Incidence of Hepatic Encephalopathy in Cirrhosis of Liver

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ABSTRACT

Introduction: Cirrhosis is diffuse septal fibrosis of the liver, associated with regenerative parenchymal nodules and a disturbed intra hepatic circulation. The most common and important causes are prolonged alcoholic liver disease and chronic hepatitis infection with Hepatitis B and C viruses. The less important causes are autoimmune hepatitis, hemochromatosis, α 1 anti trypsin deficiency, Wilson's disease, Cystic fibrosis, Glycogen storage disease, Galactosemia, Hereditary fructose intolerance. This study aimed at studying the clinical profile and the spectrum of precipitating factors of hepatic encephalopathy in cirrhosis of liver.

Material and methods: The study was a Cross Sectional descriptive study in the Department of Medicine, Down Town Hospital, Guwahati, Assam. 50 known cases of Chronic liver disease with signs and symptoms of hepatic encephalopathy were taken in the study.

Result: In this study cases of cirrhosis of liver who presented with hepatic encephalopathy were studied over a period of 12 months for precipitating factors of hepatic encephalopathy. Maximum number of patients belonged to Child Pugh Class C. Most of the patients in this study were graded under grade III or IV according to West Haven classification of hepatic encephalopathy, followed by grade I and II. 38% of patients had one precipitating factor. The commonest precipitating factors were Upper GI bleeding.

Conclusion: From this study it was concluded that in most of the cases there are different factors which play a key role in precipitating hepatic encephalopathy which is a common phenomenon in patients with cirrhosis of liver.

Keywords: Cirrhosis of liver, Hepatic Encephalopathy, Hepatitis-B and C, Ammonia

INTRODUCTION

Cirrhosis is a condition that is defined histopathologically and has a variety of clinical manifestations and complications, some of which can be life threatening. In the past, it has been thought that cirrhosis was never reversible; however, it has become apparent that when the underlying insult that has caused the cirrhosis has been removed, there can be reversal of fibrosis. This is the most apparent with the successful treatment of chronic Hepatitis C. Reversal of fibrosis is also seen in some patients with haemochromatosis who has been successfully treated and in patients with alcoholic liver disease after discontinuation of alcohol use.[1]

The common causes of cirrhosis worldwide are alcohol abuse and viral hepatitis (B and C). In urban centers in India, alcohol abuse accounts for more than 50% of cases. Hepatitis B accounts for 30% to 70% of cases, with hepatitis C following frequency. About 30% of alcoholics also have markers of hepatitis virus infection; the relative contribution of viral infection and alcohol in such patients is variable.[2]

Regardless of the cause of cirrhosis, the pathological features consist of the development of fibrosis to the point that there is architectural distortion with the formation of the regenerative nodules. This results in a decrease in hepatocellular mass, and thus function, and an alteration of blood flow. The induction of fibrosis occurs with activation of hepatic stellate cells, resulting in the formation of increased amounts of collagen and other components of the extracellular matrix.[1]

Hepatic encephalopathy (HE) is a complex, potentially reversible neuro-psychiatric condition that occurs as a consequence of acute or chronic liver disease. Hepatic encephalopathy may arise spontaneously but more commonly will develop as a result of some precipitating factor in the course of acute or chronic liver disease.[3]

Early identification of precipitating factors is extremely important in diagnosis and treatment of this fatal condition. The clinical course of hepatic encephalopathy can be interrupted in majority of patients by controlling this precipitating factors.[4]

This study aimed at studying the clinical profile and the spectrum of precipitating factors of hepatic encephalopathy in cirrhosis of liver. Early identification of precipitating factors is extremely important in diagnosis and treatment of this fatal condition. The clinical course of hepatic encephalopathy can be interrupted in majority of patients by controlling these precipitating factors. Hence early and accurate diagnosis and proper identification of precipitating factors will help in initiating the appropriate treatment and thereby bringing down the morbidity and mortality.

MATERIAL AND METHOD

The study was a Cross Sectional descriptive study in the Department of Medicine, Down Town Hospital, Guwahati, Assam. 50 known cases of Chronic liver disease with signs and symptoms of hepatic encephalopathy were taken in age group of 18- 60 years irrespective of gender were included randomly in the study. Consent was taken from the patients/ parents/ guardian. A proper history, examination according to written proforma and relevant investigations were carried out.

Inclusion criteria

- All patients of cirrhosis of liver with age 18 to 60 years, irrespective of sex.
- Known case of chronic liver disease with signs and symptoms of hepatic encephalopathy.

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Exclusion criteria

- Patients less than 18 years and more than 60 years of age
- Patients who presented with non cirrhotic portal hypertension, acute fulminant hepatitis, fulminant hepatic failure, hypo and hyperglycemic coma, stroke and uremia
- Refusal to participate in the study

Data collection technique

Primary data: - History and clinical examination. Patients were asked to sign a written informed consent form.

