

## Clinical Spectrum of Precipitating Factors of Hepatic Encephalopathy in Cirrhosis of the Liver

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### Abstract

**Background and Objectives:** Hepatic encephalopathy is an extra hepatic complication of impaired liver function and is manifested as neuropsychiatric signs and symptoms associated with acute or chronic liver disease in the absence of other neurological disorders. This study aims to ascertain the spectrum of precipitating factors of hepatic encephalopathy in patients with cirrhosis of the liver.

**Methods:** 100 cases of cirrhosis of the liver who presented in hepatic encephalopathy admitted to Sri Venkateswara Ramnarain Ruia Government General Hospital (SVRRGGH), Tirupati between May 2017 and April 2018 were studied. All patients of more than 18 years of age, manifesting with signs of hepatic encephalopathy were included, and those who had acute fulminant hepatitis or non-cirrhotic portal hypertension were excluded from the study. Detailed history, clinical examination and thorough investigations were done to look for any precipitating factor and the findings were recorded on a proforma and prognostic stratification through Child-Pugh score was done.

**Results:** Out of 100 patients, Upper GI bleed (51%), Constipation (41%), Electrolyte imbalance (38%) and Infection (22%) stood out as the most common precipitating factors. Usage of diuretics, sedatives, and excess dietary protein were the other factors.

Most patients were in grade III (30%) and grade IV (37%) of hepatic encephalopathy. Other common associations were Child Pugh class C (67%), mortality (37%), and Alcoholism (54%).

### Interpretation and Conclusion:

Upper GI bleed, Constipation, Infection, and Electrolyte imbalance were the most common precipitating factors of Hepatic encephalopathy in this study.

**Key words:** Hepatic Encephalopathy, Precipitating factors

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### I. Introduction

Hepatic Encephalopathy is a complex potentially reversible neuropsychiatric condition that occurs as a consequence of acute or chronic liver disease. It is characterized by changes in personality, consciousness, behavior, and neuromuscular function. It may arise spontaneously but more commonly will develop as a result of some precipitating factor in the course of acute or chronic liver disease.<sup>1</sup>

Hepatic encephalopathy may disable the patient from employment, driving, and self-care, and require the involvement of family or household members in the care of affected patients. The clinical importance of hepatic encephalopathy is underscored by the frequent reversibility of the precipitating factors.<sup>2</sup>

Patients who have diabetes mellitus or malnutrition seem to develop hepatic encephalopathy (HE) more frequently with cirrhosis.<sup>3</sup> Severe hyperammonemia (>150-200  $\mu\text{mol/L}$ ) with acute liver failure can cause cerebral edema that contributes to HE.<sup>4</sup>

### Patients and Methods:

#### Source of data:

The study was conducted in patients admitted to Sri Venkateswara Ramnarain Ruia Government General Hospital during May 2017 to April 2018. 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 associated with cirrhosis of liver depending on their past medical records, clinical signs of cirrhosis liver and an unequivocal ultrasonography report were taken up for the study.

**Inclusion criteria:**

1. Patients with age more than 18 years irrespective of sex.
2. Patients with clinical symptoms and signs of hepatic encephalopathy associated with cirrhosis of the liver.

**Exclusion criteria:**

1. Patients of age less than 18 years.
2. Patients who presented with acute fulminant hepatitis and non cirrhotic portal hypertension.

A proforma has been designed and used for data collection. A detailed clinical history of patients about fever, upper gastro-intestinal bleeding (hematemesis and/or melena), constipation, diarrhea, vomiting, high protein diet, any trauma or surgery, and paracentesis were taken. Drug history including the use of diuretics, sedatives/tranquilizers, NSAIDs was also enquired in detail. The past history of previous hospital admissions was also taken. All patients were carefully examined for fever, jaundice, dehydration, anemia, pedal edema, asterixis, fetor hepaticus and ascites. Hepatic encephalopathy was diagnosed on a clinical basis and graded according to West Haven criteria (Table 4). Any evidence for the presence of other co-existent complications of cirrhosis liver was also recorded and Child's 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.

**Investigations:**

The following relevant investigations were done

- Complete hemogram, Random blood sugar
- Blood urea and Serum creatinine
- Liver function tests
- Serum electrolytes
- BT, CT, PTT, INR
- Urine routine and microscopy
- Chest radiograph
- Ultrasound abdomen

**Statistical Analysis:**

Data were analyzed using descriptive statistics.

**Tools:**

- Clinical proforma
- West Haven criteria for grading of hepatic encephalopathy
- Child's Pugh score to assess the severity and prognosis in cirrhosis of the liver

**II. Results**

A total of 100 patients with cirrhosis of the liver suffering from HE were studied for different precipitating factors for 12 months.

