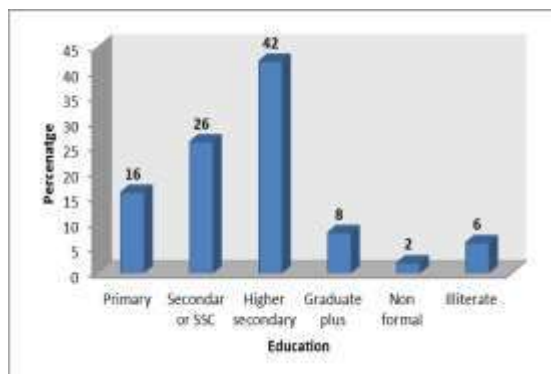
Figure 4: Distribution of patients by their education (N=50)

More than two-thirds (66%) of the patients had a monthly income of BDT 150000 or more with the median monthly income being BDT 200,000 (range: 20000 – 400000) [Table II]. Regarding viral markers, nearly three- a fifth (58%) of the patients exhibited HBsAg, 20% had Anti HCV antibodies, 6% Anti-HBc, and 14% Non-HBV [Table III]. In terms of changes in outcome variables showed that serum bilirubin decreased from 6.1 mg/dl at baseline to 5.4 mg/dl on day 3 and 3.4 at discharge; meanwhile, the serum albumin increased from 2.4 g/dl at baseline to 2.8 g/dl on 3rd day and 3.2 g/dl at discharge (Figure 5,6).

Table II: Distribution of patients by their monthly income (N=50)

Income (BDT)	N	%
<50000	04	8.0
50000-100000	05	110.0
100000-150000	08	16.0
≥150000	33	66.0

*Median income= 200000 BDT (Range: 20000-400000)

Table III: Distribution of patients by their viral markers (N=50)

Viral markers	N	%
HBsAg	29	58.0
Anti HCV	10	20.0
Anti HBc	03	6.0
Anti HEV IgM	00	0.0
Non-HBV	07	14.0

Prothrombin time was also substantially reduced from 8 seconds at baseline to 6.1 seconds on day 3 and 4.4 on the day of discharge (Figure 7). Repeated measure ANOVA analysis revealed that the improvement of the patients in terms of these variables was highly significant ($p<0.001$) [Table IV].

Table IV: Changes in outcome variables from baseline to endpoint of the study (N=50)

Variables	At 1st day	At 3rd day	At discharge	p-value
Serum bilirubin (mg/dl)	6.1±0.8	5.4±0.9	3.4±0.7	<0.001
Serum albumin (mg/dl)	2.4±0.6	2.8±0.6	3.2±0.9	<0.001
PT (second)	8.0±4.6	6.1±3.9	4.4±3.9	<0.001

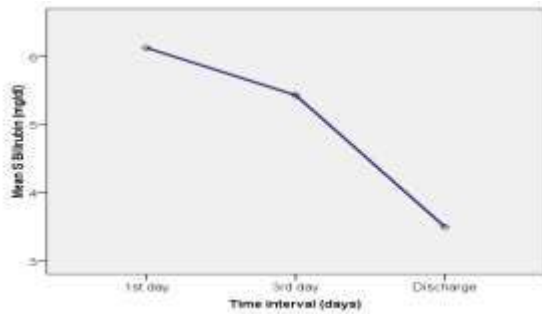***Data was analyzed using Repeated Measure ANOVA and was presented as mean ±SD**

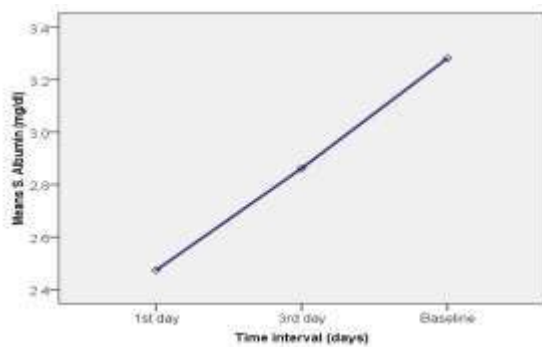**Figure 5:** Changes in S. bilirubin from baseline to end-point

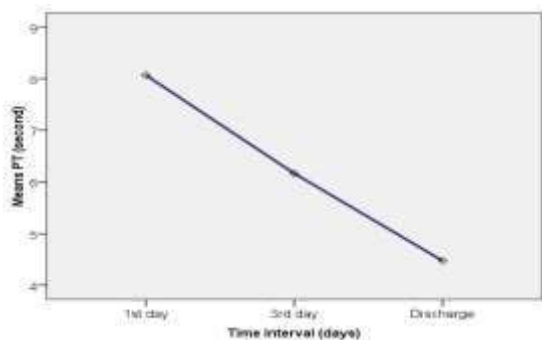**Figure 6:** Changes in S. albumin from baseline to end-point

Figure 7: Changes in prothrombin time from baseline to end-point

Table V: Distribution of patients by their USG and endoscopy (N=50)

