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PREVALENCE OF MINIMAL HEPATIC ENCEPHALOPATY IN CIRRHOTIC PATIENTS

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ABSTRACT

Aim: Psychometric hepatic encephalopathy score is considered as the simplest method for detection of minimal hepatic encephalopathy. This pilot study aims to assess the prevalence of minimal hepatic encephalopathy using PHES in patients with liver cirrhosis, thus provide appropriate treatment and to prevent its progression to overt hepatic encephalopathy**. Materials and methods:** Twelve patients with liver cirrhosis who met up with the inclusion and exclusion criteria were included in the study. All subjects underwent psychometric tests which include number connection test A and B (NCT-A), figure connection test A (FCT-A) line tracing test (LTT), serial dotting test(SDT), and digital symbol test(DST) in the same day. **Results:** Prevalence of MHE was found to be 50% which was detected with a psychometric hepatic encephalopathy score ≤ -5. Twelve patients with a mean age of 58.833±11.1667 completed all the five tests. 83.3% involved in the study were male respondents and 16.7% belongs to female population. The etiology for liver cirrhosis was found to be alcoholism (41.7%), hepatitis B (16.7%), hepatitis C (8.3%) and 33.3% due to primary sclerosing cholangitis, autoimmune hepatitis and steatohepatitis. Among subjects with MHE 62.5% belongs to CTP-B and 50% belongs to CTP-C. The mean PHES was found to be -5.41667±2.466441 points (median, -2; range, -2 to -10). **Conclusion:** MHE as undetectable mostly from any laboratory tests requires a validated diagnostic procedure but much more simple than critical flicker frequency inorder to be performed in an outpatient setting. This defines the importance of PHES in MHE detection. More studies need to be conducted on this topic as PHES has prognostic significance on survival of liver cirrhotic patients.

KEYWORDS: Psychometric hepatic encephalopathy score, Minimal hepatic encephalopathy, Liver cirrhosis.

INTRODUCTION

Minimal hepatic encephalopathy (MHE) reflects the mildest form of spectrum of hepatic encephalopathy (HE). Patients with MHE do not manifest any recognizable clinical symptoms of HE like behavioral abnormalities, altered level of consciousness, neuromuscular dysfunction etc. But MHE patients have mild cognitive and psychomotor deficits which may affect their reaction time, attention, coordination, vigilance, memory and fine motor abilities. MHE is concerned with negative health related quality of life (HRQOL), driving impairments which increases the risk of road/traffic accidents and also, it progresses to overt HE (OHE). Hence detection of MHE offers better treatment outcome in patients with liver cirrhosis.

MHE cannot be diagnosed with routine clinical and laboratory investigations. In 1998, the working party in World Congress of Gastroenterology recommended that psychometric hepatic encephalopathy score (PHES) can be considered as a gold standard diagnostic criteria for detecting MHE.[1] The PHES involves a set of five tests-number connection test A and B(NCT A/B), line tracing test(LTT), serial dotting test(SDT) and digital symbol test(DST). These are simple 'paper and pencil' tests used to assess the psychomotor speed and accuracy, visual perception, visuospatial orientation, concentration, attention and working memory.[2]

Different studies using PHES revealed that MHE is detected in 30-84% of patients with liver cirrhosis.[3,4] Studies established the fact that dietary modification[5,6], branched chain amino acids[7,8], lactulose, lacitol[9] has an beneficiary effect in improvement of MHE. Early diagnosis of MHE helps in preventing progression to OHE and improves health-related quality of life in liver cirrhotic patients. The present pilot study aim to assess the prevalence of MHE in liver cirrhotic patients with aid of psychometric hepatic encephalopathy score.

MATERIALS AND METHODS

Patient selection: A prospective study was conducted to assess the prevalence of MHE in patient with liver cirrhosis. The ethics committee of Cosmopolitan hospital a tertiary care center in TVM, Kerala approved the study. A written informed consent as per ICMR biomedical guidelines were obtained from the patients prior to inclusion in the study. From February to March of 2018, 12 patients aged between 31 to 70 years who visited inpatient and outpatient department of Gastroenterology in Cosmopolitan hospital, TVM were included in the study. Patients were then assessed for their mental state using Mini Mental State Examination (MMSE) questionnaire [Table1]. Those who scored greater than 25 points were considered to have normal mental status and were screened for MHE using PHES.

