Original Research Article

Clinico-etiological profile and outcome in hepatic encephalopathy

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Abstract

Background: Hepatic encephalopathy may arise spontaneously but more commonly will develop as a result of some precipitating factors in the course of acute or chronic liver disease. Early identification of precipitating factor is extremely important in the diagnosis and treatment of this fatal condition. **Aim:** To investigate the clinical features, etiology of hepatic encephalopathy and outcome of hepatic encephalopathy. **Material and Methods:** In this hospital based descriptive and prospective study, 100 patients manifesting with symptoms and signs of hepatic encephalopathy were taken up for study. A detailed history and clinical examination with required relevant investigations was carried out in every patient. Hepatic encephalopathy was diagnosed on clinical basis and graded according to West Haven criteria and Child –Pugh score assessed for each patient. **Results:** Abdominal distension, altered sensorium and upper gastrointestinal bleeding were the commonest presenting symptoms. Pedal edema, icterus, asterixis, pallor and ascites were the commonest presenting signs. Majority of the patients in this study were cirrhotics (81%) followed by acute liver failure (19%). The commonest cause of cirrhosis in this study was alcoholism, followed by viral hepatitis. 63% of the patients in our study were improved and got discharged and 37% were expired. **Conclusion:** In most of the cases there are different factors which play a key role in precipitating hepatic encephalopathy. The early detection and diagnosis of these precipitating factors helps in starting treatment of this fatal condition hence reducing the mortality.

Key Words: Hepatic encephalopathy, abdominal distension, liver cirrhosis, Child-Pugh classification, West Haven grading, outcome

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INTRODUCTION

Hepatic Encephalopathy (HE) is a complex, potentially reversible neuropsychiatric condition that occurs as a consequence of acute or chronic liver disease.[1] Hepatic encephalopathy is a frequent complication and one of the most debilitating manifestations of liver disease, severely affecting the lives of patients and their caregivers. Furthermore, cognitive impairment associated with cirrhosis results in utilization of more health care resources in adults than other manifestations of liver disease.[2] Hepatic encephalopathy may arise spontaneously but more commonly will develop as a result of some precipitating factors in the course of acute or chronic liver disease. They act by depressing liver cell or cerebral function, increasing nitrogenous load in the intestine or raising portal collateral flow. Gut derived neurotoxins that are not removed by the liver because of vascular shunting and decreased hepatic mass get to the brain and cause symptoms that we know of as HE. Early identification of precipitating factor is extremely important in the diagnosis and treatment of this fatal condition. Common symptoms and signs are altered sensorium, irritability, change in sleep patterns, lack of concentration, psychometric and cognitive disturbances, fetor hepaticus, asterixis (flaps) and coma. In the presence of the precipitating factors the neurological deficits are usually completely reversible upon their correction and the prognosis is better if the precipitant can be treated.[3]

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This study was conducted to investigate the clinical features, etiology of hepatic encephalopathy and outcome of hepatic encephalopathy.

MATERIAL AND METHODS

The study was conducted in patients admitted in tertiary care hospital over a period of two years. A total of 100 patients were taken up for this study.

Study design

A hospital based descriptive and prospective study.

Method of collection of data

Patients admitted to the medical wards, manifesting with symptoms and signs of hepatic encephalopathy were taken up for study. A detailed history and clinical examination with required relevant investigations was carried out in every patient.

Inclusion criteria

- Patients with age more than 12 years
- Patients with clinical symptoms and signs of hepatic encephalopathy

Exclusion criteria

- Patients with age less than 12 yrs.
- Patients with other causes of encephalopathy such as infective (bacterial or Viral), metabolic encephalopathy associated with diabetes mellitus, renal failure, intracranial hemorrhage.

A detailed history of patients about fever, upper gastro intestinal bleeding (Hemetemesis and/or Malaena), constipation, diarrhea, vomiting, high protein diet, any trauma or surgery, alcohol intake and paracentesis were taken. Drug history including use of diuretics, sedatives/tranquilizers, NSAID's was also enquired in detail. Past history of previous hospital admissions was also taken all patients were carefully examined for fever, jaundice, dehydration, anaemia, pedal edema, asterixis, fetor hepaticus and ascites. The relevant investigations were done such as complete blood count, random blood sugar, liver function tests, renal function tests, serum electrolytes, BT, CT, PT, Urine –routine, microscopy, ascitic fluid studies, viral markers (HBsAg, HCV), HIV, Ultrasound (abdomen + pelvis), Chest radiograph and ECG. Hepatic encephalopathy was diagnosed on clinical basis and graded according to West Haven criteria. Any evidence for the presence of other co-existent complications of cirrhosis of liver was also recorded and Child –Pugh score assessed for each patient. All patients were followed for the duration of their stay in hospital and whether they survived or not at the end of their stay were also recorded.

