

EPIDEMIOLOGY AND CLINICAL PROFILE OF HEPATIC ENCEPHALOPATHY IN TERTIARY CARE HOSPITAL, GGH, KAKINADA

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ABSTRACT

BACKGROUND

Hepatic Encephalopathy (HE) is defined as a spectrum of neuropsychiatric abnormalities in patient with liver dysfunction, after exclusion of other known brain diseases. It is a potentially reversible condition. Its spectrum ranges from minimal hepatic encephalopathy without recognisable clinical symptoms or signs to overt hepatic encephalopathy with risk of cerebral oedema and death. The burden of disease for cirrhosis is increasing, especially with regard to the rise in the number of patients with hepatitis C and E or non-alcoholic steatohepatitis.

MATERIALS AND METHODS

Patients with hepatic encephalopathy admitted in Department of Medicine, Government General Hospital, Kakinada were studied during the period of December 2013 - November 2016. Before commencement of study, permission was obtained from Ethics Committee, Rangaraya Medical College, Kakinada. All enrolled patients were informed about the nature of the study and their right to refuse. The informed written consent was taken before including them in the study. Sample Size was 100 patients. This study design was observational study and patients who fulfil the inclusion criteria.

RESULTS

In this study, the commonest cause of hepatic encephalopathy was found to be due to alcoholism (43%), all of them were males. HBV infection was the second commonest cause with 33%, of which 65% were females. In 12% of patients, the cause was HCV infection. Cause was not known in 8% cases of hepatic encephalopathy, which were thought to be NASH/NAFLD. In 4% of patients, both HBV and alcoholism were aetiological factors. Female preponderance was seen in non-alcohol groups, especially in cryptogenic cirrhosis.

CONCLUSION

Out of 100 patients, 51% recovered and were discharged, 49% of patients expired of which 62% were males and 38% were females. Mortality rate among patients with hepatic encephalopathy in males and females in the present study were 47% and 51% respectively. Females have relatively poor prognosis than male. Higher fatality rate were recorded with increasing severity of encephalopathy. According to West Haven classification out of the 36 patients, 34 expired in Grade IV. Out of the 31 patients, there was no mortality in Grade I hepatic encephalopathy. In Grade IV hepatic encephalopathy, the mortality was more than 80%. The number of patients who expired according to Child-Pugh score were 85% in Class C, 15% in Class B and none in Class A. Mortality of patients in Class C was 70%.

KEYWORDS

Hepatic Encephalopathy, Clinical Profile, Epidemiology.

HOW TO CITE THIS ARTICLE: Benhar NVA, Kumar HV. Epidemiology and clinical profile of hepatic encephalopathy in tertiary care hospital, GGH, Kakinada. J. Evid. Based Med. Healthc. 2017; 4(24), 1379-1388. DOI: 10.18410/jebmh/2017/270

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from minimal hepatic encephalopathy without recognisable clinical symptoms or signs to overt hepatic encephalopathy with risk of cerebral oedema and death. The burden of disease for cirrhosis is increasing, especially with regard to the rise in the number of patients with hepatitis C and E or non-alcoholic steatohepatitis.

Aim of this study was to evaluate various aetiologies and the end result of 100 patients with hepatic encephalopathy who got admitted in Department of Medicine, Govt. General Hospital, Kakinada so as to gain more awareness about the disorder, which may aid in early identification and prevention of mortality in future. Overt hepatic encephalopathy develops in 30 to 45 percent of patients with cirrhosis and in 10 to 50 percent of patients with TIPS.

Financial or Other, Competing Interest: None.

Submission 25-02-2017, Peer Review 02-03-2017,

Acceptance 16-03-2017, Published 22-03-2017.

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Source of Data

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Sample Size- 100 Patients.

Study Design- Observational Study.

Study Subjects- All patients who fulfil the inclusion criteria.

Inclusion Criteria for Cases

1. Patients with age more than 18 years irrespective of sex.
2. Patients with clinical symptoms and signs of hepatic encephalopathy.

Exclusion Criteria for Cases

1. Patients of age less than 18 years.
2. Presence of other psychiatric and neurological diseases causing cognitive dysfunction.
3. Acute alcoholic intoxication and alcoholic withdrawal state.
4. Subclinical hepatic encephalopathy.

Procedure

Details of the clinical history including symptoms like fever, gastrointestinal bleeding (haematemesis and/or melena), constipation, diarrhoea, vomiting and any trauma or surgery was taken. Drug history regarding use of diuretics, sedatives and NSAID was asked and past history was recorded.

A thorough clinical examination was done to establish the diagnosis of HE. Full blood count, urine examination, blood urea, S. creatinine, blood glucose, chest radiograph, serum electrolytes, serum albumin, coagulation profile, ultrasound of abdomen, Liver Function Test (LFT), HBsAg and Anti-HCV was done for all patients. Upper GI endoscopy, serum ceruloplasmin levels, 24 hrs. urinary copper excretion, transferrin saturation, serum ferritin, ANA, anti-LKM and serum alpha fetoprotein levels were done as and when required.

