ORIGINAL ARTICLE

FACTORS LEADING TO HEPATIC ENCEPHALOPATHY IN PATIENTS WITH LIVER CIRRHOSIS AT A TERTIARY CARE HOSPITAL IN KARACHI, PAKISTAN

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ABSTRACT

Background: To determine the frequency of factors leading to hepatic encephalopathy (HE) in patients with liver cirrhosis at a tertiary care hospital.

Material & Methods: It is a cross-sectional observation study conducted in the Department of Gastroenterology, Agha Khan University Hospital, from November 2009 to November 2012. 177 cirrhotic patients were included in this study via non-probability, purposive sampling. Data was analyzed using SPSS Version 19.

Results: A total of 177 patients were studied with the mean age of 54 $\pm$ 11 (range 20-80) years. Out these 70 (40%) were males & 107 (60%) were females. Hepatitis C (HCV) was responsible for cirrhosis in 126 (71%). Child Turcotte Pugh (CTP) class C was present in 134 (76%), while child B and A were present 41(23%) and 2 (1%) respectively. On presentation, 23(13%) patients had grade 1 HE while 80(45%), 64(36%) and 10(6%) had grades 2, 3 and 4 respectively. The most common precipitant of HE was electrolytes imbalance in 97 (55%), Hyponatremia in 95(46%), infections in 96(54%), spontaneous bacterial peritonitis (SBP) in 45 (25%), urinary tract infection (UTI) in 41(23%), respiratory tract infection (RTI) in 14 (8%), constipation in 70(39%) and gastrointestinal bleed in 12(7%). Eighty nine (50.3%) patients had one precipitant, while two precipitant were noted in 79 (44.6%). 146 (82.5%) patients improved clinically and were discharge while 31 (17.5%) patients died in the hospital. The mortality was almost three times high in those who were in child class C, had a more than one precipitants, hyponatremia and in high grade HE at presentation.

Conclusion: The hyponatremia, infections and constipation were the main precipitants of hepatic encephalopathy while frequency of GI bleed related HE had decrease. Patients had high mortality who had grade III/ IV HE at presentation, child C cirrhosis, hyponatremia, and more than one precipitant. Liver transplant is the ultimate treatment in these patients.

KEY WORDS: Hepatic encephalopathy; Cirrhosis; Precipitating factors; Viral hepatitis.

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INTRODUCTION

Hepatic encephalopathy (HE) defines a frequent neuropsychiatric manifestation of chronic and acute liver disease with disturbances of psychomotor, intellectual, cognitive, emotional/affective, behavioral and fine motor functions of varying severity.[1] HE is divided into two primary components: overt HE (OHE) and minimal HE (MHE).[2] The prevalence of hepatic encephalopathy (HE) is up to 20-80% in the cirrhosis. It has been estimated that OHE is present in 30–45% of patients, with an annual risk of development in 30% of patient with cirrhosis.[3] MHE is manifested by impairment in specialized testing and is considered by most of the clinicians to be a preclinical stage of OHE.[4] Approximately 60–80% of patients with cirrhosis tested have evidence of cognitive dysfunction or MHE.[5] While, prevalence of HE in Pakistan is about 18%.[6] The last two decades have witnessed an explosion in the knowledge of viral hepatitis which continues to be the major global health

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problem affecting millions of people worldwide.[7] Viral hepatitis particularly hepatitis B virus and hepatitis C virus infection causes considerable morbidity and mortality in human population ranging from acute viral hepatitis to chronic hepatitis, liver cirrhosis and hepatocellular carcinoma.[8] With increasing incidence and high prevalence of hepatitis-B and hepatitis C virus, more and more people are being affected by this deadly disease.[9]

According to WHO estimate, liver cirrhosis is responsible for 1.1% of all deaths occurring worldwide.[10] It is also a very common disease in Pakistan[11,12] mostly caused by hepatitis C virus followed by hepatitis B virus or a combination of both.

The exact pathogenesis of HE is not known and multifactor could contribute, but the main factor is the increase level of ammonia that leads to astrocyte swelling and cerebral edema. Many factors, like infections, SBP, constipation, gastrointestinal bleed, electrolyte imbalance, dehydration and drugs (diuretics, sedatives), will precipitate HE. Currently, the main stay of treatment is to treat the precipitating factors.[13]

The aim of this study is to determine the frequent factors leading to hepatic encephalopathy in chronic liver disease patients and to see whether there is any change of pattern of precipitants over last few years. We also want to determine the mortality during hospital and predictors for increase mortality in cirrhotic patients presented with HE.

