Original Article

Precipitating Factors of Hepatic Encephalopathy Experience at Shaheed Muhtarma Benazir Bhutto Medical University Larkana

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ABSTRACT

Objective: To know the common precipitating factors and their frequency in patients presenting with Hepatic encephalopathy. The aims of this study were to evaluate the precipitant factors and analyze the treatment outcomes of HE in LC.

Study Design: Descriptive study

Place and Duration of Study: This study was conducted at the Medical Wards of Shaheed Mohtarma Benazir Bhutto Medical University Larkana from December 2017 to June 2018.

Materials and Methods: This study included all patients (age>12 years or both genders) with diagnosis of cirrhosis of liver presented with signs and symptoms for hepatic encephalopathy were included. Patients with acute hepatic encephalopathy were excluded from study. Detailed history and examination done and all patients were graded according to clinical criteria and investigation like CBC, viral marker, LFT, serum albumin, total protein, blood sugar, serum electrolyte coagulation profile, blood culture & ascitic fluid culture were carried out and abdominal ultrasound for signs of cirrhosis of liver and child pugh score were assessed in every patient. Data were entered in on preformed proforma.

Results: We surveyed 100 patients admitted with clinical diagnosis of hepatic encephalopathy, for one or more factors responsible for encephalopathy. The commonest precipitating factors were infections 58% upper gastrointestinal bleeding 48% and constipation were present in 44%. 40% patients have electrolyte imbalance, 22% have history of paracentesis, 10% have taken drugs like benzodiazepine and only 8% have taken the high protein diet.

Conclusion: Infection, GI bleeding, constipation and electrolyte imbalance were most common precipitating factors in our setup.

Key Words: Cirrhosis liver, precipitating factors, hepatic encephalopathy.

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INTRODUCTION

Liver disease affects millions of people worldwide however it is very big problem in developing countries like Pakistan. The syndrome of hepatic Encephalopathy (H.E) describes all neuropsychiatric symptoms occurring in patient with acute or chronic liver disease in the absence of other neurological disorders. There is 30% mortality due to hepatic coma[1].

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Due to high prevalence of hepatitis B and C cirrhosis is endemic in Pakistan[2]. HE develops in 50% to 70% of patients with cirrhosis, and its occurrence is a poor prognostic indicator, with projected one- and three-year survival rates of 42% and 23%, respectively, without liver transplantation[3] Patients with CLD frequently experience episodes of exacerbations including hepatic encephalopathy precipitated by variety of established precipitants[4]. HE can occur due to acute liver failure or due to one or more precipitating factors in a cirrhotic patient, or could happen as a result of prolonged portal systemic shunting resulting in a chronic portal systemic encephalopathy[5]. Prognosis of patients having chronic HE is better than those who develop acute HE (100% vs. 70%)[6]. Common precipitating factors include gastrointestinal bleeding, infection, constipation, electrolyte imbalance[7], azotemia and high protein diet. Usage of drugs, such as sedatives[8], tranquilizers, analgesic and diuretics. Primary precipitants of hepatic encephalopathy are infection like SBP and Variceal Haemorrhag[9]. The pathogenesis of hepatic

encephalopathy is still unclear, however the basic process are failure of hepatic clearance of gut derived substances such as ammonia, free fatty acids, mercaptan etc. either through oxidative failure or shunting, nitrosamine stress both of which result in low grade cerebral edema causing depressed cerebral function[10].

MATERIALS AND METHODS

1. To know the common precipitating factors and their frequency in patients presenting with Hepatic Encephalopathy.
2. Analyze the common biochemical laboratory findings in such patients to stratify the patients according to child Pugh classification of Chronic Liver Disease.