Hepatic encephalopathy was graded according to the West Haven classification system. The severity of liver cirrhosis was assessed through Child-Pugh score system.

Grading	Clinical Features
I	Mild confusion, euphoria, anxiety or depression, reversed sleep rhythm, slurred speech
II	Drowsiness, lethargy, gross deficits in ability to perform mental tasks, relatively moderate confusion

III	Somnolent but arousable, severe confusion, inability to perform mental tasks
IV	Coma with (IVa) or without (IVb) response to painful stimuli

Table 1. Clinical Grades of Hepatic Encephalopathy

Parameters	Numerical Score		
	1	2	3
Ascites	None	Slight	Moderate to
Encephalopathy	None	Slight-to-moderate	Moderate to
Serum bilirubin	<2	2-3	>3
Albumin	>3.5	2.8-3.5	<2.8
Prothrombin time	1-3 sec	4-6 sec	>6 sec

Table 2. Child-Pugh Scoring Criteria

According to the sum of these points, patients were categorised into Child-Pugh Grades A (5 to 6 points), B (7 to 9 points) or C (10 to 15 points). Diagnosis of spontaneous bacterial peritonitis was based on demonstration of more than 250 WBC/cm³ in ascetic fluid. The presence of elevated serum creatinine (>1.5 mg/dL) in the absence of shock, haematuria or proteinuria with a normal renal sonogram was taken to be indicative of hepatorenal syndrome.

All patients were given supportive symptomatic treatment and specific treatment for hepatic encephalopathy, coagulopathy and renal failure as and when required. Patients were followed for their duration of stay in the hospital and outcomes were analysed. All the data was analysed and tabulated.

Tools

- Clinical proforma.
- West Haven classification for grading of hepatic encephalopathy.
- Child's Pugh score to assess the severity and prognosis in cirrhosis of liver.

OBSERVATIONS AND RESULTS

A total of 100 patients with hepatic encephalopathy were studied for aetiology, different precipitating factors and outcome for 23 months.

Age	Males	Females	Total Percentage
18-40	15(22.38%)	12(36.36%)	27(27%)
41-60	44(65.67%)	14(42.42%)	58(58%)
More Than 60	8(11.94%)	7(21.21%)	15(15%)
Total	67 (100%)	33 (100%)	100 (100%)

Table 3. Age and Sex Distribution

The age incidence was more in 41 to 60 years of age (58%). Followed by 20 to 40 years (27%) and more than 60 years (15%). There were no patients below the age of 20 years. The minimum age was 20 years and the maximum was 80 years with mean age of 47 years.

It was observed that 67 patients among the 100 studied were males, remaining 33 patients were females; of which 15 males and 12 females were in 20 to 40 years of age, 44 males and 14 females were in 41 to 60 years of age. In all age groups, a male preponderance (P value=0.0007) was observed.

Mean age of males was 47 and mean age of females was 47.6. Patients who were below 40 years of age were only 27%, whereas patients above 40 years were 73% (Chi squared equals 21.160 with one degree of freedom; the two-tailed P value is less than 0.0001). Patients who expired had higher mean age, which is statistically insignificant (49.20 ± 14.07 and 45.76 ± 12.31 with p value=0.1959).

Aetiological Profile

Aetiology		Percentage of Patients		Percentage
ALD	Acute hepatitis	10	0	10(10%)
	Cirrhosis	33	0	33(33%)
HBV	Acute hepatitis	2	8	10(10%)
	Chronic hepatitis/cirrhosis	9	14	23(23%)
HCV		5	7	12(12%)
Cryptogenic		2	6	8(8%)
Alcohol+HBV		4	0	4(4%)

Table 4. Aetiology of Hepatic Encephalopathy

In this study, the commonest cause of hepatic encephalopathy was found to be due to alcoholism (43%); all of them were males. HBV infection was the second commonest cause with 33%, of which 65% were females. In 12% of patients, the cause was HCV infection. Cause was not known in 8% cases of hepatic encephalopathy, which were thought to be NASH/NAFLD. In 4% of patients, both HBV and alcoholism were aetiological factors. Female preponderance was seen in non-alcohol groups, especially in cryptogenic cirrhosis.

Precipitating Factors of Hepatic Encephalopathy

Among the precipitating factors of hepatic encephalopathy, the most common causes were upper gastrointestinal bleed 9 (hematemesis 24% and melena 29%), Infection (29%), electrolyte imbalance (Hyponatremia 22% and Hypokalaemia 14%), constipation (27%), sedatives (4%) and excess protein intake (11%). In 6% patients, no precipitating factor was found. In some patients two or more precipitating factors were present. Diuretics precipitated hepatic encephalopathy in 9% of patients.