Cirrhosis was diagnosed on the basis of laboratory tests, endoscopy and liver histology. Liver cirrhotic patients were then staged using Child–Pugh (CTP) classification. Exclusion criteria include subjects with OHE, history of neurologic abnormalities like Alzheimer's disease, Parkinsonism, non hepatic metabolic encephalopathy, electrolyte disorders, history of taking lactulose or any antibiotics, gastrointestinal hemorrhage or spontaneous bacterial peritonitis during the past 30 days, hepatocellular carcinoma or other malignancy, psychoactive drug intake and visual impairmnt.

Psychometric tests: All subjects underwent NCT-A, FCT-A, LTT, SDT and DST. Patients were given with proper instructions for performing each test. For LTT separate values were calculated in terms of error (LTT_e) and time (LTT_t) and not as a sum of both. Age and education adjusted normograms were used to calculate the PHES from these psychometric tests.[11] Those subjects having PHES score ≤ -5 were considered to have MHE. These tests were performed on a quiet room with sufficient light.

RESULTS

12 cirrhotic patients with a mean age of 58.833±11.1667 satisfying the inclusion and exclusion criteria were screened for MHE. 83.3% of subjects involved in the study were male and 13.3% were female respondents [Table 2]. 66.7% of the subjects belongs to age category of 61-70 years [Table 3]. 50% (6/12) received formal education for a period of 10-12 years.[Table 4]. The etiology for liver cirrhosis was found to be alcoholism (41.7%), hepatitis B (16.7%), hepatitis C (8.3%) and 33.3% due to primary sclerosing cholangitis, autoimmune hepatitis and steatohepatitis[Table 5]. CTP classification of the 12 subjects showed that 66.6% belongs to CTP-B, 16.7% subjects each in CTP-A and CTP- C [Table 6].

The results of NCT-A, FCT-A, LTT_e, LTT_t, DST and SDT were 58.41667±17.62466, 112.6667±40.12103, 36.33333±22.11266, 58.91667±11.9275, 18.66667 ±6.03525 and 67±29.22639 respectively. The mean of PHES was found to be -5.41667±2.466441 points (median, -2; range, -2 to -10). Table 7 illustrates the demographic, clinical and biochemical characteristics of subjects involved in the study.

Using a cutoff; PHES ≤ -5, 50% (6/12) subjects screened have been detected with MHE. Among the patients with MHE 62.5% (5/8) belongs to CTP-B and 50% (1/2) belongs to CTP-C.

Table 1: Mini mental state examination questionnaire.

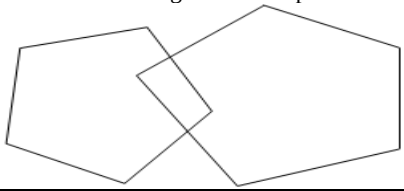
MAXIMUM SCORE	PATIENT'S SCORE	QUESTIONS
5		"What is the year? Season? Date? Day? Month?"
5		"Where are we now? State? County? Town/city? Hospital? Floor?"
3		The examiner names three unrelated objects clearly and slowly, then the instructor asks the patient to name all three of them. The patient's response is used for scoring. The examiner repeats them until patient learns all of them, if possible.
5		"I would like you to count backward from 100 by sevens." (93, 86, 79, 72, 65, …)
3		"Earlier I told you the names of three things. Can you tell me what those were?"
2		Show the patient two simple objects, such as a wristwatch and a pencil, and ask the patient to name them.
1		"Repeat the phrase: 'No ifs, ands, or buts.'"
3		"Take the paper in your right hand, fold it in half, and put it on the floor." (The examiner gives the patient a piece of blank paper.)
1		"Please read this and do what it says." (Written instruction is "Close your eyes.")
1		"Make up and write a sentence about anything." (This sentence must contain a noun and a verb.)
1		"Please copy this picture." (The examiner gives the patient a blank piece of paper and asks him/her to draw the symbol below. All 10 angles must be present and two must intersect.) 

Table 2: Gender.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Female	2	16.7	16.7	16.7
	Male	10	83.3	83.3	100.0
	Total	12	100.0	100.0	

Table 3: Age category.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	31-40	2	16.7	16.7	16.7
	41-50	1	8.3	8.3	25.0
	51-60	1	8.3	8.3	33.3
	61-70	8	66.7	66.7	100.0
	Total	12	100.0	100.0	

