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Original Research Article

Study to assess the changing pattern of clinical profile and determine the prognosis in hepatic encephalopathy

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ABSTRACT

Background: Hepatic encephalopathy (HE) is a common complication of liver disease that requires intensive care management. The prevalence of HE is increasing during recent period. The most important factors of HE are alcohol consumption, chronic hepatitis, hepatotoxic drugs and unhealthy changes in life style. There were only relatively few studies from our region on the changing profile of hepatic encephalopathy under the background of life style changes. This study was conducted with the aim to detect the changing pattern of clinical profile, precipitants and to assess the prognosis of patients with hepatic encephalopathy.
Methods: This was a prospective study for a period of 18 months since January 2012 at Academy of Medical Sciences, Pariyaram, Kannur, a tertiary care centre situated in the northern part of Kerala. Patients admitted in the medical and gastroenterology wards and intensive care units that fulfilled the inclusion criteria were enrolled in this study.
Results: Among the 76 patients with HE, 60 were suffering from CLD and 16 due to acute liver failure. The common etiologies for HE in CLD patients were Alcoholic cirrhosis (63%), Cryptogenic cirrhosis (17%) and cirrhosis due to chronic HBV (10%) and HCV hepatitis (7%) respectively. Among the CLD patients at the start of observation majority were in Child Pugh class B and C. Based on West Haven grading most of them had Grade 2 and 3 HE. Majority with Grade 1, 2 and 3 improved where as those with Grade 4 and Grade 3 in Child Pugh class C worsened. The common precipitants of HE were GI bleed, dyselectrolemia, constipation and infections. Among these precipitants a statistically significant association for a worse outcome was present only with infection. Leptospirosis and deliberate self-harm due to ingestion of hepatotoxic rodenticide and paracetamol were the leading cause of hepatic encephalopathy in acute liver failure
Conclusions: In present study HE was most commonly seen in patients with alcoholic liver disease. Cryptogenic cirrhosis associated with other life style diseases was the second common condition. Among all precipitating factors infection appeared as a statistically significant factor predicting a worse outcome. Health education among alcoholic patients and life style modifications to prevent cryptogenic cirrhosis are of paramount importance in curtailing the increase in incidence of HE in this region.

Keywords: Alcoholic liver disease, Cryptogenic cirrhosis, Hepatic encephalopathy

INTRODUCTION

Hepatic encephalopathy (HE) is a common complication due to acute or chronic liver failure. HE is characterized by personality changes, intellectual impairment and a depressed level of consciousness.[1] The pathogenesis of HE is complex and still unclear and there is no standard diagnostic modality. Subtle signs of HE are observed in

nearly 70% of patients and overt hepatic encephalopathy occurs in about 30-45% of patients with cirrhosis.[2] The common causes of chronic liver disease worldwide are Alcoholic liver disease, chronic hepatitis due to Hepatitis B and C virus infection and cryptogenic cirrhosis. Most episodes of hepatic encephalopathy in patients with CLD are due to some clinically apparent precipitating events and the common precipitants are infections, renal failure, gastrointestinal bleeding, constipation, electrolyte abnormalities, metabolic alkalosis and certain medications.

Epidemiology of liver cirrhosis, the major cause of HE depends particularly on the aetiology and shows a marked geographical difference. There is a recent increase in the incidence of liver disease attributed to many factors like increase in alcohol consumption, chronic hepatitis, hepatotoxic drugs and unhealthy life style changes. There were only relatively few studies from our region on the changing profile of hepatic encephalopathy under the background of life style changes. This study was conducted with the aim to detect the changing pattern of clinical profile, precipitants and to assess the prognosis of patients with hepatic encephalopathy.

Aims of the study

Aims of the study were to study the changing pattern of clinical profile of patients with hepatic encephalopathy and to assess the prognosis of patients admitted with hepatic encephalopathy.

METHODS

This was a prospective observational study for a period of 18 months since January 2012 at Academy of Medical Sciences, Pariyaram, Kerala, India a tertiary care centre situated in the northern part of Kerala, India.

All patients admitted in the Medical and Gastroenterology wards and intensive care units that fulfilled the West Haven criteria of hepatic encephalopathy were enrolled in the study. All patients with primary CNS disease, clinically suspected alcohol withdrawal, pre-existing psychiatric illness and metabolic encephalopathies were excluded. Subclinical hepatic encephalopathies were identified by the Number connection test (Reitan trail making test). The findings of our study were compared with similar published studies and data were analyzed using computer software SPSS 13.

RESULTS

A total of seventy six patients who fulfilled the criteria of hepatic encephalopathy were included in this study and among them sixty patients were suffering from chronic liver disease and sixteen due to acute liver failure.