Presenting Signs

The commonest signs in the present study were icterus in 91%, ascites in 68%, asterixis in 67%, pallor in 61%, pedal oedema in 61%, splenomegaly in 49%, fetor hepaticus in 11% and clubbing in 5% of patients. Clinical features like spider angioma, Dupuytren's contracture, testicular atrophy, atrophy, parotid enlargement, gynecomastia, palmar erythema and finger clubbing were uncommon in the present study.

Child-Pugh Score	Total Number of Patients
Type A	9
Type B	31
Type C	60

Table 5. Child-Pugh Score

When the patients in this study were grouped according to Child-Pugh Score 60% were in Class C, 31% in Class B and remaining 9% in Class A. Majority were in Class C showing the advanced stages of the disease.

Grade of HE	Number of Patients
I	22
II	11
III	31
IV	36

Table 6. West Haven Classification

Majority of patients of hepatic encephalopathy in the present study belong to Grade IV (36%) and Grade III (31%) of West Haven classification followed by 22% in Grade I and 11% in Grade II.

Type of Hepatic Encephalopathy	Number of Patients
Type A	20
Type B	0
Type C	80
Total	100

Table 7. Type of Hepatic Encephalopathy

Among 100 patients, 20 patients (20%) belong to type A and 80 patients (80%) belong to type C. There were no patients in type B.

Prognosis and Outcome

Outcome	Males	Females	Total	P value
Survived	35	16	51	P value = 0.8322
Expired	32	17	49	

Table 8. Prognosis and Outcome

Out of 100 patients, 51% of patients were recovered and discharged. Out of 100, 49% of patients expired, of which 65% were males and 35% were females.

Among females with hepatic encephalopathy 51% died, whereas 47% of males with hepatic encephalopathy died.

Females had relatively poor prognosis than males, which is statistically insignificant (P value equals 0.8322).

Aetiology	Total Patients	Expired	Percentage of Mortality
Alcohol	43	20	46.51%
HBV	33	16	48.8%
HCV	12	8	66.66%
Cryptogenic	8	3	37.5%
Alcohol+HBV	4	2	50%

Table 9. Mortality according to Aetiology

When patients in the present study were categorised according to mortality with respect to aetiology, 20 (46.51%) patients out of 43 patients died in ALD group. Out of 33 patients in HBV related HE, 16 (48.9%) patients expired. Out of 12 patients of HCV related HE, 8(66.6%) patients died. Out of 8 patients of cryptogenic HE, 3

(37.5%) patients died. Half of the patients (50%) died among HBV + alcohol related group. Highest mortality was observed in patients of hepatic encephalopathy with HCV aetiology in the present study.

CPS	Number of Cases	Mortality	Percentage	
A	9	0	0%	P value equals 0.0014
B	31	7	22.5%	
C	60	42	70%	

Table 10. Child-Pugh Score and Mortality

Number of patients in the present study who expired according to Child-Pugh Score was 70% in Class C, 22.5% in Class B and none in Class A expired. Child-Pugh Score C had significantly high mortality (70%) in the present study, which is statistically significant (the two-tailed P value equals 0.0014).

West Haven Classification	Number of Cases	Mortality	Percentage	
I	22	0	0%	P value equals 0.0002
II	11	3	27.2%	
III	31	12	38.2%	
IV	36	34	94.4%	

Table 11. West Haven Classification and Mortality

When all (100) patients with hepatic encephalopathy in the present study were graded according to West Haven classification of hepatic encephalopathy, 36% were in Grade IV, 31% in Grade III, 11% in Grade II and remaining 22% were in Grade I of hepatic encephalopathy.

Out of 36 patients of Grade IV hepatic encephalopathy, 34 patients (94.4%) expired, whereas out of the 31 patients in Grade III hepatic encephalopathy, 3 patients (27.2%) expired. There was no mortality in Grade I hepatic encephalopathy; the higher is the mortality in the present study. Grade IV hepatic encephalopathy had statistically

significantly high mortality in the present study (the two-tailed P value equals 0.0002).

Hepatorenal Syndrome and Mortality

In the present study, 37 patients with hepatic encephalopathy had hepatorenal syndrome. Mortality rate in the patients having hepatorenal syndrome was very high (67.57%) when compared to the patients not having hepatorenal syndrome (38.09%). The two-tailed P value equals 0.0068, which was quite significant statistically.

Parameter	Survived	Expired	P value	Significance
Haemoglobin	11.86±2.452	10.112±2.816	0.0013	Very significant
Serum Na ⁺	138.40±2.98	134.65±5.99	0.0001	Extremely significant
Serum K ⁺	3.819±0.3890	3.775±.369	0.5614	Not significant
Total Bilirubin	4.563±2.990	5.941±4.366	0.0654	Not quite significant
Albumin	3.265±0.751	2.717±0.688	0.0003	Extremely significant
Alkaline Phosphatase	113.35±48.73	134.42±59.30	0.544	Not quite significant
SGOT	122.21±200.02	225.96±321.34	0.0536	Not quite significant
SGPT	108.21±164.08	181.69±262.69	0.0939	Not quite significant
S. creatinine	1.202±0.492	1.713±0.763	0.001	Extremely significant
INR	2.29±0.87	2.77±0.59	0.0018	Very significant

Table 12. Survived Vs. Expired. Analysis of Data

Low haemoglobin, hyponatremia, hypoalbuminemia, elevated serum creatinine and elevated PT/INR were significantly associated with mortality. Elevation of liver enzymes and elevated total bilirubin were not significantly associated with mortality.

