

## Original Research Paper

## General Medicine

## LIGHTS AND SHADOWS IN DIAGNOSIS OF HEPATIC ENCEPHALOPATHY AND ITS PRECIPITATING FACTORS

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ABSTRACT INTRODUCTION: This study emphasizes on diagnosing Hepatic Encephalopathy (HE) based on prior probability of HE depending on prevalence and frequency of precipitants, recognition of clinical pattern and exclusion of alternative conditions. The study also aimed at ascertaining the common precipitating factors and their frequency in patients presenting with HE in our hospital. Appearance of HE in any patient is indicative of poor prognosis so early diagnosis and identification of precipitants is important. Finally a multidimensional approach for correct clinical reporting of HE is the concern of the study.

MATERIALS AND METHODS: Prospective, descriptive study in Department of General Medicine, Kamineni Institute Of Medical Sciences, Narketpally, Telangana was done over a period of one year from march 2020 to march 2021; which included 50 admitted patients who fulfilled the criteria of diagnosis of HE. Clinical history was elicited followed by detailed abdomen and neurological examination for every patient and

The common precipitating factors and their frequency in HE was studied.

**RESULTS:** A total of 50 admitted patients, including 92 %( 46/50) male and 08 %( 4/50) female, presenting or complicating into hepatic encephalopathy were studied. Majority i.e. 92 %( 46/50) were older than 40 years Ascites (92%) being the most common clinical feature followed by altered sensorium, jaundice.

GI bleeding (30%) being the most common precipitant followed by hyponatremia, infection.

HE phenotypes i.e. clinical grading (WEST HAVEN) was done and 20% i.e. 10 out of 50 expired were in grade3 HE

.DISCUSSION: Hepatic encephalopathy has never been less than an unsolved mystery for physicians and researchers around the globe. Correct clinical reporting of HE with exclusion of other alternative diagnosis (psychiatry disorders, head injury) along with early identification and removing of precipitating factors is still the key step in overall management. This study also emphasizes that in developing countries like India where cost of health care is always an issue, HE can be diagnosed with clinical pattern, minimal investigations and prior probability (includes prevalence of precipitants).

**CONCLUSION:** The existence of liver failure, prior HE and its precipitating factors increase the risk of HE. At present, GI bleed, hyponatremia, hypovolemia and infection are the most common precipitants of HE in our hospital. Despite the presence of shadows like measuring blood ammonia levels, computerized tests based on chronometric techniques, electrophysiological studies, neuroimaging, this study lightens the recognition of HE phenotypes and identification of precipitants for prior likelihood of HE detection shall confer a subjective degree of confidence for diagnosing HE.

## KEYWORDS: Hepatic Encephalopathy, Precipitating factors, Hepatic Encephalopathy phenotypes

## INTRODUCTION:

The syndrome of hepatic encephalopathy (HE)<sup>(1)</sup> describes all neuropsychiatric symptoms occurring in patients with acute or chronic liver diseases (CLD) in the absence of other neurological disorders. Most of the patients with cirrhosis die in hepatic coma  $^{(2)}$ . Appearance of HE in any patient is indicative of poor prognosis  $^{(3)}$ can occur either due to acute liver failure or due to one or more precipitating factors , or it could happen as a result of prolonged portal systemic shunting resulting in a chronic portal systemic encepha lopathy  $^{(4)}$ . Survival of patients having chronic portal systemic encephalopathy is better than those who develop HE acutely  $^{(5)}$ . However prognosis in the latter group can be improved if the precipitating factors are recognized early and managed accordingly  $^{(5)}$ .

Common precipitating factors include gastrointestinal bleeding, infection, azotemia, constipation, electrolyte imbalance (7) and high protein diet. Usage of drugs such as sedatives (8), tranquilizers, analgesics and diuretics, fulminant hepatic injury, large volume paracentesis have all been considered to precipitate encephalopathy in an otherwise stable cirrhotic patient. Exact pathogenic mechanism involved is unknown till date, however the basic processes are failure of hepatic clearance of gut derived substances such as ammonia, free fatty acids, mercaptans etc., either through hepatocellular failure or shunting, and altered amino acid metabolism, both of which result in changes in cerebral transmission causing depressed cerebral function (9).

Another Milestone for diagnosis of HE depends on recognition

of the phenotype of HE, hence West Haven criteria which is a clinical diagnostic criteria.