The age of patients with CLD ranges from 29 to 80 years with a mean age of 51.25 years with a SD of 9.42 years. Majority of them belonged to the age group of 46- 65 years (n= 42, 70%) followed by 26-45 (n=13, 21.7%) age group and (n=5, 8.3%) in the 66-85 age group. Among these patients with CLD, 76.66% were male and 23.33% were female. The causes for CLD were alcoholic liver disease with Cirrhosis in 63% (n=38), chronic HBV hepatitis in 10% (n= 6), chronic HCV hepatitis in 7% (n=4), auto immune hepatitis in 3 % (n=2) and cryptogenic cirrhosis in 17% (n=10) (Table 1). In present study the precipitants of HE in patients with CLD were GI bleed in 28 (47%), azotemia in 9 (15%), hypokalemia in 24 (40%), hyponatremia in 25 (42 %), hypoglycemia in 8 (13%), metabolic alkalosis 12 (20%), interventional procedures in 18 (30%), infections in 13 (22%), CNS depressants in 8 (13 %) and constipation in 32 (53.33%) (Table 2).

Table 1: Etiology of CLD in patients with hepatic encephalopathy.

Etiology	Male	Female	Total	Percentage
Alcoholic liver disease	35	3	38	63%
Chronic HBV hepatitis	4	2	6	10%
Cryptogenic cirrhosis	5	5	10	17%
Autoimmune hepatitis	0	2	2	3%
Chronic HCV hepatitis	2	2	4	7%
Total	46	14	60	100

Among the CLD patients according to the Child Pugh Scoring system at the start of observation 2 were in class A and 29 each in class B and C. According to the HE grading system 8 were in grade 1, 29 in grade 2, 17 in grade 3 and 6 in grade 4. At the end of observation all the 2 in class A became grade 0 whereas among the 29 in class B; 12 became grade 0 and 10 became subclinical. Two patients in class B worsened to grade 4 at the end of observation. In class C among the 29 patients 5 became grade 0 and 7 became subclinical and 5 patients worsened to grade 4 at the end of observation (Table 3). 7 patients out of 8 in grade 1 improved, 23 among 29 in grade 2

improved, 13 out of 17 in grades 3 improved and only 2 improved among 6 in grade 4. Outcome of patients with HE based on aetiology showed that 27 among 38 (71%) with alcoholic cirrhosis, 4 among 6 (67%) with HBV, 9 out of 10 ((90%) with cryptogenic cirrhosis, 3 out of 4 (75%) with autoimmune hepatitis and all the 2 with HCV improved.

On statistical analysis of precipitants and outcome in patients with HE, only those with infection as precipitant was noted to have a statistically significant worse outcome (Table 4). Forty five patients had precipitants up to three in number out of which 36 improved (80%) and 9 worsened (20%) where as in the group with 4-6 number of precipitants only 9 improved (60%) and 6 worsened (40%). Sixteen patients were admitted with acute liver failure causing HE, of these 38 % were due to leptospirosis and 31% due to hepatotoxic drug intake (4 following ingestion of yellow phosphorus and one following paracetamol over dosage). Other causes were acute hepatitis A virus infection (19%) and Acute Fatty Liver of Pregnancy (12%). Among these patients three were in grade 1, eight in grade 2, three in grade 3 and two in grade 4. Of these 2 in grade 1, six in grade 2 and two in grade 3 improved. All the two patients in grade 4 worsened. Among the patients with hepatic encephalopathy due to leptospirosis and yellow phosphorous fifty percent of patients recovered.

Table 2: Precipitants of hepatic encephalopathy in CLD.

Precipitant	Frequency	Percentage
GI Bleed	28	47%
Azotemia	9	15 %
Hypokalemia	24	40%
Alkalosis	12	20%
Hyponatremia	25	42%
Hypoglycaemia	8	13%
Infections	13	22%
Interventions	18	30%
Constipation	32	53%
CNS Depressants	8	13%

Table 3: Hepatic encephalopathy grade of CLD patients at the end of observation.

CPG	Hepatic encephalopathy grade at end point						Total
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Sub clinical	
A	2	0	0	0	0	0	2
B	12	2	1	0	4	10	29
C	5	3	2	3	9	7	29
Total	19	5	3	3	13	17	60

Table 4: Precipitants of hepatic encephalopathy and outcome.

