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A Study on Incidence of Minimal Hepatic Encephalopathy in Chronic Liver Disease Patients by Psychometric Methods

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Abstract: ***The quiet yet devastating effects of Minimal Hepatic Encephalopathy (MHE) have been long overlooked in the clinical management of cirrhotic patients. This study takes a closer, data-backed look at how MHE, though subtle in presentation, deeply affects cognitive functions such as attention, psychomotor speed, and visuo-spatial coordination. By using the Psychometric Hepatic Encephalopathy Score (PHES)-a straightforward paper-and-pencil battery of tests-researchers evaluated 100 cirrhotic patients and 100 healthy controls, drawing attention to the cognitive discrepancies that routine neurological exams often miss. What stands out here is the clear association between lower PHES scores (particularly below-6, as per Indian standardization), elevated MELD-Na values, and higher CTP classifications-especially Class C-indicating more severe liver dysfunction. Although factors like age, gender, etiology, or ascites didn't significantly predict MHE, elevated SGPT levels and poor PHES performance were telltale signs. This suggests that the psychometric decline precedes visible clinical deterioration. It is evident that MHE is not just a precursor to overt hepatic encephalopathy, but a standalone concern that affects quality of life, work ability, and even road safety. What this study compellingly argues is not merely the prevalence of MHE-reported here at 28%-but the urgent need for its early detection using accessible tools like PHES, especially in resource-constrained settings. In sum, this isn't just a clinical checklist-it's a call to action to prioritize subtle cognitive health in liver disease care.***

Keywords: Minimal hepatic encephalopathy, PHES testing, cirrhosis, cognitive impairment, liver disease screening

1. Introduction

Hepatic encephalopathy (HE) is defined as "a condition which reflects a spectrum of neuropsychiatric abnormalities seen in patients with liver dysfunction after exclusion of other known brain diseases".

Hepatic encephalopathy present in 30% to70% of cirrhosis patients. Symptoms and signs of HE may range from mild neurocognitive disturbances to coma. HE is a poor prognostic indicator with low 1 year and 3-year survival rates of 42% and 23% respectively.

According to SONIC classification cirrhotic patients are classified as Unimpaired, Covert HE and Overt HE

Unimpaired patients are normal on clinical examination and show normal neuropsychometric and neurophysiological test results.

Covert HE includes minimal hepatic encephalopathy (MHE) and grade1 hepatic encephalopathy.

MHE patients are clinically normal but shows abnormal neuropsychometric and neurophysiological test results.

Overt HE includes grade2-grade4 HE according to WESTHEAVEN Criteria.

Minimal hepaticencephalopathy

MHE prevalence in chronic liver disease patients is 22-74%.

Cirrhotic patients appear clinically normal and having abnormalities on specialized neuropsychometric or neurophysiological tests called Minimal hepatic encephalopathy.

MHE patients have abnormalities in:

- Areas of attention
- Executive function
- Visuo-spatial coordination
- Psychomotor speed and
- Reaction time.

MHE patients exhibit severe impairment in psychosocial aspects of social interaction, alertness and emotional behavior. MHE also affects sleep, work, driving ability, home management and health related quality of life. MHE predicts the development of overt HE and it is a predictor of death and hospitalization independent of MELD score. Even though the impact of MHE in cirrhotic patients is high, testing for MHE is not routinely done and remain untreated because of lack of standardization, simple tools, expertise to administer tests.

MHE is not detected by routine physical or neurological examinations and specific psychometric test is needed for diagnosis of MHE.

PSYCHOMETRIC TEST includes:

- Paper and pencil test
- Computerized test
- Neurophysiological test.

PAPER AND PENCIL TEST includes:

- NCT-A: Number connection test A

- NCT-B: Number connection test B
- LTT: Line Tracing Test
- SDT: Serial Dotting Test
- DST: Digit Symbol Test

With the help of paper and pencil battery test we can calculate the PHES (psychometric hepatic encephalopathy score) and the score ranges from 6 to-18.

According to Indian standardization values PHES score <-6 considered as MHE positive.

Early diagnosis of MHE and initiation of treatment improves Health related quality of life and prevents progression to OHE and improves survival.

This study aims to determine the incidence of minimal hepatic encephalopathy in cirrhotic patients with psychometric test i. e. paper and pencil battery test with PHES score, which is gold standard, simple bed side test which can be used in resource constraints areas where EEG is not available and helps in improving patients health related quality of life, driving ability and decrease development of overt HE.

2. Methods and Material

The study was done in Department of Gastroenterology, Government General Hospital, Kurnool medical college Kurnool, Andhra Pradesh.