MATERIAL AND METHODS

It is a cross-sectional study. It was conducted from November 2009 to November 2012 in the Department of Gastroenterology, Aga Khan Hospital, Karachi. Proportion of least precipitating factor was hypoglycemia that is 8%. So P =0.08, margin of error, d = 0.04 with 95% confidence interval so 177 patients will be included in this study via non probability, purposive sampling. Patients who were 18 years and above, of either gender, diagnosed with liver cirrhosis presenting with altered mental state (i.e confusion, drowsiness, increase sleep or coma without any unilateral weakness on clinical examination) were included. Their severity was graded according to West Heaven criteria. Whereas, patients with fulminant hepatic failure (i.e. rapid and massive impairment of liver function leading to encephalopathy without previous known liver disease within 8 weeks of onset of jaundice), any history of stroke and mental retardation and patients with previous history cardiac (heart failure), end stage renal disease, or chronic obstructive air way disease were excluded from this study. Data was analyzed using SPSS Version 19. Patients are stratified on basis of severity of hepatic encephalopathy, age and sex to control confounders.

RESULTS

A total of 177 patients were studied with the mean age of 54 $\pm$ 11 (range 20-80) years. Out these 70 (40%) were males & 107 (60%) were females. Hepatitis C was responsible for cirrhosis in 126 (71.2%), hepatitis B in 19(10.7%), mix viral in 6 (3.4%) and 26 (14.7%), others like alcohol, cryptogenic. (Fig. 1)

According to Child Turcotte Pugh (CTP), 134 patients were CTP class C, while CTP class B and A were 41 and 2 respectively. With further break up of CTP-C, 77 patients had score between10 12 and 57 had score above 13/15.On presentation based on West Haven criteria 23 (13%) patients were in grade I hepatic encephalopathy, while 80 (45.2%) had grade II, 64 (36.2%) grade III and 10 (5.6%) had grade IV HE.

The most common precipitant was electrolyte imbalance that was present in 97 (54.8%) patients. Out of these, hyponatremia was found in 95(53.7%) while hypokalemia in only 13(7.3%) patients presented with HE. The next most frequent factor responsible for HE precipitation was infection in 96 (54.2%). In the infection the most common infection was SBP in 45 (25.4%) followed by urinary tract infection (UTI) and respiratory tract infection in 41 (23.2%) and 14 (7.9%) patients respectively. Constipation was identified in 70 (39.5%) while gastrointestinal bleed in 12(6.8%) and hypoglycemia in only 2(1.1%) of the patient of HE (Table 1).

According to severity of the hepatic encephalopathy, infection and electrolyte imbalance still the main precipitating factors in all grade of encephalopathy. The infection and electrolyte disturbances were more in patient above 40 years of age as compared to below 40 year.

146 (82.5%) patients improved clinically and discharge home while 31 (17.5%) patients died in the hospital. 29 patients died were in child C, 2 in child class B and none in child class A. in the 31 died patients hyponatremia was seen in 21 while 10 had normal sodium level. Grade III and IV hepatic encephalopathy were present at time of presentation in 25 died patients, grade II in 6 while none in grade I.

Similarly, eighty-nine (50.3%) patients had one precipitant, 79 (44.6%) patients had two and eight (4.5%) had three precipitant factors at the time of presentation. Out of 31 patients who died, 9 (29.1%) had 1 precipitant and 22 (70.9%) had > 2 precipitant factors (p=.003)

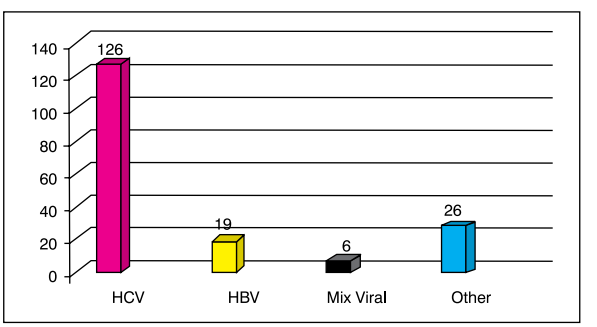

Figure 1 : Etiology of liver cirrhosis in our study

Table 1: Frequency of precipitating factors of hepatic encephalopathy

S. No	Factors	Frequency(n=177)	Percentage (%)
1	Electrolyte imbalance	97	54.8
2	Hyponatremia	95	46.3
3	Hypokalemia	13	7.3
4	Infection	96	54.2
5	Spontaneous bacterial peritonitis	45	25.4
6	Urinary tract infection	41	23.2
7	Respiratory tract infection	14	7.9
8	Constipation	70	39.5
9	Gastrointestinal bleed	12	6.8
10	Hypoglycemia	2	1.1

DISCUSSION

Hepatic encephalopathy is a high mortality complication in patients with decompensated chronic liver disease. Increased cerebral extraction of ammonia in CLD patients is believed to be major pathological factor in patients with hepatic encephalopathy.[14]

In our study mean age of the patients presetting with encephalopathy was calculated to be 54 years. Out of which 70 (40%) were male and 107(60%) were female showing higher prevalence of the complication than in female patients in our setting.

