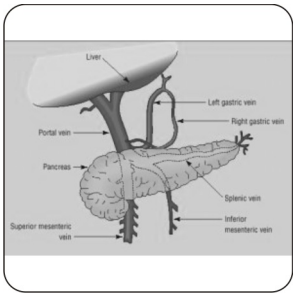
ORIGINAL PROF-1335

HEPATIC ENCEPHALOPATHY;
PRECIPITATING FACTORS IN PATIENTS WITH CIRRHOSIS



COL. DR. MANZAR ZAKARIA
Classified Medical Specialist
Department of Medicine
CMH, Lahore

DR. MUJEEB-UR-REHMAN ABID BUTT
Classified Medical Specialist
Department of Medicine
CMH, Lahore

DR. SYED RIZWAN HUSSAIN
Resident Department of Medicine
CMH, Lahore

Dr. Ghulam Farid Rana
Resident Department of Medicine
CMH, Lahore

ABSTRACT... gujri@hotmail.com **Introduction:** Hepatic encephalopathy is a common complication of cirrhosis. Its development heralds a poor prognosis. Hepatic encephalopathy is often precipitated by an identifiable factor. Prompt diagnosis of precipitating factors is the key to management of this reversible complication of cirrhosis. **Objective:** To determine the frequency of precipitating factors for hepatic encephalopathy in patients diagnosed with cirrhosis. **Study Design:** Descriptive Study. **Place and Duration of study:** The study was carried out at Combined Military Hospital Lahore from 18.6.07 to 18.12.2007. **Patients and methods:** Eighty Consecutive patients, 18 years and above of both genders suffering from hepatic encephalopathy were included in the study. Precipitating factors of hepatic encephalopathy were identified with the help of clinical examination and investigations. **Results:** Majority of patients (63.8%) had one precipitating factor; more than one factor was found in 27.5%. Upper gastrointestinal bleed (56%) and infections (27%) (spontaneous bacterial peritonitis and urinary tract infections) were the leading precipitating factors. Use of diuretics/ electrolyte imbalance and constipation were found in 19% and 7% of patients respectively. No precipitating factor was detected in 9% of patients. **Conclusion:** In majority of patients with hepatic encephalopathy, precipitating factor/ factors could be easily identified.

Key words: Cirrhosis, Hepatic Encephalopathy, Precipitating Factors.

INTRODUCTION

Hepatic encephalopathy is a common complication of cirrhosis[1]. It includes the spectrum of potentially reversible neuropsychiatric abnormalities such as personality changes, intellectual impairment, and a depressed level of consciousness seen in patients with liver dysfunction after exclusion of unrelated neurological and/or metabolic abnormalities[1].

In patients with cirrhosis admitted to hospital hepatic encephalopathy has been reported in 19% to 50% % of patients[2,3,4]. Most manifestations of hepatic encephalopathy are reversible with prompt medical treatment[1].

The diversion of portal blood into the systemic circulation appears to be a prerequisite for the syndrome. Many pathogenetic theories have been postulated. Patients may have altered brain energy metabolism and increased permeability of the blood-brain barrier[5].

Ammonia is fundamental to the pathogenesis of hepatic encephalopathy. Detoxification of ammonium by the astrocytes results in some neuro-chemical alterations. Many factors such as hyponatremia, cytokine elevations, and alterations in the ligands of astrocytes interact with ammonium, causing alterations in the astrocytes, thereby producing an anatomic substrate and neuro-chemical synergism that can increase the development of hepatic encephalopathy. The role of Endogenous benzodiazepines is not well understood. A decrease in branched-chain amino acids can favor the entrance into the brain of aromatic Amino Acids, which are precursors of false neurotransmitters that alter glutamine synthesis. Branched chain amino acids have a direct effect in muscle increasing ammonium detoxification.

In patients with stable cirrhosis, hepatic encephalopathy often follows a clearly identifiable precipitating event. Early recognition of the precipitating factors improves the prognosis and final outcome[6]. The importance of this study is to have a better understanding of causative factors of hepatic encephalopathy in our hospital. This may reduce the mortality and morbidity associated with this grave but treatable condition.

PATIENTS AND METHODS

The study was conducted at Department of Medicine, Combined Military Hospital Lahore. The study was conducted from the 16 June 2007 to 15 December 2007.Eighty consecutive patients of hepatic encephalopathy aged 18 years and above from both genders were included in the study. Patients with Intracranial lesions such as subdural hematoma, cerebral infarction, meningitis, encephalitis, brain abscess were excluded from the study. Patients with hypoxia, hypercarbia, ketoacidosis, uraemia, post seizure encephalopathy and neuropsychiatric disorders were also excluded.Diagnosis of cirrhosis was based on ultrasound abdomen showing increased echogenicity of liver and increased diameter of portal vein.