Study participants include healthy volunteer controls who visited gastroenterology OPD and cases are those patients who were admitted in gastroenterology ward for a period of two years

With a sample size of 100 controls and100 cases

Inclusion criteria:
- Patients above 18 years age
- Chronic liver disease patients who were diagnosed as cirrhosis on the basis of clinical examination, laboratory test, imaging and endoscopy evidence or liver histology

Exclusion criteria:
- History of overt hepatic encephalopathy
- Presence of neurological or psychiatric disorders or MMSE<25 Alcohol consumption >50 gm/day within past 3 months
- Inability to read or write.
- Unable to complete the psychometric test.

Methodology
All controls who are normal or not having liver disease with MMSE>25 is allowed to participate in study. All controls are subjected to PHES battery paper and pencil tests which includes NCT-A, NCT-B, LTT, Errors, DST, SDT and each test results are calculated as mean values and standard deviation. All cases who fulfill the inclusion criteria were included in the study.

Blood samples for liver biochemistry, renal function test, complete blood picture, ultrasound abdomen, ascitic fluid analysis, upper gastrointestinal endoscopy, serum electrolytes were sent and values are obtained and CTP scores and MELD-Na score was calculated.

After initial demonstration, cases are subjected to PHES paper and pencil psychometric test under bright light and in quite room. Patients are allowed to perform NCT-A, NCT-B, LTT, Errors, DST, SDT test and test completion is noted in time duration i. e in seconds.

Each Test result of cirrhotic patients are compared with controls with same age and education level. Test results of each test (NCT-A, NCT-B, LTT, Errors, DST, LTT) found between mean+_1Standard deviation were assigned score of 0. If test result found in between+1 and+ 2 SD then-1 score and if found between +2and+3 SD score of-2 and if test result >+3 SD score of-3 points given and if test result with mean less than-1 SD score of +1points given.

Then total PHES score was calculated. In Indian standardization PHES score <-6 is considered as minimal hepatic encephalopathy.

Statistical analysis:
For data analysis SPSS 22 version software was used and then data entered into Microsoft EXCEL. Data was analysed and expressed as categorical variables and calculated mean and standard deviation and Chi square test, Paired t test and Student t test wherever needed and p value calculated.

3. Results

The study enrolled 100 healthy volunteer controls and 100 cases of cirrhosis diagnosed based on clinical examination, laboratory test, imaging. All cases and controls subjected to pencil and paper psychometric test

Table 1: Distribution of age among cases and control

	Controls (N=100)		Cases (N=100)		Mean Difference	95% Confidence Interval	t – value (P Value)
	No. of Patients	%	No. of Patients	%			
19-20 Years	28	28	7	7	4.87	1.83-7.90	3.184** (0.000)
30-39 Years	29	29	33	33			
40-49 Years	24	25	35	35			
50-60 Years	29	29	25	25			
Total	100	100	100	100			
Mean Age	37.29±11.35		42.16±8.79				

Mean age of controls is 37.29±11.35 is lower than mean age of cases is 42.16±8.79 and p value is <0.05 which shows significant difference in age groups between controls and cases.

Table 2: Distribution of PHES test values among cases and controls

TEST	N	Cases (Mean ± SD)	Control (Mean ± SD)	Mean Difference	95% Confidence Interval	t-value (P Value)
NCT-A	100	82.89±18.70	63.28±18.14	19.610	13.57-25.649	6.443** (0.000)
NCT-B	100	180.17± 54.90	125.44± 40.43	54.730	40.59-68.87	7.680** (0.00)
LTT	100	181.00±42.983	141.37± 32.114	39.630	29.229-50.031	7.561** (0.00)
DST	100	275.09± 76.938	197.27± 43.068	77.820	59.146 – 96.494	8.269** (0.00)
SDT	100	88.55 ± 26.039	70.71± 13.567	17.840	11.641 – 24.039	5.710** (0.000

NCT-A NCT-B LTT DST SDT mean values in cases are significantly higher than controls which shows significant difference cases and controls with P value <0.05.

