ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 05 | May - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

CHRONIC LIVER DISEASE AND HEPATIC ENCEPHALOPATHY CLINICAL PROFILE AND OUTCOME.

Medicine

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ABSTRACT

Background: Hepatic encephalopathy (HE) is a serious neuropsychiatric complication of acute and chronic liver diseases. Hepatic encephalopathy (HE) is a common complication due to acute or chronic liver failure. HE is characterized by personality changes, intellectual impairment and a depressed level of consciousness. A study was undertaken for determining the clinical profile and outcomes associated with the chronic liver disease and Hepatic Encephalopathy among the patients visiting the Medicine Department of Tertiary care centre. Early and accurate diagnosis of & proper identification of underlying factors of Hepatic Encephalopathy will help in initiating the appropriate treatment and thereby bringing the morbidity and mortality. **Methods:** Patient admitted under the Department Medicine in tertiary care centre and meeting the inclusion and exclusion criteria were included in the study after obtaining written informed consent from patients/relatives/legal guardians. Demographic details were recorded. Detailed past history and history of present illness were recorded. Personal history, including addictions and details of alcohol intake were recorded. Detailed physical examination was done. Any abnormal findings were noted. Ascites was evaluated by the examination maneuvers and radiological examination. **Results:** All patients in our study were male with mean value of age(years) of study subjects was 43.29 ± 10.77 with median of 42. Alcohol consumption of 97.52% cases was frequent, and 0.83% cases was occasional. 1.65% cases were non-drinkers. Viral hepatitis was present in 1.65% cases only. Grade of hepatic encephalopathy of 64.46% cases was 0, 20.66% cases was 1, 14.05% cases was 2 and 0.83% cases was 3. Child Pugh class of 72.73% cases was C, 26.45% cases was B and 0.83% cases was A. Mean value of Child Pugh score of study subjects was 10.44 ± 1.43 with median of 11. Patients presented with various complaints like abdominal distension, high coloured urine, Yellowish Discolouration of Sclera, pedal oedema, black stools, general weakness, altered sleep cycle, loss of appetite, altered sensorium and hematemesis. Splenomegaly was seen in 65.29% cases. Ultrasound study of abdomen showed that 99.17% cases had liver parenchymal disease, 61.16% cases had splenomegaly, 8.26% cases had hepatomegaly, 2.48% cases had signs of portal hypertension and 0.83% cases had liver cirrhosis. Mean value of serum ammonia levels(/dL) of study subjects was 73.63 ± 41.69 with median of 45. Significant correlation was seen between mortality and grade of Hepatic encephalopathy. **Conclusions:** In our study, majority of patients belong to 3rd and 4th decade of their life with all being male patients. Majority of patients belong to Grade 0 hepatic encephalopathy and Child Pugh class C. Mortality rate in our study was 10.74%. Most common cause of mortality was multi organ failure, secondary to chronic liver disease. Significant association was seen between mortality rate and grade of hepatic encephalopathy. All the patients with Child Pugh class A shows good recovery. Child pugh Class C patients showed poor outcome as compared to Child pugh class A and B. Current treatment strategies are symptomatic therefore better characterization of the disease will assist in developing new management strategies in the future. Early and active management of patients in hepatic encephalopathy can help in reducing morbidity and mortality rate.

KEYWORDS

Hepatic Encephalopathy, Child Pugh Score, Chronic Liver Disease,

INTRODUCTION

Hepatic encephalopathy (HE) is a serious neuropsychiatric complication of acute and chronic liver diseases. Hepatic encephalopathy (HE) is a common complication due to acute or chronic liver failure. HE is characterized by personality changes, intellectual impairment and a depressed level of consciousness. The pathogenesis of HE is complex and still unclear and there is no standard diagnostic modality. Subtle signs of HE are observed in nearly 70% of patients and overt hepatic encephalopathy occurs in about 30-45% of patients with cirrhosis.

Chronic liver disease (CLD) is a progressive deterioration of liver functions for more than six months, which includes synthesis of clotting factors, other proteins, detoxification of harmful products of metabolism, and excretion of bile. CLD is a continuous process of inflammation, destruction, and regeneration of liver parenchyma, which leads to fibrosis and cirrhosis.

The occurrence of organ failure in patients with cirrhosis indicates a dismal prognosis.

It is classified according to the clinical severity into five grades (0-4) ranging from confusion in grade I up to deep coma in grade IV. Other symptoms such as change in sleep pattern, loss of coordination and disorientation also can be found. The pathophysiology of the condition is attributed to increased blood levels of ammonia and other neurotoxins, associated with inflammatory response in form of astrocyte swelling and cerebral edema.