Tools

- Clinical proforma
- West haven criteria for grading of hepatic encephalopathy
- Child– Pugh score to assess the severity and prognosis.

Statistical analysis

Data was analyzed using Chi-square goodness of fit test, Z test for proportion, mortality rate and graphical presentation wherever applicable.

RESULTS

It was observed that 75 (75%) patients among the 100 studied were males, remaining 25 (25%) patients were females. The age incidence was more in 41 to 50 years of age, followed by 31 to 40 years and then 51 to 60 years. The minimum age was 27 years and the maximum was 75 years. Majority of the patients (42%) were in the age group of 41 to 50yrs. In all age groups male preponderance was observed.

Table 1: Age and sex distribution

Age (years)	Males	Females	Total
12-20	0	0	0
21-30	5	2	7
31-40	18	4	22
41-50	32	10	42
51-60	14	5	19
>60	6	4	10
Total	**75**	**25**	**100**

The most common mode of presentation was abdominal distension seen in 70 (70%) patients and altered sensorium [disorientation 63 (63%), confusion 62 (62%) and coma 37 (37%)], which were statistically highly significant ($p<0.01$). Hematemesis seen in 32 (32%) patient followed by malaena in 23 (23%), altered sleep pattern in 22 (22%), fever in 20 (20%), vomiting in 18 (18%), constipation in 18 (18%) and diarrhea in 15 (15%) patients.

Table 2: Presenting clinical features

Symptom	No. of cases	p value	Signs	No. of cases	p value
Abdominal distension	70	Chi-square test= 123.45, D.F.= 10, p<0.01	Pedal edema	77	Chi-square test= 115.29, D.F.= 9, p<0.01
Disorientation	63		Icterus	73	
Confusion	62		Ascitis	67	
Coma	37		Asterixis	63	
Hemetemesis	32		Pallor	61	
Malaena	23		Splenomegaly	48	

Altered sleep pattern	22	Signs of chronic liver cell failure	34
Fever	20	Hepatomegaly	30
Vomiting	18	Fetor hepaticus	11
Constipation	18	Dehydration	11
Diarrhea	15		

The commonest sign was pedal edema seen in 77 (77%) patients, followed by icterus in 73 (73%), asterixis in 63 (63%), ascites in 67 (67%) and pallor in 61 (61%), which were statistically highly significant ($p<0.01$). Splenomegaly seen in 48 (48%) patients, while signs of chronic liver cell failure seen in 34 (34%) patients, hepatomegaly in 30 (30%), dehydration in 11 (11%) and fetor hepaticus in 11 (11%) patients.

Table 3: West Haven and Child-Pugh classification

Classification	No. of Patients
West Haven	
Grade I	15
Grade II	18
Grade III	30
Grade IV	37
Child-Pugh	
Class A	23
Class B	10
Class C	67

Out of the 100 patients when they were graded according to West Haven classification, 37% were in grade IV, 30% in grade III, 18% in grade II and remaining 15% in grade I. When the patients in this study were grouped according to Child-Pugh Score, 67% were in Class C, 10% in Class B and the remaining 23% in Class A. Majority were in Class C showing the advanced stages of the disease. In the analysis of laboratory findings, anaemia was found in 72(72%) patients. Leucocytosis (TLC >10,000/mm3) was found in 20 (20%) patients. Serum bilirubin level more than 3 mg% was found in 62(62%) patients. Hypoalbuminemia (serum albumin <3 g/dl), hyponatremia (<135mmol/L), hypokalemia (<3.5mmol/L) and hypoglycaemia (BSL<70mg%) were found in 41 (41%), 18 (18%), 13 (13%) and 2 (2%) patients respectively. USG (A+P) shown cirrhosis of liver in 81 (81%) patients, ascites in 67 (67%), hepatitis in 19 (19%), hepatomegaly in 30 (30%) and splenomegaly in 48 (48%) patients. Prothrombin time was prolonged more than 6 seconds in 67 (67%) patients. Among the precipitating factors the most common cause was Upper GI bleed [Hemetemesis (32%) and Malaena (23%)] which was statistically highly significant ($p<0.01$), followed by electrolyte imbalance [hyponatremia (18%) and hypokalemia (13%)], infection (20%), vomiting/diarrhoea (18%), constipation (18%), heavy bout of alcohol (12%), excess protein intake (10%), drugs [diuretics (3%) and sedatives (2%)] and large paracentensis (1%). In 6% of patients no precipitating factor was found.

