

Precipitating factors of Hepatic Coma

Saira Afzal,¹ Maaz Ahmad²

Abstract

Objective: The objective of this study was to: Find the age and gender distribution and frequency of precipitating factors of hepatic coma in chronic liver disease.

Study Design: Comparative cross – sectional study.

Material and Methods: In the Gastroenterology Unit and East Medical Ward KEMU. The study duration was one year and started in May 2005.

Fifty cases of hepatic encephalopathy due to chronic liver disease were selected. It was probability sampling and random table was used. The complete record of the patients was maintained on the structured proforma. After informed consent all record was kept confidential.

Results: Constipation, upper gastrointestinal bleeding, and infection were the common precipitating factors. It was found that constipation was more in old age group (75%) and the difference was found significant ($p < 0.05$). The upper gastrointestinal bleeding was found more in young group (44%) and this was found significant ($p < 0.05$).

Conclusions: The precipitating factors of hepatic

encephalopathy should be early recognized and awareness should be created. Lifestyle modifications like exercise, low fat diet, high fibre diet and active work should be encouraged to prevent constipation. Emergency endoscopic facilities should be made available.

Keywords: Cirrhosis, encephalopathy, hepatic.

Introduction

Liver disease is common worldwide; in United Kingdom 5000 deaths from cirrhosis and its complications like coma have occurred in a year.¹ In United States chronic liver disease is the 7th leading cause of death, according to the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).² Pakistan is included in high prevalence area for hepatitis B and C which is 8% and 6% respectively.³ Thus the life of large number of population is at stake due to the large impact of hepatitis B and C viral infections that leads to chronic liver disease.

Hepatic encephalopathy is a common complication of chronic liver disease. Hepatic encephalopathy is defined as a spectrum of neuropsychiatric abnormalities in patients with liver dysfunction, after exclusion of other known brain diseases.⁴ Hepatic encephalopathy is characterized by personality changes, intellectual impairment, and a depressed level of consciousness. An important prerequisite for the syndrome is diversion of portal blood into the systemic circulation through portosystemic collateral vessels.⁵ Hepatic encephalopathy is also described in patients without cirrhosis with either spontaneous or surgically created portosystemic shunts.⁶ The development of hepatic

Afzal S.¹
Assistant Professor Community Medicine
King Edward Medical University, Lahore – Pakistan

Ahmad M.²
Dean of Public Health and Preventive Medicine
Professor of Community Medicine
King Edward Medical University, Lahore – Pakistan

encephalopathy is explained, to some extent, by the effect of neurotoxic substances, which occurs in the setting of cirrhosis and portal hypertension.⁷

Subtle signs of hepatic encephalopathy are observed in nearly 70% of patients with cirrhosis.⁸ Symptoms may be debilitating in a significant number of patients and are observed in 24 – 53% of patients who undergo portosystemic shunt surgery.⁹ Approximately 30% of patients dying of end-stage liver disease experience significant encephalopathy, approaching coma.¹⁰ Hepatic encephalopathy is seen as a clinical manifestation of low – grade chronic cerebral edema, which is accompanied by alterations in glioneural communication.¹¹ Different factors such as ammonia, inflammatory cytokines, benzodiazepines and electrolyte imbalance, upper gastrointestinal bleed, constipation, drugs specifically diuretics, excess dietary protein intake, infections including spontaneous bacterial peritonitis, urinary tract infections, paracentesis, acute hepatitis, hepatocellular carcinoma may precipitate or aggravate glial edema.¹² Patient passes through progressive stages of encephalopathy resulting in increased hospital admissions, more consumption of health care resources and above all the longer – hospital stays contribute to increase in off work hours and loss of man power resources. It is a fact that with proper nutrition, avoidance of certain toxins (i.e., alcohol), vitamin supplementation, and management of complications of cirrhosis, hepatic encephalopathy can be avoided. Health education, specific protection, early diagnosis of the precipitating factors of hepatic encephalopathy and prompt management decreases the mortality due to this fatal condition. Early recognition of precipitating factors improves the outcome, thus the awareness about those factors was the aim of this study, in order to decrease the morbidity and mortality due to dreadful but preventable condition of hepatic encephalopathy in chronic liver disease.

