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PRECIPITATING FACTORS OF HEPATIC ENCEPHALOPATHY IN WITH CIRRHOCIS OF LIVER

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ABSTRACT

OBJECTIVE: *To determine the precipitating factors and outcome of Hepatic encephalopathy in patients of cirrhosis of liver.*
STUDY DESIGN: *Prospective Descriptive study*
PLACE AND DURATION: The study was conducted in the department of Medicine Liaquat University of Medical and Health Sciences Jamshoro / Hyderabad from July 2009 to December 2009.
PATIENTS AND METHOD: *Ninety patients of cirrhosis of liver presented with hepatic encephalopathy were included in the study. Patients presented with hepatic encephalopathy due to fulminate hepatic failure, hyper and hyperglycemic coma, stroke and uremia were excluded from the study. Precipitating factors of encephalopathy were recognized on the basis of history, clinical examination and laboratory investigations. Statistical analysis was done using SPSS version 16.0*
RESULTS: *Out of 90 patients of hepatic encephalopathy Hypokalemia was found to be the commonest precipitating factor 34(37.8%), dehydration 22(24.4%), hyponatremia in 12 (13.3%), constipation in 28(31.1%), Hematemasis 9(10.0%), Infection in 27(27.8%). while in 12(13.3%) patients precipitating factor was not identified. 41(45.6%) patients were found in grade II encephalopathy with 61-70 years age group patients 30(33.3%) were more affected than younger age group. Whereas viral infection was the commonest etiological factor of cirrhosis of liver, anti HCV was found in 53(58.9%), hepatitis B 8(8.9%) while hepatitis B and HCV both positive in one patient (1.11%).*
CONCLUSION: *In most of the patients the precipitating factors for hepatic encephalopathy were electrolyte imbalance, dehydration, constipation and infection because of over use of diuretic therapy, dietary restrictions, poverty and poor hygienic measures.*

KEYWORDS: Hepatic encephalopathy, precipitating factors, cirrhosis of liver.

INTRODUCTION:
Hepatic encephalopathy is a state of disordered central nervous system function resulting from failure of the liver to detoxify noxious agents of gut origin because of hepatocellular dysfunction and porto systemic shunting. The clinical scale ranges from day-night reversal and mild intellectual impairment to coma.(1) Patients with minimal hepatic encephalopathy have no recognizable clinical symptoms but show mild cognitive and psychomotor deficits and attention deficits on standardized tests and an increased rate of traffic accidents.(1) The stages of overt encephalopathy are: (1) mild confusion (2) drowsiness (3) stupor, and (4) coma.
In our part of the world cirrhosis of liver is a common cause of mortality and the viral hepatitis is a common etiological factor, hepatitis C (28%) and hepatitis B (22%)(2) .Hepatic encephalopathy lead to death in 30% of cirrhotic patients.(3)
Hepatic encephalopathy has not been ascribed to any one toxic substance or altered mechanism but is considered to result from the collective effect of several factors.(4) Traditionally, ammonia has been regarded as the most important factor in the progress of the Hepatic encephalopathy. Ammonia reaches the systemic circulation via Porto systemic shunting and the failure of the liver to metabolize ammonia.(5) extreme levels of ammonia have can be seen in the basal ganglia and cerebellum of cirrhotic patients with H.E.(6) It is believed that this contributes to the increase occurrence of motor dysfunction and the extra pyramidal symptoms exhibited with hepatic encephalopathy.

It is reported that 60-80% of patients with hepatic encephalopathy, arterial blood samples show greater than before ammonia levels suggesting an important role of ammonia accretion in the pathogenesis of hepatic encephalopathy.[7] Even more believable, although arterial blood levels of ammonia are not generally high there is an augmented diffusion of ammonia into the brain.[8] The problem has always been the lack of association between the levels of ammonia and the clinical stage of hepatic encephalopathy. When high levels of ammonia are reached in the brain numerous neurochemical changes have been observed. The principal neuro-inhibitory neurotransmitter gamma-amino-butyric acid (GABA) is also increased in the cerebral spinal fluid (CSF) of patients with encephalopathy. GABA receptor complex localized in post-synoptic membranes comprise the major inhibitory set-up within the CNS and has been a key provider at neuronal inhibition in Hepatic encephalopathy.[9] Central to the pathogenesis is low grade cerebral edema and astrocyte swelling accompanied by augmented production of reactive oxygen and nitrogen oxide species that trigger RNA and protein modifications and there by affect brain function.[1] Factor that contributes to cerebral edema are ammonia, hyponetremia, cytokines and benzodiazepines, bleeding in to the intestinal tract may significantly increase the amount of protein in the bowel and precipitate encephalopathy. Other precipitants include constipation, alkalosis, and potassium deficiency induced by diuretics, opioids, hypnotics and sedatives: medications containing ammonium or amino compounds; paracentasis with attendant hypovolemia; and protosystemic shunt (including tips). The diagnosis is based primarily on recognition of characteristic symptoms and signs, including asterixis.[1] The role of neuroimaging studies (e.g. cerebral position emission tomography, magnetic resonance spectroscopy) in the diagnosis of hepatic encephalopathy is growing.[1] Thus, the pathophysiology of Hepatic encephalopathy is a result of several complex factor rather than a single mechanism.