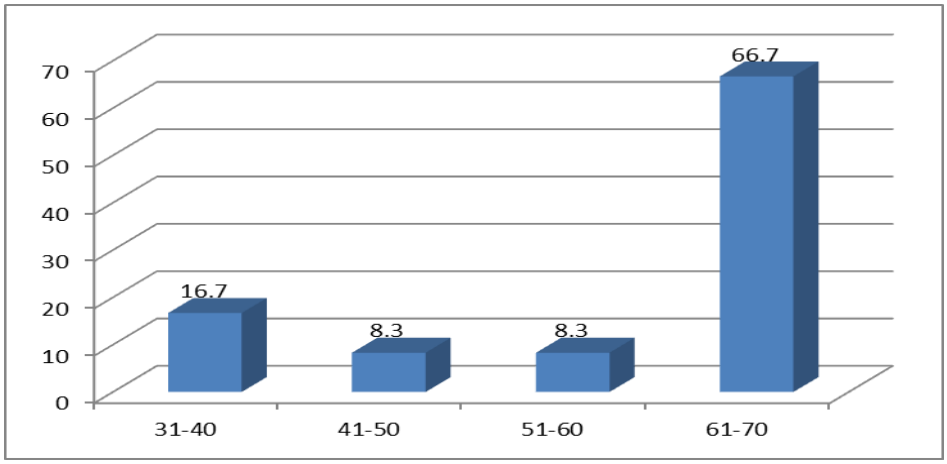


Table 4: Education years.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	7-9	4	33.3	33.3	33.3
	10-12	6	50.0	50.0	83.3
	13-15	2	16.7	16.7	100.0
	Total	12	100.0	100.0	

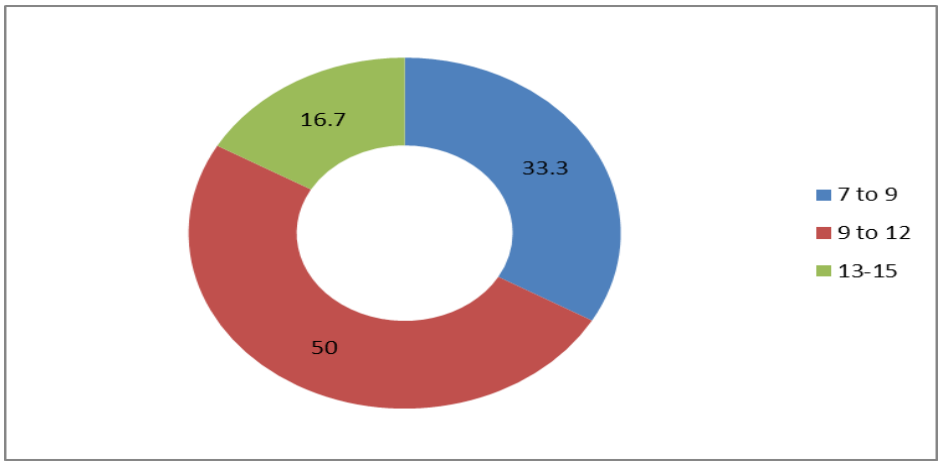


Table 5: Etiology.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Alcohol	5	41.7	41.7	41.7
	Hepatitis B	2	16.7	16.7	58.3
	Hepatitis C	1	8.3	8.3	66.7
	Others	4	33.3	33.3	100.0
	Total	12	100.0	100.0	

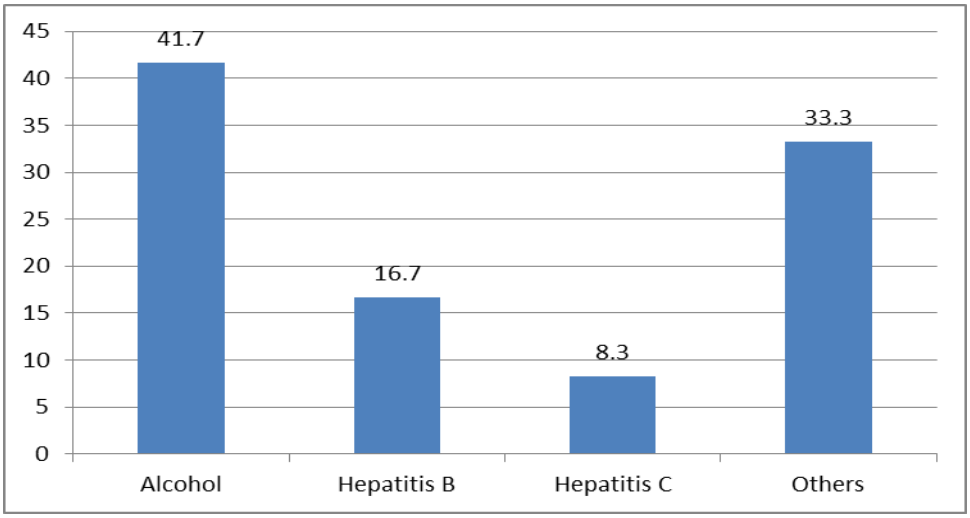


Table 6: CTP classification.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	A(1-6)	2	16.7	16.7	16.7
	B(7-9)	8	66.7	66.7	83.3
	C(>10)	2	16.7	16.7	100.0
	Total	12	100.0	100.0	

