Evaluation and Clinical Profile of Hepatic Encephalopathy in Liver Cirrhosis Patients at Tertiary Care Center

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Abstract

Problem: A poor prognosis is linked to cirrhosis's prevalent consequence, hepatic encephalopathy (HE). This research intends to examine the clinical profile for worse outcomes in patients with hepatic encephalopathy caused by liver cirrhosis. **Approach:** With 110 patients as the study group, this cohort study were conducted over the course of two years. An ultrasonography of the liver verified the presence of cirrhosis. **Findings:** 110 patients with HE related to hepatic cirrhosis were included in the study; 81.8% of the patients were men, and 41.8% and 46.3% of the patients, respectively, met grade 2 and grade 3 of the West Haven criteria. Almost 65 to 67% of patients had asterexis, ascites, or icterus.65% of population had alcohol dependence. In our study, the most common form of treatment for 75.89% of patients was lactulose. **Conclusion;** The majority of the patients had grade III HE, the most common cause of cirrhosis was alcohol, the most common symptom of liver cell failure was icterus, and the most frequently prescribed medication was lactulose.

Keywords: alcohol, chronic liver, cirrhosis, hepatic encephalopathy, lactulose

Introduction: Hepatic encephalopathy (HE) describes a wide range of neuropsychiatric abnormalities which are the result ofhepatic insufficiency or portosystemic shunting. HE can bebroadly classified into overt HE (in which neurologic and neuropsychiatric abnormalities are detected using bedsideexaminations and bedside tests) or minimal HE (where mentalstatus is normal and neurologic examination is normal inconjunction with abnormalities on psychometric testing).[1,2]

Overt HE will occur in 30%–40% of patients suffering from cirrhosis of liver, and incidence rate of HE is ashigh as 30%–50% in patients who undergo transjugularintrahepatic portosystemic shunting (TIPS), whereas 60%of patients suffering from cirrhosis are likely to develop minimal HE. Very poor prognosis and reduced survivalare the two basic outcomes after the onset of HE in patientsof cirrhosis of liver.Although some of the precise details about the cause of HEremains unknown, a general consensus has been achievedregarding raised levels of ammonia and its central role inthe disease by acting as a neurotoxin that results in astrocyte swelling.[3-5]

Cirrhosis and chronic liver disease were found to be the10th leading cause of death for men and the 12th for women in theUnited States in 2001, killing about 27,000 people each year. In India, in patients with cirrhosis, HE is often considered an indicator of poor prognosis, with 1- and 3-year survival afterits first occurrence being 42% and 23%, respectively, in theabsence of liver transplantation. Furthermore, the cost ofcirrhosis in terms of human suffering, hospital costs, and lostproductivity are very high. [1]

Alcohol consumption is the primary contributing factor to chronic liver disease in western nations, which is a serious global health issue. Hepatitis B is more common than 10% throughout the Asia-Pacific area, although the prevalence of chronic hepatitis C varies from 4 to 12% in the same region.[1,2]

A variety of neuropsychiatric anomalies that develop as a result of liver failure are referred to as hepatic encephalopathy. The earliest recorded paper on HE was written in the seventeenth century by Giovanni Battista Morgagni. The instance of a man with liver cirrhosis who went into a coma, died, and whose thorough brain examination revealed no abnormalities was described in Morgagni's book of medicine .[3]

There have been numerous theories put forth and battles fought to determine the precise pathophysiology of H.E. It is discovered that an essential component of the illness is the diversion of portal blood into the systemic circulation through Porto systemic collateral arteries. It occurs along with portal-systemic shunting of venous blood, which can be caused by cirrhosis, non-cirrhotic portal hypertension, or can be surgically induced by porto-caval anastomosis or trans-jugular intra-hepatic porto-systemic shunt (TIPS), both of which are intended to treat portal hypertension.[4]

60% of people with cirrhosis are likely to develop mild HE, but 30%–40% of patients with liver cirrhosis will experience overt HE. The incidence rate of HE is as high as 30%–50% in patients who undergo transjugular intrahepatic portosystemic shunting (TIPS). [5,6] After the development of HE in individuals with liver cirrhosis, the two main consequences are a very poor prognosis and shortened survival.

