

Precipitating Factors of Hepatic Encephalopathy in Patients With Liver Cirrhosis

Hepatic
Encephalopathy
With Liver Cirrhosis

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ABSTRACT

Objective: The objective of this study was to know the frequency of various precipitating factors in patients with hepatic encephalopathy secondary to hepatic cirrhosis.

Study Design: Descriptive cross sectional study

Place and Duration of Study: This study was conducted at the King Abdullah Teaching Hospital Mansehra for one year from January to December 2019.

Materials and Methods: One hundred and two patients both male and female having age ≥ 16 years with hepatic encephalopathy secondary to liver cirrhosis were included in this study. All the patients with encephalopathy due to causes other than hepatic cirrhosis were excluded from the study. After taking detailed history, physical examination and investigations precipitating factor was identified. All the data was analyzed using SPSS version 19.

Results: One hundred and two patients with hepatic encephalopathy were studied. Mean age of the population was 52.68 ± 17.69 years and the male to female ratio of 1.13:1. In most of the patients cause of cirrhosis was hepatitis C (60.78%) and most of the patients presented with hepatic encephalopathy grade III (39.2%) and IV (33.3%). The most common precipitating factor was infection (24.50%) followed by upper gastrointestinal bleeding (20.58%) and combination of factors (15.68%).

Conclusion: Infection is one of the most common precipitating factors of hepatic encephalopathy and hence need timely identification and treatment.

Key Words: Hepatic encephalopathy, precipitating factors, liver cirrhosis, West haven criteria, ammonia, portosystemic shunting.

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INTRODUCTION

Liver diseases are classified as the second most common cause of death among all the digestive diseases and accounts for about 66,000 deaths in the united states of America.^{1,2} If not diagnosed and treated timely, liver disease can lead to cirrhosis which in turn give rise to serious complications like hepatic encephalopathy, ascities and varices.³

Hepatic encephalopathy is described as a combination of neurological and psychiatric symptoms and signs in patients with acute or chronic liver disease or portosystemic shunting after exclusion of other causes of encephalopathy.⁴ Hepatic encephalopathy is a very serious complication of liver disease and very badly

affects the quality of life of the patient and the caregivers and also puts heavy burden on health care resources and economy.^{5,6,7} The prevalence of overt hepatic encephalopathy varies from 10 to 25 % in patients with cirrhosis and upto 50% in patients with transjugular intrahepatic portosystemic shunts.⁴ The severity of hepatic encephalopathy can be graded according to West Haven classification from grade 0 assigned to normal patients to grade 4 to patients with coma.⁸ Several factors have been studied in the pathophysiology of hepatic encephalopathy but the most important neurotoxin is ammonia. In normal state ammonia generated in intestine is metabolized in the liver to urea and excreted through kidneys. In cirrhosis liver is unable to metabolize ammonia and bypasses to brain through collateral circulation and causes brain dysfunction through various mechanisms eg, increase intracranial pressure, brain edema and altered neurotransmitters level.⁹

Hepatic encephalopathy is almost always induced by one or more precipitating factors. The most common precipitating factors involved in hepatic encephalopathy are gastrointestinal bleeding, constipation and heavy protein intake. This leads to increased production of nitrogenous waste products especially ammonia by the intestinal bacteria. Ammonia crosses the blood brain

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barrier and leads to encephalopathy through various mechanisms. The other precipitating factors implicated in hepatic encephalopathy are infections, dehydration, azotemia, sedatives and hypnotics, opioid derivatives and electrolytes imbalance.^{10,11} The identification of precipitating factors is of utmost importance as fixation of these factors usually results in rapid reversal of hepatic encephalopathy.¹²

The rationale behind doing these study was to identify the frequency of the most common precipitating factors implicated in hepatic encephalopathy. As the frequency of different precipitating factors vary in different populations, this study will provide us local statistics of the precipitating factors of hepatic encephalopathy.

MATERIALS AND METHODS

This descriptive cross sectional study was conducted at King Abdullah Teaching Hospital, Mansehra from January to December 2019 after approval from hospital research and ethical committee. Informed written consent was taken from the patients or attendants. One hundred and two patients presenting with hepatic encephalopathy were identified through consecutive non probability sampling. All the patients having age 16 years or above diagnosed with hepatic encephalopathy secondary to liver cirrhosis (type C) were included. All patients with psychiatric diseases, structural renal diseases with creatinine ≥ 2 mg/dl, intracranial infections, head injury and stroke were excluded. Detailed history including present and past medical history, physical examination, biochemical tests and ultrasound was performed in all patients. History included present history of gastrointestinal bleeding, constipation, fever, vomiting, motions, drugs etc and past history of similar episodes. Investigations included blood complete picture, blood culture, albumin, bilirubin, blood sugar, coagulation profile, urea, creatinine, ascetic fluid analysis and culture, viral profile (A, B, C, D, E if not already done), electrolytes, urine routine examination and culture, X ray chest and ultrasound for liver, spleen, ascities and portal vein. The diagnosis of covert hepatic encephalopathy (minimal hepatic encephalopathy + grade I) was based on Psychometric Hepatic Encephalopathy Score¹³. Child Turcotte Pugh score was used for classification of severity of liver cirrhosis while West Haven criteria was used for classification of severity of hepatic encephalopathy^{14,15}. All the parameters were recorded on a predesigned proforma. All the patients were managed according to gastroenterology department protocol.

RESULTS

SPSS version 19 was used for data analysis. Mean \pm standard deviation were used for quantitative variables like age while frequencies and percentages were used

for qualitative variables like gender and precipitating factors. The data was presented in the form of tables.

