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Original Article

A REVISIT STUDY OF HEPATIC ENCEPHALOPATHY IN PATIENTS WITH CIRRHOSIS OF LIVER

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ABSTRACT

Objective: To understand the triggering causes and dynamics of Hepatic encephalopathy in cirrhotic liver patients.
Study Design: Prospective Descriptive study
Place And Duration: The study was conducted in a private setup at Karachi from March 2014 to December 2014.
Patients and Method: This study included 90 patients which were reported during the study period at a private setup. Patients presented with other comorbidities were excluded. Informed consent was taken from all patients. Data was collected on a predesigned study proforma. Declaration of Helsinki was followed for ethical purpose. Study data was stored on SPSS 16 and same was used for statistical analysis.
Results: Ninety patients out of 41(45.6%) male and 49(54.4%) females were included in the study. The mean age + SD were 54.74 + 14.26 (range 22 - 80 years) commonest age group affected were between 61-70years (33.3%). Majority of the patients were in stage II hepatic encephalopathy 41 (45.6%), while 22(24.4%) stage IV, 18(20.0%) stage I and9 (10.0%) stage III coma. Anti HCV was positive in 53(58.9%). HBsAg in 08(8.9%) and both Anti HCV + HBsAg were positive in 01(1.11%) of patients. While viral markers were negative in 30(33.3%) of patients.
Conclusion: In most of the patients the precipitating factors for hepatic encephalopathy were improper hygienic measures, related to less privileged social class, unhealthy food, diuretics abuse, various infections and irregular bowel habits.

Keywords: Cirrhosis of liver, hepatic encephalopathy, causative factors.

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INTRODUCTION

Hepatic encephalopathy is a contingency of chaotic central nervous system function which results from inability of hepatic system to cleanse noxious agents of gut origin because of hepatocellular dysfunction and porto systemic shunting. The clinical scale varies from day-night reversal and insignificant intellectual

weakening to coma.[1] Patients with insignificant hepatic encephalopathy have no identifiable clinical symptoms but demonstrates slight cognitive and psychomotor discrepancies and attention deficits on standardized assessments and an amplified frequency of traffic accidents.[1] The phases of explicit encephalopathy are mild confusion, drowsiness, stupor, and coma.

Cirrhosis of a liver is frequently cause of death in our region. The most common etiological factor is viral hepatitis. [2]. Most of patients with cirrhosis of liver face mortality due to hepatic encephalopathy. [3]

It is not safe to label any single factor responsible for hepatic encephalopathy rather a group of events and multifactorial altered mechanism needs to be understood.[4]. One of the most frequent factor found responsible for hepatic encephalopathy is ammonia. Usually, ammonia has been considered as the utmost significant influence in the development of the Hepatic encephalopathy. Ammonia spreads in the systemic circulation via Porto systemic shunting and the failure of the liver to metabolize ammonia.[5] dangerous levels of ammonia have been observed in the basal ganglia and cerebellum of cirrhotic patients with hepatic encephalopathy.[6]

It is understood that this adds to the upsurge incidence of motor dysfunction and the extra pyramidal symptoms shown with hepatic encephalopathy.

It is also presented that a higher number of patients with hepatic encephalopathy, arterial blood samples exhibits larger than previously ammonia levels signifying an imperative part of ammonia addition in the pathogenesis of hepatic encephalopathy.[7]

It is also believed that even if the arterial blood levels of ammonia are not high still there is an increased diffusion to the brain. [8] The issue is always the deficiency of link between the levels of ammonia and the clinical stage of hepatic encephalopathy. Various different neurological changes can be seen in brain on accumulation of higher levels of ammonia. The main neuro-inhibitory neurotransmitter gamma-amino-butyric acid (GABA) is also amplified in the cerebral spinal fluid (CSF) of hepatic encephalopathy patients. GABA receptor complex contained in post-synoptic membranes encompass the major inhibitory set-up within the CNS and plays an essential role at neuronal inhibition in Hepatic encephalopathy.[9] Necessary to the pathogenesis is low grade cerebral edema and astrocyte swelling joined by increased making of reactive oxygen and nitrogen oxide species that cause RNA and protein adaptations and hence they affect brain function.[1]

Characteristics that adds to cerebral edema are ammonia, hyponetremia, cytokines and benzodiazepines, hemorrhage within the intestinal tract might expressively upsurge the quantity of protein in the bowel and precipitate encephalopathy. Additional precipitants comprise constipation, alkalosis, and potassium insufficiency tempted by diuretics, opioids, hypnotics and sedatives: drugs containing ammonium or amino compounds; paracentasis with associated hypovolemia; and protosystemic shunt.

The analysis is grounded principally on acknowledgement of typical symptoms and signs, including asterixis.[1] The role of neuroimaging studies in the identification of hepatic encephalopathy is increasing.[1] Hence it is understood that the several complex factors induces the hepatic encephalopathy rather than a single factor. Although the precise way which is thought to be the main reason of causing hepatic encephalopathy is not yet known, therefore this study was designed to observe the various elements which are involved in this disease.