A hospital based descriptive observational study was carried out on 100 patients in Medical wards of Shaheed Mohtarma Benazir Bhutto Medical University Larkana from December 2017 to June 2018. All patients above 12 years of cirrhosis liver with signs and symptoms of hepatic encephalopathy, either at presentation or during the course of hospital stay were included in this study. Patients with acute fulminant hepatic failure were excluded from study. For data collection, Proforma was prepared. Detailed history regarding fever, abdominal pain, gastro intestinal bleeding either Hemetemesis or malena, constipation, high protein intake, H/O paracentesis, surgery. Use of drugs like sedatives, tranquilizers, excessive use of diuretics, analgesics, cough syrups were carefully examined for jaundice, temperature, anemia, asterixis and ascites. Encephalopathy was graded according to clinical criteria as given in Table-I Following investigations were done from each patient. CBC, Viral markers, liver function tests, serum electrolytes, coagulation profile, blood sugar, total protein were carried out abdominal ultrasound was done for signs of cirrhosis of liver, in case of ascites paracentesis was done to look for spontaneous bacterial peritonitis. Child's pugh score was assessed for each patient based on parameters in Table-II. All patients were followed for the duration of their stay in hospital and whether they survived or died at the end of stay was also recorded.

RESULTS

A total number of 100 patients underwent study out of which 71 (71%) were male and 29 (29%) were females, (Table-II) presenting with encephalopathy. Majority of our patients were older than 40 years including 26 males and 12 females. Only 8 patients were below 20 years of age. The age, gender distribution in different clinical presentation and grades of patients with hepatic encephalopathy is given in table II. The precipitating factors of Hepatic Encephalopathy, most commonly found in our patients were infection 58%, Hemetemesis 48% constipation 44%, electrolyte disturbance 40% Drugs likes Benzodiazepine, Diuretics 10% and 8% have history of high protein intake. Anti HCV were positive in 60 (60%) cases HBsAg in 25 (25%) cases and HBsAg Anti HDV and anti HCV in 10 (10%) cases. 5 (5%) cases no cause was detected. In analysis of laboratory findings Hypokalemia, Hyponatremia and hypoglycemia were found in 40 (40%) cases. Hypoalbuminia were found in 80% cases. Leukocytosis were present in 58 (58%) cases 48 (48%) patient have deranged coagulation profile with prothrombin time > 6 seconds. However 22 (22%) patients were pancytopenic. When the cirrhotic patients were grouped according to child pugh classification 68% patients were found to be in class C (Table III). Majority of our patients who expired were in class C of child's Pugh grading.

Table No.I: Clinical Grading of Hepatic Encephalopathy

Clinical Grade	Clinical Sign
Grade 1	Poor concentration, slurred speech, slow mentation, disordered sleep rhythm
Grade II	Drowsy but easily arousable, occasional aggressive behavior , lethargic
Grade III	Marked Confusion, drowsy, sleepy but responds pain and voice, gross disorientation
Grade IV	Unresponsive to voice , may or may not respond to painful stimuli, unconscious

Table No.2: Age & Gender Distribution

Grades of Hepatic Encephalopathy	No N = 100	No. of Patients according to age & Gender							
		12 - 20		21 – 40		41 – 50		> 50	
		M	F	M	F	M	F	M	F
I	8	0	0	0	0	0	0	4	4
II	16	2	2	0	0	8	2	2	0
III	50	1	1	2	3	26	12	4	1
IV	26	6	1	3	0	6	0	7	3

Table No.3: Precipitating factors found in our patients were

Precipitating factors	Male	Female	Total	%
Infection	38	20	58	58%
G.I bleeding	26	22	48	48%
Constipation	20	24	44	44%
Paracentesis	12	10	22	22%
Drugs	8	2	10	10%
High protein intake	8	0	8	8%