In India, HE is frequently seen as a sign of poor prognosis in cirrhotic patients, with 1 and 3 year survival rates after its initial incidence being 42% and 23%, respectively, in the absence of liver transplantation. [7] In addition, the cost of cirrhosis is very significant in terms of human misery, medical expenses, and lost productivity.

Hence the aim of the current research is to find out the clinical profile & risk factors for adverse outcome in patients of HE due to cirrhosis of liver.

Material & methods: The study included all cirrhotic liver patients who had been admitted to the hospital. This study has a cohort design. Two years were spent doing the study. The study's inclusion criteria were Patients showing any one signs of HE such as:

- Slowing down or sluggish movement
- Drowsiness or severe confusion
- Strange conduct or drastic personality changes

• Flapping tremors or strange movements
• Coma: unresponsive and unconscious.

Patients with acute fulminant hepatitis, noncirrhotic portal hypertension/TIPS, surgical portosystemic shunts, central nervous system manifestations (such as prior cerebrovascular event and dementia), or intake of toxins (such as benzodiazepines) that would make the neurological examination challenging were excluded from the study, as were patients with terminal illnesses (e.g., advanced hepatocarcinoma).

Data collection on name, age, sex, hospital registration number, address, and occupation was done using a standardised questionnaire. Patients were evaluated according to the West Haven criteria, they were also checked for signs of liver cell failure, and they underwent laboratory investigations including liver and kidney function tests, coagulation profile, and serum ammonia before receiving treatment. The detailed history of patients' alcohol intoxication was assessed by CAGE scoring. Hepatitis B and C examination was also performed.

Grading for HE was done as follows:

West Haven criteria These criteria are based on severity:[8]

- Grade 0: Normal
- Grade I: Mild impairment: sleep alterations, subtly impaired intellectual function, heightened irritability, metabolic tremor, and impaired muscular coordination
- Grade II: Moderate impairment: lethargy, grossly impaired intellectual function, disorientation to time, inappropriate or bizarre behavior, slurred speech, hypoactive reflexes, and ataxia
- Grade III: Severe impairment: somnolence, confusion, disorientation, paranoia or anger, clonus
- Grade IV: Coma: unconsciousness and dilated pupils

Statistical analysis: Data was collected and subjected to statistical analysis using SPSS software version 24. Chi square test was used to find the significant association with level of significance set at <0.05.

Results: The study population's initial characteristics are shown in Table 1. In our analysis of 110 patients, the mean age of those with cirrhosis was 44.55 years; there were 20 female patients and 90 male patients.

Of the 110 patients, 72 individuals provided a positive alcohol consumption history, while 38 patients provided no such information.

When the serum ammonia levels of all 110 patients were examined, a mean value of 118.73 was discovered, with values ranging from 60 to 411.

Of the 110 participants, 10 were determined to be in Grade I of the West Haven criteria for HE at admission, 46 patients were found to be in Grade II, 51 patients were under Grade III of the criteria, while just three patients were found to be under Grade IV.

Table 1 Basic characteristics of study population		
Variable		Number of subjects N, (%)
Mean age (years), mean±SD (range)		44.55±12.05,(16-84)
Gender	Male	90 (81.8)
	Female	20 (18.1)
History of alcohol	Yes	72 (65.4)
	No	38 (34.5)
Clinical investigations (serum ammonia), mean±SD (range)		118.73±66.46 (60-411)
HE Grading	Grade I	10 (9.0)
	Grade II	46 (41.8)
	Grade III	51 (46.3)
	Grade IV	3 (2.7)
Etiology	Constipation	61 (55.45)
	Diuretics Induced Dyselectrloemia	28 (25.45)
	Unknown	21 (19.09)

In Table 2, according to our study in population of 110 patients,67.43% of persons had icterus, 65.26% of persons had ascites,66.48% of persons had asterixis, ecchymotic patches were present in 42.45% of persons, fetor hepaticus was present in40.67% of patients, gynecomastia was present in 36.81% of patients, male pattern baldness was present in 19.87% of patients,s pider naevi were present in 16.79% of patients, Dupuytren'scontracture was present in 7.89% of patients, purpura was presentin 5.89% of patients, testicular atrophy was present in 6.51% of patients and leukonychia was present in 0.81% of patients.