Table 4: Precipitating factors of hepatic encephalopathy

Precipitating factors	No. of patients
Hemetemesis	32
Malaena	23
Infection	20
Constipation	18
Vomiting/Diarrhoea	18
Na(<135)	18
K(<3.5)	13
Heavy bout of alcohol	12
Excess protein	10
Diuretics	3
Sedatives	2
Large paracentesis	1

Chi-square test= 66.61, D.F.= 11, $p<0.01$.

Out of the 100 patients, 33 (33%) patients had only one precipitating factor, 31 (31%) patients had two precipitating factors and patients with more than two factors were 30 (30%).

Table 5: Etiology of hepatic encephalopathy

Etiology	No. of patients	Percentage	P value
Acute liver failure	19	19%	
Liver cirrhosis			Z test =6.2, p<0.01
Alcoholism	54	54%	
Viral hepatitis*	24	24%	
Autoimmune	3	3%	
Total	**100**	**100 %**	

*In viral hepatitis out of 24 cases, 17 were HBsAg positive and 7 were HCV positive. Out of 100 patients of HE, majority of the patients [81 (81%)] had liver cirrhosis which was statistically highly significant (p<0.01) and 19 (19%) patients had acute liver failure. In this study the commonest cause of cirrhosis was found to be alcoholism in 54 patients (54%), of which 49 (49%) were male and 5 (5%) were females. Secondly viral hepatitis was the commonest cause with 24 patients (24%). Autoimmune hepatitis accounts for 3 (3%) cases which were all females. Out of 19 cases of acute liver failure, 16 patients were had alcoholic hepatitis, 2 were had viral hepatitis and 1 had drug Induced hepatitis (isoniazid).

Table 6: Prognosis and outcome

Age	Male		Female		Total
	Discharge	Death	Discharge	Death	
12-20	0	0	0	0	0
21-30	3	2	2	0	7
31-40	11	7	2	2	22
41-50	20	12	9	1	42
51-60	9	5	3	2	9
>60	3	3	1	3	10
Total	**46**	**29**	**17**	**8**	**100**

Out of 100 patients, 63 (63%) patients recovered and were discharged, 37 (37%) patients were expired, of which 29 were males and 8 were females. Majority of the patients [13 out of 37 (35.13%)] expired in the age group of 41- 50 yrs. Thus, mortality rate in males was 38.66% whereas in females it was 32%.

DISCUSSION

In majority of the patients with hepatic encephalopathy, a clearly defined precipitating factor is usually identified, and the reversal or control of these factors is a key step in the management. A total of 100 patients admitted in medical wards, presented with symptoms and signs of hepatic encephalopathy were taken up for the present study. All possible factors which could be responsible for precipitation or aggravation of HE were looked for and analyzed. In this study abdominal distension (70%), altered sensorium [disorientation (63%), confusion (62%) and coma (37%], hemetemesis (32%) and malaena (23%) were the most common presenting symptoms, and most common signs were pedal edema (77%), icterus (73%), ascites (67%), Asterixis (63%), pallor (61%) and splennomegaly (48%). Shah D *et al*[4] conducted a study in 50 admitted patients of HE, they found abdominal distension (72%), hemetemesis (56%), constipation (52%) and fever (20%) were the most common presenting symtoms, while icterus (76%), ascites (72%), splenomegaly (68%), fetor hepaticus (52%) and pedal edema (40%) were the common presenting signs. Alam I *et al*[3] conducted a study in 50 admitted patients in which they found asterixis (66%), icterus and ascites were the most common presenting signs. Maqsood S *et al*[5] found that ascites (64%) was the most common presenting sign in their study of 50 admitted patients of HE. Majority of the patients in this study had higher grades of encephalopathy with 37 (37%) patients in grade IV, 30 (30%) patients in grade III, 18 (18%) patients in grade II, while 15 (15%) patients were in grade I hepatic encephalopathy of WHC. Child Pugh classification of patients in this study had 67(67%) patients in class C, 10 (10%) patients in class B and 23(23%) patients in class A. Alam I *et al*[3] found 38(76%) patients in grade III and grade IV of WHC. Shah D *et al*4 found 4 (8%) patients in grade I, 4 (8%) patients in grade II, 4 (8%) patients in grade III and 38 (76%) patients in grade IV of West Haven Classification. Maqsood S *et al*[5] found 4 (8%) patients in grade I, 9 (18%) patients in grade II, 26 (52%) patients in grade III and 11 (22%) patients in grade IV of West Haven Classification, while in the same study they found 2 (4%) patients in class A, 14 (28%) patients in class B and 31 (62%) patients in class C of child Pugh Classification. Tariq M *et al*[6] found 58 (29%)patients in grade I, 83 (41.5%) patients in grade II, 38 (19%) patients in grade III and 21 (10.5%) patients in grade IV of West Haven Classification, while in the same study they found 67 (33.5%) patients in class B and 133 (66.5%) patients

