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PRECIPITATING FACTORS AND OUTCOME OF HEPATIC ENCEPHALOPATHY IN LIVER CIRRHOSIS – OUR CENTER EXPERIENCE

Gastroenterology

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KEYWORDS

INTRODUCTION:

Hepatic encephalopathy is a spectrum of potentially reversible neuropsychiatric abnormalities seen in patients with liver dysfunction and/or portosystemic shunting. It is defined as a spectrum of neuropsychiatric abnormalities in patients with liver dysfunction, after exclusion of other known causes of brain disease.[1]

Despite of increasing incidence of hepatic encephalopathy , we do not have a clear understanding of its pathogenesis. However, studies from last few years have suggested that there is increase in ammonia concentration is implicated and that there may be a role for inhibitory neurotransmission through gamma-aminobutyric acid (GABA) receptors in the central nervous system and changes in central neurotransmitters and circulating amino acids.

Cognitive findings in patients with hepatic encephalopathy vary from subtle deficits that are not apparent without specialized testing (minimal hepatic encephalopathy), to more overt findings, with impairments in attention, reaction time, and working memory [2]

Hepatic encephalopathy can be categorized based on four factors: the underlying disease, the severity of manifestations, the time course, and whether precipitating factors are present [3,4,5] . Episodes of hepatic encephalopathy can be described as being either nonprecipitated or precipitated. If precipitated, the precipitating factors should be specified.

There are several conditions that may precipitate an episode of hepatic encephalopathy in patients with liver disease or a portal-systemic shunt [2,6,7,8,]

These factors include :Gastrointestinal bleeding, Infection (including spontaneous bacterial peritonitis, pneumonia and urinary tract infections), Hypokalemia and/or metabolic alkalosis, renal failure, Hypovolemia, Hypoxia, sedatives or tranquilizers, hypoglycaemia, constipation, rarely hepatocellular carcinoma and/or vascular occlusion (hepatic vein or portal vein thrombosis)

Patients with hepatic encephalopathy should be evaluated for potential precipitating causes. This evaluation should include: history to determine if the patient has been exposed to any medications or toxins (including alcohol), Physical examination to look for signs of gastrointestinal bleeding or hypovolemia, search for sources of infection with blood and urine cultures, as well as paracentesis for patients with ascites ,routine serum chemistries to look for metabolic and electrolyte abnormalities and serum alpha-fetoprotein.

Depressed cerebral function due to hepatic failure of clearance of gut-derived substances is probably an accepted explanation [9]. However, the exact pathogenic mechanism involved is still unknown.

AIM OF THE STUDY

To determine precipitants of hepatic encephalopathy (HE) and their impact on hospital stay and mortality.

STUDY DESIGN:

Cross-sectional, analytical study.

Place and duration of Study:

Department of Digestive Health and Diseases (DDHD), Kilpauk Medical College, Chennai and Government Royapettah Hospital, Chennai and from January 2018 to April 2018.

MATERIALS AND METHODS:

A total of 104 consecutive patients admitted with different grades of HE were evaluated between January 2018 and April 2018. The precipitants of HE were correlated with the different grades of HE; length of hospital stay and mortality. Chi-square test was used for statistical analysis with significance at $p<0.05$.

A detailed clinical history of each patient was taken from the patient and a close accompanying relative regarding the present complaints and the past illnesses. The history specifically included presence or absence of gastrointestinal bleeding, fever, constipation, high protein diet, recent trauma, surgery, or abdominal paracentesis. Patients were investigated about recent intake of alcohol, sedatives, tranquilizers, analgesics, or cough syrups.

INCLUSION CRITERIA:

All adult patients admitted with diagnosis chronic liver disease with hepatic encephalopathy after applying exclusion criteria.

EXCLUSION CRITERIA:

1 - Patients with intracranial lesions such as subdural hematoma, cerebral hemorrhage, cerebral infarction, brain abscess, meningitis, or encephalitis.
2- Patients with hypoxia, hypercarbia, uremia, ketoacidosis,
3. Fulminant hepatic failure,
4. Neuropsychiatric disorders
5. Post-seizure encephalopathy

The diagnosis of liver cirrhosis was based on clinical, biochemical, ultrasonographic, or liver histological data obtained from the in-hospital patients' data records.

All patients were carefully examined with special stress on the presence of jaundice, spider naevi, parotid enlargement, anemia, ascites, flapping tremors, lower limb edema, and gynecomastia.

Following table was used to grade hepatic encephalopathy: (West Heaven criteria)

Grade	Features
I	Mild lack of awareness, shortened attention span, impaired addition or subtraction, mild asterixis or tremors
II	Lethargic, disoriented, inappropriate behaviour, obvious asterixis and slurred speech
III	Somnolent but arousable, gross disorientation; bizarre behavior,muscular rigidity, clonus and hyperreflexia
IV	Coma, decerebrate posturing

Routine labs were carried out for each patient including liver function tests, renal function tests, complete blood count, serum electrolytes, random blood glucose, urine analysis, and the coagulation profile.

Imaging in form of chest radiography and abdominal ultrasonography, to assess liver, splenic size and echogenicity, and portal vein diameter were performed. A diagnostic tap was performed for ascites, if present. Patients were also categorised using Child- Turcotte Pugh (CTP) scoring criteria:

Parameters	Numerical score			Total Numerical score	CTP score
	1	2	3		
Ascites	None	Slight	Moderate to severe		
Encephalopathy	None	Slight	Moderate to severe		
Sr. Bilirubin (mg/dl)	<2	2-3	>3	5-6	A
Sr. Albumin (g/dl)	>3.5	2.8 -3.5	<2.8	7-9	B
Prothrombin time (sec)	1-3	4-6	>6	10-15	C

RESULTS:

Total 104 patients were evaluated out of which 80 (76.92%) were males and 24 (23.08%) were females. The cause of cirrhosis was predominantly ethanol in 60 patients followed by hepatitis B, hepatitis C and NAFLD (Non Alcoholic Fatty Liver Disease).