**TABLE: 1 - Age And Sex Distribution**

Age (years)	Females	Males
20-40	3	17
41-60	15	52
More than 60	8	5

The age incidence was more in 41 to 60 years of age, followed by 20 to 40 years and more than 60 years. There were no patients below the age of 20 years. The minimum age was 22 years and the maximum was 68 years with a mean age of 47.5 years.

It was observed that 74 patients among the 100 studied were males, remaining 26 patients females; of which 17 males and 3 females were in 20 to 40 years of age, 52 males and 15 females were in 41 to 60 years of age and 5 males and 8 females were in more than 60 years of age. In all age groups, a male preponderance was observed except in more than 60 years of age, in which females were more in number.

**Table: 2** Child Pugh Score

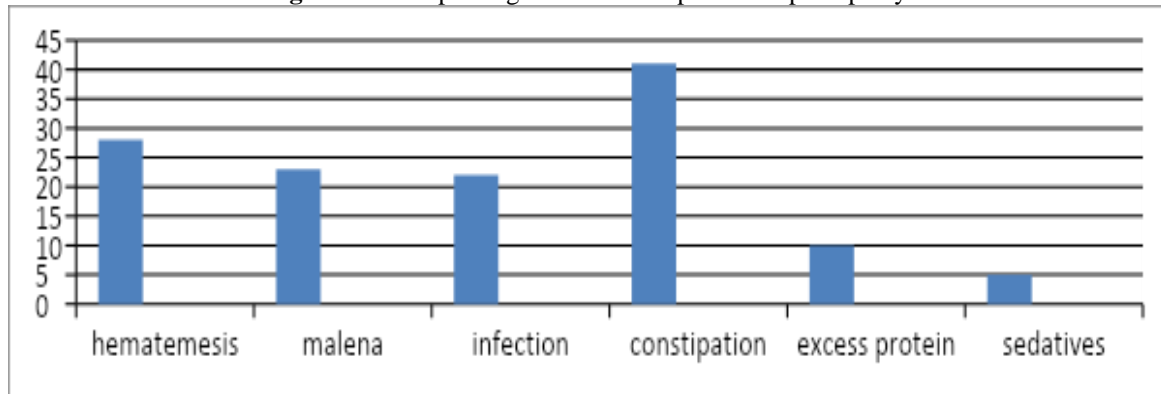
Class	Child Pugh Score
A	23
B	10
C	67

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.

**Table: 3** Precipitating Factors of Hepatic Encephalopathy

Precipitating factors	No. of pts.
Hematemesis	28
Melaena	23
Infection (TC>10,000)	22
Constipation	41
Excess protein	10
Sedatives	5
Diuretics	9
Na (<135)	25
K (<3.5)	13

**Figure 1-** Precipitating Factors Of Hepatic Encephalopathy



Among the precipitating factors the most common cause was Upper GI bleed (Hemetemesis 28 % and Malena 23 %), Constipation 41 %, Electrolyte imbalance (Hyponatremia 25 % and Hypokalemia 13 %), Infection 22 %, Drugs (Diuretics 9 % and Sedatives 5 % ), and Excess protein intake 10 %. In 6 % no precipitating factor was found.

**TABLE: 4** west haven classification

West Haven Classification (Grades of HE)	No. of pts.
I	23
II	10
III	30
IV	37

Out of the 100 patients when they were graded according to West Haven classification, 37 % were in grade IV, 30 % in grade III, 10 % in grade II and remaining 23 % in grade I HE.

**Table 5 -** Mortality According To Risk Factors

Precipitating factors	No. of cases	Mortality	%
Hematemesis	28	13	46
Melaena	20	11	55
Infection (TC>10,000)	22	17	77
Constipation	40	11	27
Excess protein	4	1	25
Sedatives	4	1	25
Diuretics	8	4	50
Na (<135)	25	4	16
K (<3.5)	13	1	7

Of the mortality cases, patients who presented with Upper GI bleed, Infection and Drug overdose had a higher mortality rate compared to other precipitating factors

