Original Article

Study of Hepatic Encephalopathy in Department of Medicine at PMCH Nawabshah

Hepatic Encephalopathy

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ABSTRACT

Objectives: To assess the frequency of Hepatic Encephalopathy in patients with chronic liver disease admitted in the medical ward.

Study Design: Cross sectional Study

Place and Duration of Study: This study was conducted in the department of Medicine at PMCH Nawabshah from January 2016 to December 2016.

Materials and Methods: For this study both male and female were included, informed consent was taken from all the relatives of patients or conscious patients. Data collected using Questionnaires' translated into local languages Sindhi and Urdu. Statical analysis was done using SPSS 15 Version.

Results: 53 were males and 47 were females. Common age group was middle age, mean age(46.93) .6 patients were in stage 1, 17 patients were in stage 2, 56 patients were in stage 3, 21 patients were in stage 4. Anti HCV positive in 72 patients, HBsg positive in 10 patients, both antiHCV and HBsAg positive in 18 patients SGPT raised in 87 patients, PT prolonged in 94 patients, BILIRUBIN raised in10 patients, UREA and Creatinine raised in 8 patients.

Conclusion: Majority of the patients admitted with history of infection irregular diet pattern , electrolyte imbalance, portal hypertention, irregular treatment and use of herbal medicines. Proper treatment, education of the patient and preventive measures patients quality of life and mortality can be reduced.

Key Words: Chronic liver disease, hepatic encephalopathy, mortality, portal hypertention, ammonia, HE, OHE, CLD.

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INTRODUCTION

Hepatic encephalopathy is reversible neuropsychiatric abnormalities seen in chronic liver disease patients without any neurologic and metabolic abnormality. By collateral vessels portal blood enters into systemic circulation.[1] and inability of the liver to clear toxic agents of gut origin. Symptoms include cognitive impairment, personality changes impaired consciousness, altered sleep pattern[2], disorientation, confusion, agitation and coma can occur.[2] Chronic liver disease is common cause of death in Pakistan. Main causes of chronic liver disease are hepatitis C and B virus.[3] Hepatic Encephalopathy is main cause of death in majority of the patients with chronic liver disease.[3] MRI and MRS are helpful for the pathophysiological mechanism of Hepatic Encephalopathy.[4] Ammonia is important factor responsible for the Hepatic Encephalopathy, ammonia enters via port systemic shunting and liver fails to metabolize ammonia.[5]

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Due to increased level of ammonia irritability, aggressiveness and convulsions occur.[6] Increased level of ammonia was observed in patients with coma.[7] Ammonia produced mainly by intestinal bacteria, catabolism of ingested protein is their main source of energy.[7] Helicobacter pylori is another source of ammonia production and precipitate Hepatic Encephalopathy.[7] Alkalosis due to prolonged diuretic therapy, impaired renal function and intravascular volume depletion can affect renal excretion of ammonia. Muscle wasting in chronic liver disease increase ammonia level, muscle is main site for extra hepatic ammonia removal.[7] Neurons are more to the effect of ammonia than astrocytes which absorb ammonia and convert it to glutamine minimize its toxic effect on neurons.[8] Increased levels of ammonia increase brain glutamine levels with the result increased brain water and impaired neuropsychological function.[9] Increase ammonia level causes increase uptake of brain neutral amino acid I.e. the L –aminoacid transporter at the blood brain barrier increase conversion of ammonia into glutamine. By this mechanism increase amount of tyrosine, phenylalanine and tryptophan into CNS affecting many neurotransmitters dopamine, nor epinephrine and serotonin.[10] Many toxic chemicals are produced by enteric flora increase the neurotoxic effect of ammonia. These are mercaptans, phenols, oxindole and short chain fatty acids. Oxindole cause sedation, coma, hypotension and muscular weakness.[11] Oral neomycin is effective. Neurological features are altered sleep pattern, bradykinesia, asterixis, hperreflexia and

decrebrate posturing . 80% patients improve with lactulose and lactitol treatment.[12] Ammonia level lowered by Rifaximin, neomycin, paromomycin and metronidazole, improve quality of life and recurrence rate are decreased of OHE.[13] Hospital stay is decreased, rifaximin improve psychomotor abnormality. Use of probiotics improve Hepatic Encephalopathy and decrease ammonia level,[14] Administration of branched chain amino acids shown mixed mixed results, treatment recommended in protein intolerant patients.[15] Liver transplantation advised for fulminant or subfulminant liver failure, improve Hepatic Encephalopathy with cirrhosis. Flumazenil is effective for Hepatic Encephalopathy.[16]

MATERIALS AND METHODS

This study was conducted in department of medicine at PMCH Nawabshah from January 2016 to December 2016. Both males and females were selected for this study, informed consent was taken from all relatives of patients and conscious patients. Study was done using Questionnaires translated into local languages Urdu and Sindhi. Detailed history was taken including dietary history, melana, hemetemesis and constipation. History of herbal medicine, fever and previous history of admission in the hospital. Clinical examination including general physical examination and examination of abdomen to see jaundice, spleen liver size and ascites. Routine investigations and specific investigations were done including blood CP, serum electrolyte, urea, creatinine, LFT, PT, HBsAg and anti HCV. U/S was done to assess hepatomegaly , shrinkage in size of liver, spleenomegaly and ascites. X-ray chest was done to see pleural effusion. Treatment given with rifaximin, lactulose, branched chain amino acids and K, Na replacement.

