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# A Study on Clinical Characteristics of Cirrhotic Patients in Bangladesh

Dr. Md. Shayedul Ashik[1*], Dr. Irfat Yasmin[1], Professor Dr. Mamun Al Mahtab[2], Dr. Muhammad Rezaul Karim[3], Dr. Arifa Tasnim[4], Dr. Md. Arif Uddin Sumon[5]

[1]Assistant Registrar, Shaheed Tajuddin Ahmad Medical College and Hospital, Gazipur, Bangladesh
[2]Professor and Head, Interventional Hepatology Division, Dept of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka
[3]Junior Consultant (Medicine), OSD, DGHS, Deputation - Bangladesh National Parliament Secretariat Medical Centre, Dhaka, Bangladesh
[4]Assistant Registrar, National Gastroliver Institute and Hospital, Dhaka, Bangladesh
[5]Registrar, Dept of Hepatology, Mymensingh Medical College and Hospital, Mymensingh, Bangladesh

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***Corresponding author:** Dr. Md. Shayedul Ashik
Assistant Registrar, Shaheed Tajuddin Ahmad Medical College and Hospital, Gazipur, Bangladesh

## Abstract

***Background*:** Cirrhosis is a chronic liver condition characterized by significant morbidity and mortality. Hepatic encephalopathy (HE), a neuropsychiatric complication of cirrhosis, is associated with vitamin D deficiency, which may exacerbate liver dysfunction. Understanding the clinical and laboratory characteristics of cirrhotic patients with and without HE is crucial for improving management strategies. ***Objective*:** To evaluate the clinical characteristics of cirrhotic patients and investigate the association between serum 25-hydroxyvitamin D levels and the severity of HE. ***Methods*:** This cross-sectional observational study was conducted at Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, from December 2019 to August 2020. A total of 54 cirrhotic patients were divided into two groups: 27 with HE (cases) and 27 without HE (controls). Clinical history, physical examination, and laboratory parameters, including serum 25-hydroxyvitamin D levels, were assessed. Data analysis involved chi-square tests, t-tests, and ANOVA, with a significance level of $p < 0.05$. ***Results*:** The mean age of participants was 50.2 years, with a male predominance (63%). Serum 25-hydroxyvitamin D levels were significantly lower in patients with HE (6.6 ± 2.1 ng/ml) compared to controls (13.6 ± 4.2 ng/ml; $p < 0.0001$). Vitamin D levels decreased progressively with higher HE grades. Cases exhibited significantly higher serum bilirubin, prothrombin time, INR, Child-Pugh scores, and MELD scores than controls ($p < 0.05$). ***Conclusion*:** Vitamin D deficiency is strongly associated with the severity of HE in cirrhotic patients. Lower vitamin D levels correspond to higher grades of encephalopathy, emphasizing its potential role in HE pathophysiology. Future studies should explore the therapeutic implications of vitamin D supplementation in this population.

**Keywords:** Cirrhosis, Hepatic Encephalopathy, Vitamin D Deficiency.



## INTRODUCTION

Cirrhosis is a chronic liver condition characterized by irreversible scarring and distortion of the liver's normal architecture due to sustained injury and repair processes. It represents the advanced stage of various liver diseases, including viral hepatitis, alcoholic liver disease, and non-alcoholic fatty liver disease (NAFLD). The condition poses significant health challenges, as it is associated with high morbidity and mortality rates globally, particularly in regions with limited healthcare resources. Understanding the clinical characteristics of cirrhotic patients is vital for improving diagnostic accuracy, treatment strategies, and patient outcomes [1-4].

He clinical presentation of cirrhosis can vary widely, ranging from asymptomatic cases detected incidentally to severe, life-threatening complications. Common features include jaundice, ascites, variceal bleeding, and hepatic encephalopathy, reflecting the progressive loss of liver function and the impact of portal hypertension. Additionally, systemic manifestations, such as fatigue, weight loss, and muscle wasting, often complicate the disease course and further compromise quality of life [4-6].