**TABLE 6** Presenting Symptoms

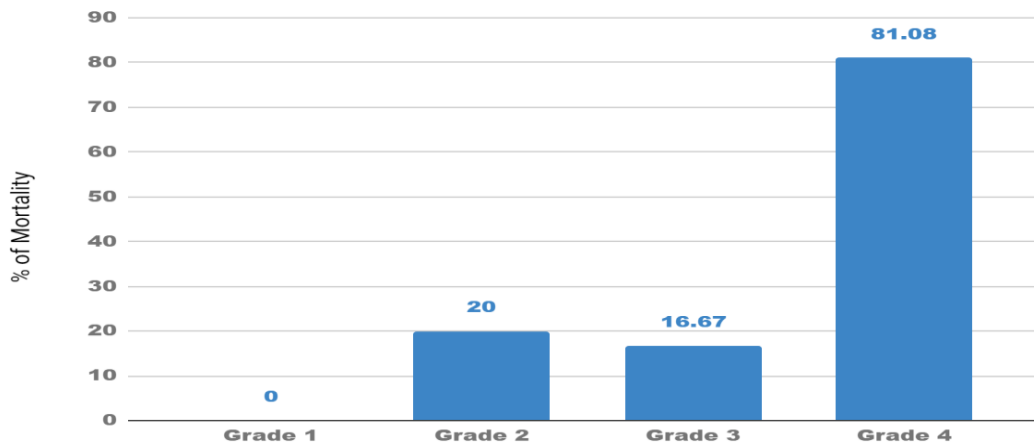
Symptoms	No. of cases
Fever	22
Vomiting	21
Diarrhea	19
Constipation	40
A. Distension	70
Hematemesis	28
Malena	20
Disorientation	68
Confusion	67
Coma	32

The most common mode of presentation was abdominal distension 70 % and altered sensorium (Disorientation 68 %, confusion 68 % and coma 32 %), followed by constipation 40 %, Hematemesis 28 %, Malena 20 %, fever 22 %, vomiting 21 % and diarrhoea 18%.

**Table 7 - West Haven Classification And Mortality**

West Haven Classification	No. of Cases	Mortality	%
I	23	0	-
II	10	2	20
III	30	5	17
IV	37	30	81

**Figure 2 - West Haven Classification And Mortality**



According to West Haven classification, out of the 37 patients, 30 expired in grade IV, out of the 30 patients in grade III, 5 expired and out of the 10 patients in grade II, 2 expired. There was no mortality in grade I HE. In grade IV the mortality was more than 80 %.

### III. Discussion

In majority of the patients with HE, a clearly defined precipitating factor usually is identified, and the reversal or control of these factors is a key step in the management. In the present study 100 patients of cirrhosis of liver presenting with HE, all possible factors which could be responsible for precipitation or aggravation of HE were looked for and analyzed.

In this study the majority of the patients were males, constituting about 74% of cases compared to females 26%, with the majority of patients 80% above 40 years of age. About gender, the male were dominant in our study, while similar findings were observed in a retrospective study of hepatic encephalopathy in Pakistan.

In our study, the majority of patients were alcoholics 54%, followed by HBV 17% and HCV 7% being the other leading causes of liver cirrhosis. In the western world alcoholism is the main cause of liver cirrhosis

where there is a definite male preponderance, making it the fourth commonest cause of death in males in the USA. The etiology of cirrhosis has been hepatitis C virus in majority of the cases in most of the studies done in Pakistan. Gastrointestinal bleeding (51%) and constipation (41%) were the common precipitating factors in this study similar to some other studies. Other causes include electrolyte imbalance (hypokalemia in 13% and hyponatremia in 25%), excess protein intake in 10%, drugs (diuretics in 9% and sedatives in 5%) and infections in 22%. Most of the patients with electrolyte imbalance had a history of diarrhea or vomiting or were already on diuretic therapy. For a comparison of the frequency of different precipitating factors in different international studies is given in the following.

**Studies comparing precipitating factors of HE**

Study	GIB	Constipation	Infection	K <sup>+</sup>	Na <sup>+</sup>	Excess dietary protein
Shaikh S <sup>5</sup> (n=50)	56%	52%	15%	70%	28%	-
Hameed <sup>6</sup> (n=50)	56%	52%	28%	68%	28%	52%
Souheil <sup>7</sup> (n=100)	18%	3%	3%	11%	-	9%
Aisha <sup>8</sup> (n=100)	76%	36%	52%	-	-	-
Conn <sup>9</sup> (n=100)	18%	3%	4%	9%	-	9%
Faloon <sup>10</sup> (n=39)	33%	6%	-	18%	-	-
Present Study (n=100)	51%	41%	22%	13%	25%	10%

Amongst the clinical features, jaundice in 67%, altered conscious state (ranging from confusion to coma) in 68%, asterixis in 67%, and ascites in 70% were the most common presenting features in this study. Anemia was seen in 61%, splenomegaly in 48%, and pedal edema in 67%. The findings of low hemoglobin (55%) and hypoalbuminemia (79%) in patients with HE correspond well with advanced stages of liver cirrhosis.

Child Pugh classification of patients in this study had 67% in class C, 10% in class B and 23% in class A. Similarly majority of the patients in this study had higher grades of encephalopathy with 37% in grade IV, 30% in grade III, 10% in grade II, while 23% had grade I HE.

The mortality rate of HE is high as shown by the study of Sargent and Fullwood,<sup>11</sup> while in this study the mortality rate was 37%. Patients who did expire were mostly in class C of Child Pugh classification and grade III and IV of HE.

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