DATA COLLECTION PROCEDURE

Permission for the conduct of study was obtained from the hospital administration. All the information was filled in a performa containing details of patients.

History of hematemesis, malena, constipation, fever, burning micturition, pain abdomen, diarrhea, jaundice, benzodiazepines and diuretics intake was recorded. Excessive protein intake was assessed. Past history of hepatic encephalopathy, kidney disease, stroke, space occupying lesion of brain, diabetes mellitus, epilepsy and head injury was asked. A detailed physical examination was carried out including record of vital signs and mini-mental state examination. Jaundice, asterixis, edema, ascites, abdominal tenderness and hepatosplenomegaly were looked for. Investigations were requested to aid in the identification of precipitating factors of hepatic encephalopathy. Investigations included complete blood counts, prothrombin time serum ammonia, albumin, urea creatinine, electrolytes, liver function tests , blood sugar and urine microscopic examination. All patients with ascites had their ascitic fluid examination. Ultrasound abdomen was carried out in every case.

Following precipitating factors were identified:-

1. Upper gastrointestinal bleed.
2. Constipation.
3. Drugs specifically diuretics and benzodiazepines.
4. Excess dietary protein intake.
5. Infections including spontaneous bacterial

peritonitis and urinary tract infections.
6. Paracentesis.
7. Electrolyte imbalance like hypokalemia and hyponatremia.
8. Acute hepatitis.
9. Hepatoma.
10. No precipitating factor found.

STATISTICAL ANALYSIS

Data were analyzed using descriptive statistics

RESULTS

Eighty patients were included in this study. Maximum age was 68 years and minimum was 26 years. The mean was 51.2 years. Fifty were males and 30 were females. Majority of patients (63.75%) had one precipitating factor; more than one factor was found in 27.5%. Upper gastrointestinal bleed and constipation were the leading precipitating factors followed by infections , hypokalemia and drugs. Results are tabulated in table I and II. Sixty patients were anti HCV positive; ten were HBsAg positive, while ten were positive for both.

Table-I. Characteristics of patients (n=80)

Age (years)		Sex		Hepatitis serology positivity	
Range	Mean	M (%)	F (%)	HbsAg (%)	HCV (%)
26-68	51.9 ± 8.9	50 (62.5)	30 (37.5)	10 (12.5)	60 (75)
10 (12.5%) patients were positive for both hepatitis B and C serology					

Table-II. Precipitating factors of hepatic encephalopathy

Precipitating factors	No. Of patients	%age of patients
Upper GI Bleed	45	56.3
Infections	22	27.5
Diuretic and Electrolytes Imbalance	20	25
Constipation	5	6.3
Excessive protein intake	1	1.3
Hepatoma	2	2.5
Paracentesis	1	1.3
Acute hepatitis	6	6.3
Benzodiazepines	3	3.8
No factor found	7	8.8
In certain patients, there were multiple factors, so percentages do not add to 100.		

DISCUSSION

Patients of cirrhosis having hepatic encephalopathy at time of admission were selected. Precipitating factors leading to encephalopathy were ascertained. Males out numbered females. This is probably because males are given preference for hospitalization and treatment. Strauss in a similar study reported that male–female ratio was 3:1.14[7]. The male preponderance in west is explained by patterns of alcohol consumption where 77% cases of chronic liver disease are related to alcoholism[8]. Interestingly 75(94%) patients had viral etiology of cirrhosis in this study.

In our study upper GI bleed was the most common precipitant. In contrast Souheil found GI bleed responsible in only 18% of cases, Fallon in another study found GI bleed as a precipitating factor in 33% of cases[9,10]. Our results are however similar to earlier local studies; Sheikh and Hameed found upper GI bleed responsible in 76% and 56% of their cases respectively[11, 12].

Infections were second most common cause of hepatic encephalopathy. Souheil found infections responsible in only 3% of cases[9]. In another study by Conn infections were responsible in only 4% of cases.[13] The high frequency of infections in our study was probably because of unhygienic conditions and poor nutritional status of the patients.

Compared to study done by Alam et al[14] in which diuretics and electrolyte imbalance were found to be a leading precipitating factor it was on third place in our study. Suheil and conn found electrolyte imbalance in 11% and 9% of cases respectively[12,15].