Table 3: Table showing Biochemical variables

Variables	Mean and SD (Cases n=100)
Serum creatinine	1.476±0.814
HB	8.082±1.732
TB	3.505± 2.121
SGPT	42.120± 22.890
SGOT	55.670± 51.507
ALP	92.660±22.824
S. Alb	2.473±0.515
INR	1.777±1.565
MELD-Na	22.580± 5.429
CTPCLASS:	
Class-A	6 (6%)
Class-B	38 (38%)
Class-C	56 (56%

Hb-haemoglobin; TB-Total bilirubin, SGPT-alanine transaminase, SGOT-aspartate transaminase, ALP-alkaline phosphatase, S. ALB-albumin-prothrombin time, INR-International Normalised ratio, MELD Na-Model for end stage liver disease, CTP-Child pugh Turcotte score

Table 4: Distribution of subjects according to age

Age	Cirrhosis patients (n=100)						Chi-square
	No MHE (n=72)		MHE (n=28)		Total		
	No. of Patients	%	No. of Patients	%	No. of Patients	%	
Below 25 Years	3	4.2	0	0	3	3	$\chi2$=1.788[at]; (p=0.775); df= 4;
26-35Years	16	22.2	6	21.4	22	22	
36-45Years	29	40.3	10	35.7	39	39	
46-55Years	20	27.8	10	35.7	30	30	
>55Years	4	5.6	2	7.1	6	6	
Total	72	100	28	100	100	100	
Mean Age	41.42±8.91		44.07±8.32		42.16±8.79		

The mean age of patients in No MHE (41.42 ± 8.91 years) was slightly lower than those with MHE (44.07 ± 8.32 years). Chi-square test did not show significant association between age and the occurrence of MHE (χ^2 = 1.788, p= 0.775).

Table 5: Distribution of subjects according to sex

Gender	Cirrhosis patients (n=100)					
	No MHE (n=72)		MHE (n=28)		Total	
	No. of Patients	%	No. of Patient s	%	No. of Patients	%
Male	62	86.1	25	89.3	87	87
Female	10	13.9	3	10.7	13	13
Total	72	100	28	100	100	100
Chi-square	$\chi2$=0.180[at]; (p=0.672); df= 1;					

Gender distribution showed male predominance in both groups, with 89.3% of MHE patients being male, compared to 86.1% in the non-MHE group.

3.9% females in No MHE group and10.7% in MHE group.

Difference was not statistically significant (χ^2=0.180, p=0.672).

Table6: Distribution of subjects according to ETIOLOGY

Etiology	Cirrhosis patients (n=100)						Chi-square
	No MHE (n=72)		MHE (n=28)		Total		
	No. of Patients	%	No. of Patients	%	No. of Patients	%	
Alcohol	47	65.3	18	64.3	65	65.0	$\chi2 = 1.807$[at]; (p = 0.875); df= 5;
HCV	2	2.8	0	.0	2	2.0	
Cryptogenic	4	5.6	1	3.6	5	5.0	
HBV	13	18.1	6	21.4	19	19.0	
NASH	5	6.9	3	10.7	8	8.0	
Wilson	1	1.4	0	.0	1	1.0	
Total	72	100.0	28	100.0	100	100.0	

In both groups (65% in the non-MHE group and 64.3% in the MHE group), followed by HBV infection HBV 18.1% vs 21% in No MHE and MHE group respectively. The chi-square test results ($\chi^2 = 1.807$, p = 0.875) suggests No significant difference in incidence of MHE with respect to etiology.

Table 7: Distribution of subjects according to Ascites

ASCITES	Cirrhosis patients (n=100)						Chi-square
	No MHE (n=72)		MHE (n=28)		Total		
	No. of Patients	%	No. of Patients	%	No. of Patients	%	
No	7	9.7	2	7.1	9	9.0	$\chi2 = 1.139$[at]; (p =0.768); df= 3;
GradeI	10	13.9	2	7.1	12	12.0	
Grade II	21	29.2	9	32.1	30	30.0	
Grade III	34	47.2	15	53.6	49	49.0	
Total	72	100.0	28	100.0	100	100.0	

Grade 3 ascites present in 53.6% of MHE group vs 47% in no MHE group No ascites is present in 7 % of MHE patients. Presence of ascites and grades of ascites does not have significant difference between two groups Chi-square $\chi2 = 1.139$ (p = 0.768)

Table 8: Distribution of subjects according to SBP

SBP	Cirrhosis patients (n=100)					
	No MHE (n=72)		MHE (n=28)		Total	
	No. of Patients	%	No. of Patients	%	No. of Patients	%
Yes	14	19.4	7	25.0	21	21.0
No	58	80.6	21	75.0	79	79.0
Total	72	100.0	28	100.0	100	100.0
Chi-Square	$\chi2=0.375$[at]; (p=0.540); df= 1;					

SBP incidence is slightly higher in MHE group (25%) than in noMHE group (19.4%) but no significant difference the two groups with regarding to SBP $\chi2 = 0.375$ (p = 0.540)