METHODOLOGY

Setting and Duration of Study: The study was conducted in a private setup at Karachi from March 2014 to December 2014.

Data Collection Tool: A predesigned proforma was used to collection all the study variables.

Data Collection Procedure: After explaining the purpose of study in local language, all patient who gave informed consent were included in this study. All patients went through history and clinical examination with a focus on any previous history of liver diseases, high protein diet, blood in stool, constipation, gastrointestinal hemorrhage, and any drug usage. All patients with hepatic encephalopathy for any other reasons like acute fulminant failure, hyperglycemia, infection, hypoglycemia, stroke or meningitis were excluded from this study. Diagnosis and grading of hepatic encephalopathy was done on clinical grounds.

All baseline investigations were done, in addition patients also underwent ascetic fluid detail report, serum albumin, creatinine and liver function test (LFT). Ultrasonography was used to confirm the size of liver and spleen also portal vein diameter was noted and ascites was checked. Child-Pugh classification was used to evaluate the grade of severity of liver disease.

All patients were given nutritional support along with fluid management and electrolyte balance check. Antibiotic cover was provided along with bowel washing during the hospital stay.

Data Analysis Tool: SPSS version 16 was used for statistical analysis.

RESULTS

Ninety patients out of 41(45.6%) male and 49(54.4%) females were included in the study. The mean age + SD were 54.74 + 14.26(range 22 - 80 years) commonest age group affected were between 61-70years (33.3%) group wise age distribution is given in table. I

Majority of the patients were in stage II hepatic encephalopathy 41 (45.6%), while 22(24.4%) stage IV, 18(20.0%) stage I and 9 (10.0%) stage III coma. Anti HCV

TABLE NO. 1
DEMOGRAPHIC PARAMETERS (N = 90)

	N	Percentage (%)
Gender:		
Male	41	45.6
Female	49	54.4
Age groups (years)		
21 to 30	6	6.7
31 to 40	14	15.6
41 to 50	16	17.8
51 to 60	20	22.2
61 to 70	30	33.3
71 to 80	04	4.4
Grade		
Stage I	18	20.0
Stage II	41	45.6
Stage III	9	10.0
Stage IV	22	24.4
Etiology		
HCV	53	58.9
HBV	08	8.9
HBV + HCV	01	1.11
Unknown	30	33.33

TABLE NO. 2.
BIOCHEMICAL PARAMETERS (N = 90)

	N	Percentage (%)
Ascites:		
Mild	21	23.3
Moderate	59	65.6
Severe	10	11.1
Bilirubin:(mg)		
< 2	37	41.1
2 to 3	6	6.7
> 3	47	52.2
Albumin:(gm)		
> 3.5	15	16.7
2.8 to 3.5	16	17.8
< 2.8	59	65.6
Prothrombine Time:(sec)		
12 to 15	25	27.8
16 to 20	11	12.2
> 20	54	60.0

was positive in 53(58.9%). HBsAg in 08(8.9%) and both Anti HCV + HBsAg were positive in 01(1.11%) of patients. while viral markers were negative in 30(33.3%) of patients shown in table 1.Biochemical parameters of patients were shown in Table 2.

Amongst the precipitating factors Hypokalemia was found to in 34(37.8%), Hyponatremia in 12(13.3%) and Dehydration in 22(24.4%), Hematemasis 9(10.0%), constipation in 28(31.1%) and infection in 27(27.8%). While in 12(13.3%) of patients no precipitating factor was identified shown in chart 1.

Out of 80 patients in whom precipitating factors were found

CHART NO. 1.
PRECIPITATING FACTORS (N = 90)

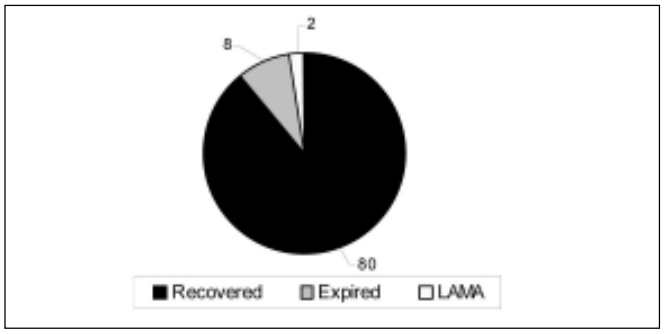


CHART NO. 2.
OUTCOME (N = 90)

