

## Frequency of Minimal Hepatic Encephalopathy in Cirrhotic Patients with Normal Neurological Examination

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### ABSTRACT

**Aim:** To determine the frequency of minimal hepatic encephalopathy in patients with cirrhosis who have normal neurological examination presenting in tertiary care setting.

**Materials:** This cross-sectional study was carried out in the Department of Gastroenterology, Medical Unit III, Services Hospital Lahore, Pakistan over a period of six months from 21-09-2011 to 20-03-2012. A total of 150 cases were included in this study. Bispectral index of the patients was calculated by researcher herself by applying bispectral index monitor pad on the forehead and graded from 0 to 100. Minimal hepatic encephalopathy was defined by impairment in bispectral index score (>84 and <100).

**Results:** Regarding age distribution of patients, 22 patients (14.7%) were 20-40 years old, 98 patients (65.3%) were 41-60 years of age while 30 patients (20%) were between 61-70 years of age. Mean age of the patients was observed  $51.25 \pm 11.32$ . Out of 150 patients, 90 patients (60%) were male and remaining 60 (40%) were female. Minimal hepatic encephalopathy was noted in 91 patients (60.7%)

**Conclusion:** It is concluded that minimal hepatic encephalopathy (MHE) is highly prevalent among patients with cirrhosis.

**Keywords:** Minimal hepatic encephalopathy, Cirrhosis, Bispectral index

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### INTRODUCTION

Cirrhosis of liver globally affects millions of people. In developing countries, however, liver cirrhosis and its complications like hepatic encephalopathy are always a major health problems as in these countries the cost of the health care has always been an issue. These complications imply a grave challenge to health economy.<sup>1</sup> Hepatic encephalopathy is defined as a chronic neuropsychiatric syndrome secondary to liver cirrhosis and it carries prognostic implications<sup>2,3</sup>. It can be classified into overt and minimal hepatic encephalopathy. Approximately 30% patients, approaching coma experience significant encephalopathy before dying of end-stage liver disease<sup>4</sup>.

Minimal hepatic encephalopathy is a prevalent problem but often neglected by the doctors because of its occult nature. In the spectrum of hepatic encephalopathy it is the mildest one and refers to the subtle changes in electrophysiological parameters, cognitive function and cerebral neurochemical, neurotransmitter and fluid homeostasis<sup>5</sup>. Detailed clinical history and neurological examination cannot identify these changes but these can be detected by abnormalities in neurophysiological or neuropsychometric tests that can be performed in out-patient setting<sup>6</sup>.

The effect of minimal hepatic encephalopathy on the psychosocial and medical aspects of the patients is profound. It is associated with decreased working capability and poor quality of life especially for patients doing jobs requiring physical coordination. Patients with minimal encephalopathy have poor independent survival<sup>7</sup>. These patients have attention, response inhibition and working memory difficulties associated with navigation and driving impairment leading to high incidence of motor vehicle accidents and falls<sup>7,8</sup>. In different studies, prevalence of minimal hepatic encephalopathy in patients of liver cirrhosis reported to be between 30% and 84%. The prevalence is higher in patients with poor liver function and reported to be 55% in one study<sup>4,9,10</sup>.

Risk factors for development of minimal hepatic encephalopathy are increasing age of the patient, alcohol abuse, advanced liver disease, presence of esophageal varices and previous episode of overt hepatic encephalopathy.<sup>11</sup> Bispectral index is a bedside tool to monitor electroencephalographic activity<sup>12</sup> and it is not only helpful for earlier detection of cerebral dysfunction but also for classifying the degree of presence of hepatic encephalopathy. This monitor has an advantage to avoid the learning effects which are usually seen in psychomotor tests and is also helpful for patients of low educational background in whom psychomotor test will be difficult to perform<sup>11,12</sup>.

Recently another grade of hepatic encephalopathy i.e., grade 0 on West Have Criteria

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has been added, which cannot be detected on routine clinical examination but only be detected with certain psychometric tests. We do not look for this early abnormality in patients with liver cirrhosis in our clinical set up and thus allow patients to step into higher stages of hepatic encephalopathy. By doing this study, we want to know that how many patients with normal clinical examination have underlying minimal hepatic encephalopathy. This will not only produce magnitude of this important problem in our population but will enable us to recommend that psychometric analysis with the help of Bispectral index monitor be made a part of routine screening of these patients if frequency of such patients comes out to be significant. Moreover no local literature regarding this is available.

## PATIENTS AND METHODS

It was a cross-sectional survey conducted at Department of Gastroenterology, Medical Unit-III, Services Hospital, Lahore carried out over a period of six months from 21-09-2011 to 20-03-2012. Total 150 cases were enrolled in the study. Patients from 18-70 years of age, of both genders having cirrhosis with normal mental status on clinical examination (mini mental examination) score >24 were included. Alcoholic patients (minimum of two units of alcohol per week), patients with visual impairment (with visual acuity 6/18 or less), patients with cirrhosis and uncontrolled co-morbidities like chronic renal failure (history of renal disease with serum creatinine 1.5mg/dl), hypertension (systolic BP > 160mmHg and diastolic > 90mmHg) and cerebrovascular accident (diagnosed clinically or on CT scan brain), patient with history of head injury and patients with history of poisoning were excluded. According to the exclusion and inclusion criteria, 150 patients from our patients department were selected. After informed consent, patients were offered short admission at Medical unit-III. The demographic data and history of patients were noted during admission and their clinical examination was performed. Bispectral index was calculated by applying bispectral index monitor pad on the forehead by researcher herself and grading was done from 0 to 100. Patients with impairment in bispectral index score (> 84 and < 100) were classified as having minimal hepatic encephalopathy.