Table 9: Distribution of creatinine values between two groups

	Group	N	Mean ± S. D	Std. Error Mean	t – value (p-value)
Serum creatinine	MHE	28	1.72± 0.948	.179	1.906 [at] (0.060)
	No MHE	72	1.38± 0.740	.087	

Mean Serum creatinine value is slightly higher in MHE patients than in patients without MHE No statistical significance is seen between the two groups P value (0.060)

Table 10: Distribution of subjects according to varices

Varices	Cirrhosis patients (n=100)						Chi-square
	No MHE (n=72)		MHE (n=28)		Total		
	No. of Patients	%	No. of Patients	%	No. of Patients	%	
No	12	16.7	6	21.4	18	18.0	$\chi2= 3.471$[at]; (p= 0.325); df= 3;
Grade I	17	23.6	4	14.3	21	21.0	
Grade II	15	20.8	10	35.7	25	25.0	
Grade III	28	38.9	8	28.6	36	36.0	
Total	72	100.0	28	100.0	100	100.0	

Distribution of varices showed no significant difference between the groups, despite a trend toward higher grades of varices in the MHE group (Grade II in 35.7% of MHE patients vs.20.8% in non-MHE patients) (p = 0.325)

Table 11: Distribution of subjects according to UGI bleed

UGI Bleed	Cirrhosis patients (n=100)					
	No MHE (n=72)		MHE (n=28)		Total	
	No. of Patients	%	No. of Patients	%	No. of Patients	%
Yes	27	37.5	9	32.1	36	36.0
No	45	62.5	19	67.9	64	64.0
Total	72	100.0	28	100.0	100	100.0
Chi-square	$\chi2$=0.251[at]; (p=0.616); df= 1;					

UGI bleed present in 36% of MHE patients vs37.5% of patients without MHE group and not significant between the two groups Chi-square $\chi2$= 0.251, (p= 0.616)

Table12: Biochemical variables between two groups

		N	Mean ±S. D	S. E	Mean Difference	t – value (p-value)
HB	MHE	28	7.91±1.59	0.30	0.23	0.602 (0.549)
	No MHE	72	8.15±1.79	0.21		
TB	MHE	28	3.88±1.39	0.26	-0.52	1.099 (0.274)
	No MHE	72	3.36±2.34	0.28		
DB	MHE	28	2.70±1.18	0.22	-0.49	1.557 (0.123)
	No MHE	72	2.21±1.48	0.17		
SGPT	MHE	28	52.79±25.43	4.81	-14.81	3.023** (0.003)
	No MHE	72	37.97±20.55	2.42		
SGOT	MHE	28	58.93±24.10	4.56	-4.53	0.393 (0.695)
	No MHE	72	54.40±58.93	6.94		
ALP	MHE	28	91.29±30.12	5.69	1.91	0.374 (0.709)
	No MHE	72	93.19±19.50	2.30		
S. ALB	MHE	28	2.37±0.42	0.08	0.15	1.277 (0.205)
	No MHE	72	2.51±0.54	0.06		
PT	MHE	28	20.93±3.54	0.67	-0.64	0.915 (0.362)
	No MHE	72	20.29±2.95	0.35		
INR	MHE	28	2.26±3.10	0.59	-0.44	0.881 (0.380)
	No MHE	72	1.82±1.83	0.22		
MELD-Na	MHE	28	25.61±4.78	0.90	-4.20	3.692** (0.000)
	No MHE	72	21.40±5.23	0.62		

Hb-haemoglobin; TB-Total bilirubin, DB-Direct bilirubin, SGPT-alanine transaminase, SGOT-aspartate transaminase, ALP-alkaline phosphatase, S. ALB-albumin-prothrombin time, INR-International Normalised ratio, MELD Na-Model for end stage liver disease.

Haemoglobin, Total bilirubin, SGOT, ALP, Albumin, INR values are not statistically significant difference between the MHE and No MHE groups

SGPT is significantly higher in MHE group 52.79 ± 25.43and 37.97 ± 20.55patients without MHE group (p <0.003)

MELD-Na score was significantly higher in the MHE group (25.61 ± 4.78 vs.21.40 ± 5.23, p < 0.001

Table13: Distribution of subjects according to CTP class

CTP Class	Cirrhosis patients (n=100)						Chi-square
	No MHE (n=72)		MHE (n=28)		Total		
	No. of Patients	%	No. of Patients	%	No. of Patients	%	
A	5	6.9	1	3.6	6	6.0	$\chi2$= 10.884**; (p= 0.004); df= 2;
B	34	47.2	4	14.3	38	38.0	
C	33	45.8	23	82.1	56	56.0	
Total	72	100.0	28	100.0	100	100.0	

