



CODEN [USA]: IAJPBB

ISSN : 2349-7750

INDO AMERICAN JOURNAL OF PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

<http://doi.org/10.5281/zenodo.4412101>Available online at: <http://www.iajps.com>

Research Article

DETECTION OF TRIGGERING FACTORS OF HEPATIC ENCEPHALOPATHY IN PATIENTS WITH CHRONIC LIVER DISEASE IN A TERTIARY CARE HOSPITAL

Manoj Kumar Yadav¹, MD Sakil², Matiullah Alam³^{1,2,3}Jalalabad Ragib-Rabeya Medical College & Hospital, Bangladesh.

Article Received: November 2020 Accepted: December 2020 Published: January 2021

Abstract:

Introduction: Doctors in hospital practice often face chronic liver disease (CLD). Hepatic encephalopathy is a serious complication of chronic liver disease, most commonly in people with advanced cirrhosis. In patients with stable cirrhosis, hepatic encephalopathy is often followed by easily identifiable triggering events. The aim of the study is to understand the triggering factors and their frequency in CLD patients with hepatic encephalopathy in order to prevent mortality and morbidity.

Methods: This descriptive observational study was conducted to identify triggers and their frequency among 50 cases of diagnosed chronic liver disease with hepatic encephalopathy at the Medicine department of Jalalabad Ragib-Rabeya Medical College & Hospital, Bangladesh for one-year duration from March 2019 to March 2020.

Results: Among 50 patients, 36 patients (72%) were men, 14 (28%) women. The study found that the incidence of age 14 (28%) was 41 to 50 years, and 08 (16%) 51 to 60 years, 12 (24%) > 60 years. Of the 50 patients, the etiology of cirrhosis was hepatitis B virus in 28 (56%), hepatitis C virus in 4 (8%), both hepatitis B and C in 02 (4%). Among 50 patients 13 (26%) were grade 3 and 11 (22%) in grade 2 hepatic encephalopathy. According to Child-Pugh with a score of 16 (32%) in class C and 09 (18%) in class B. The most common triggers were gastrointestinal bleeding (28%), infection (26%), mixed (16%) and unknown (20%). In this study, the mortality rate was 32% of the majority of patients in Child-Pugh Class C.

Conclusions: The most common triggers of hepatic encephalopathy in this study were the upper G.I. bleeding, infection, mixed factor and electrolyte imbalance. To prevent hepatic encephalopathy, caution should be exercised in administering diuretics to patients with chronic liver disease. Maintaining early and effective infection control measures and better hygiene conditions in government hospitals are imperative.

Key words: precipitating factors, hepatic encephalopathy, chronic liver disease.

Corresponding author:**Manoj Kumar Yadav,**

Jalalabad Ragib-Rabeya Medical College & Hospital, Bangladesh.

QR code



Please cite this article in press Manoj Kumar Yadav et al. *Detection Of Triggering Factors Of Hepatic Encephalopathy In Patients With Chronic Liver Disease In A Tertiary Care Hospital*, Indo Am. J. P. Sci, 2021; 08(1).

INTRODUCTION:

Liver disease affects millions of people around the world every day. However, in developing countries, where health care costs have always been an issue, long-term diseases such as cirrhosis and its complications are a serious health problem and a major challenge to the health economy [1-2]. Due to poverty, poor hygiene, insufficient education and a lack of counseling, the number of patients with cirrhosis of the liver is increasing, and most of them end up in wards with various complications. Hepatic encephalopathy syndrome (HE) describes all neuropsychiatric symptoms that occur in patients with acute or chronic liver disease (CLD) in the absence of other neurological disorders [3-4]. About 30% of cirrhotic patients die in hepatic coma. A patient with chronic liver disease is common in our country due to the frequent occurrence of hepatitis B and C. A 2008 report showed a positive result of 5.5% of HbsAg among the general population living in Savar, a suburban area on the outskirts Dhaka in Bangladesh. The appearance of HE (hepatic encephalopathy) in any patient indicates a poor prognosis [5-6]. HE can occur as a result of acute liver failure or one or more triggers in a patient with cirrhosis, or it can occur as a result of prolonged systemic portal shunt resulting in chronic systemic portal encephalopathy. Patients with chronic portal systemic encephalopathy survive better than those who develop acute HE (100% vs 70%). However, the prognosis for the latter group can be improved if triggering factors are identified early and treated appropriately [7-8]. Common triggers are gastrointestinal bleeding, infection, Azotemia, constipation, electrolyte imbalance, and a high-protein diet. The use of drugs such as tranquilizers, sedatives, analgesics and diuretics, fulminant liver injury, and high-volume paracentesis is believed to induce encephalopathy in a patient with stable cirrhosis. The exact pathogenic mechanism is unknown to date; however, the basic processes are disturbances in the hepatic clearance of intestinal substances such as ammonia, free fatty acids, mercaptans, etc., caused by liver cell failure or transfusion and altered metabolism of amino acids in changes in brain transmission resulting in impairment brain function [9-10]. This study will aim to establish common triggers and their frequency in patients with hepatic encephalopathy.

METHODS:

This was a descriptive observational study involving 50 patients admitted to the medical ward at Jalalabad Ragib-Rabeya Medical College & Hospital, Bangladesh for one-year duration from March 2019 to March 2020. All adult patients admitted to the medical department have biochemical, sonological evidence of chronic liver disease and symptoms suggestive of hepatic encephalopathy or confusion were included in this study. Patients were selected by deliberate sampling. Patients with acute fulminant liver failure or patients with clinical, biochemical and microbiological evidence of other causes of liver failure and encephalopathy were excluded from the study. A data collection sheet is designed to record all interesting information. A detailed clinical history of patients was collected regarding the current and past disease. Questions were asked about upper gastrointestinal bleeding (bloody vomiting, melaena), constipation, a high-protein diet, and the use of medications such as diuretics, tranquilizers, painkillers, paracentesis, and trauma or surgery. Some patients had more than one risk factor (a mixed factor). Particular attention was paid to the presence of jaundice, anemia, fever, asterisk and ascites. Encephalopathy was assessed according to criteria. A complete blood count, liver function test, kidney function test, random blood sugar test, serum electrolytes, serum albumin and clotting profile were performed for each patient. Abdominal ultrasound was performed to determine the size of the liver and spleen, echogenicity of the parenchyma and ascites. Any evidence for the presence of other comorbid complications of cirrhosis was also recorded, and each patient was scored on the Child-Pugh Score. All patients were followed throughout their hospital stay. Participants were encouraged to participate voluntarily in the study. Consent was obtained after presenting all respondents with a short study in Bengali. Confidentiality was ensured and anonymity was maintained; special care should be taken to ensure that no participant can be identified in any report or publication within this study.

RESULTS:

A total of 50 patients were enrolled in the study. The mean age of the study population was 44.3 years (SD 12.83 years), and 72% were male. Most of the patients are Muslim, most of the patients are house wives, and most of the patients are of low socioeconomic status (Table I).

Table-I
General characteristics of the whole study population

Variables	Values (Number/percentage)	SD
Age	44.3 years	±12.83
Sex		
• Male	36 (72%)	
• Female	14 (28%)	
Religion		
• Muslim	42 (84%)	
• Hindu	8 (16%)	
• Others	0 (0%)	
Occupation		
• Service	6 (12%)	
• Business	14 (28%)	
• Housewife	13 (26%)	
• Others	17 (34%)	

Table-II
Age distribution of patients (n=50)

Age (Years)	No. of patient	SD
<20 years	2	4%
20 – 30	6	12%
31 - 40	8	16%
41 – 50	14	28%
51 – 60	8	16%
>60	12	24%

The mean age of the patients was 44.3 years (STD-12.83). The maximum number of patients (14) in this study was in the age group 41-50 years, then (12) in the age group > 60 years and the age group 31-40 years (Table II). 26 (52%) patients had Grade III encephalopathy, 11 (22%) had Grade IV, 9 (18%) patients had Grade II and 4 (8%) patients had Grade I encephalopathy.