Although controversy about the exact pathogenetic mechanism exists, certain factors like hyper ammonia and increased blood-brain permeability to ammonia, increased brain concentration of manganese and inhibitory neurosteroids (allopregnanolone) have been documented. Based on the underlying hepatic abnormality, encephalopathy is subdivided into three types; type A (associated with acute liver disease), type B (associated with portosystemic bypass and no intrinsic hepatocellular disease), and type C (associated with chronic liver disease).

Implications of the study:

A study will be undertaken for determining the clinical profile and outcomes associated with the chronic liver disease and Hepatic Encephalopathy among the patients visiting the Medicine Department of Tertiary care centre .Early and accurate diagnosis of & proper identification of underlying factors of Hepatic Encephalopathy will help in initiating the appropriate treatment and thereby bringing the morbidity and mortality.

METHODS

Study design:

This is a Hospital based 50% prospective & 50% retrospective, descriptive and observational study.

Study area: Department of Medicine of tertiary care centre.

Study population: Patients admitted under the Department Medicine of tertiary care centre.

Inclusion criteria:

1. Patients with clinical and/or laboratory evidence of liver dysfunction.
2. Patients of either gender aged between 18 and 70 years
3. Patients having laboratory evidence of liver dysfunction (deranged LFTs) and/or radiological evidence of cirrhosis.(deranged liver function is defined as a chronic inflammatory reaction in the liver present on clinical or other grounds (biochemical/serological) without improvement for 6 months or longer.radiological signs of cirrhosis of liver in ultrasound are nodular liver surface, round edge, and hypoechoic nodules in liver parenchyma which represent regenerative nodules of cirrhotic liver

4. Patients with signs of hepatic encephalopathy as:
a. Flapping tremors/abnormal movements
b. Drowsiness or severe confusion
c. Slowed or sluggish movements
d. Coma: unconscious/unresponsive

Exclusion criteria:
1. Patients aged less than 18 years or more than 70 years
2. Patients with primary CNS disease or pre-existing psychiatric illness
3. Patients with other causes of encephalopathy like septic encephalopathy or toxins, etc
4. Patients having underwent surgery like portosystemic shunt, TIPS, etc.
5. Patients with intrinsic renal disease, obstructive jaundice
6. Patients with the history of Hepatocellular carcinoma or other cancers
7. Patients with any disseminated malignancy or HIV/AIDS
8. Pregnant women
9. Cases where relatives/legal guardians refuse to participate in the study.

Sample Size:
The prevalence of HE in India is 59.7% Formula
Where n= sample size
p = prevalence of HE = 59.7% q = 100-p = 40.3%
l = Allowable error (15% of p)
Thus, minimum sample size required is 121
Rounding off the sample size for convenient purpose and taking it as 121. Out of 121 sample size 60 sample will be included as prospective and 61 sample will included as retrospective cases.

Sampling Technique: Simple random technique (may be changed to consecutive sampling)

Methodology:
Patient admitted under the Department Medicine in tertiary care centre and meeting the inclusion and exclusion criteria will be included in the study after obtaining written informed consent from patients/ relatives/ legal guardians.

Demographic details will be recorded. Detailed past history and history of present illness will be recorded. Personal history, including addictions and details of alcohol intake will be recorded. Detailed physical examination will be done. Any abnormal findings will be noted. Ascites will be evaluated by the examination maneuvers (shifting dullness will indicate more than 1000 ml of ascitic fluid, horseshoe dullness will indicate atleast 500 ml of ascitic fluid, fluid thrill will indicate massive ascites) and radiological examination (USG abdomen for detection of less than 500 ml of free fluid). Other specific signs of liver failure such as gynecomastia, testicular atrophy, asterixis, icterus, purpura, spider naevi, etc will be noted.

HE: It is defined as a range of neuropsychiatric manifestations in patients with hepatic dysfunction, after exclusion of neurological cause.

AIMS AND OBJECTIVES
To study the clinical Profile and Outcomes of Chronic liver disease and Hepatic Encephalopathy among the patients admitted in the Medicine Department of tertiary care centre.

OBJECTIVES-
1. To identify various liver diseases and other co-morbid conditions associated with Hepatic Encephalopathy (HE)
2. To identify various precipitating factors related to HE
3. To identify various presenting manifestation of HE
4. To know survival of hospitalized HE patients & its correlation with severity of cirrhosis and HE.