82% of MHE patients belongs to CTP class C when compared to 33% of patients without MHE which shows significant between the two groups (p = 0.004)

Table14: Distribution of PHES tests among MHE and No MHE groups

	Group	N	Mean ± S. D	S. E Mean	Mean Difference	t – value (p-value)
NCTA	MHE	28	104.14 ±18.487	3.494	-29.52	10.052** (0.000)
	No MHE	72	74.63 ±10.487	1.236		
Score 1	MHE	28	-2.04±.793	.150	1.97	12.665** (0.000)
	No MHE	72	-.07±.657	.077		
NCTB	MHE	28	224.79 ±66.847	12.633	-61.97	5.860** (0.000)
	No MHE	72	162.82 ±37.580	4.429		
Score 2	MHE	28	-1.64± 1.283	.242	1.12	4.806** (0.000)
	No MHE	72	-.53±.934	.110		
LTT	MHE	28	220.79 ±49.155	9.289	-55.26	7.051** (0.000)

	No MHE	72	165.53 ±28.112	3.313		
Score 3	MHE	28	-1.82± 1.278	.242	1.61	7.171** (0.000)
	No MHE	72	-.21±.887	.105		
Errors	MHE	28	40.32 ±29.133	5.506	-10.15	2.711** (0.008)
	No MHE	72	30.17±8.217	.968		
Score 4	MHE	28	-.46±1.071	.202	0.28	1.490[at](0.139)
	No MHE	72	-.18±.757	.089		
DST	MHE	28	375.11 ±64.260	12.144	-138.91	13.911** (0.000)
	No MHE	72	236.19 ±34.704	4.090		
Score5	MHE	28	-2.82±.476	.090	2.11	11.309** (0.000)
	No MHE	72	-.71±.941	.111		
SDT	MHE	28	113.29 ±32.950	6.227	-34.36	7.336** (0.000)
	NoMHE	72	78.93 ±14.052	1.656		
Score 6	MHE	28	-2.04± 1.170	.221	1.84	8.342** (0.000)
	NoMHE	72	-.19±.914	.108		
PHES	MHE	28	-10.82 ±3.031	.573	9.03	17.052** (0.000)
	NoMHE	72	-1.79± 2.076	.245		

Table 15: Distribution of Mean values of PHES tests among No MHE and MHE groups

Test	NOMHE group Mean ± S. D	MHE group Mean ± S. D	Mean Difference	P value
NCTA	74.63±10.487	104.14 ±18.487	-29.52	(0.000)
NCTB	162.82 ±37.580	224.79 ±66.847	-61.97	(0.000)
LTT	165.53 ±28.112	220.79 ±49.155	-55.26	(0.000)
Errors	30.17±8.217	40.32±29.133	-10.15	(0.008)
DST	236.19 ±34.704	375.11 ±64.260	-138.91	(0.000)
SDT	78.93±14.052	113.29 ±32.950	-34.36	(0.000)
PHES	-1.79± 2.076	-10.82±3.031	9.03	(0.000)

NCT A: Number connection test A, NCT-B: Number connection test B, LTT: Line Tracing Test, DST: Digit Symbol Test, SDT: Serial Dot Test, PHES: Psychometric hepatic encephalopathy score
NCT A, NCT-B, LTT, DST, SDT all these tests show significant difference between MHE and no MHE group (p value <0.005)

Mean values of total PHES have significant difference in MHE and No MHE group (-10.82 ± 3.031score in MHE when compared with-1.79 ± 2.076 score in No MHE group, p value <0.005)

Table 16: Distribution of mortality between two groups

Mortality	Cirrhosis patients (n=100)						Chi-square
	No MHE (n=72)		MHE (n=28)		Total		
	No. of Patients	%	No. of Patients	%	No. of Patients	%	
Expired	15	20.8	7	25.0	22	22.0	$\chi 2 = 0.204$[at];
Recovered	57	79.2	21	75.0	78	78.0	
Total	72	100.0	28	100.0	100	100.0	(p=0.652); df=1

Mortality rates did not significantly differ between the two groups (χ^2=0.204, p= 0.652), with 25% of MHE patients and 20.8% of non-MHE patients died.

4. Discussion

Routinely cirrhotic patients are not screened for MHE and remain untreated because of lack of standardization, simple tools, expertise to administer tests. MHE is not detected by routine physical or neurological examinations so it is difficult to diagnose and specific psychometric test is needed for MHE diagnosis. PHES is a neuro-psychometric test which is a gold standard test for the MHE diagnosis. It is very simple and easily performed in an outpatient setting. PHES values are normalized and standardized according to age and education levels in each country and values normally ranges from +6 to-18. In India PHES values <-6 are diagnostic for minimal hepatic encephalopathy whereas in Germany PHES score <-4 and in Thai population PHES score <-3 considered as diagnostic of MHE.