Table 2 Patient distribution based on clinical signs of liver failure	
Clinical signs	N (%)
Icterus	74 (67.43)
Male pattern baldness	22 (19.87)
Fetor hepaticus	45 (40.67)
Spider naevi	18 (16.79)
Gynecomastia	40 (36.81)
Ascites	72 (65.26)
Testicular atrophy	7 (6.51)
Purpura	6 (5.89)
Ecchymotic patches	47 (42.45)
Leukonychia	1 (0.81)
Paper money skim	5 (4.67)
Asterixis	73 (66.48)
Dupuytrens contracture	9 (7.89)

In Table 3, lactulose was used as treatment modality in 83 (75.89%) persons, l-ornithine-l-aspartate was used in 38 (34.48%) patients, cefotaxim was used in 41 (37.13%) persons, mannitol was used in 42 (38.25%) persons, and rifaximin was used for treating 70 (64.20%) patients of HE in the study population.

Table 3: Distribution of subjects according to the treatment protocol

Treatment	Number of subjects (%)
Lactulose	83 (75.89)
l-ornithine-l-aspartate	38 (34.48)
Cefotaxim	41 (37.13)
Mannitol	42 (38.25)
Rifaximin	70 (64.20)

Table 4 shows the distribution of patients according to the etiology of cirrhosis of liver. In our research out of 110 patients, 72 patients were found to be alcoholic which was significantly higher in males (70) than in females (2). Hepatitis B surface antigen status was positive in 8 persons of which 7 were males and 1 was female. According to our study, HCV was found positive in 8subjects. NFLD status was positive in 8 subjects of which six were male persons and two were female. Wilson's disease was found to be positive in two female patient which was significantly higher (P = 0.030) than that in male patients. Sixteen subjects suffered from cryptogenic cirrhosis and were significantly higher in females (13) than in males (3).

Table 4: Distribution of subjects according to etiology of cirrhosis of liver

Etiology	Number of patients (%)	Male (%)	Female (%)	P value
Alcoholic	72 (65.45)	70 (63.6)	2 (1.8)	0.001
HBsAg	8 (7.27)	7 (6.3)	1 (0.9)	0.015
HCV	4 (3.63)	4 (3.6)	-	0.050
NFLD	8 (7.27)	6 (5.4)	2 (1.8)	0.065
Wilsons disease	2 (1.81)	-	2 (1.8)	0.030
Cryptogenic	16 (14.5)	3 (2.7)	13 (11.8)	0.001
Total	110 (100)	90 (81.8)	20 (18.1)	

Table 5 represents the laboratory parameters of all the subjects with cirrhosis of liver. All the important parameters with their mean value are shown.

Table 5: Laboratory parameters of all subjects with cirrhosis of liver

Variable	Minimum	Maximum	Mean ±SD
Total bilirubin	0.56	11.42	3.55 ± 2.11
Conjugated bilirubin	0.13	7.30	1.70 ± 1.67
Unconjugated bilirubin	0.16	5.45	1.96 ± 1.38
Total protein	2.65	7.89	6.50 ± 0.99
Serum albumin	1.21	4.79	2.87 ± 0.78
Serum globulin	1.91	6.89	3.64 ± 0.99
Serum urea	20.01	167.20	40.68 ± 33.41
Serum creatinine	0.56	8.67	1.27 ± 1.07
Serum potassium	2.21	6.54	4.11 ± 0.68
Serum sodium	124.03	153.90	138.23 ±5.01
INR	1.03	4.30	1.55 ±0.40
Prothrombin time	11.32	41.20	19.71 ±6.20
aPTT	29.11	70.32	28.39 ±8.01
Serum Ammonia	50.04	413.05	117.83 ±68.45

Discussion: Hepatic encephalopathy has never been less than anunsolved mystery for physicians and researchers around the globe. Since the time of Hippocrates, it has been difficult to diagnose and manage any patient of hepaticencephalopathy. In majority of patients with hepaticencephalopathy, clearly definable precipitating factors are identified and reversal or control of these factors is the key step in the management. The present research was conducted to determine the clinical profile of a patient suffering with HE in cirrhosis of liver. The factors studied were signs of liver cell failure, etiology of cirrhosis, and treatment used among these subjects.

