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Clinical Spectrum of Precipitating Factors of Hepatic Encephalopathy in Patient of Liver Cirrhosis

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Abstract: ***Objective****: To determine the precipitating factors of hepaticencephalopathy (HE) in patients with liver cirrhosis*

Background and Objectives:

Hepatic encephalopathy is an extra hepatic complication of impairedliver 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 liver.

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TABLE 1: Precipitating Factors of HE[1]

1. Dehydration
2. Gastrointestinal bleeding
3. Infections (especially Spontaneous bacterial peritonitis, Urinary tract, Skin infection, or Pulmonary infection)
4. Constipation
5. Excessive dietary protein
6. Central nervous system acting drugs
7. Hypokalemia
8. Renal failure
9. Hyponatremia
10. Superimposed liver injury (Acute hepatitis, Drug-induced liver injury)
11. Hepatocellular carcinoma
12. Terminal liver disease

I. Introduction

Hepatic Encephalopathy (HE) is a complex, potentially reversibleneuropsychiatric condition that occurs as a consequence of acute orchronic liver disease.2 It is a well recognized clinical complication of cirrhosis of liver and the presence and prompt identification of well defined precipitating factors is extremely important in diagnosis and treatment of this fatal condition. Cirrhosis of liver is common in our day to day clinical practice, besides alcoholic In the management of patients with HE in cirrhosis of liver it isimportant to stage the encephalopathy into four clinical stages and thentry to identify and treat the precipitating factors. In the presence of theprecipitating factors the neurologicaldeficits are usually completely reversible upon their correction and the prognosis is better if the precipitant can be treated.3This study aims at studying the clinical profile and the spectrum of precipitating factors of HE in cirrhosis of liver, hence identifying themand initiating the appropriate treatment can bring down the morbidityand mortality

II. Methods

100 cases of cirrhosis of liver who presented in hepatic encephalopathyAdmittedsubharti medical college, Meerut between June 2016 and may2018 were studied. All patients of more than 18 years of age,manifesting with signs of hepaticencephalopathy were included and those who had acute fulminant hepatitis or non-cirrhotic portalhypertension were excluded from the study. Detailed history, clinicalexamination 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.

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

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

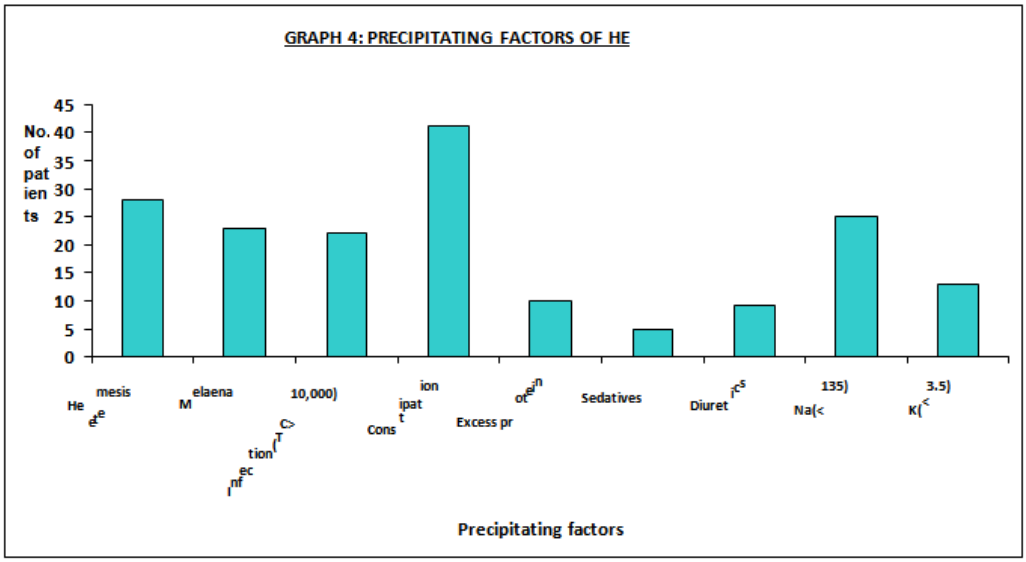
Parameters	1 point	2 points	3 points
Serum bilirubin total (mg/dL)	<34 (<2)	34-50 (2-3)	>50 (> 3)
Serum albumin (mg/dL)	>35	28-35	<28
INR*	<1.7	1.71-2.20	>2.20
Ascites	None	Suppressed with medication	Refractory
Hepatic encephalopathy	None	Grade I-II (or suppressed with medication)	Grade III-IV (or refractory)