## RESULTS

Twenty two patients (14.7%) were having age of 20-40 years, 98 patients (65.3%) were 41-60 years old while 30 patients (20.0%) were between 61-70 years of age. Mean age of the patients was observed to be 51.25±11.32 years. Out of 150 patients, male

patients were 90(60%) and remaining 60(40%) were female patients. In 91 patients (60.7%) minimal hepatic encephalopathy was noted (Table 1).

Table 1: Demographic data of the patients (n = 150)

| Variable                              | n  | %age |
|---------------------------------------|----|------|
| <b>Age (years)</b>                    |    |      |
| 20-40                                 | 22 | 14.7 |
| 41-60                                 | 98 | 65.3 |
| 61-70                                 | 30 | 20.0 |
| <b>Sex</b>                            |    |      |
| Male                                  | 90 | 60.0 |
| Female                                | 60 | 40.0 |
| <b>Minimal hepatic encephalopathy</b> |    |      |
| Yes                                   | 91 | 60.7 |
| No                                    | 59 | 39.3 |

## DISCUSSION

Hepatic encephalopathy (HE) is a potentially reversible, metabolic cause of disturbed central nervous system function that occurs in acute or chronic liver disease patients. It comprises a wide spectrum of neurological symptoms of varying severity and is classified according to etiology or clinical symptoms<sup>13</sup>.

Minimal hepatic encephalopathy (MHE) is the subtype of hepatic encephalopathy (HE). It is highly prevalent (22-74%) among patients with liver dysfunction. MHE is defined as HE with cognitive deficits but without grossly evident neurologic abnormalities that can be revealed by psychometric testing<sup>13</sup>. These findings are comparable with results of our study where frequency of minimal hepatic encephalopathy among cirrhotic patients was noted to be 60.7%.

Das et al<sup>14</sup> reported in their study that minimal hepatic encephalopathy was present in 62.4% patients. They found the Picture Completion tests and Number and Figure Connection Block Design were the most useful in the detection of MHE. Severity of MHE, was greater in patients with more severe liver disease as assessed by the number of abnormal tests. Although other clinical complications were similar in different groups, overt hepatic encephalopathy seen more commonly in those patients who had MHE at entry compared to those who did not (22.6 vs. 5.6%, P = 0.044)<sup>14</sup>.

Minimal hepatic encephalopathy (MHE) is characterized by some minimal non specific alterations of cerebral functions that can only be detected by neurophysiologic or neuropsychological diagnostic tests. It interferes with the patient's daily living. Its progression can be prevented and the development of the overt hepatic encephalopathy can be delayed by early recognition of these impairments<sup>15</sup>.

Zamora-Nava and Torre-Delgadillo<sup>17</sup> demonstrated the prevalence of MHE as high as 84% in patients with cirrhosis by a study that was conducted in Mexico<sup>16</sup>. Similarly Maldonado-Garza et al. reported the prevalence of minimal hepatic encephalopathy to be of 55.8%. Mittal et al<sup>18</sup> carried out a study in New Delhi, India in which they reported that 160 patients of cirrhosis (49.69%) out of 322 had MHE. Results of these studies are also supporting our findings. Minimal hepatic encephalopathy (MHE) is present intermittently in up to two third of patients with chronic liver disease. It causes impairment of their daily living but can be treated. Except for psychometric methods, for the rest of diagnostic criteria's there is no consensus<sup>19</sup>.

Minimal hepatic encephalopathy is a serious complication of cirrhosis as it commonly impairs the health-related quality of life (HRQoL) and daily functioning in well-compensated cirrhotic patients. In patients of liver cirrhosis with MHE, Acetyl-L-carnitine (ALC) has been shown to be useful in improving cognitive functions and blood ammonia levels<sup>21</sup>.

A 'gold standard' for the assessment of minimal hepatic encephalopathy remains the Psychometric Hepatic Encephalopathy Score (PHES), but between studied populations its results clearly differ.<sup>19</sup> Between 30 to 50% of the patients with cirrhosis who do not show symptoms of clinical hepatic encephalopathy usually have MHE with mild cognitive impairment. MHE increases the risk of suffering accidents, impairs the patient's quality of life, predicts the occurrence of overt HE, and is linked with shortened lifespan. Therefore, early detection of MHE would be very useful in identifying patients with MHE and hence for saving lives<sup>20</sup>.

## CONCLUSION

It is concluded that there is high prevalence of minimal hepatic encephalopathy (MHE) among patients with cirrhosis, who have a specific cognitive impairment that has a negative impact on their work performance and driving capabilities and most important is that it is not evident to the patients themselves. Although testing for MHE and subsequently its treatment is not standard of care at this time but it is imperative to consider this in patients with cirrhosis in order to improve their quality of life.

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