In our study PHES score <-6 were considered as MHE positive. PHES values will decrease with age and less educational years. According to Weissen born K et. al, PHES test sensitivity was 96%andthe specificity was 100% for diagnosing HE.

According to EASL/AASLD combining PHES with other test ICT (Inhibitory control test) CFF (critical flicker frequency test) which are computer based test, improves MHE detection rate.

Age and Gender Distribution

In our study 100 controls were taken and 100 cases of cirrhosis were taken Mean age of controls were 37.29 ± 11.35 years and Mean age of cases is 42.16 ± 8.79 years which is statistically significant with p value<0.05. Among cases the mean age of patients without MHE (41.42±8.91years) was slightly lower than those with MHE (44.07±8.32years). However, the chi-square test did not indicate a significant association between age and the occurrence of MHE (χ^2=1.788, p = 0.775).

In Dhiman et al[1] study included 104 patients with mean age of cirrhosis is 48.44 years, mean age of cirrhotics with MHE is 50.98years and mean age in without MHE 45.46years. Dhiman et al not considered age as a demographic variable. Larissa Pessidjo et al which is a Cameroonian population study showed that mean age in volunteers was 38.1±12.55years and mean age in cirrhotic patients was 49.3±15.6years, which shows age is a significant variable, which correlates with our study. Our study consists of 72 males (72%), 28 females (28%) in control group and 87 males (87%) 13 (13%) females as cases were included. Among these 25 males (89%) and 3 females (10.7%) have MHE. In Dhiman et al[1] study done for detection of MHE with PHES and critical flicker frequency test included 104 cirrhotic patients in which 83 were males and 21 were females.48 patients found to have MHE out of which 38 (86%) were males and 10 (20%) were females. Our study correlates with Dhiman et al regarding the gender demographics. Larissa Pessidjo Djomatcho et al which is a Cameroonian population study included 54 males (52.90%), 48 females (48.10%) in controls and in cirrhosis group 29 males (58%) and 21 (42%) females were included. Similar to our study this study does not show any significance between gender groups. Incidence of MHE in our study is 28% (28 cirrhotic patients were MHE positive out of 100 cirrhosis patients). Prevalence of MHE in Dhiman et al study is 48% (48 patients positive for MHE). Forty-eight patients had minimal hepatic encephalopathy as indicated by altered psychometric hepatic encephalopathy score (PHES). Yu-Yuan Li et al with the help of NCT and SDT battery psychometric test MHE was found in 50.9% of cirrhotic patients. In Thai study incidence of MHE in cirrhosis is 27% with PHES psychometric test. This incidence is similar to our study.

In seoys et al study the incidence of MHE is 25.6% (41 patients positive for MHE) by performing PHES test. The incidence in this study is similar to our study. In Su Wenli et al study the incidence of MHE is 49.1% (26 patients MHE positive) by performing PHES test.

Gomez et al study showed 53% (34 patients MHE positive out of 63) prevalence of MHE based on NCT test and evoked potentials. MHE prevalence in chronic liver diseases is estimated at 30–80% (44). MHE is prevalent in up to 80% of cirrhotic patients[2, 3, 4, 5].

Reason for wide range of prevalence of MHE in cirrhotic patients is lack of standardized research methods and the specificity of the studied populations. Prevalence of MHE among different studies are due to prior episodes of overt HE[6] severity of liver disease[7, 8, 9, 10] age, presence of oesophageal varices[6] and surgical porto-systemic shunts. Depending on both the examinable dimensions of the disease and fixed diagnostic cut-offs prevalence of MHE vary between 22% and 74% in patients with liver cirrhosis[7.11, 12].

Etiology

In our study out of 100 cases the most common etiology is alcohol cirrhosis 65% (65 patients) followed by HBV cirrhosis 19% (19 patients) followed by NASH 8% (8 patients). Alcohol consumption was the leading cause of liver disease in both groups (65% in the non MHE group and 64.3% in the MHE group), followed by HBV infection. The chi-square test results (χ^2=1.807, p=0.875) suggest no significant difference between the two groups concerning etiology. This implies that while alcohol and HBV are common risk factors for liver diseases, they may not directly influence the development of MHE.

In Dhiman et al study 49% (51patients) belongs to alcohol cirrhosis etiology followed by HBV 11.5% (12 patients).43.7% (21) patients with alcoholic cirrhosis are MHE positive.