Table No.4: Frequency according to child Pugh classification

Child's Class	No N=100	%
A	12	12%
B	20	20%
C	68	68%

In analysis of laboratory funding, HCV antibodies were found positive in 60 (60%) patients, HBsAg in 25 (25%) and all virus HBsAg, HDV and anti Hcv were found positive in 10 (10%) patient. In (5%) patient, no cause was detected. Hypo kalemia, hyponatremia and hypoglycemia were found in 40 (40%) cases, in 60% cases blood urea was found high while Creatinine was slightly raised in 28 (28%) cases. Hypoalbuminia was found in 80 (80%) cases Leukocytosis (TLC count > 11000 umm) was found in 58 (58%) cases. Coagulation profile was abnormal in 48 (48%) cases with prothrombin time patient > 6 seconds of control. While pancytopenia was detected in 22 (22%) patient, however only thrombocytopenia was found in 36 (36%) cases. When the cirrhotic patients were grouped according to child pugh classification 68% of patients were found to be in class C, as show in table- IV. Out of 100 patients, 34 (34%) died including 20 (20%) males 14 (14%) were females. 50 patients were in grade III and 26 patients were in grade IV hepatic encephalopathy respectively. All those cirrhotic patients who expired were found to be in class C of child's Pugh classification.

DISCUSSION

Liver Cirrhosis is one of the common, challenging and rising health problem in Pakistan. Although the exact pathogenic mechanism is yet to be determined[11] We conducted study on 100 patients, majority of patients were above forty years old, comparable in other studies at PIMS Islamabad[12] Baluchistan[13] also there is male predominance in advanced stages of cirrhosis, also reported internationally at Saudi Arabia[14]. In our study anti HCV was found in 60% of cases, that is epidemic in Pakistan, that was comparable in other studies conducted in Pakistan. Alam in Khyber Pakhtoon Khwah[15] at PIMS Islamabad[12]. Most of our patient were in end stage of cirrhosis in which hepatitis C was commonest cause. That is against the studies conducted in western countries, which showed alcohol is the main etiological factor[16]. Infection was most common precipitant factor i.e SBP in our study, there has been lot of differences in precipitants across the studies. This was consistent with a study done in Pakistan by Mumtaz et al. and Abid et al. who also reported SBP as the most common precipitant in HE [17-18]. Our finding is, however, contradicting studies done in the USA by Souheil et al., who observed that infections were responsible in only 3% of cases. This could be related to adherence to therapy and regular monitoring of patients with LC in the USA, which resulted in early detection and treatment of infections[19].Infection, gastrointestinal bleeding, constipation was important precipitating factors[12] that was also proved in our study. After reviewing literature we assessed that our findings match with studies conducted locally by khuram[18] and Saad Masood[12] only one study conducted by Hameed Ahmed[17] shows electrolyte imbalance was the main cause of HE but the foreign studies revealed infection is less common cause abroad, which may be due to better hygienic conditions of patients and hospitals. In our study 40% patients having electrolyte imbalance, may be because of excessive use of diuretics, or vomiting Leukocytosis were found in 58% cases which supports infection was the most common precipitating factor in our study findings of low haemoglobin, hypoalbuminia correspond with advanced stages of cirrhosis[19] majority of our patient, having high blood urea and Creatinine may be a contributor factor for hepatic encephalopathy. The mortality in our patients was 34% which is comparable with study conducted by Saad Maqsood Islamabad[12]. All those patients who expired were mostly in class C of child's classification and grade III or IV hepatic encephalopathy. The limitations of our study include it involving a single center and the small sample size. Further, large-scale, multicenter trials should be evaluated using robust clinical outcomes.

CONCLUSION

Infection, gastrointestinal bleeding, constipation and electrolyte in balance were the most common precipitating factors in our set up.

Author's Contribution:

Concept & Design of Study:	Hakim Ali Abro
Drafting:	Azizullah Jalbani, Chandur Lal
Data Analysis:	Mumtaz Ali, Abdul Raheem, Sultan Ahmed
Revisiting Critically:	Hakim Ali Abro, Azizullah Jalbani
Final Approval of version:	Hakim Ali Abro

Conflict of Interest: The study has no conflict of interest to declare by any author.

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