Table-III
Grading of patients according to Child Pugh's classification of cirrhosis

Grade	Patients	Percentage
B	18	36%
C	32	64%

Table-IV
Etiology of chronic liver disease

Etiology	Frequency	Percentage
HBV	28	56%
HCV	4	8%
Both B & C	2	4%
Wilson's	1	2%
Alcohol	1	2%
Unknown	15	30%
Total	50	100%

The etiology of chronic liver disease was hepatitis B in 28 (56%), hepatitis C in 4 (8%), HBV and HCV in 2 (4%), alcohol in 1 (2%), Wilson's disease 1 (2%), and different in 15 (30%) patients (Table IV).

Table-V
Clinical presentations of patients with hepatic encephalopathy

Sign/Symptom	Frequency	Percentage
Jaundice	50	100%
Hematemesis	14	28%
Edema	36	72%
Fever	18	36%
Constipation	12	24%
Ascites	50	100%
Splenomegaly	45	90%
PalmarErythema	10	20%

Table-VI
Outcome of patients according to Precipitating Factors

Risk Factor	Survival (% of factor)	Death (% of factor)	Total Cases (% of total)
GI bleeding	06 (42.85%)	08 (57.14%)	14 (28%)
Infection	11 (84.62%)	2 (15.38%)	13 (26%)
Hypokalemia	03 (100%)	0 (0%)	3 (6%)
Constipation	02 (100%)	0 (0%)	2 (4%)
Mixed	05 (62.5%)	03 (37.5%)	8 (16%)
Unknown	07 (70%)	03 (30%)	10 (20%)
Total	34 (68%)	16 (32%)	50 (100%)

All patients present with jaundice and ascites, and 90% of patients with spleen enlargement (Table V). Gastrointestinal bleeding (28%) and infection (26%) were the most common triggers of hepatic

encephalopathy (Fig. 2). In this study, the mortality rate was 32%, mostly from gastrointestinal bleeding (57.14%) (Table VI).

DISCUSSION:

Chronic liver disease is one of the most common causes of morbidity and mortality worldwide. Hepatic encephalopathy (HE) is the major neuropsychiatric complication of chronic liver disease, and its appearance indicates poor prognosis. HE is the most common cause of death in patients with chronic liver disease [11]. A clearly defined trigger factor is usually identified in most HE patients, and reversing or controlling these triggers is a key step in management. In this study, 50 patients with CLD with symptoms of hepatic encephalopathy were examined in a tertiary hospital. All possible important factors that may be responsible for the induction or aggravation of hepatic encephalopathy were searched for and analyzed. In our study, men (72%) outnumbered the female patients (28%) and most patients (68%) over 40 years of age, which is more in line with the studies by Kumar et al. Most of the patients in this study were from rural areas and should be to a weak socio-economic group. The negative aspect for the rural population is that they reached at the late-stage in tertiary hospital. In this study, the majority of patients were in the 3rd stage of coma 26 (52%), 11 (22%) in the 4th stage, 9 (18%) in the 2nd stage and 4 (8%) in the 1st stage [12-13]. Various studies show grade I to grade IV encephalopathy with varying frequency. The most common clinical symptoms were jaundice (100%), altered state of consciousness (100%), splenomegaly (90%), and ascites (100%) in patients with hepatic encephalopathy. The amalgamation of all these poor prognostic symptoms is not surprising when considering uncontrolled chronic liver disease in these selected patients. In this study, gastrointestinal bleeding is the most important factor in causing HE cases (28%), which is more in line with the studies by Kumar et al. (39%) where Maqsood et al. is the second leading cause, Kumar et al. was the second (26%) most common trigger of hepatic encephalopathy in this study. Kumar et al., Devrajani et al., Maqsood et al., Alam et al. Found this in 67%, 58%, 44%, 24% of cases, respectively. Souheil said infections are only responsible in 3% of cases. In another study by Conn, infections were only responsible in 4% of the cases. The high frequency of infections in this study was likely due to unhygienic conditions and poor nutritional status of the patients [14]. In our study, multiple factors (ie infection and gastrointestinal bleeding, infection and constipation or hypokalaemia) were found in the same patient as the cause of HE in 16% of the cases. Hypokalemia was found in 6% of cases as an isolated trigger compared to the study by Alam et al. In which drugs (diuretics, tranquilizers) and electrolyte disturbances (hyponatraemia and hypokalemia) were the main cause that was very high.