The mean age of the subjects in our study was 44.55 years, and most of them were male, i. e., 81.8% of total patients and 41.8% and 46.3% of patients were in Grade 2 and Grade 3 of the West Haven criteria of HE, respectively. The mean age of patients with HE was 49.9 ± 18.9 years old in a research done by Kowo PM et al [9] . The relatively young age of these patients could be explained by the etiology of cirrhosis. Indeed, the most common cause of cirrhosis in chronic HBV infection, which affects mostly young people [10]Cirrhosis in Nepal by Poudyal et al., 78% of patients included were male [11]. In another study by Gad et al. in Egypt 63.3% of patients with HE in liver cirrhosis were male [12]. This could be as the result of men being more exposed to various risk factors of cirrhosis.

In 65% of patients, liver cirrhosis was linked to alcohol dependence. Icterus, ascites, and asterixis were the three most prevalent symptoms of liver cell failure in the population of the

current study, each present in over 65% of patients, followed by ecchymotic patches, fetor hepaticus, and gynecomastia. When compared to research conducted in other nations, it is evident that alcoholism is the main factor contributing to liver cirrhosis. As a result, raising public awareness about alcohol abstinence can have a substantial impact on how cirrhosis develops in the context of our study. Drinking is the primary cause of liver cirrhosis in the Western world, where there is a clear male majority to the extent of 77:33, making it the fourth-most common cause of death for men in the USA.[13,14]

In our research, 75.89% of patients received lactulose as a form of treatment, while 64.20% of patients received rifaximin, the second-most often prescribed medication for the management of HE.Lactulose is the most often prescribed medication for individuals with chronic liver disease, according to a study by QaziArisar et al. [15] conducted at Aga Khan university.

NFLD, which was present in 7.27% of patients and was the second-most frequent cause of cirrhosis of the liver in our patients, alcohol was found to be first present in 65.45% of the 110 patients investigated in our study. Nearly 14.5% of patients had conditions for which there was no known cause or which could not be identified. In patients with alcoholic liver cirrhosis, men predominated, whereas women predominated in the group where the diagnosis could not be made and the aetiology of the cirrhosis of the liver was still unknown (cryptogenic).Contrary to our studythe predominance of hepatitis B as the etiology of cirrhosis was explained by Kowo PM et al [9] explained by the high prevalence of HBV in the subjects. Chronic HCV was found in 22.6% of patients. The high prevalence of HCV reported by several studies in the Cameroonian population might explained this finding [10,16].

The aforementioned findings make it abundantly evident that over two thirds of the patients had coagulopathy; additionally, more than half of the study group has hyperammonemia, hypoalbuminemia, and hyperbilirubinemia. Numerous haematological, vascular, and other abnormalities that are present in cirrhotic individuals make them more likely to suffer from morbidity and mortality. The majority of these patients also had extended PT and low serum albumin levels. The findings of our study were consistent with those of Maqsood et al. [17], who found that 86% of the patients had hypoalbuminemia and 44% of the patients had liver cirrhosis. Prolonged PT is a relatively late manifestation of liver disease and clearly indicates the progression of liver cirrhosis in our subjects by the time of their presentation in the hospital.

There were several limitations to our study firstly we did not perform a brain CT scan to rule out primary neurological disease in this investigation due to the high cost of imaging the patients; nonetheless, the majority of these individuals already had liver disease. Secondly due to a lack of technical requirements and patient and family resistance to the procedure, liver biopsy could not be performed to confirm the histological diagnosis of patients with cirrhosis of the liver and lastly due to the patients' illiterate and careless behaviour during the follow-up period, poor patient follow-up compliance was a significant restriction in our study setting. This is also the same cause for the patients' poor compliance with their medications and regular hospital visits.

Conclusion

Alcohol was discovered to be the primary cause of liver cirrhosis in the current investigation, followed by NFLD. In our investigation, icterus, ascites, asterixis, and ecchymotic patches were the most often observed clinical features. Our research revealed that lactulose and rifaximin are the most often prescribed medications for HE.

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