One hundred and two patients who presented with hepatic encephalopathy due to hepatic cirrhosis were included in this study. There were 55(53.9%) male and 47(46.1%) female with a male to female ratio of 1.13:1. The minimum age of the population was 17 years, maximum 89 years and mean 52.68 ± 17.69 standard deviation. Most of the patients were in the age group ≥ 61 followed by those ranging from 41-60 years.

Table No.1: Modified West Haven Criteria¹⁵

	Grade	Features
Covert	minimal	No evidence of mental change but detectable on psychometric or neurophysiological tests
	I	trivial lack of awareness, euphoria or anxiety, shortened attention span, altered sleep pattern
Overt	II	Lethargy, disorientation in time, Obvious personality change, dyspraxia, asterixis
	III	somnolence, confusion, gross disorientation
	IV	Coma with or without response to stimuli

Table No.2: Demographics of patients

Variables		No. of patients	Percent
Gender	Male	55	53.9
	Female	47	46.1
Age	16-40	27	26.5
	41-60	35	34.3
	≥ 60	40	39.2
Cause of Cirrhosis	Hepatitis C	62	60.78
	Hepatitis B	31	30.39
	B+C	3	2.94
	Autoimmune	2	1.96
	Unknown	4	3.92
Child' class	A	9	8.8
	B	38	37.3
	C	55	53.9

Table No.3: Frequency of patients according to West Haven classification

	Grades of Encephalopathy	No. of patients	Percent
Covert hepatic encephalopathy	Minimal	2	1.96
	I	6	5.88
Overt hepatic encephalopathy	II	20	19.6
	III	40	39.2
	IV	34	33.3
	Total	102	100

The most common cause of cirrhosis was chronic hepatitis C in 62(60.78%) followed by Chronic Hepatitis B in 31(30.39%) patients. The other less

common causes were co-infection with both hepatitis B and C in 3 (2.94%), Autoimmune Hepatitis in 2 (1.96%) and unknown causes in 4 (3.92%) patients. Most patients presented with Child's Turcotte Pugh score C in 55 (53.9%) and B in 38 (37.3%).

Majority of the patients (40/39.2%) presented in hepatic Encephalopathy grade III while only 8 (7.8%) with covert hepatic encephalopathy.

Table No.4: Frequency of precipitating factors of hepatic encephalopathy

Precipitating factors	No. of patients	Percent
Infection	25	24.50
Gastrointestinal bleeding	21	20.58
Excess protein intake	15	14.70
Constipation	10	9.80
Drugs	8	7.84
Electrolytes	5	4.90
Paracentesis	2	1.96
Combination	16	15.68
Total	102	100

The most common precipitating factor in this population was infection in 25 (24.50%) followed by Upper gastrointestinal bleeding in 21 (20.58%). 16 (15.8%) patients had Hepatic Encephalopathy due to combination of factors. Among the patients who presented with hepatic encephalopathy secondary to infections, respiratory tract infection was the most common site in 12 (48%). The other sites of infection in decreasing frequency were multiple sites in 7/25 (28%), spontaneous bacterial peritonitis in 4/25 (16%) and urinary tract infection in 2/25 (8%) patients.

DISCUSSION

The development of hepatic encephalopathy in patient with hepatic cirrhosis characterizes decompensation and carries poor prognosis without liver transplantation. In our study chronic hepatitis C was the most common cause of cirrhosis (60.78%) compared to study by Kabir A et al in which hepatitis B was the most common cause (56%) and in western countries where alcoholic cirrhosis is the most common cause.^{11,16} In our study majority of the patients presented with hepatic encephalopathy grade III (39.2%) while only 8 (7.8%) presented with covert hepatic encephalopathy of which 6 (5.88%) were in grade I and only 2 (1.96%) were in minimal hepatic encephalopathy. The frequency of grade I hepatic encephalopathy varies in different studies. Maqsood S et al reported 8% while Sing G reported 24% frequency of grade I encephalopathy^{17,18}. The reason for this may be that our patients come from far areas and due to lack of awareness and facilities they report very late to proper health care facility. In almost all cases precipitating factors can be identified

easily. Early recognition and treatment of precipitating factor is of utmost importance in the management of hepatic encephalopathy. In our study infection (24.50%) was the most common precipitating factor similar to studies conducted by Wang et al and Devrajani BR et al^{19,16}. In a study by Kabir A et al, gastrointestinal bleeding was the most common precipitating factor and in a study by Husain W et al, constipation was the most common precipitating factor²⁰. The most common site of infection in our study was respiratory tract (48%), in addition to multiple sites (28%), spontaneous bacterial peritonitis (16%) and Urinary tract infections (8%). Upper gastrointestinal bleed, high protein intake and constipation leads to high protein load in the intestine which is converted to ammonia and carried to brain through portal vein and collateral circulation. Drugs especially diuretics are integral part of treatment of ascities and can lead to precipitation of hepatic encephalopathy either by causing dehydration or electrolytes imbalance.

CONCLUSION

From this study it is concluded that most of the patients presented with hepatic encephalopathy were in grade III and IV. Illiteracy and poor socioeconomic status of the patients are important hurdles in prevention, identification and treatment of precipitating factors before the patients progress to high grade encephalopathy and thus high rate of morbidity and mortality. Most of the precipitating factors can be easily prevented if we educate and create awareness among the patients and caregivers.

Author's Contribution:

Concept & Design of Study: Tahir Ullah
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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