Secondary data: - Systematic reviews and research data.

Tools – Clinical performance.

West Haven criteria for grading of hepatic encephalopathy. Child Pugh score to assess the severity and prognosis of cirrhosis of liver.

Primary Data collection

A hospital based descriptive study was conducted. All patients having age between 18-60yrs having the symptoms and signs of hepatic encephalopathy presenting during the course of hospital stay were evaluated and studied. 50 patients were included in the study according to the above described inclusion and exclusion criteria. Proper Consent was taken and patient identification numbers were given to each patient to protect their identity. Precipitating factors of encephalopathy were recognized on the basis of detailed history (like fever, hematemesis, melena, constipation, diarrhoea, vomiting, diet, trauma, surgery, drugs like diuretics, sedatives, or tranquilizers, NSAID were enquired), clinical examination, routine and relevant investigations according to the study proforma. The hepatic encephalopathy has been graded according to the West Haven classification system. The severity of liver cirrhosis has been assessed through Child Pugh score system in the present study.

The different laboratory tests and methods done in our hospital for this study are:

- Serum Ammonia- Dry Bio-chemistry VITROS Method
- Blood urea- Dry Bio-chemistry VITROS Method
- Serum creatinine- Dry Bio-chemistry VITROS Method
- Serum Sodium- Ion Selective electrode method
- Serum Potassium- Ion Selective electrode method
- Serum bilirubin- Dry Bio-chemistry VITROS Method
- Serum protein- Dry Bio-chemistry VITROS Method
- Serum albumin- Dry Bio-chemistry VITROS Method
- Serum globulin- Dry Bio-chemistry VITROS Method
- ALP (Alkaline phosphatase)- Dry Bio-chemistry VITROS Method
- AST (Aspartate transaminase)- Dry Bio-chemistry VITROS Method
- ALT (Alanine transaminase)- Dry Bio-chemistry VITROS Method
- HBsAg- Electro Chemiluminisence
- HCV- Electro Chemiluminisence

STATISTICAL METHODS

Data has been analyzed using descriptive statistics. Results of continuous measurement were presented on Mean ± SD (Min-Max) and results on categorical measurements were presented in number (%). Data's were presented in charts, table formats, Bar diagram, pie diagram for ease of understanding and interpretation.

RESULTS

A total of 50 admitted patients with cirrhosis of liver suffering from HE were studied for different precipitating factors for 12 months in down town hospital, Guwahati, Assam.

In the present study, out of 50 patients, the age incidence was more in 20 to 40 years of age, followed by 40 to 60 years. There was only one case found to have below the age of 20 years. The minimum age was 18 years and the maximum was 60 years with a mean age of 40.48 ± 11.38 years. It was observed that 43 patients among the 50 studied were males, remaining 7 patients females; of which 27 males and 2 females were in 20 to 40 years of age, 15 males and 5 females were in 41 to 60 years of age and only 1 male patient was found in <20 years of age group. In all age groups a male preponderance was observed more in number than female.

From the present study we have found, out of 50 cases, 8 patients were HBsAg positive, 2 were HCV antibodies positive and the remaining 40 patients were negative for both HBsAg and Anti HCV. Not even a single patient in this study was found to be positive for both Hepatitis B and C.

In this study the patients were grouped according to Child-Pugh Score, the majority of the patients 60 % were found in Class C which showing the advanced stages of the disease followed by 24 % in Class A and the remaining 16 % in Class B.

Among the precipitating factors the most common cause was (Upper GI bleed) 19 cases were Hemetemesis and Melena 15 cases followed by Constipation 17 cases. Electrolyte imbalance (Hyponatremia 12 cases and Hypokalemia 7 cases), Infection in 13 cases, Diuretics 6 cases and Sedatives 3 cases (Drugs). Excess protein intake found in 7 cases while in 3 cases no precipitating factor was found.

Out of the 50 patients when they were graded according to West Haven classification, 18 cases were found in grade IV, 15 cases in grade III, 5 cases in grade II and remaining 12 cases were in grade I HE.

From the above table the mortality cases, patients who presented with Upper GI bleed, Infection and on Diuretics had a higher mortality rate compared to other precipitating factors.