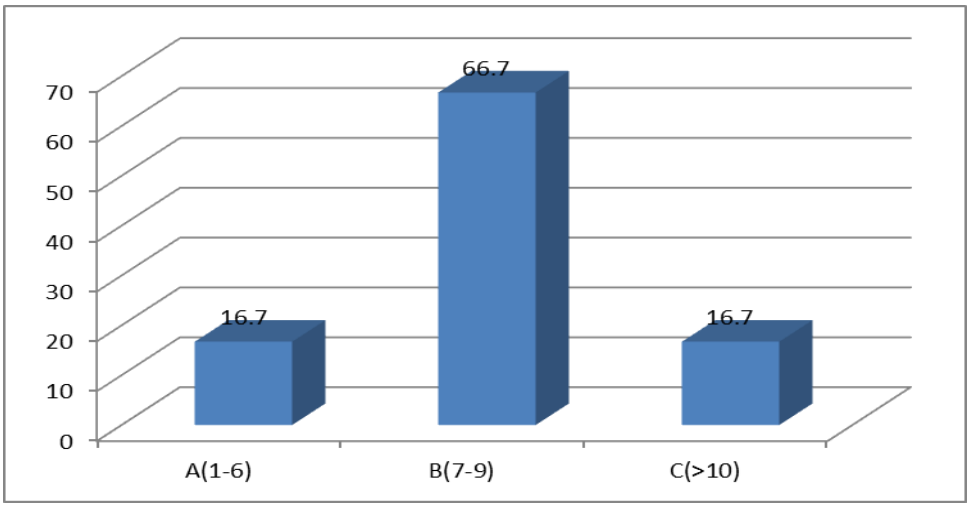


Table 7: Demographic, clinical and biochemical characteristics of subjects.

	Mean	Standard deviation	Variance
Age(years)	58.83	11.1667	124.697
Education status(years)	10.91667	2.4664	6.0833
Hemoglobin(g/dl)	10.48333	2.104037	4.42697
Total count(cells/mm^3)	8650.833	3766.161	14183972
Platelet count(cells/mm^3)	197416.7	236128.4	5.58E+10
Total bilirubin(mg/dl)	2.358333	2.044709	4.180833
Serum albumin(g/dl)	3.058333	0.569622	0.32447
INR	1.6	0.376612	0.141836

DISCUSSION

MHE affects the psychomotor functioning, attention abilities and information processing skills adversely. This defines the need for early and accurate detection of MHE in liver cirrhotic patients. Certain researches indicated that MHE patients have significantly higher rates of impairment in daily functioning including sleep, social interactions, emotional behavior, alertness etc and may accelerates the risk of car accidents, difficulty in handling complex machines etc. PHES is an inexpensive, simple and appropriate diagnostic procedure for this purpose in an outpatient clinic. Detecting subjects with MHE enables early treatment with drugs including

lactulose, lactitol, rifaximin etc thus preventing its progression to OHE.

PHES is largely affected by educational status as well as age. Hence normative data are required to apply it for diagnosis of MHE. PHES has been standardized in Germany[1], Spain[14], India[11], Mexico[15], China[16], Korea[17], Turkey[18] and Cuba.[19] Dhiman et al[11] standardized PHES in India replacing NCT-B with FCT-A which made PHES system more acceptable and simple for illiterate subjects.

Previous studies reported the prevalence of MHE in between 30-84%.[3,4] Mina et al[18] reported the prevalence of MHE as 44%, Maldonado et al[19] as 34.6%, Wang et al[20] as 39.9%, Ananya et al[21] as 62.4%, Coskun et al[22] as 31.6% and Dhiman et al[11] as 48%. Our study supported these results with a prevalence rate of 50%. However controversy exists in certain conclusions. Gilberstedt et al[12] reported that the severity of liver injury is related with MHE. Sood et al[13], Rikkers et al[6] was unable to establish a relationship between them. Our study concluded that there is not much relation between severity of liver injury and prevalence of MHE. From the result its evident that prevalence of MHE is more profound in CTP-B (62.5%), CTP-C (50%) classes respectively.

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