DISCUSSION

Hepatic encephalopathy has never been less than an unsolved mystery for physicians and researchers around the globe. Since the time of Hippocrates, it has been difficult to diagnose and manage any patient of hepatic encephalopathy. In majority of patients with hepatic encephalopathy, clearly definable precipitating factors are

identified and reversal or control of these factors is the key step in the management. In the present study of 100 patients of hepatic encephalopathy, all possible factors which could be responsible for precipitating or aggravating hepatic encephalopathy were looked for and analysed.

Age Distribution

In this study, the majority of the patients (85%) were above 41 years of age. The age incidence was more in 41 to 60 years of age (58%), followed by 20 to 40 years (27%) and more than 60 years (15%). There were no patients below the age of 20 years. Minimum age was 20 years and maximum age was 80 years in the present study.

Patients who were below 40 years of age were only 27%, whereas patients above 40 years were 63% which was quite significant (the two-tailed P value equals 0.0020).

Durrani B et al reported that hepatic encephalopathy was most common in patients with age more than 40 years. Majority (64%) of patients were more than forty years by Saira Afzal et al.¹ Most common age group affected by hepatic encephalopathy was 41-60 in Bikhram Ram Devrajani et al,² whereas 64% were in the age group of 45-60 years by Alam et al. Most common age group affected was 41-60 years by Shivani A. Patel et al.

Mean Age

The mean age of the present study subjects was 47 years, and the mean age of the males and females were comparable (47.4 years and 47.6 years respectively) Onyekwere CA et al.³ Reported that there was no significant difference in the mean ages of males and females in patients with hepatic encephalopathy.

The mean age of presentation of 47 years shows a high prevalence of the disease among the productive age group, a result similar to previous studies that are shown below as table.

Patients who expired had higher mean age, which is statistically insignificant (49.20 ± 14.07 and 45.76 ± 12.31 with p value=0.1959).

GENDER

Male preponderance was observed in the present study, while similar findings were observed in various other studies shown below. The two-tailed P value equals 0.0007.

Marked male preponderance was noted especially in patients with chronic liver disease due to alcohol (male: female (44.0)).

In contrast, slight female preponderance was seen in patients with hepatitis B (female: male (23.10)), cryptogenic chronic liver disease (female, male (6:2)) and HCV related chronic liver disease (female: male (7.5)). Variation in male preponderance in various studies may be due to variation in the drinking pattern or medical care seeking practice between sexes in these geographic locations.

Aetiology

In the present study, the majority of patients were alcoholics (43%), followed by HBV (33%) and HCV (12%) being the other leading causes of hepatic encephalopathy.

Alcohol

The high incidence of ALD in the present study may be due to alcohol intake in India is steadily increasing with decrease in the initiation age to 20. This alarming trend is noticed in many areas of the country. The absolute value of AST and ALT in alcoholic hepatitis patients was <300 u/L in the present study. AST/ALT >2 was observed in majority of these patients.

Studies done in industrialised nations of the West such as by Conn and by Faloon showed alcohol as the main aetiological factor. In the Western world alcoholism is the main cause of hepatic encephalopathy, where there is a definite male preponderance, making it the 4th commonest cause of death in males in USA.

Medha Y Rao et al reported that incidence of alcohol associated cirrhosis was 58.1% in Bangalore. In the present study alcohol intake was contributory factor in 48% of patients, which is significantly more than a prior study from Eastern India. This may be a reflection of referral bias, socioeconomic situation or can be a reflection of a changing trend.

In the present study alcoholic liver disease was not observed in females, whereas in other local study it was seen in 3.5% of female cases. This may be because patients denied alcoholic consumption. All the patients of ALD were males in a study by Ajitpal Singh Gil, Punjab. Alcoholic liver disease (68%) was the most common CLD by Dhiman RK et al, Chandigarh.⁴

Hepatitis B Infection

The results of the current study had shown that HBV infection (33%) was more common than HCV infection (12%). HCV is the dominant cause of non-alcoholic Chronic Liver Disease (CLD) in several parts of the world, whereas in India there are conflicting reports. Some report hepatitis B, while others hepatitis C viruses as the most important infection in CLD patients. HBV was the most prevalent viral infection than HCV in chronic liver disease patients in North India as reported by Sarin SK et al.⁵

HBsAg was positive in 9% of patients with ALD. Seroprevalence in cirrhosis was 16%. Seroprevalence in acute hepatitis was 50%.