Material and Methods

Setting: In Gastroenterology Unit Medical-1 Allied hospital Faisalabad and East Medical Ward KEMU Lahore.

Duration: The study was carried out in one year starting from May 2005 to 2006.

Sample Size: In the study 30 males and 20 females having hepatic coma due to chronic liver disease were included. Epi-info2000 was used to find sample size at 95% confidence level. The estimated population of

patients of chronic liver disease was 5000. The expected frequency of hepatic coma in these patients was 5%, the worst acceptable was 11%. The sample size was calculated as 50.

Sampling Technique: It was probability sampling. Random table was used for simple random sampling.

Sample Selection: The sample was selected according to the following inclusion and exclusion criteria.

Inclusion Criteria: Diagnosed cases of cirrhosis of liver suffering from hepatic encephalopathy grade 4, Child Pugh Class A and B. They were 20 – 80 years of age of any sex.

Exclusion Criteria: Following unconscious patients were excluded from the study: renal failure due to any cause including hepatorenal syndrome, hypertension, hypotension, diabetes, hypoglycaemia, electrolyte disturbances, alcohol intoxication, sedative overdose, cerebrovascular accidents including hemorrhage and infarctions.

Study Design: Comparative cross-sectional study.

Data Collection Procedure:

Permission for the conduct of the study was obtained from the Ethical Research Committee of Punjab Medical College and Allied Hospital Faisalabad. Informed consent was taken. Risks and benefits were explained. All the information about the patient was kept confidential. History of hematemesis, Malena, bleeding, constipation, fever, burning micturition, swelling of abdomen, pain in abdomen, jaundice, diuretics, vomiting and diarrhea, use of sedative drugs were assessed. The patients were diagnosed to have hepatic coma on both clinical features and relevant investigations. Clinical features included palmar erythema, fetor hepaticus, jaundice, spider naevi, gynaecomastia, caput madusae, reduced liver span, splenomegaly, ascites and unconsciousness. The investigations done included hepatitis B and C, D status, serum albumin, serum globulin, blood sugar levels, serum electrolytes, blood urea and creatinine, complete blood count, liver function tests, CT brain, ascitic fluid examination, ultrasound abdomen for liver and spleen, endoscopy for variceal bleed.

Structured Proforma and check list was used as data collection tool.

Data Analysis:

The descriptive statistics were given in frequency and percentages. On qualitative data Chi-square test was applied on proportions to find the statistical signifi-

Table 1: Age and Gender distribution of hepatic encephalopathy.

Age (range)	Mean Age	Males (%)	Females (%)
Group I = 20 – 40	51.9 ± 8.9	30 (60%)	20 (40%)
Group 2 = 41 – 80			

Table 2: Distribution of causes of hepatic encephalopathy in Males and Females.

S. No.	Cause	Males	Percentage	Females	Percentage	p-value
1.	Constipation	20	67	10	50	0.23
2.	Bleeding	04	13	05	25	0.29
3.	Infection	02	07	03	15	0.33
4.	others	04	13	02	10	0.72

Table 3: Distribution of causes of hepatic Coma in two groups.

S. No.	Cause	Group1 n = 18	%	Group2 n = 32	%	p-value
1.	Constipation	06	34	24	75	0.003
2.	Bleeding	08	44	01	03	0.0002
3.	Infection	00	00	05	16	0.07
4.	Others	04	22	02	06	0.09

cance. P value less than 0.05 was considered as significant. Tables were used to present the data. SPSS version 13 was used for analysis.

Results

Out of total 50 patients of hepatic encephalopathy due to chronic liver disease, mean age was 51.9 ± 8.9 . They were divided in two groups according to the age. Group 1 was 20 – 40 years and Group 2 was 41 – 80 years. There were more males (60%) than females (40%). The frequency of precipitating factors show that bleeding and infection was more in females, that is 25% and 15% respectively. However no significant difference was found in gender distribution of the precipitating factors of hepatic encephalopathy ($p < 0.05$). When two age groups were compared for the precipitating factors of hepatic encephalopathy, it was found that constipation was more in old age group (75%) and the difference was found significant ($p < 0.05$). The upper gastrointestinal bleeding was found more in group 1 (44%) and this was found significant ($p < 0.05$). Infections and other factors like paracentesis, use of benzodiazepines and drugs, excessive protein intake was not found significant ($p > 0.05$).