Precipitants at the start of observation	Total patients (N=60)	Improved (N=45)	Worsened (N=15)	Chi square test statistic	P value
GI bleed	28	20	8	0.357	0.550
Azotemia	9	7	2	0.044	0.835
Hypokalemia	24	20	4	1.481	0.224
Hyponatremia	25	16	9	2.766	0.096
Hypoglycaemia	8	7	1	0.769	0.380
Interventional procedures	18	13	5	0.106	0.745
Infection	13	7	6	3.961	0.047
CNS depressants	8	5	3	0.769	0.380
Constipation	32	23	9	0.357	0.550

DISCUSSION

In this study a total of seventy six patients were admitted with hepatic encephalopathy and among them sixty patients were suffering from chronic liver disease and sixteen due to acute liver failure. Among the patients admitted with acute liver failure causing HE, leptospirosis was the most common cause and hepatotoxic drug intake following ingestion of yellow phosphorus and paracetamol were the next common cause. Other causes were Acute Hepatitis due to HAV and Acute Fatty Liver of Pregnancy. Among the 60 patients with CLD, mean age of patients were 51.25 years with a SD of 9.42 and majority were male with a M: F ratio of 3.34:1. Patients in the age group of 46-65 were affected the most. Alcoholic liver disease with cirrhosis was the most common cause and cryptogenic cirrhosis the second most common condition.

Cirrhosis due to chronic HBV hepatitis, chronic HCV hepatitis and autoimmune hepatitis were the other causes of chronic liver disease causing hepatic encephalopathy. Pattern of alcohol intake around the world is constantly changing and have a strong bearing on the prevalence and incidence of cirrhosis due to alcohol. According to the Global Status report on alcohol and health 2014, released by WHO states that the amount of alcohol consumption has increased significantly in India recently. The per capita consumption of alcohol in the country has increased from 1.6 litres from the period of 2003-2005, to 2.2 litres from the period of 2010-2012 and Kerala lead the states in terms of alcohol consumption.[3] This change might have resulted alcoholic liver disease becoming the leading cause of chronic liver disease in patients with hepatic encephalopathy in our region.

Cryptogenic cirrhosis was the second most common cause of hepatic encephalopathy in present study. The frequency of obesity, diabetes mellitus and dyslipidemia are much higher in patients with cryptogenic cirrhosis.[4] With the growing epidemic of diabetes and obesity due to unhealthy life style changes, the prevalence and impact of NAFLD continues to increase, making NASH potentially a major cause of advanced liver disease. Since there is no specific therapy, prevention of the risk factors of NAFLD such as obesity, insulin resistance, T2DM and dyslipidemia will be the key strategy to reduce the incidence rate of NAFLD.[5]

Hepatitis B Virus related cirrhosis came as the third major cause of hepatic encephalopathy in present study. India represents the second largest pool of chronic HBV infection worldwide with an estimated 40 million infected and with a HBsAg prevalence rate of 2.97% among the rural population and 3.3% in the general population of India.[6-8] Compared to other states, HBsAg prevalence of Kerala is low with 0.5% in the normal population in northern Kerala and 1.5% among voluntary blood donors from South Kerala, India.[9,10] The prevalence of Hepatitis C also in the normal population of northern part of Kerala is only 0.24%, compared to other areas of India this is very low.[9] This low prevalence was evident in our study as cryptogenic cirrhosis causing more people with hepatic encephalopathy than due to HBV and HCV related cirrhosis. As there is no vaccine and no post-exposure prophylaxis for HCV, the focus of primary prevention efforts should be safer blood supply, safe injection practices in health care and other settings, and decreasing the number of people who initiate injection drug abuse.[11]

In the present study the most common precipitants of HE were GI bleed, dyselectrolemia, constipation, interventional procedures and infections. One of the earlier and quotable studies on the incidence of precipitants of hepatic encephalopathy was done by Fessel JM & Conn HO in 100 consecutive patients at West Haven, Connecticut. The most common precipitant in that study was azotemia and next common cause was due to CNS depressant medications. The most severe encephalopathy in that study occurred in association with gastrointestinal bleeding, infection, or azotemia. In our study statistical analysis of the presence of precipitating factors in patients and the outcome of these patients was done in both chronic and acute liver disease. It was found that in patients with HE and chronic liver disease, the presence of infections at the time of diagnosis had a statistically significant association with a worse outcome. Prompt recognition of infections and early treatment with appropriate antibiotics may be needed to improve the outcome. Those with gastrointestinal bleed also were found to have a worse outcome but not statistically significant. Statistical analysis of the number of precipitating factors and duration of stay in hospital was done for both chronic liver disease patients as well as those acute liver failures, with no statistically significant association. Of the total 60 patients with HE and chronic liver disease, none of the precipitating factors was found to have a statistically significant association with the grade of HE at the time of presentation or the duration of hospital stay.

CONCLUSION

In our study hepatic encephalopathy was most commonly observed in patients with cirrhosis due to Alcoholic liver disease. Cryptogenic cirrhosis associated with other life style diseases was the second common condition. The common precipitants like GI bleed, constipation, infections and electrolyte abnormalities were preventable and correctable. Among all the precipitating factors infection appeared as the only statistically significant factor predicting a worse outcome. Health education among alcoholic patients and life style modifications to prevent cryptogenic cirrhosis are of paramount importance in curtailing the increase in incidence of hepatic encephalopathy in this region.

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