Efforts at improving the coverage of current immunisation campaign against Hepatitis B certainly will help reduce the burden of Hepatitis B virus infection, while promotion of sensible use of alcohol should be encouraged.

Hepatitis C Infection

Seroprevalence of HCV in hepatic encephalopathy in the present study was 12%. All were having decompensated cirrhosis. No patient with acute hepatitis was seropositive for HCV in the present study. HCV had high mortality in the present study (66%) when compared to other groups.

The aetiology of type C HE had been hepatitis C virus infection in majority of the cases in most of studies done in Pakistan. Anti-HCV was positive in 60% patients by Bikha Ram Devrajani et al.² 70% patients by Mumtaz K et al.⁶ and 62% patients by Maqsood S et al.⁷ Hepatitis C was the major aetiological factor of HE by Sheik et al.⁸

Hepatitis C virus was the commonest of Cirrhosis by Muhammad Khurram et al.⁹ This high prevalence in other areas may be due to nasal and ear-pricking by unsterilised instruments and wide spread quack practice. Unawareness in general population regarding the spread of viruses. Non-disposable syringes and low incidence of alcoholism.

Alcohol + viral (Co-infection)

In our study, there was a lower prevalence of hepatitis B and HCV infection among ALD patients with only 9% of ALD were positive for HBsAg. These findings correlate with Gautham Ray et al.

Rare Causes

None of the patients in current study were positive for rare causes of type C hepatic encephalopathy, such as Wilson's disease and hemochromatosis.

Cryptogenic Cirrhosis

No aetiology could be found for type C hepatic encephalopathy in 8% patients, therefore they were labelled as idiopathic. This high frequency of idiopathic liver cirrhosis in the recent study was due to financial restriction as well as limited availability of advanced and specific diagnostic tools to determine other underlying causes of chronic liver disease in the current study were HBsAg negative. However, serum anti-hepatitis B core antibody and serum HBV DNA were not done in all. All patients with cryptogenic chronic liver disease in the current study were HCV antibody negative; however, serum HCV RNA was not done in all. The frequency of idiopathic CLD also varies in different areas of the world. Commonest aetiology for cirrhosis was cryptogenic (35%), chronic liver disease by Ashish Goel et al.¹⁰ Vellore, India. In UK it is about 5%-10%, whereas other areas such as France and urban parts of USA where alcoholism is prevalent have a lower proportion of idiopathic CLD. No aetiology could be found in 19.4% patients by Trimukhe R et al.¹¹ With increase of specific diagnostic facilities, there will be a decrease in the percentage of idiopathic CLD.

However, better designed prospective studies are needed to investigate the precise causes of idiopathic chronic liver disease in our area. Drug intake history is at times inadequate and an occasional role of a drug (methotrexate, amiodarone, diclofenac, methyldopa, herbal medicines) in the aetiology of cirrhosis of liver should be remembered.

These overall findings provide strong evidence that the aetiology of cirrhosis in Indians continues to change. A larger survey of the current epidemiological status of cases from Andhra Pradesh with hepatic encephalopathy is greatly needed, because the aetiology of hepatic

encephalopathy varies widely with socioeconomic, regional and educational variables.

Type of Hepatic Encephalopathy

Majority of the patients (80%) in the present study had encephalopathy complicating underlying chronic liver disease with only 20% patients had acute fulminate hepatic failure. No cases of type B were seen in the present study. Type C was the most common type in majority of the studies as shown in the table.

Precipitating Factors

Haematemesis (24%), melena (29%), constipation (27%) and infections (29%) were the common precipitating factors in this study. Other causes were electrolyte imbalance (hypokalaemia in 14% and hyponatremia in 22%). Excess protein intake in 11% and sedatives in 4%. Most of the patients in the present study with electrolyte imbalance had history of diarrhoea or vomiting or were already on diuretic therapy. Patients having constipation and hypokalaemia as precipitating factors had good outcome, whereas patients having upper GI bleed had poor outcome.

As shown in the table gastrointestinal bleeding, constipation and infections stand out as the most common precipitants of hepatic encephalopathy in almost all the studies. It can be assessed from the table that findings of the present study match those studies done in this subcontinent, such as Alam et al.¹² and Khurram et al.⁹

Gastrointestinal bleeding and infections were the most common precipitating factors for hepatic encephalopathy. This is especially true for the province of Punjab where Aisha⁸ and Khurram⁹ revealed gastrointestinal bleeding, infection and constipation as the main factors precipitating HE.

Infection, gastrointestinal bleeding and constipation have been repeatedly demonstrated as important precipitating factors of hepatic encephalopathy, a fact also borne out by this study.

Foreign studies such as by Conn¹³ et al and by Floon¹⁴ et al, however, revealed infection as a less common cause as precipitant of hepatic encephalopathy in abroad which was understandably due to better hygienic conditions of the patients and hospitals in the Western countries.