Discussion

Hepatic Encephalopathy can be prevented by the early recognition of its precipitating factors so these factors were ascertained in selected cases of hepatic encephalopathy due to chronic liver disease. In this study males were more than females. Strauss et al reported the male to female ratio in the study of hepatic encephalopathy as 3:1.1.¹³

In our study majority (64%) of patients were more than forty years old. Durrani 12 had reported similar findings in Pakistan.¹⁴

Constipation and gastrointestinal bleeding and have been described as important precipitating factors of Hepatic Encephalopathy and same was emphasized in our study.¹⁵⁻¹⁷ Our findings match those studies done locally. This is especially true for Pakistan where Sheikh and Khurram reveal constipation and bleeding as the main factors.^{18,19}

In our study, the most common precipitating cause of hepatic encephalopathy was found to be constipation. In western studies by Souheil, Fallon, and Conn had reported the constipation in 6%, 3%, 3% of their patients respectively.²⁰⁻²² In local studies same results were presented as our study. Hameed and Alam found constipation in 52%, and 32% of their patients

respectively.²³⁻²⁴ It is an eye opener for us. It may be due to the reason that the mortality of active gastrointestinal bleeding is very high in our population due to limited resources. Many patients die of hypovolemic shock even before the actual treatment is instituted in the hospital. The reasons are lack of transport facilities, lack of blood banks and donors, non-availability of emergency sclerotherapy and banding in cities and rural health centres, limited availability of drugs for the control of bleeding, poor compliance of our patients to drugs and infrequent follow-ups. Meta-analysis of randomized control trials of propranolol versus no therapy has demonstrated a 47% reduction in variceal bleed, a reduction of 45% in death; from bleeding and a 22% overall reduction in mortality ($p, 0.05$). Thus poor compliance to drugs increases the rate of mortality in patients due to upper gastrointestinal bleed.²⁵

Constipation is the significant precipitating factor in old age in our study due to the fact that increasing age effects the bowel habits, however it is easily treatable and preventable. In old age life style modifications, lactulose and fibre rich diet may do a lot by preventing the dangerous condition of hepatic encephalopathy in chronic liver disease.²⁶ In group I upper gastrointestinal bleeding was more common and significant. Sheikh and Hameed have reported upper gastrointestinal bleed as cause of hepatic encephalopathy in 76% and 55% of their patients respectively.^{18,23}

Studies done by Sheikh and Hameed have also shown electrolyte imbalance as precipitating factor of hepatic encephalopathy.^{18,23} But in this study we have excluded electrolyte imbalance because hyponatremia and hypernatremia, may cause coma in any person, even in the absence of hepatic disease due to the edema of neurons and the condition may mimic hepatic coma. Souheil found infections responsible in only 3% of cases and Conn reported infections in only 4% cases.^{20,22} In foreign studies infection was found less common than our study (22%) due to better hygienic conditions of the patients and hospitals in the western countries than public sector hospitals in Pakistan.

Most cases of hepatic encephalopathy have identifiable risk factor. Thus the awareness, health education, specific protection from these precipitating factors like use of lactulose, high fibre diet, life style modifications, prophylaxis against upper gastrointestinal bleed, proper follow ups, early diagnosis and control of infections, emergency sclerotherapy or banding, blood banks and proper screening and safe blood transfusions can save lives from hepatic encephalopathy.

Conclusions

Constipation and upper gastro intestinal bleed are the most common factors of Hepatic Encephalopathy in Pakistan. Priority should be given to these factors in terms of hospital funds, blood banks, medicines and human efforts. No stone should be left unturned in providing better and effective infection control measures and better hygienic conditions in government hospitals. The proper disposal of infected hospital waste and especially syringes, blades should be performed. Consistent use of lactulose and fibre, lifestyle modifications like exercise, low fat diet and activity should be encouraged to prevent constipation. Emergency endoscopic facilities should be made available nationwide and especially in big cities including Faisalabad in Public sector hospitals for prompt control of gastrointestinal bleeding. The every effort should be made to control increasing incidence of hepatitis B and C through health education, prevention and immunization.

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