Inclusion Criteria: Coma due to CLD
HBsAg positive
Anti HCV positive

Exclusion criteria: Coma due to any other cause
HBsAg negative
Anti HCV negative

RESULTS

Hundred patients were selected for this study, 53 were males 47 were females, antHCV positive in 72 patients, HBsAg positive in 10 patients. HBV and anti HCV positive in 18 patients. Decreased potassium level in 30 patients, decreased sodium level in 20 patients, history of malena 8 patients, hematemesis in 7 patients, constipation in 60 patients, fever in 26 patients, serum urea creatinine raised in 8 patients, serum bilirubin raised in 10 patients and SGPT raised in 87 patients. Hb% 6-8 in30 patients,9-10 in 60 patients, 11-12 in 10 patients. Leukocyte count raised in 60 patients and PT raised in 94 patients. 6 patients were in grade 1, 17 patients in grade 2, 56 patients in grade 3 and 21 patients in grade 4.

Table No.1: Age

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	26.00	1	1.0	1.0	1.0
	32.00	1	1.0	1.0	2.0
	38.00	3	3.0	3.0	5.0
	39.00	3	3.0	3.0	8.0
	40.00	2	2.0	2.0	10.0
	41.00	3	3.0	3.0	13.0
	42.00	4	4.0	4.0	17.0
	43.00	2	2.0	2.0	19.0
	44.00	5	5.0	5.0	24.0
	45.00	8	8.0	8.0	32.0
	46.00	8	8.0	8.0	40.0
	47.00	10	10.0	10.0	50.0
	48.00	10	10.0	10.0	60.0
	49.00	8	8.0	8.0	68.0
	50.00	6	6.0	6.0	74.0
	51.00	4	4.0	4.0	78.0
	52.00	3	3.0	3.0	81.0
	53.00	3	3.0	3.0	84.0
	54.00	2	2.0	2.0	86.0
	55.00	4	4.0	4.0	90.0
	56.00	2	2.0	2.0	92.0
	57.00	2	2.0	2.0	94.0
	58.00	2	2.0	2.0	96.0
	59.00	2	2.0	2.0	98.0
	60.00	2	2.0	2.0	100.0
	Total	100	100.0	100.0	

Table No.2: Grades of HE

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1.00	6	6.0	6.0	6.0
	2.00	17	17.0	17.0	23.0
	3.00	56	56.0	56.0	79.0
	4.00	21	21.0	21.0	100.0
	Total	100	100.0	100.0	

Table No.3: Prothrombin Time

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	12.00	5	5.0	5.0	5.0
	17.00	2	2.0	2.0	7.0
	18.00	2	2.0	2.0	9.0
	19.00	1	1.0	1.0	10.0
	20.00	2	2.0	2.0	12.0
	21.00	6	6.0	6.0	18.0
	22.00	9	9.0	9.0	27.0
	23.00	8	8.0	8.0	35.0
	24.00	8	8.0	8.0	43.0
	25.00	12	12.0	12.0	55.0
	26.00	8	8.0	8.0	63.0
	27.00	6	6.0	6.0	69.0
	28.00	9	9.0	9.0	78.0
	29.00	5	5.0	5.0	83.0
	30.00	6	6.0	6.0	89.0
	31.00	5	5.0	5.0	94.0
	32.00	2	2.0	2.0	96.0
	33.00	2	2.0	2.0	98.0
	34.00	2	2.0	2.0	100.0
	Total	100	100.0	100.0	