The most common precipitating factors for hepatic encephalopathy detected were infection (67%), constipation (49%) and gastrointestinal bleeding (45%) by Bikha Ram Devrajani et al.² Most common precipitants of hepatic encephalopathy were infections (20.5%) and constipation (18.3%) by Mumtaz K et al.⁶ The identified precipitants for hepatic encephalopathy were sepsis (29%), electrolyte imbalance (14%), gastrointestinal bleed (24%) and drugs (5%) by Onyekwere CA et al.³ Infection (44%), gastrointestinal bleeding (38%) and constipation (38%) stood out as the most common precipitating factors for hepatic encephalopathy by Maqsood S et al.⁷ Islamabad.

Electrolyte imbalance in 56% patients, diarrhoea in 40%, constipation in 32%, infections in 24% and

gastrointestinal bleed in 22% patients were amongst the commonest precipitating factors for hepatic encephalopathy by Islam et al, whereas 30% had constipation, 29% had upper gastrointestinal bleed in patients with HE by Mohammad Tariqbb et al,¹⁵ constipation (32.9%) and upper GI bleed (31.4%) were the commonest precipitating factors by Khurram et al.¹⁶

Souheil et al¹⁶ found that infections were responsible in only 3% of cases and Conn reported infections were responsible in only 4% cases.

Studies that were done by Shaik and Hameed showed electrolyte imbalance as most common precipitating factors for hepatic encephalopathy. Overzealous diuretic abuse may be contributing factor for this high prevalence of electrolyte disturbances.

GI Bleed

Percentage of patients with gastrointestinal bleeding as precipitating factor for hepatic encephalopathy in the present study was 29%, which matches with majority of studies.

Infection

Percentage of patients with infection as precipitating factor for hepatic encephalopathy in the present study was 29%, which matches with majority of above studies except with Conn et al, which was carried out in West.

Present study is correlating with majority of the studies done in Indian subcontinent, such as Onyekwere CA et al³ and Hameed et al.

Amongst the infections Spontaneous Bacterial Peritonitis (SBP) was found in 52% patients, Urinary Tract Infection (UTI) in 36% patients, while another 12% patients had lobar pneumonia and septicemia.

Constipation

Percentage of patients with constipation as precipitating factor for hepatic encephalopathy in the present study was 37%. This correlates with various studies in subcontinent, such as by Alam¹² (32%). Aisha⁸ (36%) and Khyrrm (32%). In Western studies by Souhell,¹⁶ Fallon¹⁴ and Conn¹³ had reported constipation in 6%, 3% and 3% of their patients respectively. Higher percentage of constipation over GI bleed may be due to the reason that the mortality of active gastrointestinal bleeding is very high in local population due to limited resources. Constipation was significant precipitating factor in old age in the present study due to the fact that increasing age affects the bowel habits. However, it is easily treatable and preventable. In old age lifestyle modifications, lactulose and fibre rich diet may do a lot by preventing the dangerous condition of hepatic encephalopathy in chronic liver disease.

Sedatives

Usage of sedatives and tranquilisers was observed in 04% patients with hepatic encephalopathy in the present study. When the history was taken from the attendants and the patients themselves (when recovered from hepatic coma or

in a hepatic encephalopathy Grade 0 or 1), history was suggestive of self-prescription of such drugs and this shows the lack of proper counselling and knowledge in these patients. This finding is in accordance with Onyekwere CA et al,³ in which sedatives were precipitating factors in 5% of patients with hepatic encephalopathy.

High Protein Diet

The intake of high protein diet was precipitating factor in 11% of patients with hepatic encephalopathy in the present study. This could be due to lack of guidance regarding nutritional supplements for the patient or unavailability of a nutritionist. This is most easily preventable precipitating factor for hepatic encephalopathy. Hence, there is a great need for proper counselling regarding food habits for patients with liver disease.

Bikha Ram Devrajani et al² reported high protein diet as precipitating factor in 26% of patients with hepatic encephalopathy.

Clinical Features

Amongst the clinical features jaundice (91%), ascites (68%) and asterixis (67%) were the most common presenting features in this study. Anaemia was seen in 61%, splenomegaly in 49% and pedal oedema in 64% of patients. Clinical features like spider angioma. Dupuytren's contracture, testicular atrophy, parotid enlargement, gynecomastia, palmar erythema and finger clubbing were uncommon. The high incidence of oedema and ascites in the present study indicated fairly advanced disease with decompensation. These findings are correlating with C. Willis et al.¹⁷

Anaemia

Anaemia was seen in 61% in the present study, which correlates with other studies. Anaemia was seen in almost 85% of cases by Jadumani Nayak et al.¹⁸ Anaemia of diverse aetiology was reported in about 75% of patients with chronic liver disease by McHutchison et al.¹⁹