However, Suheil and Conn found electrolyte imbalances in 11% and 9% of the cases, respectively. If hypokalemia were included in the mixed component, this percentage would be high. In our study, hypokalemia was mainly caused by diarrhea, vomiting, and treatment with diuretics. In our study, we did not find any documented or prescribed medication that could cause hepatic encephalopathy. Constipation was the lowest trigger (4%) in this study as an isolated cause, consistent with Souheil20 Fallon and Conn reported constipation in 6%, 3%, and 3% of the cases, respectively. In turn, Sheikh et al., Hameed et al., And Alam found it in 36%, 52% and 32% of cases, respectively. This could be due to dietary restrictions, poverty, lack of use, or inappropriate dosing of lactulose. In this study, no causative factors were found in a significant percentage of cases (20%), unlike Maqsood et al., In which no causative agent of hepatic encephalopathy was found in 10% of cases [15]. A greater percentage of unknown factors may be due to the illegal taking of a drug from a pharmacy without a prescription, a lack of knowledge about its disease, poverty, illiteracy, the communication gap between the doctor and the patient and, above all, due to economic constraints that we could not do some important research on some patient. In our study, the mortality rate was 32%, which was consistent with the 30% in the Maqsood et al. Study; All expired patients with chronic liver disease were classified as child grade C (in this study, 64% of patients were in childhood grade C and the rest 36% were in childhood grade B).

CONCLUSION:

The most common triggers of hepatic encephalopathy in this study were upper G.I. bleeding, infection, mixed factor and electrolyte imbalance. To prevent hepatic encephalopathy in patients with chronic liver disease, diuretics should be used with caution in patients with chronic liver disease. Maintain early and effective infection control measures and better hygiene in government hospitals. The consistent use of lactulose and fiber should be encouraged to prevent constipation. More and more urgent endoscopic facilities need to be made available nationwide for the rapid control of gastrointestinal bleeding, and most importantly. Implementing an effective screening program for the early detection of HBV nationwide should be the primary focus of official health concerns.

REFERENCES:

1. Ullah T, Qasim MI, Shah SF, Ullah I. Precipitating Factors of Hepatic Encephalopathy

- in Patients With Liver Cirrhosis. *InMed. Forum* 2020 Apr (Vol. 31, No. 4, p. 54).
- Sethuraman VK, Balasubramanian K. Clinical Spectrum of Precipitating Factors of Hepatic Encephalopathy in Cirrhosis of Liver and Its Relation to Prognosis in a Tertiary Care Hospital- A Retrospective Study. *Age (Mean±STD)*. 2019;49:12-26.
 - Terefe Tesfaye B, Gudina EK, Boshu DD, Mega TA. Short-term clinical outcomes of patients admitted with chronic liver disease to selected teaching hospitals in Ethiopia. *PLoS one*. 2019 Aug 30;14(8):e0221806.
 - Aidoo M, Mohammed BS. Distribution and Determinants of Etiologies and Complications of Chronic Liver Diseases Among Patients at a Tertiary Hospital in a Lower Economic Region of Ghana. *Education*. 2020 Sep 25;60(28):15-6.
 - Poudyal NS, Chaudhary S, Sudhamshu KC, Paudel BN, Basnet BK, Mandal A, Kafle P, Chaulagai B, Mojahedi A, Paudel MS, Shrestha B. Precipitating Factors and Treatment Outcomes of Hepatic Encephalopathy in Liver Cirrhosis. *Cureus*. 2019 Apr;11(4).
 - Khiangte B, Kothakota SR, Sasidharan M, Kareem H, Joshi S, Kumar VV, Kanala JR, Kumar P, Nair AK. Prevalence and determinants of hepatopulmonary syndrome in decompensated chronic liver disease. *Indian Journal of Gastroenterology*. 2020 Aug;39(4):362-9.
 - Jang WY, Chung WJ, Jang BK, Hwang JS, Lee HJ, Hwang MJ, Kweon YO, Tak WY, Park SY, Lee SH, Lee CH. Changes in Characteristics of Patients with Liver Cirrhosis Visiting a Tertiary Hospital over 15 Years: a Retrospective Multi-Center Study in Korea. *Journal of Korean medical science*. 2020 Jul 27;35(29).
 - Bohra A, Worland T, Hui S, Terbah R, Farrell A, Robertson M. Prognostic significance of hepatic encephalopathy in patients with cirrhosis treated with current standards of care. *World Journal of Gastroenterology*. 2020 May 14;26(18):2221.
 - Mane M, Bhosale T, Mane P, Mankar P, Mane CA. A CORRELATION OF PROGNOSTIC AND PRECIPITATING FACTORS OF HEPATIC ENCEPHALOPATHY. *Journal of Critical Reviews*. 2020;7(13):417-22.
 - Tauseef A, Zafar M, Rashid B, Thirumalareddy J, Chalfant V, Farooque U, Mirza M. Correlation of Fasting Lipid Profile in Patients With Chronic Liver Disease: A Descriptive Cross-Sectional Study in Tertiary Care Hospital. *Cureus*. 2020 Oct;12(10).
 - Oluremi AS, Opaleye OO, Ogbolu DO, Alli OT, Ashiru FT, Alaka OO, Suleiman IE, Enitan SS, Adelakun AA, Adediji IO, Olowoyeye EA. Serological evidence of HIV, Hepatitis B, C, and E viruses among liver disease patients attending tertiary hospitals in Osun State, Nigeria. *Journal of Immunoassay and Immunochemistry*. 2020 Sep 25:1-3.
 - Yousaf MK, Nourin S, Khan A, Yousaf MI, Ullah SA, Lodhi S. Diabetes Mellitus Among Patients with Cirrhosis Due to Hepatitis C Virus and its Association with Hepatic Encephalopathy. *Annals of King Edward Medical University*. 2020 Jun 4;26(1):36-40.
 - Montagnese S, Russo FP, Amodio P, Burra P, Gasbarrini A, Loguercio C, Marchesini G, Merli M, Ponziani FR, Riggio O, Scarpignato C. Hepatic encephalopathy 2018: A clinical practice guideline by the Italian Association for the Study of the Liver (AISF). *Digestive and Liver Disease*. 2019 Feb 1;51(2):190-205.
 - Shah ND, Ventura-Cots M, Abraldes JG, Alborae M, Alfadhli A, Argemi J, Badia-Aranda E, Arús-Soler E, Barritt IV AS, Bessone F, Biryukova M. Alcohol-Related liver disease is rarely detected at early stages compared with liver diseases of other etiologies worldwide. *Clinical Gastroenterology and Hepatology*. 2019 Oct 1;17(11):2320-9.
 - Raju B, Andani A, Kolhapure S, Agrawal A. Need for hepatitis A prevention in patients with chronic liver disease in the changing epidemiological setting of India. *Human Vaccines & Immunotherapeutics*. 2020 Nov 23:1-0.