USG & endoscopy	At 1st day N (%)	At 3rd day N (%)	At discharge N (%)
USG of the whole abdomen			
Hepatomegaly	5 (10.0)	4 (8.0)	3 (6.0)
Splenomegaly	41 (82.0)	39 (78.0)	39 (78.0)
Ascites	36 (72.0)	34 (68.0)	33 (66.0)
Upper GIT-varix (by endoscopy)	34 (68.0)	32 (64.0)	33 (66.0)

USG examination at baseline showed that 10% of the patients had hepatomegaly, 82% splenomegaly, and 72% had ascites which reduced to 8%, 78%, and 68% respectively on 3rd day of admission and 6%, 78%, and 66% respectively on the day of discharge [Table V]. Finally outcome was evaluated with help of West Haven Criteria (WHC). According to WHC 10%, 20%,40%, and 30% of the patients at baseline were classified as unimpaired, grade 0-1, grade 2, and coma respectively. But at discharge, only 2% of the patients were classified as WHC grade-2, and 10% as comatose (Figure 8). McNemaer Chi-square demonstrated significant improvement in encephalopathy grade (p-0.001).
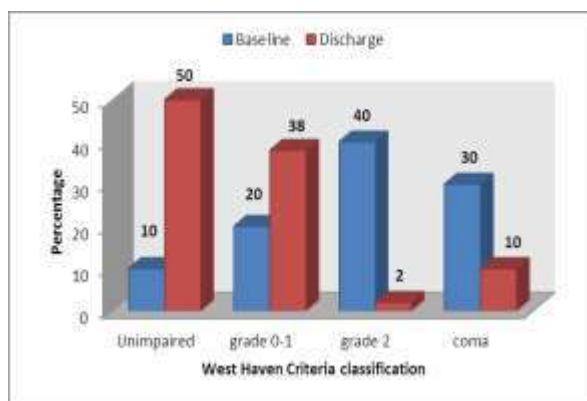
Figure 8: Distribution of patients by West Haven Criteria of classification (N=50)

DISCUSSION

In the present study, the mean age of the patients was 50 years with the youngest and the oldest patients being 29 and 69 years respectively. This age distribution was quite relatable to another study [11]. The patients were predominantly male (78%), urban residents (76%), service holders & businessmen (66%), and belonged to the affluent class (66%). Another study also showed a similar scenario [12]. Regarding viral markers, nearly three- a fifth (58%) of the patients exhibited HBsAg, 20% had Anti HCV antibodies, 6% Anti-HBc, and 14% Non-HBV. In a study, the etiology of cirrhosis was 41 in alcoholic, HCV infection in 18, HBV infection in 6 (association with HDV in 1 patient), and combined factors in 23 patients (HCV and alcohol in 12 patients, HBV, and alcohol in 6), which was somewhat similar to this present study [13]. Changes in outcome variables showed that serum bilirubin decreased from 6.1 mg/dl at baseline to 5.4 mg/dl on day 3 and 3.4 at discharge; meanwhile, the serum albumin increased from 2.4 g/dl at baseline to 2.8 g/dl on 3rd day and 3.2 g/dl at discharge. Prothrombin time was also substantially

reduced from 8 seconds at baseline to 6.1 on day 3 and 4.4 on the day of discharge. The improvement of the patients in terms of these three variables was highly significant ($p < 0.001$). Consistent with these clinical features, a study described that hepatic encephalopathy can present with a wide spectrum of neurocognitive manifestations [14]. In the case of MHE, there may not be any obvious clinical changes. However, these patients have abnormal psychometric tests and subtle personality changes may be reported by caregivers [15]. Regarding clinical features, Motor abnormalities such as hypertonia and hyperreflexia as well as extrapyramidal dysfunction such as rigidity, bradykinesia, dyskinesia, hypokinesia, and slowness of speech are also often present [16]. Sleep disturbances with excessive daytime sleepiness are another common manifestation of OHE [17]. Grading of HE is necessary to assess the evolution of the condition and the response to the effects of therapy. Several methods are based on clinical findings or the combination of neurophysiological and neuropsychological tests, but the simplest grading of HE is based on clinical findings. The West Haven index is widely used [18]. According to WHC 40 and 30% of the patients in the present study had grade-2 and grade-3-4 (coma) encephalopathy at baseline. But at discharge only 2% of the patients were classified as WHC grade-2 10% as grade-4 ($p < 0.001$). This prognostic picture was quite similar to a study conducted by another author [19]. A study conducted by another author also found a relatable prognosis [20].

Limitations of the Study

The study was conducted in a single hospital with small sample size for a short duration. So, the results may not represent the whole community.

CONCLUSION

It can be concluded that the majority of the HE of moderate to severe grade in the present study came down to grade 0-1 or unimpaired state. The diagnosis and grading of the severity of HE using West Haven Criteria is of utmost importance in deciding the treatment options for a favorable outcome.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

RECOMMENDATION

The grading of the severity of HE must be done, before augmenting treatment. The discharge of patients should also be based on grading of severity using the same criteria as are used in the initial evaluation of the severity of the disease on admission.

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