Splenomegaly

Sherlock (1997) stated that if there is no splenomegaly in a case of portal hypertension, the diagnosis is erroneous. Splenomegaly was seen in 49% patients in the present study. Clinically, the spleen might have been shrunken due to acute GI bleed in the remaining cases. Splenomegaly was seen in 62% of cases by Jadumani Nayak et al.¹⁸ Splenomegaly was found in 80% cases by Alam et al.¹²

Child-Pugh Score

Patient Distribution according to Child-Pugh Score

Child-Pugh score is a simple and convenient prognostic measure in patients with liver cirrhosis that has been repeatedly shown to be useful in this assessment. When the patients in the current study were grouped into Child-Pugh classification, 9% were assigned to class A, 31% were considered as class B and 60% were in class C. High

preponderance of HE in Child-Pugh C indicates HE is a feature of advanced liver disease.

Mortality according to Child-Pugh Score

Majority of patients in Child-Pugh C were expired in the present study, which correlates with previous studies. Child-Pugh C had significantly high mortality (70%) in the present study (the two-tailed P value equals 0.0014).

Majority of expired patients had Child-Pugh score of 10-15 in Bikha Ram Devrajani study in Pakistan.² Mortality percentage is comparable to Fakhar Ali Qazi Arisar et al²⁰ as shown below in graph.

Udayakumar et al reported that Child-Pugh-Turcotte's score did not predict the outcome. This may be due to interobserver variation as two parameters in Child-Pugh-Turcotte's score (ascites and encephalopathy) are observer dependent.

West Haven Classification

Majority of the patients in this study had higher grades of encephalopathy with 36% in Grade IV, 31% in Grade III, 11% in Grade II, while 22% had Grade I HE. The higher the grade, higher is the mortality in the present study. Grade IV HE had significantly high mortality (<90%) (Two-tailed P value equals 0.0002).

Majority of expired patients were in Grade IV of hepatic encephalopathy in Bikha Ram Devrajani study in Pakistan.² Majority (76%) of patients were having either Grade III or IV coma by Alam et al.¹²

Serum Ammonia

Serum ammonia was raised in 8 patients (80%) in the present study. It was done in 10 patients only because of financial constraints. This correlates with Sheila Sherlock.²¹ (Serum ammonia was raised in 85.5% with hepatic encephalopathy by D. Sinniah et al).²²

Newly Diagnosed Cirrhosis in Hepatic Encephalopathy

Prevalence of newly diagnosed cirrhosis in hepatic encephalopathy in the present study was 7%. This shows that overt hepatic encephalopathy is a relatively uncommon presentation at the time of cirrhosis diagnosis. A study of 466 Danish patients showed that 11% had overt hepatic encephalopathy at the time of cirrhosis diagnosis. The results of these studies indicate that in the majority of patients, there is time to intervene and prevent the development of hepatic encephalopathy.

Patients who have already developed cirrhosis complications are much more likely to develop hepatic encephalopathy. The risk of first episode of overt hepatic encephalopathy was compared in a study in West between patients who had not developed cirrhosis complications and patients who had already had variceal bleeding or ascites. Those who had not developed complications had a 5-year risk of first episode of overt hepatic encephalopathy of 7% compared with 26% in those with other complication.

Outcome and Mortality

Out of 100 patients, 51% recovered and were discharged; 49% of patients expired, of which 62% were males and 38% were females. Mortality rate among patients with hepatic encephalopathy in males and females in the present study were 47% and 51% respectively. Females have relatively poor prognosis than male. Higher fatality rate were recorded with increasing severity of encephalopathy. According to West Haven classification out of the 36 patients, 34 expired in Grade IV. Out of the 31 patients, there was no mortality in Grade I hepatic encephalopathy. In Grade IV hepatic encephalopathy, the mortality was more than 80%. The number of patients who expired according to Child-Pugh score were 85% in Class C, 15% in Class B and none in Class A. Mortality of patients in Class C was 70%.

Comparison of Mortality with Other Studies

The mortality rate of hepatic encephalopathy in the present study (49%) is as high as that of other study by the study of Sargent and Full Wood All Giandan et al²³ (40%), Garget et al (48%) and Onyekwere CA et al³ (51%). Patients who did expire were mostly in Class C of Child-Pugh classification and Grade III and IV of West Haven classification. Majority of our patients came in with fairly advanced stage of liver dysfunction (Child-Pugh class B and C), which may have contributed to the observed mortality. The mortality rate in our patients was 49%, which is in excess that what reported by Sheila Sherlock.²¹

Gender Based Mortality

Fifty one percent of females with hepatic encephalopathy died, whereas 47% of males with hepatic encephalopathy died in the present study.

This showed that female sex was associated with increase mortality. This could be due to hormonal factors along with the delayed health care seeking practice among female patients. The Z score is -0.3531, the P value is 0.72634, the result is statistically insignificant.