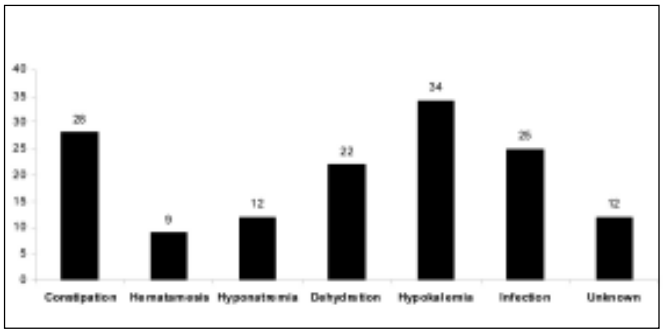


TABLE NO. 3.
SEVERITY OF DISEASE ACCORDING TO CHILD'S CLASS (N = 90)

Child's class	N	Percentage(%)	Numerical score
A	0	0	5 – 6
B	31	34.4	7 – 9
C	59	65.6	10 – 15

70 patients had 2 or more than 2 whereas in 10 patients single precipitating factor was accountable for Hepatic Encephalopathy.

Severity of liver disease was assess according to child's classification .Non of the patient were found in A class, 59(65.6%) in class C, whereas 31(34.4%) in class B shown in Table3

Eighty patients improved from encephalopathy, 8 patients were expired and 2 patients left against Medical advice. Most of the patients improved within 24 hours of therapy and the average duration of stay in hospital was about one week shown in chart 2.

DISCUSSION

Though the exact mechanism implicated in the pathogenesis of hepatic encephalopathy is not known and reports shows 19 to 50% cases of hepatic encephalopathy in cirrhotic patients,[3,10] and its emergence is indicative of poor prognosis.[11] The present study was focused on the assessment of precipitating factors because researches has proved that recognition and treatment of precipitating factor is the key step in the management of hepatic encephalopathy.[12] Slight female dominance 49(54.4%) was observed and most of the patients were between the age of 40-70 years in our study. Whereas male dominance was observed in other studies but commonly affected age group was more than 40 years [13, 14, 15] similar to our study.

Pakistan carries one of the world highest burdens of chronic hepatitis c and mortality due to liver failure.[16] The increasing concern regarding hepatitis c virus becoming an epidemic and an important cause of liver cirrhosis is justified yet again in our study which shows 53(58.9%) Anti HCV positivity in patients, this is supported by other studies done in Pakistan Saad Maqsood shows 62%, Manzar Zikaria 60%and Alam 48%.[13,14,17] In our study the Hepatitis B infection was found in 8%(8.9%) patients. Similarly Saad Maqsood 8%, Mohd Tarique 15%and Manzer Zikaria 12.5%, while Sadique Husain and Intekhab Alam shows 46% and 28% Hepatitis B positive patients in their studies.[13,15,17,18,19] The reason for low percentage is because of increasing knowledge concerning vaccination against Hepatitis B virus. One patient had both B and C. (1.11%) likewise 4% of patients had both B and C positive in Saad Maqsood study.[13] Surprisingly non of the patient give history of alcohol ingestion in our study .In contrast studies done in industrialized nations of the west ,shows alcohol as the main etiological factor.[20]

Majority of patients in our study were from rural areas and belongs to poor socioeconomic group. The negative aspect for the rural population is that the reached tertiary care hospital in late phase .In this study ,the majority of patients were in stage II coma 41(45.6%) while 22(24.4%) stage IV ,18(20.0%) stage I and 9(10.0%) stage III coma. Different studies shows encephalopathy from grade I to grade IV with diverse frequency.[13-18]

In our study Hypokalemia was found in 28(31.1%), Dehydration in 22(24.4%) and Hyponatremia in 12(13.3%) The main reason for this water and electrolyte imbalance was over use of diuretic therapy. Similar studies also support our results.[13,15,16] The commonest single reason in our study found was constipation in 28(31.1%) of patients this may be because of dietary restriction, poverty, lack of use or

inappropriate dosing of lactulose. Infection as a reason for encephalopathy was found in 25(27.8%) patients because of SBP, UTI and RTI.while hematemasis was found in 9((10.0%), On the other hand different studies conducted in different setup and hospital revealed the similar precipitating factors but with dissimilar frequencies. [13, 15, 16, 18,)]

In 10% of patients the precipitating factor for hepatic encephalopathy was not identified, in the same way Saad Maqsood did not find precipitating factor in 10% and Manzar Zakaria in 9% of patients.[13,15] The underlying etiology of hepatic encephalopathy in these patients may be because of use of sedatives, high protein diet and some trace element deficiency like zinc.[21]

Out of 90 patients 80(88.9%) improved from encephalopathy, while 10(11.1%) expired most of them were in grade III and IV coma and class c of child's classification. whereas other study shows high mortality rate of 30 %.[13]

CONCLUSION

Commonest precipitating factors of hepatic encephalopathy in this study were electrolyte imbalance, infection and constipation. To prevent hepatic encephalopathy in cirrhotic patients, counseling concerning the use of diuretic therapy, appropriate use of lactulose and how to prevent infection and judicious use of antibiotic are important. Hygienic condition of home, dietary substance and government hospital needs to be maintained.

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