When etiology of hepatic encephalopathy was studied, hepatitis C was found to be the most common etiological factor with prevalence of 71.2%, hepatitis B was found in 10.7%, and mix viral in 3.4% and 14.7% had other factors like alcohol or cryptogenic. Similar result was seen in a research conducted by Mumtaz K et al at AKU hospital Karachi in 2010 where hepatitis was found in 70% of patients with CLD in hepatic encephalopathy[15]. Another study conducted in Hyderabad by Devrajani et al reported 60% patients with hepatitis C when studying precipitating factors of hepatic encephalopathy[16], validating our results and showing high burden of virus in our society leading to hepatic encephalopathy.

Accordingly when patients were classified according to the Child Turcotte Pugh (CTP) score to access the severity of cirrhosis or classification of liver dysfunction, 75.7% were CTP class C, 23.2% were class B and while 2.6% were labeled class A. Further breakup of patients with CTP class C, 77 (57.5%) patients had score between 10-12, and 57 (42.5%) had score between 13-15. Similar results were seen by Mumtaz k et al were CTP class C was seen in 78% patients.[15] Ananya Das et al concluded in their study that overt hepatic encephalopathy was more common in patients with CTP score of more than 6 accounting for 40% of case than more with CTP score on less than 6 accounting for just 5% of cases.[17] Onyekwere CA also reported 61% of patients with CTP class C[18] showing that majority of patients presented in the advanced stage of liver disease.

In accessing severity of encephalopathy that patients presented with 13% were in grade I hepatic encephalopathy, while 80 (45.2%) had grade II, 64 (36.2%) grade III and 10 (5.6%) had grade IV Hepatic encephalopathy. Mumtaz et al also reported similar results with most patients 44% in grade II of hepatic encephalopathy at presentation.[15] While Devrajani et al found their 80% of patients to be in grade IV hepatic encephalopathy at presentation.[16] Maqsood et al in their study conducted in Islamabad had most patients in grade III hepatic encephalopathy when presented, followed by 22% in grade II hepatic encephalopathy.[19]

When most common precipitant factors of hepatic encephalopathy were studied, infection was the most common factor seen in 54.2% patients constipation was seen in 39.5%, GI bleed in 6.8% and hypoglycemia in 1.1%. Infection due to SBP was most common (25.4%), followed by UTI in 23.2% and respiratory tract infection in 7.9%. Wang QM et al [20] in their study conducted in 2013 also found infection as the most common precipitant factor in hepatic encephalopathy, in these infection respiratory tract infection was most common followed by peritoneal and urinary tract infection. Strauss [21] in their study found SBP as most common infection in precipitating acute HE and urinary tract infection in chronic HE. Mumtaz K at al[15] in their study quoted similar results as in this study, with SBP as most common precipitant in HE in 20.5%, followed by constipation in 18.3% and UTI in 15.3%.[15] Devrajani BR[16] and Maqsood S[19] quoted similar results validating our results in this study.

Mortality of patients studied was found to be 17.5%, out of which 93.5% were in child C. Strauss E found mortality higher in acute HE patients than in chronic HE associated with CTP class C.[21] Onyekwere et al[18] quoted mortality of 48% in patients with hepatic encephalopathy with average stay of patient in hospital of 1 to 7 weeks. Devrajani BR in their study found mortality highest in patients with CTP score

10-15.[16]

CONCLUSION

Hyponatremia, infections and constipation are the main precipitants of hepatic encephalopathy while frequency of GI bleed related HE has decreased may be due to early intervention of GI bleed with antibiotic and gut cleansing agents. There is a definite need for liver transplant in patients with child C cirrhosis with hyponatremia, grade III/IV HE and recurrent episode of HE. Patient and family education is compulsory for early detection of precipitant and prophylactic intervention to prevent HE.

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
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AUTHORS' CONTRIBUTION

Conception and Design:	MSA, HS, AM, SM, ABK, MTU, US
Data collection, analysis & interpretation:	MSA, HS, AM, SM, ABK, MTU, US
Manuscript writing:	MSA, HS, AM, SM, ABK, MTU, US