*INR: International Normalized Ratio; Child-Pugh A=5-6 points, Child-Pugh B=7-9 points, Child-Pugh C=10 or more points

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

Precipitating Factors of He

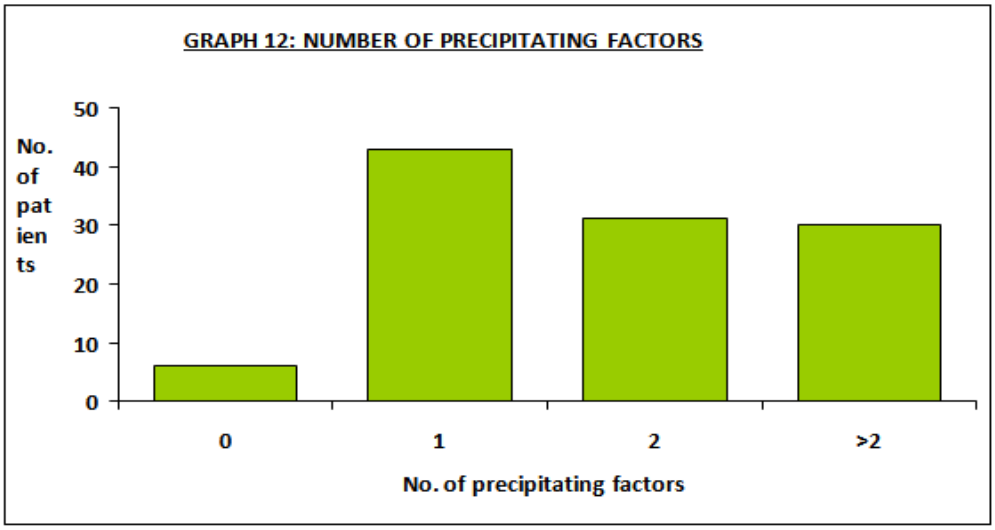
Precipitating factors	No. of pts. (%)
Hemetemesis	28 %
Melaena	23 %
Infection (TLC>10,000)	22 %
Constipation	41 %
Excess protein	10 %
Sedatives	5 %
Diuretics	9 %
Na (<135)	25 %
K (<3.5)	13 %



Among the precipitating factors the most common cause was Upper GI bleed (Hemetemesis 28 % and Malaena 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: NUMBER OF PRECIPITATING FACTORS