#### West Haven Criteria:

| Grade   | Intellectual function   | Neuromuscular function         |
|---------|-------------------------|--------------------------------|
| 0       | Normal                  | Normal                         |
| Minimal | Normal examination      | Minor abnormalities of         |
|         | findings; subtle        | visual perception or on        |
|         | changes in work and     | psychiatric or on              |
|         | driving                 | psychometric or number         |
|         |                         | tests                          |
| 1       | Personality changes,    | Tremor and incoordination      |
|         | attention deficits,     |                                |
|         | irritability, depressed |                                |
|         | state                   |                                |
| 2       | Changes in sleep        | Asterixis, ataxic gait, speech |
|         | awake cycle,            | abnormalities ( slow and       |
|         | lethargy, mood and      | Slurred)                       |
|         | behavioral changes,     |                                |
|         | cognitive dysfunction   |                                |
| 3       | Altered level of        | Muscular rigidity,             |
|         | consciousness,          | nystagmus, clonus, Babinski    |
|         | confusion,              | sign , hyporeflexia            |
|         | disorientation and      |                                |
|         | amnesia                 |                                |
| 4       | Stupor and coma         | Oculocephalic reflex,          |
|         |                         | unresponsiveness to noxious    |
|         |                         | stimuli.                       |

## Child turcot Pugh classification:

It's a prognostic indicator comprising of

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Class B 7-9 points Class C 10-15 points

The higher the grade, worst the prognosis.

| Clinical Variable   | l point      | 2 point      | 3 point      |
|---------------------|--------------|--------------|--------------|
| Encephalopathy      | None         | Stage 1-2    | Stage 3-4    |
| Bilirubin (mg/dl)   | <2           | 2-3          | >3           |
| Albumin (g/dl)      | >3.5         | 2.8 - 3.5    | > 2.8        |
| Prothrombin time    | <4 seconds   | 4 seconds    | >6 seconds   |
| ( seconds prolonged | or INR < 1.7 | or INR 1.7 - | or INR > 2.3 |
| or INR )            |              | 2.3          |              |
| Ascites             | None         | slight       | Moderate to  |
|                     |              |              | severe       |

The diagnosis of HE, as with every clinical diagnosis, results from the a priori probability of HE before any observation, and the probability that a clinical finding relates to HE. This should be compared with the probability of alternative conditions.

# Thus, the degree of certainty for the diagnosis of HE depends on three key steps:

- (1) The prior probability of HE,
- (2) The recognition of a clinical pattern suggestive of HE, and
- (3) The consideration of alternative conditions.

### AIMS AND OBJECTIVES:

This study was carried out with the main objective of ascertaining the most common precipitating factor and their frequency in a group of patients presenting with hepatic encephalopathy

## Method of data collection:

This study included 50 admitted patients whofulfilled the criteria of diagnosis of HE .Clinical history was elicited followed by detailed abdomen and neurological examination was done for every patient. The common precipitating factors and their frequency in HE was studied.

## Study Design:

Prospective, descriptive study

## Place & Duration:

Department of general Medicine, Kamineni Institute of Medical Sciences, Narketpally, Telangana.

## Study Period:

Study was done over a period of one year from March 2020 to march 2021.

## Patient & Procedure:

#### Inclusion Criteria:

- Patients with Hepatic encephalopathy, belonging to either sex
- Age above 12 years

### Exclusion Criteria:

- Patients with psychiatric disorders or on treatment for psychiatric Disorders
- 2. Those with altered sensorium due to other metabolic disease or head injury
- 3. Acute alcoholic intoxication and alcoholic withdrawal states

## Investigation

- 1) Haemogram HB, TC, DC, ESR, PCV
- 2) UrineAlbumin, Sugar, Deposits, Bile Salts, Bile Pigments
- 3) LFT: Total bilirubin, direct bilirubin, SGOT, SGPT, ALP, Serum Albumin, Serum Globulin.'
- 4) Coagulation Profile: BT, CT, PT, aPTT, INR
- 5) RFT: Serum Urea, serum creatinine, serum sodium, potassium, chloride, bicarbonate
- 6) ASCITIC FLUID ANALYSIS: Glucose, Cell Count, Culture,

- Gram Stain, SAAG
- 7) Chest X ray, ECG, USG Abdomen
- 8) Urine Culture, blood culture and sputum culture
- 9) EEG, CT ABDOMEN, MRI BRAIN if needed.