Etiology of cirrhosis	Total patients	Males	Females
Ethanol	60	56	4
Hepatitis B	24	16	8
Hepatitis C	10	4	6
NAFLD	10	4	6

Patients were admitted with various grades of encephalopathy. We classified them based on West Heaven criteria. Most of the patients were in Grade II (n= 45) and Grade III (n= 30) encephalopathy.

Grade of HE	No. of patients	Percentage
I	16	17.3
II	45	43.26
III	30	28.84
IV	11	10.57

Among all precipitating factors upper GI bleed was far most common precipitating factor (48%) followed by constipation (25%), Infections (9.6 %) and dyselectrolytemia (3.84 %). About 14.42 % patients had 2 or more precipitating factors. Constipation and UGI bleed were consistent in multiple precipitating factors.

In case of infections as precipitating factors respiratory tract infections were most common (n =6) followed by SBP (Spontaneous Bacterial Peritonitis) and UTI (Urinary Tract Infections). Hyponatremia was the precipitating factors in all 4 patients with dyselectrolytemia.

Following were the precipitating factors for hepatic encephalopathy in the study:

Precipitating factor	No. of patients	Percentage
UGI bleed	50	48
Constipation	25	24
Infection	10	9.6
2 or more factors	15	14.42
dyselectrolytemia	4	3.84

The Mean Hospital stay was 5+/- 2 days in patients with UGI bleed and almost similar length of hospital stay in all patients with single precipitating factor. Patient with multiple precipitating factors had mean hospital stay of 7+/- 3 days.

The Mean Hospital stay of the patients in this study:

Precipitating factor	Hospital stay
UGI bleed	5+/- 2 days
Constipation	5+/- 2 days
Infection	6+/- 1 day
dyselectrolytemia	4+/- 2 days
2 or more factors	7+/- 3 days

Out of 104 patients 100 patients (96.15 %) were discharged. Out of 100 patients 90 patients were discharged without encephalopathy and 10 patients with grade I HE. During the course of hospital stay 4 patients died all those patients were admitted with grade IV encephalopathy and had 2 or more precipitating factors.

Outcome of the patients:

Outcome	No. of patients		
Discharged	100	90 without HE	10 - with Grade I HE
Death	4	-	

DISCUSSION:

Cirrhosis represents a late stage of progressive hepatic fibrosis characterized by distortion of the hepatic architecture and the formation of regenerative nodules. Patients with cirrhosis are susceptible to a variety of complications, and their life expectancy can be markedly reduced. Hepatic encephalopathy describes the spectrum of potentially reversible neuropsychiatric abnormalities seen in patients with liver dysfunction. Disturbance in the diurnal sleep pattern (insomnia and hypersomnia) is a common early feature that typically precedes overt neurologic signs. There are several conditions that may precipitate an episode of hepatic encephalopathy in patients with liver disease or a portal-systemic shunt. In our study, we concentrated on the precipitating factors of HE and their outcomes at our center.

In our study, the study population was consisting of predominantly males as cirrhosis is common in males as compared to females in India. The most common cause of cirrhosis in our patient group was alcohol followed by hepatitis B and C. Less commonly cirrhosis was found to be related to Non Alcoholic Fatty Liver Disease (NAFLD). The grade of encephalopathy with patients were admitted was predominantly grade II and grade III based on West Heaven criteria.

The most common precipitating factor was found to be upper GI bleed in our population. All these patients had clinically detected upper GI bleed in form of Hematemesis of melena. The etiology of UGI bleed was due to esophageal varices. All those patients with bleeding esophageal varices were treated with either Endoscopic Variceal Ligation (EVL) or sclerotherapy using 1.5 % Polidoconal. Constipation was second most common precipitating factor in our study group. Infections including respiratory tract infections, Urinary Tract Infections (UTI) and Spontaneous Bacterial Peritonitis (SBP) were third most common precipitating factors. All those patients were treated for 5 to 7 days of IV antibiotics as per guidelines. Hyponatremia was found to have precipitating factor in few cases and it was treated with Na+ supplements and regular serum electrolyte monitoring. We found out that almost 15 % patients had two or more precipitating factors including UGI bleed and constipation or one of the either in addition to other precipitating factors.

The overall hospital stay was 5+/- 2 days for all patients with single precipitating factors. In case of 2 or more precipitating factors the mean hospital stay was 7=/- 3 days. So, overall patients with 2 or more precipitating factors had longer mean hospital stay.

We discharged 100 patients out of 104 patients. Total of 90 patients were discharged without signs and symptoms of hepatic encephalopathy and 10 patients were discharged with grade I HE. Total 4 patients were died during the hospital stay and all were admitted with grade IV HE. Total 3 out of 4 patients had 2 or more precipitating factors and 1 patient had UGI bleed as precipitating factor.

CONCLUSION:

From our study it was concluded that there are different factors which play a key role in precipitating hepatic encephalopathy. Patients presenting with 2 or more precipitating factors and advanced grade of HE had a prolonged hospital stay and increased mortality rate. Upper GI bleeding was the most common precipitating factor at our center.

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