Even though the exact mechanism involved in the pathogenesis of hepatic encephalopathy is not known, the present study was done to observe precipitating factors which are avoidable and treatable.

METHODOLOGY:

This prospective descriptive study was conducted from July 2009 to December 2009 in the Department of Medicine at Liaquat

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

University of Medical and Health Sciences Jamshoro. A written informed consent was obtained from all patients with history of hepatic encephalopathy in cirrhosis of liver. Data was collected in a preformed questioner based on inclusion criteria. A detailed clinical history and physical examination of each patient was done. Evaluation of the mental status was performed using West Haven scale. Especial enquiry was done concerning the past history of hepatic encephalopathy, gastrointestinal bleeding including hematemasis and melena, constipation, fever, high protein diet, paracentasis and any h/o trauma or surgery, use of any sedatives, tranquillizers, analgesics and diuretics. Hepatic encephalopathy is a diagnosis of exclusion, therefore Patients suffering from other reasons for encephalopathy like hypertension. Uremia, stroke, meningitis, septicemia, hypo and hyperglycemic coma, acute fulminant hepatic failure etc were excluded from the study. Diagnosis of Hepatic Encephalopathy was made on clinical basis and graded according to clinical criteria.

Laboratory investigations of each patient were done which include liver function test. Full blood count, Anti HCV. HbsAg. Prothormbine time, serum Albumin, serum creatinine, urine DR, Ascetic fluid DR, S. Electrolytes, Blood sugar. While blood ammonia was not done in our patients because of lack of services to test ammonia at liquate university hospital laborite. An abdominal ultrasound was done to look for liver and spleen size, parenchyma echogenicity, portal vein diameter and ascites. The degree of severity of liver disease was assessed using the child-Pugh classification. All patients were managed with good antibiotic cover, bowel washing, and maintanence of fluid and electrolyte balance, nutritional support and were followed for the duration of their stay in hospital and the outcome whether survived or expired.

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

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

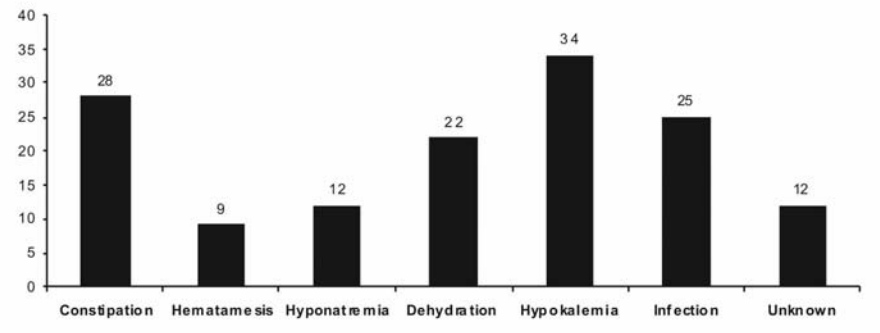
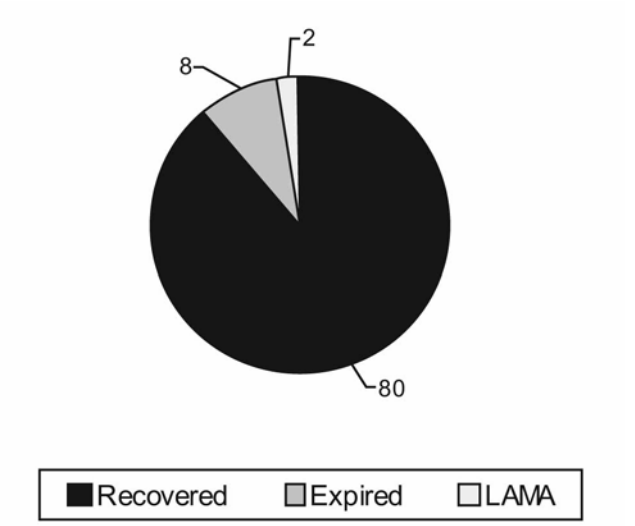


CHART NO. 2.
OUTCOME (N = 90)



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 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 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 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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