#### Observations:

A total of 50 admitted patients presenting or complicating into hepatic encephalopathy were studied.

Table 1 Age and Gender Distribution

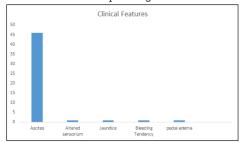
| Age       | Male | Female |
|-----------|------|--------|
| <40 years | 2    | 2      |
| >40 years | 44   | 2      |
| Total     | 46   | 4      |

The above table describes distribution of hepatic encephalopathy patients were predominantly male and majority of patients (92%) were above 40 years.

Table 2 Common Clinical features in patients with HE

|                   | -                  |
|-------------------|--------------------|
| Clinical Features | Number of patients |
| Ascites           | 46                 |
| Altered sensorium | 1                  |
| Jaundice          | 1                  |
| Bleeding tendency | 1                  |
| Pedal edema       | 1                  |
| Total             | 50                 |
| Total             | 50                 |

The above table describes that majority of patients with hepatic encephalopathy presented with ascites (92%) followed by altered sensorium, jaundice, bleeding tendency, pedal edema which are of equal magnitude.

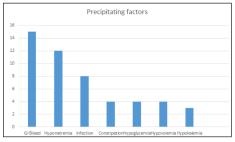


Graph 1: Common Clinical features in patients with HE

Table 3: Precipitating factors for hepatic encephalopathy

| Precipitating factor   | Number of patients |
|------------------------|--------------------|
| Gastrointestinal bleed | 15                 |
| Hyponatremia           | 12                 |
| Infection              | 8                  |
| Constipation           | 4                  |
| Hypoglycemia           | 4                  |
| Hypovolemia            | 4                  |
| Hypokalemia            | 3                  |
| Total                  | 50                 |

The above table demonstrates the most common precipitating factor for HE is GI bleed (30%) followed by hyponatremia (24%), infection (16%), constipation, hypoglycemia, hypovolemia each (8%), followed by hypokalemia (6%).



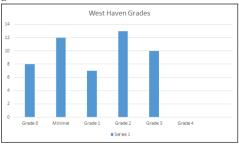
Graph 2: Precipitating factors for hepatic encephalopathy

Table 4: Distribution of HE phenotypes according to West Haven criteria

| West Haven criteria - Grade | Number of patients |
|-----------------------------|--------------------|
| 0                           | 8                  |
| Minimal                     | 12                 |
| 1                           | 7                  |
| 2                           | 13                 |
| 3                           | 10                 |
| 4                           | 0                  |
| Total                       | 50                 |

The above table describes that majority of HE phenotypes 26% were into grade 2 West Haven criteria followed by 24% minimal grade and 20% grade 3

And 10/50(20%) expired were all from grade 3 of west haven criteria



Graph 3: Distribution of HE phenotypes according to West Haven criteria

Table 5: Distribution of cases according to Child Turcotte Pugh Score

| Child Turcotte Pugh Score class | Number of Cases |
|---------------------------------|-----------------|
| Class A                         | 4               |
| Class B                         | 14              |
| Class C                         | 32              |
| Total                           | 50              |

The above table describes that majority of the cases belong to child Pugh class C (64%) followed by child Pugh class B and then child Pugh class A.

#### 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. Although the exact pathogenic mechanism is yet to be determined, modern research has proved time and again that identifying and removing precipitating factors is still the key step in the overall management.

Study conducted by DR. K. B. R SASTRY, DR. SUNIL KUMAR, DR.P ANURADHA et al $^{\mbox{\tiny (10)}}$   $\alpha$  hospital based descriptive and prospective study done in Department of General Medicine, Gandhi Hospital, Secunderabad over a period of one year from March 2014 to March 2015 included 100 sample size out of which 96 were male and 4 were female. Majority of them above 40 years i.e. 92%.

This study goes in par with our study in which out of 50, 46 were male and 4 were female and majority belong to age group more than 40 years (i.e. 92%).

Coming to clinical features presenting as Hepatic Encephalopathy, ascites was most common clinical feature (92%), followed by altered sensorium, jaundice, bleeding tendency, pedal edema which constitute 2% of each, whereas in DR. K. B. R SASTRY, DR. SUNIL KUMAR , DR. P ANURADHA et al $^{(10)}$  ascites is a most common clinical feature followed by bleeding tendency and altered sensorium.