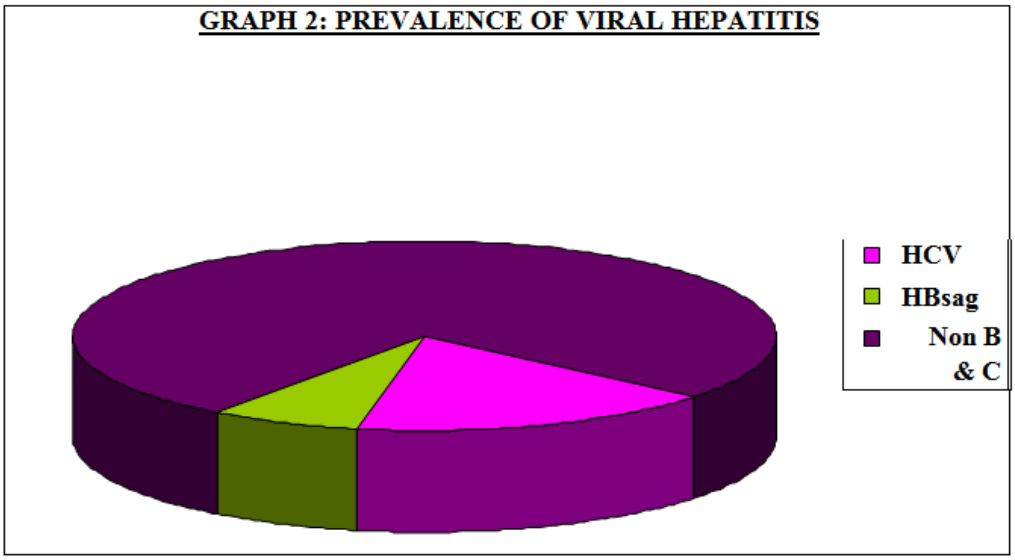
Precipitating Factors	Cases
0	6
1	43
2	31
>2	30



Out of the patients who presented with precipitating factors, 43 % had only one factor, which was the majority, followed by patients with two factors 31 % and patients with factors more than two factors 30 %.

PREVALENCE OF VIRAL HEPATITIS

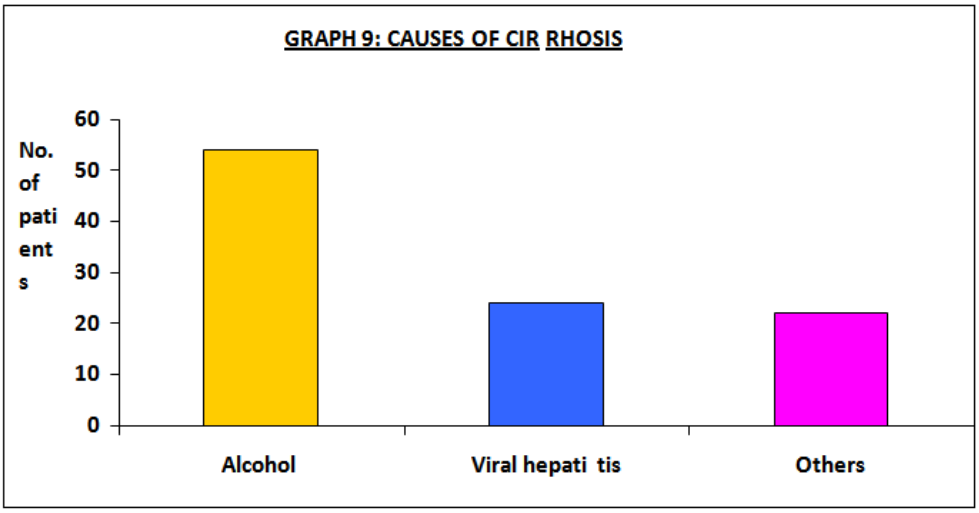
Viral Hepatitis	Cases
HBsAg	7
HCV	17
Non B & C	76



7 patients were HBsAg positive, 17 were HCV antibodies positive and the remaining 76 patients were negative for both HBsAg and Anti HCV