Table No.4: One way ANOVA

		Sum of Squares	Df	Mean Square	F	Sig.
Age	Between Groups	1026.381	3	342.127	13.772	.000
	Within Groups	2384.929	96	24.843		
	Total	3411.310	99			
Sex	Between Groups	.478	3	.159	.626	.600
	Within Groups	24.432	96	.254		
	Total	24.910	99			
Occupation	Between Groups	.478	3	.159	.626	.600
	Within Groups	24.432	96	.254		
	Total	24.910	99			
HCV	Between Groups	.637	3	.212	2.437	.069
	Within Groups	8.363	96	.087		
	Total	9.000	99			
HBV	Between Groups	11.188	3	3.729	5.155	.002
	Within Groups	69.452	96	.723		
	Total	80.640	99			
Bilirubin	Between Groups	36.131	3	12.044	2.391	.073
	Within Groups	483.645	96	5.038		
	Total	519.776	99			
SGPT	Between Groups	28205.432	3	9401.811	13.287	.000
	Within Groups	67929.318	96	707.597		
	Total	96134.750	99			
PT	Between Groups	955.433	3	318.478	23.016	.000
	Within Groups	1328.357	96	13.837		
	Total	2283.790	99			
Sodium	Between Groups	580.203	3	193.401	3.896	.011
	Within Groups	4765.507	96	49.641		
	Total	5345.710	99			
potasium	Between Groups	1.110	3	.370	2.126	.102
	Within Groups	16.706	96	.174		
	Total	17.816	99			
Hemoglobin	Between Groups	69.820	3	23.273	11.998	.000
	Within Groups	186.220	96	1.940		
	Total	256.040	99			
Urea	Between Groups	418.697	3	139.566	.333	.801
	Within Groups	40229.893	96	419.061		
	Total	40648.590	99			
Creatinine	Between Groups	.880	3	.293	.670	.572
	Within Groups	42.011	96	.438		
	Total	42.890	99			
L.count	Between Groups	74839447.863	3	24946482.621	27.779	.000
	Within Groups	86212043.137	96	898042.116		
	Total	161051491.000	99			

Out of 100 patients 81 patients recovered completely, 19 patients expired due to severity of the disease. In statical analysis HCV is denoted by 1, HBV by 2, male by 1, female by 2, farmer occupation by 1 and housewife by 2. Statical analysis was done using SPSS 15 version

DISCUSSION

In our study major cause of Hepatic Encphalopathy is CLD due to HCV and HBV, rarely due to alcohol or any other cause, as compared to western countries where alcohol is main cause of chronic liver disease.[17] Precipitating factor found commonly constipation, high

protein diet, esophageal varices and excessive diuretic use with electrolyte abnormality. Commonest cause of chronic hepatitis in our study are viral infections not treated properly with investigations and treatment. Preventive measures like hand washing for CLD proper cooked food and boiled water or purified water necessary.vaccination of HAV to non immune and HEV for CLD patients are necessary preventive measures to precipitate HE. Aavoidence of herbal medicines which are hepatotoxic and anti tuberculoses drugs can precipitate HE. High mortality rate observed with MELD score more than 27 a study done in western india.[18] With concomitant renal failure mortality increased.[19] Electrolyte imbalance with diuretic use or diarrhea vomiting causes low sodium and low potassium death ratio increased.[20] Increase ammonia level and various other inflammatory cytokines cause increase in glutamine within astrocytes and swelling of astrocytes causes brain edema and neurotoxic effect.[21] Increase in white matter of brain in HE is due to astrocytes swelling during progress of disease, decreased gray matter volume detorioted with HE progression. These are reported in CT and MRI studies.[22] Increased in thalamus has been observed in patients with OHE. All information from cortex through striato-pallidal system to thalamus, filter for sensory in puts. Basal ganglia dysfunction leads to disinhibition of thalamus and results neurocognitive dysfunctions. Portal flow steal is important factor in the development of HE in cirrhotic patients. Ammonia level is dependent on portal blood flow . There are trials of lactulose for maintenance of remission from OHE.[22] Lactulose as prevention of HE with upper GI bleeding is helpful[23] in another study lactulose can prevent first episode of OHE.[24] Liver transplantation is best option for treatment of HE with its risks.[25] Control of precipitating factors in the treatment of OHE is important majority of patients treatment is correction of the precipitating factors.[26] Rifaximin with lactulose is excellent to maintain improvement with OHE.[27] BCAA improve HE either OHE or MHE.[28] Treatment of OHE include treatment of of underlying cause, supportive measures and specific treatment. All patients of overt HE should be given prophylactic treatment to reduce recurrence.[29]

CONCLUSION

Prevention of precipitating factors and use of lactulose with rifaxamixin risk of HE can be reduced, patients quality of life can be improved. In our study main cause of HE with CLD is HCV and HBV, early diagnosis and treatment mortality rate can be reduced. Avoidence of high protein diet, avoidance of animal protein and use of vegetable protein risk of HE can be reduced. Maintenance of nutrition, supportive measures and specific treatment HE canbe prevented. All patients of OHE should be given prophylactic treatment to reduce recurrence. By appropriate treatment we can reduce hospital admission and risk of further readmission. To get maximum benefit from treatment early diagnosis and treatment are essential.

Author's Contribution:

Concept & Design of Study:	Jeando Khan Daidano
Drafting:	Jeando Khan Daidano & Akbar Yousfani
Data Analysis:	Akbar Yousfani
Revisiting Critically:	Rafique Ahmed Memon & Saeed Khan
Final Approval of version:	Jeando Khan Daidano

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