In this study the commonest cause of cirrhosis was found to be Alcoholism, as 38 cases were belonged to this group, of which 31 were male and 7 were female's patients. Viral hepatitis was the second most common cause with 10 cases followed by 2

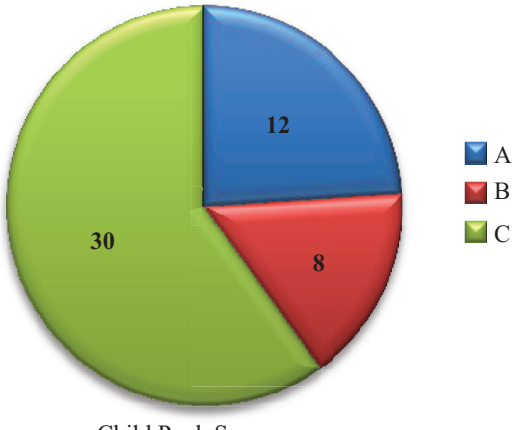

Figure-1: Pie chart showing child pugh score.

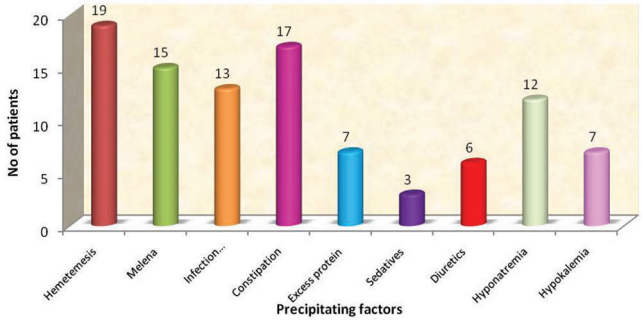

Figure-2: Bar diagram showing precipitating factors of HE

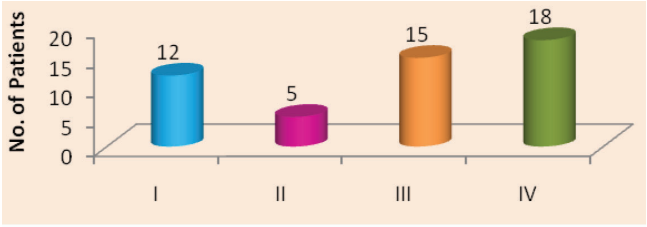

Figure-3: Bar diagram showing West Haven Classification.

patients of which the cause of disease was not known.

In this study we found that the most common presenting symptoms was abdominal distension and altered sensorium (Disorientation, confusion and coma), followed by Hemetemesis, Melena, constipation, fever, vomiting and diarrhea. There was no history of any seizure.

The commonest presenting sign was Pedal edema, followed by Icterus, Asterixis, Ascitis, Pallor, Splenomegaly, Dehydration, fetor hepaticus and clubbing were found in the current study. None of the patients presented with gynaecomastia.

According to Child Pugh score (CPS) the highest mortality rate occurred in Class C, where 11 cases expired out of 30 patients (mortality rate 37%). In Class B out of 8 patients, 1 patient was expired (rate is 13%) and none in Class A in rest of 12 patients.

According to West Haven classification, the highest mortality rate found in grade –IV, followed by grade III. There was no mortality found in grade I and II.

DISCUSSION

Hepatic Encephalopathy has never been less than an unsolved mystery for physicians and researchers around the globe. Since the time of Hippocrates it has been difficult to diagnose and manage any patient of hepatic encephalopathy. Although the exact pathogenic mechanism is yet to be determined, modern research has proved time and again that identifying and removing precipitating factors is still the key step in the overall management.[5] In majority of patients with HE, a clearly definable precipitating factors are identified and reversal or control of these factors is the key step in the management. In the present study 50 patients of cirrhosis of liver presenting with HE, all possible factors which could be responsible for precipitation or aggravation of HE were looked for and analyzed.

In this study the majority of the patients were males, constituting about 86% of cases compared to females 14%, with majority of patients 54% are between the age group of 20-40 years. And on the other hand, the male cases were dominant in our study, while similar findings were observed in a retrospective study of hepatic encephalopathy in Pakistan. Male dominance in progression to advanced stages of chronic liver disease was found in our patients. Al-Gindan[6] also reported the same pattern in a study in Saudi Arabia.

The most common cause of Cirrhosis liver in this study is Alcohol intake 38 (76%) person were alcoholic. This is similar with the studies done by, Faloon[7] and Conn[8], which showed alcohol as the main etiological factor.

In our study, HBV were 16% and HCV 4% being the other leading causes of liver cirrhosis. The etiology of cirrhosis has been hepatitis C virus in majority of the cases in most of the studies done in Pakistan.

Gastrointestinal bleeding was the most common precipitating factor for HE. Khurram[9] and Aisha[10] had also similar types of finding as gastrointestinal bleeding, infection and constipation as the main factors.

The studies done by Sheikh[11] and Hameed[12] the electrolyte imbalance as main precipitating factor followed by infection, G.I. bleed, constipation.