Constipation was the fourth in the list of precipitating factors (7%). Souheil[9] Fallon[10] and Conn[13] reported constipation in 6%, 3% and 3% 0f their cases respectively. In contrast in local literature Sheikh[11], Hameed[12] and Alam[14] found it in 36%, 52% and 32% of their cases respectively. In our study all patients were veterans or their families. They were provided lactulose by the hospital, this probably explains the lower frequency of constipation in our patients.

In 8.75% of patients in this study no precipitating factor was found. Maqsood reported almost similar finding in the study carried out at Pakistan Institute of Medical Sciences Islamabad who found no precipitating factor of hepatic encephalopathy in 10% of cases[15].

In majority of cases hepatic encephalopathy was secondary to a precipitating factor. It is therefore recommended that it should be diagnosed and treated properly. Patients and their families need to be educated about the complications of the cirrhosis in particular hepatic encephalopathy.

The limitations of this study are, it is confined to a single institution, it has small number of patients, and the patients studied are from a specific class that is servicemen, ex-servicemen and their families. Therefore results cannot be generalized.

There is a wide variation in the frequency of various precipitating factors of hepatic encephalopathy in the literature. This is probably explained by how closely the patients are followed up, their education and drug compliance.

CONCLUSION

Most cases of hepatic encephalopathy had an identifiable precipitating factor. Upper GI Bleed, infections, diuretics/electrolyte imbalance and constipation were the most common precipitating factors. Prophylactic use of beta-blockers and nitrates along with prompt control of infection and prevention of constipation by laxatives needs to be given importance. Sedatives and diuretics should be used judiciously. Priority should be given to control of these factors by allocation of hospital funds, medicines and human efforts.

REFERENCES

1. Ferenci P, Lockwood A, Mullen K, Tarter R, Weissenborn K, Blei AT. **Hepatic encephalopathy--definition, nomenclature, diagnosis, and quantification: final report of the working party at the 11th world congresses of Gastroenterology,** vienna, 1998. Hepatology 2002; 35:716-21.

2. Nadeem M, Yousaf MA, Zakaria M, Hussain T, Ali N. **The value of clinical signs in diagnosis of cirrhosis.** Pak J Med Sci 2005; 21: 121-4

3. Marchesini G, Bianchi G, Amodio P, Salerno F, Merli M, Panella C et al. **Factors associated with poor health-related quality of life of patients with cirrhosis.** Gastroenterology 2001; 120:170-8.

4. Wein C, Koch H, Popp B, Oehler G, Schauder P. **Minimal hepatic encephalopathy impairs fitness to drive.** Hepatology 2004; 39:739-45.

5. Haussinger D, Kircheis G, Fischer R. **Hepatic encephalopathy in chronic liver disease: a clinical manifestation of astrocyte swelling and low-grade cerebral edema.** J Hepatol 2000; 32:1035-7.

6. Mehboob F. **Frequency of risk factors for Hepatic encephalopathy in patients of chronic liver disease.**

Ann King Edward Med Coll 2003; 9:29-30.

7. Strauss E, da Costa MF.**The importance of bacterial infections as precipitating factor of chronic hepatic encephalopathy in cirrhosis. Hepatogastroenterology.** 1998; 45:900-4.

8. Mennon KV. **Pathogenesis, diagnosis and treatment of alcoholic liver disease.** Mayo Clin Proc 2001; 76:1021.

9. Abbou-Assi S, Vlaeevi Z. **Hepatic encephalopathy: metabolic consequences of cirrhosis are often reversible.** Postgrad Med J; 1099(2): 52-65.

10. Faloon WW, Evans GL. **Precipitating factors in genesis of hepatic coma.** N Y Stage J Med 1970; 70:2891.

11. Sheikh A, Ahmed SI, Naseemullah M. **Etiology of hepatic encephalopathy and importance of upper gastrointestinal bleeding and infections as precipitating factors.** J Rawalpindi Med Coll 2001; 5:10-2.

12. Hameed A, Masood R, Ilyas S. **Factors precipitating hepatic encephalopathy in cirrhosis liver.** J Post grad Med 2001; 15: 91-7.

13. Conn HO, Leiberlhal MM. **The hepatic coma syndrome and lactulose.**1st edition. Baltimore: Williams and Wilkins; 1980:106.

14. Alam I, Razaullah, Haider I, Hummayun M, Taqween M, Nisar M. **Spectrum of precipitating factors of Hepatic encephalopathy in Liver cirrhosis;** Pakistan J Med Res 2005; 44(2): 96-100.

15. Maqsood S, Saleem A, Iqbal J, Butt J. **Precipitating factors of hepatic encephalopathy: experience at Pakistan institute of medical sciences Islamabad.** Ayub Med Coll2006; 18(4): 57-60.