in class C of Child-Pugh Classification. Ortiz M *et al*[7] found 7 (19%) patients in class B and 29 (81%) patients in class C of child Pugh Classification. Devrajini *et al*[8] found most of the patients (70%) in grade IV of WHC. Mumtaz K *et al*[9] found 17% patients in grade I, 44% patients in grade II, 29% patients in grade III and 10% patients in grade IV while 78% patients found in class C of Child-Pugh classification. Gad YZ10 found 57 (24%) patients in grade II, 128 (54%) patients in grade III and 52 (22%) patients in grade IV of West Haven Classification, while in the same study they found 12 (5%) patients in class A, 91 (30%) patients in class B and 154 (65%) patients in class C of Child-Pugh Classification. In present study, 19 (19%) patients had acute liver failure and 81 (81%) had liver cirrhosis. In this study leading cause of liver cirrhosis was alcoholism found in 54 (54%) patients, followed by viral hepatitis in 24(24%) patients [HbsAg positive (17%) and HCV positive (7%)]. Out of 19 cases of acute liver failure, 16 patients had alcoholic hepatitis, 2 were had viral hepatitis and 1 had drug Induced hepatitis (isoniazid). In this study liver cirrhosis was statistically highly significant underlying etiology of HE. Patel S *et al*[11] conducted a study in 100 admitted patients, they found that 34% patients were had acute liver failure and 68%were had cirrhosis, while alcoholism was the most common cause of cirrhosis. Maqsood S *et al*[5] found that 8% patients were had acute liver failure and 92% were had liver cirrhosis, while viral hepatitis (70%) was the most common cause of cirrhosis. Ortiz *et al*[7] conducted a study in 36 admitted patients, they found that viral hepatitis (36%) was the leading cause of cirrhosis, while alcoholism was the second most common cause of cirrhosis found in 31% of patients. Shah D *et al*[4] found viral hepatitis in 76% of the cirrhotic patients. In this study, out of 100 patients, 63 (63%) patients recovered and were discharged, 37 (37%) patients were expired, of which 29 were males and 8 were females. Majority of the patients [13 out of 37 (35.13%)] expired in the age group of 41- 50 yrs. Mortality rate was more in males (38.66%). Al-Gindan YM12 was also found 41%mortality in their study, of which majority were males of age more than 40 yrs. The mortality rate of hepatic encephalopathy was high as shown by the study of Sargent and Fullwood[13] Maqsood S *et al*[5] were shown 30% mortality in their study, of which majority were males of age more than 40 yrs. Devrajini *et al*8 were shown 23% mortality in their study, of which majority were males in the age group of 40-60 yrs. Gad YZ10 was shown 32.48% mortality in their study, of which majority were males in the age group of 40-60 yrs.

CONCLUSION

From this study it was concluded that in most of the cases there are different factors which play a key role in precipitating hepatic encephalopathy which is a common phenomenon in patients with cirrhosis of liver. Mortality rate was high when patients were presented in late stages of hepatic encephalopathy and also when presented with acute liver failure. There is a definite need for health education in patients who are diagnosed with cirrhosis of liver regarding the risk of hepatic encephalopathy and its precipitating factors. Hence, the early detection and diagnosis of these precipitating factors helps in starting treatment of this fatal condition hence reducing the mortality.

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