In Bajaj et al study33% (45 patients) belongs to HCV etiology followed by 14% (19) patients belongs to alcohol. Incidence of psychometric alterations in alcoholics were same with other etiology. Our study does not show any statistical significant difference between etiology and incidence of MHE and this correlates well with studies of Dhiman et al and Bajaj et al which also showed etiology of cirrhosis is not significant with incidence of MHE.

Biochemical Variables

In our study univariant variables analysis like serum creatinine, total bilirubin (TB), SGOT, ALP, Serum Albumin, INR, Hemoglobin doesn't show any significant difference between cirrhosis with MHE and without MHE. Among the biochemical markers, serum creatinine levels were higher in the MHE group (1.72±0.948) compared to the non-MHE group (1.38±0.740), approaching statistical significance (p = 0.060). Liver enzymes such as SGPT and SGOT were elevated in both groups, with a significant difference in SGPT levels between MHE and non-MHE patients (p=0.003). This may be due to more number of complications and severity of liver disease (CTP, MELD Na) in the MHE group. But This should be validated with large sample studies for further confirmation.

Larissa Pessidjo Djomatcho et al study also showed univariant variables analysis like serum creatinine, total bilirubin (TB), SGOT, SGPT, ALP, Serum Albumin, INR, Hemoglobin doesn't show any significant difference between cirrhosis with MHE and without MHE.

Dhiman et al study showed that bilirubin is significantly higher in MHE patients and considered as prognostic marker. Remaining variables like SGPT, SGOT, SGPT, ALP, Serum Albumin, INR, Hemoglobin doesn't show any significant difference between MHE and without MHE group.

Clinical Variables (Ascites, Varices)

In our study, a larger proportion of patients with MHE had more severe grades of ascites, with 53.6% having Grade III ascites compared to 47.2% in the non-MHE group. However this difference was not statistically significant (χ^2=1.139, p=0.768). Similarly, the distribution of varices showed no significant difference between the groups, despite a trend toward higher grades of varices in the MHE group (GradeII in 35.7% of MHE patients vs.20.8% in non-MHE patients). This suggests that while these complications are more common in MHE patients, they are not significantly different enough to be predictive markers for MHE.

Our study correlates with Ananya das et al study which also showed that ascites and SBP doesn't have any significance

difference between MHE and without MHE patients.

GoenewegMetalstudyshowedpresenceofoesophagealvarices willhaveaneffect on prevalence of MHE but in our study we did not find any difference in incidence of MHE with relation to esophageal varices.

CTP Scores and MHE:
Our study shows correlation between incidence of MHE and severity of liver disease.82% (23) patients belongs to CTP class C are MHE positive which shows that severity of liver disease correlates with incidence of MHE.14% (4) patients belongs to CTP class B are MHE positive and our study also shows that incidence of MHE is less (3.6%) in patients with CTP class A which clearly shows that incidence of MHE have a significant association with severity of liver disease.

Dhiman et al study showed 8 (36.4%) of 22 patients with CTP class A cirrhosis, 27 (45%) of 60 patients with CTP class B and 13 (72.2%) of 18 patients with CTP class C had MHE which shows incidence of MHE is more in CTP class C which correlates with our study. Same study showed that CTP score >8 is a poor prognostic factor in MHE patients.

Das et al study also showed that MHE patients with CTP score >6 develop overt HE in 26.3% patients vs 2.9% with CTP score <6 during follow up. This study shows that risk of progression to overt HE is more common with severity of liver disease.

In Yen et al study risk of progression to overt HE increases with increase in CTP scores.72% of MHE patients developed Overt HE at 6 months of follow up period.

Gitlin *et al* [13] and Sood *et al* [14] did not find any significant correlation between the liver disease severity (CTP score) and the extent of psychometric test impairment. Overall literature shows that MHE incidence and risk of progression to Overt MHE increases with liver disease severity.

MELD Na and MHE:
MELD-Na score, an important marker of liver function, was significantly higher in the MHE group (25.61 ±4.78 vs.21.40 ±5.23, $p < 0.001$). These findings suggest that MELD-Na could be potential predictor of MHE development in patients with liver disease.

Hirano Het al[15] and NabiE et al[16] studies showed that higher MELD scores had significance with relation to MHE incidence and progression. Dhiman et al and das et al and Thai studies doesn't show any significant difference in incidence of MHE with relation to MELD scores.

Neurocognitive and Psychometric Test Scores (PHES)
Significant differences were observed in psychometric test scores between the two groups. The number connection test (NCT-A and NCT-B), LTT, DST, LTT score results, were substantially worse in MHE patients, with all comparisons yielding p-values < 0.01. This highlights the marked cognitive decline in MHE patients, reaffirming the importance of psychometric testing in detecting MHE in liver disease patients.