Shivani A Patel et al reported that females had worst outcomes in hepatic encephalopathy. The number of females who passed away was more than males with the female: male ratio being 7:3 by CA Onyekwere et al.³

Hepatic encephalopathy affects not only mortality, but quality of life. Cirrhosis and to an even greater extent hepatic encephalopathy affects the physical domains of the patient. Hepatic encephalopathy also imposes a great burden on the caregivers of these patients. This was not studied in the present study.

Management of patients with HE in an intensive care unit with newer therapeutic measures may have improved the outcome. Identification of early grades of hepatic encephalopathy by screening of those at risk (patients with pre-existing liver disease) using the psychometric tests will go a long way in reducing the fatal outcome since presentation at advanced stage as was documented in this study is associated with less favourable outcome.

Analysis of various parameters in survived and expired patients; it was revealed that low haemoglobin, hyponatremia, hypoalbuminemia, elevated serum creatinine and elevated PT/INR were significantly associated with mortality. Elevation of liver enzymes and elevated total bilirubin were not significantly associated with mortality.

Predictive factors of mortality in patients with hepatic encephalopathy in the present study were female sex, alcohol intake, Grade III and IV hepatic encephalopathy, Child-Pugh Class C, HBsAg, HCV antibody, hyponatremia, elevated PT/INR elevated renal parameters and low haemoglobin.

On multivariate analysis of hepatic encephalopathy, low serum sodium and high PT/INR were found to be independent baseline predictors of mortality by Garg et al. Present study revealed alcoholism as most common cause of hepatic encephalopathy, therefore every effort should be taken to counsel the patients regarding alcohol abstinence.

HBV infection was the second most common aetiology of hepatic encephalopathy, therefore early detection and treatment of HBV infection should be conducted, particularly in all high risk individuals. In order to prevent the spread of infection, HBV-infected persons should be advised not to share tooth brushes and dental or shaving kits. Public awareness regarding the spread of the disease and avoidance of risk factors is strongly needed.

Patients with hepatic encephalopathy presented with a fairly advanced stage of the disease in the present study. Early detection of hepatic encephalopathy and cirrhosis will lead to a genuine survival benefit.

In fact complete recovery is possible, especially if the encephalopathy was triggered by a reversible cause. Therefore, the goal should be to identify and manage the particular precipitating factor and effective measures and steps must be taken to avoid precipitants for hepatic encephalopathy.

Gastrointestinal bleeding, infection, constipation and electrolyte disturbances were the most common factors of hepatic encephalopathy in this study. Priority should be given to these factors in terms of hospital funds, medicines and human efforts.

Caution must be exercised in putting cirrhotic patients on diuretics early and effective infection control measures and better hygienic conditions in Government hospitals should be maintained.

Consistent use of lactulose and fibre should be encouraged to prevent constipation. More and more endoscopic facilities should be made available nationwide for prompt control of gastrointestinal bleeding. Only then there are any chances of combating cirrhosis and even worse hepatic encephalopathy.

There is a need for large multicentre trials and maintenance of some sort of registry to monitor patients with cirrhosis and hepatic encephalopathy. This will give a better understanding of the disease and its natural course.

From this study, it was concluded that in most of the cases there are different factors which play a key role in

precipitating hepatic encephalopathy which is a common phenomenon in patients with liver disease. Infections, upper GI bleed, constipation and electrolyte imbalance were the most common precipitating factors.

There is definite need for health education in patients who are diagnosed with cirrhosis of liver regarding the risk of hepatic encephalopathy and its precipitating factors. Priority should be given to these factors in terms of hospital funds, blood banks, medicines and human efforts. No stone should be left unturned in providing better and effective infection control measures and better hygienic conditions in Government hospitals. The proper disposal of infected hospital waste and especially syringes, blades should be performed. Consistent use of lactulose and fibre, lifestyle modifications like exercise, low-fat diet and activity should be encouraged to prevent constipation. Emergency endoscopic facilities should be made available nationwide in public sector hospitals for prompt control of gastrointestinal bleeding. Every effort should be made to control increasing incidence of hepatitis B and C through health education, prevention and immunisation. Judicial use of sedatives and diuretics and proper advice regarding diet must be an integral part of all counselling protocol to cirrhotic patients. Hence, the early detection and diagnosis of these precipitating factors help in starting treatment of this fatal condition, hence reducing the mortality.

CONCLUSION

Out of 100 patients, 51% recovered and were discharged, 49% of patients expired of which 62% were males and 38% were females. Mortality rate among patients with hepatic encephalopathy in males and females in the present study were 47% and 51% respectively. Females have relatively poor prognosis than male. Higher fatality rate were recorded with increasing severity of encephalopathy. According to West Haven classification out of the 36 patients, 34 expired in Grade IV. Out of the 31 patients, there was no mortality in Grade I hepatic encephalopathy. In Grade IV hepatic encephalopathy, the mortality was more than 80%. The number of patients who expired according to Child-Pugh score were 85% in Class C, 15% in Class B and none in Class A. Mortality of patients in Class C was 70%.

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