Inclusion Criteria:
5. Patients with clinical and/or laboratory evidence of liver dysfunction.
6. Patients of either gender aged between 18 and 70 years
7. Patients having laboratory evidence of liver dysfunction (deranged LFTs) and/or radiological evidence of cirrhosis.(deranged liver function is defined as a chronic inflammatory reaction in the liver present on clinical or other grounds (biochemical/serological) without improvement for 6 months or longer.radiological signs of cirrhosis of liver in ultrasound are nodular liver surface, round edge, and hypoechoic nodules in liver parenchyma which represent regenerative nodules of cirrhotic liver
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Sampling Technique: Simple random technique (may be changed to consecutive sampling)

RESULTS
Table 1 :- Alcohol intake distribution.

Alcohol intake	Frequency	Percentage
Classification of alcohol consumption		
Non drinker	2	1.65%
Occasional excessive drinker	1	0.83%
Frequent excessive drinker	118	97.52%
Frequency based on drinking		
Non drinker	2	1.65%
Once a week	1	0.83%
More than three times/week	1	0.83%
Every day	117	96.69%

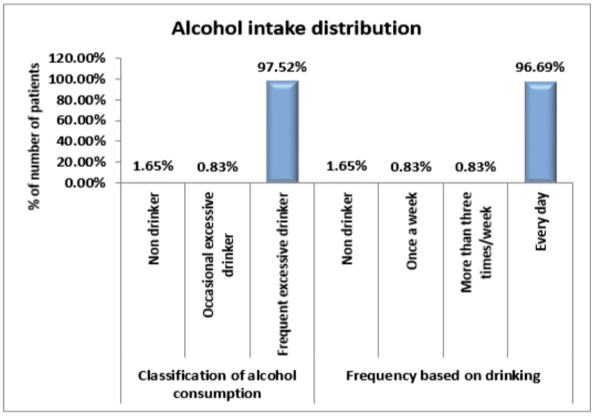

Figure 1:- Alcohol intake distribution.
Alcohol consumption of 118(97.52%) cases was frequent, and 1(0.83%) cases was occasional. 2(1.65%) cases werr non drinkers.

Frequency based on drinking of 117(96.69%) cases was every day, and 1(0.83%) case was once a week and more than three times/week each. (Table 1, figure 1).

Table 2:- Viral hepatitis distribution.

Viral hepatitis	Frequency	Percentage
No	119	98.35%
Yes	2	1.65%
Total	121	100.00%

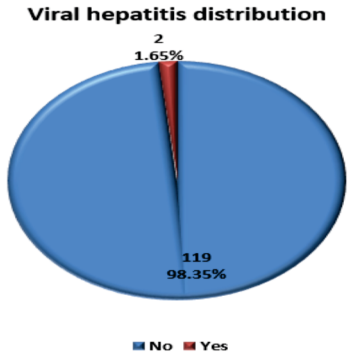

Figure 2:- Viral hepatitis distribution.
Viral hepatitis was present in 2(1.65%) cases. (Table 2, figure 2).

Table 3:- Autoimmune hepatitis distribution.

Autoimmune hepatitis	Frequency	Percentage
No	121	100.00%
Total	121	100.00%

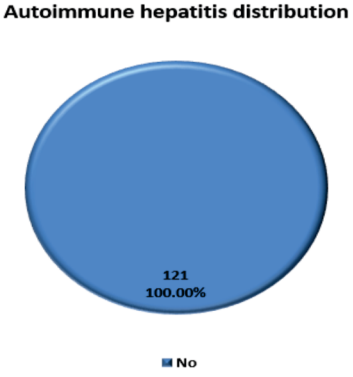

Figure 3 :- Autoimmune hepatitis distribution.
Autoimmune hepatitis was absent in all cases. (Table 3, figure 3).

Table 4:- Precipitating factor distribution.