Table 6: Comparison of precipitating factors of Hepatic Encephalopathy among different studies.

| Precipitating factors | Present Study       | Faloon et al <sup>11</sup> |
|-----------------------|---------------------|----------------------------|
|                       | ( n=50) Year - 2022 | (n=200)                    |
| GI bleed              | 15                  | 58                         |
| Hyponatremia          | 12                  | 3                          |
| Infection             | 8                   | 60                         |
| Constipation          | 4                   | 60                         |
| Hypoglycemia          | 4                   | 0                          |
| Hypovolemia           | 4                   | 0                          |
| Hypokalemia           | 3                   | 9                          |
| Diarrhea              | 0                   | 6                          |
| Sedation/increased    | 0                   | 4                          |
| protein intake/ ATT   |                     |                            |
| induced               |                     |                            |
| total                 | 50                  | 200                        |

the above table describes that most common precipitating factor in present study is GI BLEED ( 30% ) followed by hyponatremia ( 24% ), infection ( 16% ), constipation, hypoglycemia and hypovolemia each included ( 8% ) each and hypokalemia least the order (6%).

Faloon et al, study includes 200 participants out of which Infection, Constipation was the most common precipitating factor ( 30% ), followed by GI bleed ( 29% ), Hypokalemia ( 4.5%), diarrhea ( 3% ), sedation/increased protein intake/ATT induced ( 2% ), hyponatremia ( 1.5% ).

Identification of these precipitating factors gave a clue of prior diagnosing hepatic encephalopathy and treating accordingly.

Table 7: comparison of phenotypes of Hepatic encephal opathy with other studies

| West haven criteria | Present study | Maqsood S,          |
|---------------------|---------------|---------------------|
|                     | (n=50)        | Saleem A et al (12) |
|                     | Year 2022     | 2006 (n=50)         |
| Grade 0             | 8             | 0                   |
| Grade Minimal       | 12            | 0                   |
| Grade 1             | 7             | 4                   |
| Grade 2             | 13            | 9                   |
| Grade 3             | 10            | 26                  |
| Grade 4             | 0             | 11                  |
| Total               | 50            | 50                  |

Maqsood S, Saleem A et al $^{(12)}$  is a hospital based non-interventional descriptive study was carried out on 50 patients in Medical Unit III of Pakistan Institute of Medical Sciences Islamabad. All patients who were aged 13 years or above manifesting signs and symptoms of HE either at presentation or during the course of hospital stay were studied. This also included patients with acute fulminant hepatitis or known liver cirrhosis developing HE.

Majority of patients belong to grade 3 of West Haven criteria (52%), followed by grade 4 (22%), grade 2 (18%) and grade 1 (8%) and none belong to grade 0 and minimal.

In the present study, majority of patients belong to grade 2 ( 22%) followed by minimal ( 24% ), followed by grade 3 ( 20% ) and grade 0 ( 16% ) and grade 1 ( 14% ) and none belong to grade 4.

Table 8: Distribution of cases according to Child Turcotte Pugh score and comparison with other study.

| Child Turcotte Pugh<br>class | Present study<br>( n=50) Year 2022 | Faloon et al <sup>11</sup> ( n=200) |
|------------------------------|------------------------------------|-------------------------------------|
| Class A                      | 4                                  | 0                                   |
| Class B                      | 14                                 | 67                                  |
| Class C                      | 32                                 | 133                                 |
| Total                        | 50                                 | 200                                 |

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The above table describes, that majority of patients belong to Child Pugh class C (64%), and followed by Class B (28%) followed by class a (8%).

Whereas study conducted by faloon et al, (n=200), majority of patients belong to Class C (66.5%) followed by Class B (33.5%) and none belong to Class A.

#### CONCLUSION:

The existence of liver failure, prior HE and its precipitating factors increase the risk of HE. At present, GI bleed, hyponatremia, hypovolemia and infection are the most common precipitants of HE in our hospital. Despite the presence of shadows like measuring blood ammonia levels, computerized tests based on chronometric techniques, electrophysiological studies, neuroimaging, this study lightens the recognition of HE phenotypes and identification of precipitants for prior likelihood of HE detection shall confer a subjective degree of confidence for diagnosing HE.

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