CAUSES OF CIRRHOSIS

Cause of Cirrhosis	No. of pts.
Alcohol	54
Viral hepatitis	24
Others	22

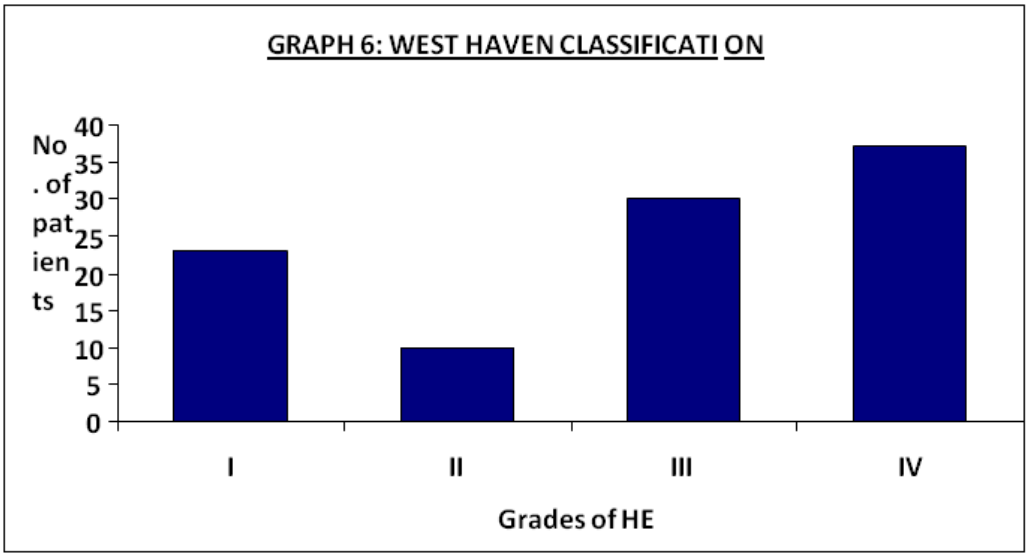


In this study the commonest cause of cirrhosis was found to be Alcoholism 54 %, of which 49 % were male and 5 % females. Secondly viral hepatitis was the commonest cause with 24 %. In 22 % of patients the cause wasnot known.

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

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 HEAmongst the clinical features, jaundice in 67%, altered conscious state (ranging from confusion to coma) in 68%, asterixis in 67%, and ascitis 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

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 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 7% and HCV 17% 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 4thcommonest cause of death in males in USA. The etiology of cirrhosis has been hepatitis C virus in majority of the cases in most of the studies done in Pakistan. Gastro intestinal bleeding (51%) and constipation (41%) were the common precipitating factors in this study similar to some other studies. Other causes included 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 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 Table.

Table : Studies comparing precipitating factors of HE

Study	GIB	Constipation	Infection	K^+	N^+	Excess dietary protein
Shaikh S[4] (n=50)	56%	52%	15%	70%	28%	-
Hameed[5] (n=50)	56%	52%	28%	68%	28%	52%
Souheil[6] (n=100)	18%	3%	3%	11%	-	9%
Aisha[7] (n=100)	76%	36%	52%	-	-	-
Conn[8]					-	

(n=100)	18%	3%	4%	9%		9%
Faloon[9] (n=39)	33%	6%	-	18%	-	-
Present Study (n=100)	51%	41%	22%	13%	25%	10%

In study of Sheikh_etGastro-intestinal bleeding, constipation and infections stand out as the most common precipitantIn study of Hameed_etGastro-intestinal bleeding, constipation and infections stand out as the most common precipitant

As shown in the above Table Gastro-intestinal bleeding, constipation and infections stand out as the most common precipitant of HE in almost all the studies. The mortality rate of HE is high as shown by the study of Sargent andFullwood[10]while in this study the mortality rate was 37%. Patientswho did expire were mostly in class C of Child Pugh classification andgrade III and IV of HE.

IV. 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.GI bleed,constipation, infections, diuretics, electrolyteimbalance and were the most common precipitatingfactors.

There is a definite need for health education in patients who arediagnosedwith cirrhosis of liver regarding the risk of hepaticencephalopathyand its precipitating factors. Prompt control of infections,routine upper GI endoscopy and follow up, prevention of constipation by laxatives, judicial use of sedatives and diuretics andproper advice regarding diet must be an integral part of all counselingprotocol to cirrhotic patients.

Hence the early detection and diagnosis of these precipitating factorshelps in starting treatment of this fatal condition hence reducing themortalityencephalopathy in this study

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