Precipitating factor	Frequency	Percentage
None	42	34.71%
Azotemia	9	7.44%
Hypokalemia	21	17.36%
Hyponatremia	10	8.26%
Infection	4	3.31%
Malena	35	28.93%
Total	121	100.00%

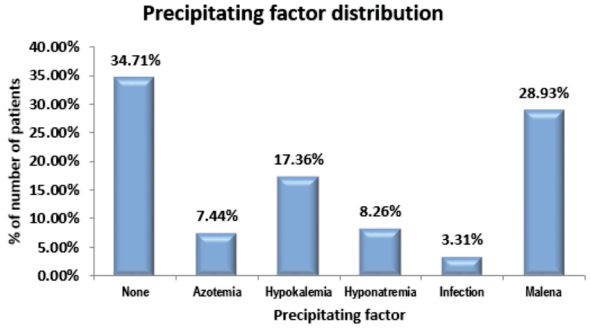

Figure 4:- Precipitating factor distribution.
Precipitating factor of 35(28.93%) cases was malena, 21(17.36%) cases was hypokalemia, 10(8.26%) cases was hyponatremia, 9(7.44%) cases was azotemia and 4(3.31%) cases was infection. 42(34.71%) cases did not have any precipitating factor. (Table 4, figure 4).

Table 5:- Grade of hepatic encephalopathy distribution.

Grade of hepatic encephalopathy	Frequency	Percentage
Grade 0	78	64.46%
Grade 1	25	20.66%
Grade 2	17	14.05%
Grade 3	1	0.83%
Total	121	100.00%

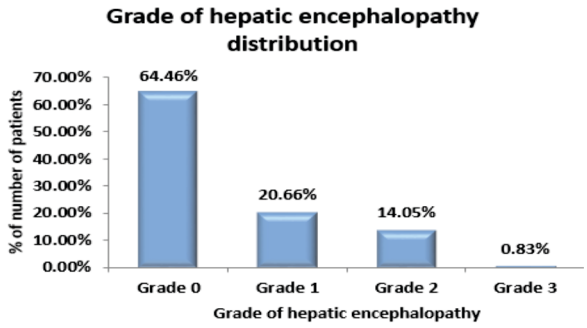

Figure 5:- Grade of hepatic encephalopathy distribution.
Grade of hepatic encephalopathy of 78(64.46%) cases was 0, 25(20.66%) cases was 1, 17(14.05%) cases was 2 and 1(0.83%) cases was 3. (Table 5, figure 5).

Table 6:- Acute/ Chronic liver disease distribution.

Acute/ Chronic liver disease	Frequency	Percentage
Chronic liver disease	121	100.00%
Total	121	100.00%

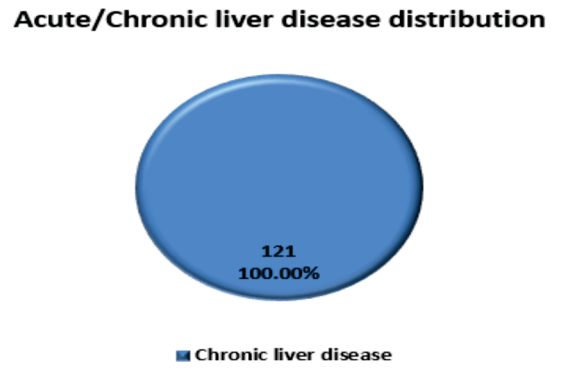

Figure 6:- Acute/ Chronic liver disease distribution.
All cases had chronic liver disease. (Table 6, figure 6).

Table 7:- Child Pugh score and class distribution.

Child Pugh score and class	Frequency	Percentage
Child Pugh class		
A	1	0.83%
B	32	26.45%
C	88	72.73%
Child Pugh score		
Mean ± SD	10.44 ± 1.43	
Median(25th-75th percentile)	11(9-12)	
Range	6-13	

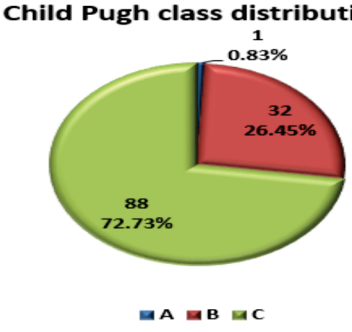

Figure 7:- Child Pugh score and class distribution.

Table 8:- Presenting clinical manifestation distribution.

Presenting clinical manifestation	Frequency	Percentage
HCU/YDS	88	72.73%
Abdominal distension	112	92.56%
Black stools	38	31.40%
Altered sleep cycle	23	19.01%
Altered sensorium	11	9.09%
General weakness	25	20.66%
Loss of appetite	14	11.57%
Pedal oedema	55	45.45%
Hematemesis	1	0.83%

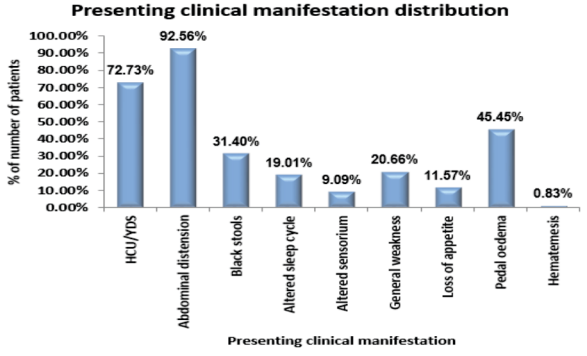

Figure 8:- Presenting clinical manifestation distribution.