In our study among PHES battery test mean values of **NCT-A** test is 104.14 ±18.487s in MHE patient vs 74.63±10.487s in without MHE patients and mean values of**NCT-B** test is 224.79±66.847s in MHE patient vs162.82±37.580s in without MHE patients and mean values of **LTT** test is 220.79±49.155s in MHE patient vs 165.53± 28.112s in without MHE patients and mean values of **errors** is 40.32 ± 29.133s in MHE patient vs 30.17±8.217 in without MHE patients and mean values of **DST** test 375.11 ± 64.260s in MHE patient vs 236.19 ± 34.704s in without MHE patients and mean values of **SDT** test is 113.29 ± 32.950s in MHE patient vs 78.93 ± 14.052s in without MHE. All the above tests showed significant difference between MHE and without MHE patients.

With above tests PHES score calculated and compared with controls. A score <-6 is diagnosed as MHE positive. In MHE patients mean PHES score was-10.82 ±3.031 and in without MHE patients PHES score is-1.79±2.076 with P value<0.001 which is highly significant. So PHES score is a useful diagnostic test used to estimate the incidence of MHE in cirrhosis patients.

In Cameroon study by performing PHES tests: in cirrhotic group, mean values of NCT-A, NCT-B, SDT, DST, LTT test are 164.72±169.93s; 255.96±203.69s; 150.26±93.26s; 22.62±11.36 points; 183.03±134.54s. Mean PHES score was−7.66±5.62 (range−14to+3) and in volunteer group the mean PHES score was −0.08±1.28 and cut-off was set at −3 points between normal and pathological values. This score was significantly lower in cirrhotic patients. This study showed MHE prevalence as74% in cirrhotic patients. Similarly in Thai study with PHES test, mean values of NCT-A, NCT-B, LTT, DST, SDT calculated in cirrhosis group were 59.8±36.6s, 137.8±78.0s, 148.7±72.8, and 29.1± 12.7 points, 99.7 ± 50.9s respectively. The mean PHES score in cirrhosis patients was −2.6±3.1 points (median−2; range−14to4). The mean PHES in cirrhotics was significantly lower than in healthy subjects (p<0.001). Using a cut-off for MHE of ≤−5 points, 54 of 203 patients (26.6%) were diagnosed with MHE.

All these studies showed PHES test is a valuable diagnostic tool for detection of MHE patients in cirrhosis and is considered as gold standard.

Mortality and Clinical Outcome
Mortality rates did not significantly differ between the two groups ($\chi^2 = 0.204$, p =0.652), with 25% of MHE patients and 20.8% of non-MHE patients succumbing to their condition.

However, the high MELD-Na score in MHE patients points toward a worse overall prognosis despite the lack of statistical significance in mortality rates. This suggests that while MHE may not directly increase mortality, it reflects a more severe disease state that warrants closer monitoring and management.

5. Conclusions

Prevalence of MHE in common among cirrhosis patients so all cirrhotic patients should be screened for MHE. Prevalence of MHE vary among different studies due to lack of

standardisation of tests.

Age, gender, etiology, and clinical parameters like ascites, varices and biochemical parameters like total bilirubin, SGOT, ALP, Albumin, Haemoglobin, serum creatinine do not significantly differ between MHE and non-MHE groups. Biochemical markers such as SGPT levels and MELD Na and CTP score are key differentiators between MHE and non-MHE groups. Severity of liver disease CTP class C and high MELD Na scores correlates with increased incidence of MHE. Mortality rate is not vary in patients with MHE and without MHE patients and this mortality is not due to perse MHE but due to underlying complications of CLD. PHES score<-6is considered as MHE positive and PHES score is also independent predictor of prognosis in cirrhosis patients.

PHES test is simple neuropsychometric, reliable and gold standard test for diagnosis of MHE in cirrhosis patients where resources like EEG, MRI are not available. This test is simple and can perform in outpatient set up. The marked differences in cognitive function tests such as the NCT, LTT, and DST, highlight the need for regular screening of liver disease patients, even in the absence of overt hepatic encephalopathy (HE) symptoms. So all cirrhotic patients should be screened for MHE and if positive consider initiation of treatment. Early detection of MHE and initiation of treatment improves quality of life, driving ability and decrease the rate of progression to Overt HE and improves survival. These findings highlight the importance of early detection of MHE through psychometric testing (PHES) and monitoring of liver function to improve patient outcomes.

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