Other causes included electrolyte imbalance (hypokalemia in 14% and hyponatremia in 24%), excess protein intake in 14%, drugs (diuretics in 12% and sedatives in 6%) and infections in 26%. Most of the patients with electrolyte imbalance had history of diarrhea or vomiting or were already on diuretic therapy.

Findings of low hemoglobin, thrombocytopenia and hypo-albuminemia correspond well with advanced stages of cirrhosis.[13] Raised total leukocyte count supports infection[10] as a common precipitant in our settings.

Serum ammonia was raised in 38 (76%) patients. The figure correlates with Sheila Sherlock[14] (serum ammonia is raised in 90% 0f patients with hepatic encephalopathy). Raised urea and creatinine is seen in most of the patients, highlight the fact that azotemia is an important pathogenic contributor to the onset of HE.[15]

Amongst the clinical features, jaundice in 72%, altered conscious state (ranging from confusion to coma) in 68%, asterixis in 66%, and ascitis in 66% were the most common presenting features in this study. Anemia was seen in 60%, splenomegaly in 48%, and pedal edema in78%. Hypo-albuminemia in patients with HE correspond well with advanced stages of liver cirrhosis.

Child Pugh score of patients in this study had 60% in class C, 16% in class B and 24% in class A. Similarly majority of the patients in this study had higher grades of encephalopathy with 36% in grade IV, 30% in grade III, 10% in grade II, while24% had grade I HE**.** The mortality rate of HE is high as shown by the study of Sargent and Fullwood,[16] while in this study the mortality rate was 24%. Patients who did expire were mostly in class C of Child Pugh classification and grade III and IV of HE. The patients who expired were mostly in Class C of CPS. Gastrointestinal bleeding, electrolyte disturbances, infection, constipation were the most common factors of hepatic encephalopathy in this study. For a comparison of the frequency of different precipitating factors in different international studies are given in the following Table.

As shown in the Table Gastrointestinal bleeding, constipation and infections stand out as the most common precipitant of HE in almost all the studies.

Study	GIB	Constipation	Infection	Hypokalemia+	Hyponatremia	Excess dietary protein	Diarrhoea
Faloon WW[7] (n=39)	33%	6%	-	18%	-	-	-
Conn HO[8] (n=100)	18%	3%	4%	9%	-	9%	12%
Souheil Abu Assi[17] (n=100)	18%	3%	3%	11%	-	9%	-
Sheikh S[11] (n=50)	56%	52%	15%	70%	28%	-	22
Ahmed H.[12] (n=50)	56%	52%	28%	68%	28%	52%	22
Khurram[9]	11%	33%	31%	-	33%	-	-
Aisha[10] (n=100)	76%	36%	52%	-	-	-	-
Mahboob[18]	30%	19%	47%	-	-	1%	5%
Alam I[19] (n=50)	24%	32%	22%	18%	24%	-	-
Maqsood S [20] (n=50)	38%	38%	44%	-	-	-	-
Devrajani BR[21] (n=87)	45%	49%	67%	9%	24%	-	-
Tariq H[22] (n=200)	29%	30%	19.5%	4.5%	1.5%	0.5%	3%
Masood N[23] (n=90)	10%	31.1%	27.8%	34%	13.3%	-	-
Afzal S[24] (n=50)	44%	77%	10%	-	-	-	-
Khan AU[25] (n=150)	37.3%	42.7%	12	1.3	-	1.3	-
Gad YZ[26] (n=237)	36.7	13.92	15.61	2.95	2.95	11.39	-
Arisar Q[27] (n=150)	34	11.33	-	-	-	-	-
Present Study (n=50)	68%	34%	26%	24%	14%	14%	8%

Table-1: Studies comparing precipitating factors of HE

CONCLUSION

From this study it was concluded that in most of the cases there are different factors which play a key role in precipitating hepatic encephalopathy which is a common phenomenon in patients with cirrhosis of liver. Upper GI bleed, infections, diuretics, electrolyte imbalance and constipation were the most common precipitating factors. There is a definite need for health education in patients who are diagnosed with cirrhosis of liver regarding the risk of hepatic encephalopathy and its precipitating factors. Prompt control of infections, routine upper GI endoscopy and follow up, prevention of constipation by laxatives, judicial use of sedatives and diuretics and proper advice regarding diet must be an integral part of all counseling protocol to cirrhotic patients. Caution must be exercised in putting cirrhotic patients on diuretics. Early and effective infection control measures and better hygienic conditions in hospitals are needed to be maintained. Consistent use of lactulose and fiber should be encouraged to prevent constipation. More and more endoscopic facilities should be made available nationwide for prompt control of gastrointestinal bleeding. Screening and Prophylactic measures should be strongly committed to control the increase incidence of hepatitis B. The early detection and diagnosis of these precipitating factors helps in starting treatment of this fatal condition hence reducing the mortality.

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