In present study, 112(92.56%) cases had abdominal distension, 88(72.73%) cases had HCU/YDS, 55(45.45%) cases had pedal oedema, 38(31.40%) cases had black stools, 25(20.66%) cases had general weakness, 23(19.01%) cases had altered sleep cycle, 14(11.57%) cases had loss of appetite, 11(9.09%) cases had altered sensorium and 1(0.83%) cases had hematemesis. (Table 8, figure 8).

DISCUSSION

The increasing burden of Chronic liver disease with acute event worldwide should raise concerns regarding the prevention of morbidity and mortality in these patients. Chronic and excessive alcohol abuse is the most commonly known causes of chronic liver disease worldwide. Chronic alcohol abuse can result in a spectrum of liver injury that ranges from mild fatty infiltration to cirrhosis and hepatocellular carcinoma. The proportion of global deaths attributable to alcohol differs based on gender, with 7.6% of deaths among males and 4.0% of deaths among females attributable to alcohol as shown in a study done by WHO. The factors predisposing to this development may include amount, type and duration of alcohol consumed along with certain less obvious facts like a person genetic predisposition, race sex and other co morbid conditions.

Alcohol intake distribution (Table 1, figure 1)

In our study, alcohol consumption of 97.52% cases was frequent, and 0.83% cases was occasional. 1.65% cases were non drinkers. Frequency based on drinking of 96.69% cases was every day and 0.83% case was once a week and more than three times/week each. Study done by **Bhattacharyya M et al** demonstrated that there were about 85.7% patients having history of alcohol intake.

Viral hepatitis distribution (Table 2, Figure 2)

In our study, Viral hepatitis was present in 1.65% cases. Study done by **Bhattacharyya M et al** demonstrated that viral hepatitis was present in 8.2% cases, which is more than our study outcome.

In our study, precipitating factor of 28.93% cases was malena, 17.36% cases was hypokalemia, 8.26% cases was hyponatremia, 7.44% cases was azotemia and 3.31% cases was infection. 34.71% cases did not have any precipitating factor. Study done by **Bhattacharyya M et al** demonstrated that all cases had underlying cirrhosis and the commonest aetiology of underlying cirrhosis was alcohol abuse in 85.7% patients followed by chronic HBV infection in 8.1%. Studies done by **Pati GK et al** and **Zauner C et al** document alcoholic cirrhosis as the most frequent aetiology of chronic liver disease and viral hepatitis in the studies from Asian subcontinent. Recent trends have shown alcohol as the commonest cause of underlying cirrhosis in the Indian subcontinent too as shown in a study done by **Khatun et al** and **Singh N et al .** Most common precipitating factors in study done by **Bhattacharyya M et al** was flare of hepatitis B which was seen in 60% of the Hepatitis B infection patients followed by alcoholic hepatitis (46.6%) and drugs (45%) and sepsis in 29% patients. A study by **Garg et al** showed that 85% of the cases was due to flare of Hepatitis B. Similar findings were seen in most of the Asian studies done by **Gildea TR et al** and **Tsai et al**. Most Western literature however documents alcoholic hepatitis, sepsis and Upper GI bleed as the common precipitating factors. Alcoholic Hepatitis was responsible for acute insult in 46% of our patients with acute on chronic liver failure similar to studies by **Dhiman et al**

CONCLUSION

In our study, majority of patients belong to 3rd and 4th decade of their life with all being male patients. Majority of patients belong to Grade 0 hepatic encephalopathy and Child Pugh class C.

Mortality rate in our study was 10.74%. Most common cause of mortality was multi organ failure, secondary to chronic liver disease. Significant association was seen between mortality rate and grade of hepatic encephalopathy.

All the patients with Child Pugh class A shows good recovery. Child pugh Class C patients showed poor outcome as compared to Child pugh class A and B.

Current treatment strategies are symptomatic therefore better characterization of the disease will assist in developing new management strategies in the future. Early and active management of patients in hepatic encephalopathy can help in reducing morbidity and mortality rate.

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