Cirrhosis is often classified into compensated and decompensated stages. Compensated cirrhosis may remain clinically silent for years, while decompensated cirrhosis is marked by the emergence of complications like ascites, gastrointestinal bleeding, or encephalopathy. The Child-Turcotte-Pugh (CTP) score and Model for End-Stage Liver Disease (MELD) score are widely used to assess disease severity and predict prognosis. These scoring systems help clinicians stratify patients for interventions such as liver transplantation [7-9].

The etiology of cirrhosis influences its clinical manifestations. For instance, cirrhosis due to viral hepatitis often presents with higher rates of hepatocellular carcinoma, while alcohol-related cirrhosis is frequently associated with malnutrition and other systemic comorbidities. Identifying the underlying cause is essential for tailoring treatment approaches and addressing modifiable risk factors, such as alcohol cessation or antiviral therapy [10-12].

Advanced diagnostic tools, including imaging studies, liver biopsy, and non-invasive fibrosis markers, have enhanced our understanding of the pathophysiological changes in cirrhosis. These tools, coupled with clinical assessments, are crucial for detecting complications like variceal bleeding or spontaneous bacterial peritonitis (SBP) early in their course. Timely interventions, such as endoscopic variceal ligation or antibiotic prophylaxis, can significantly improve survival rates.

**Objective:** To assess the clinical characteristics of cirrhotic patients.

## METHODOLOGY

**Study Design:** This was a cross-sectional observational study.

**Study Setting**

The study was conducted in the Department of Hepatology at Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka.

**Study Period:** The study was carried out from December 2019 to August 2020.

**Study Population**

The study included hospitalized cirrhotic patients, with or without hepatic encephalopathy, who met the inclusion and exclusion criteria.

**Sampling Method:** Purposive sampling was employed to recruit participants.

**Sample Size**

The sample size was determined by the following formula-

$$n = \frac{\left\{ u\sqrt{[\pi(1-\pi)]} + v\sqrt{[\pi_0(1-\pi_0)]} \right\}^2}{(\pi-\pi_0)^2}$$

Where,

n was estimated sample size,

- u= 0.84, v= 1.96,
- $\pi$ = 29 % or 0.29, $\pi_0$ = 10 % or 0.10 (Vidot *et al*., 2017)
- So calculated sample size was 27 in case and 27 in control for statistically significant result.

**Selection Criteria**

**Inclusion Criteria**

- **Case Group**:
  1. Adult patients (>18 years) with liver cirrhosis and hepatic encephalopathy, diagnosed based on the West Haven criteria.
  2. Liver cirrhosis diagnosed through clinical features (e.g., vascular spiders, palmar erythema, gynecomastia, leukonychia, testicular atrophy) and laboratory findings (e.g., prolonged prothrombin time, reduced serum albumin).
  3. Additional supportive evidence such as esophageal varices on endoscopy and coarse liver texture on ultrasonography.

- **Control Group**:
  1. Adult patients (>18 years) with liver cirrhosis but no history or symptoms of hepatic encephalopathy.

**Exclusion Criteria**

1. Chronic renal failure.
2. Alcohol intoxication.
3. Malignancy.
4. Parathyroid disorders.
5. Rheumatological diseases.
6. History of taking vitamin D supplements.
7. History of hepatic encephalopathy.

**Variables**

- **Dependent Variable**:
  - Serum 25-hydroxyvitamin D levels.
- **Independent Variables**:
  - Age, sex, grades of hepatic encephalopathy, Child-Pugh (CTP) score, and MELD score.

**Study Procedure**

Patients admitted to the Department of Hepatology at BSMMU with liver cirrhosis were screened for eligibility. A total of 27 patients with hepatic encephalopathy (case group) were classified into four groups based on the West Haven criteria (WHC), while 27 patients without encephalopathy (control group) were selected.

Data collection involved a detailed history, clinical examination, and laboratory investigations. Demographic and clinical data such as age, sex, and cirrhosis-related complications (e.g., ascites, variceal bleeding, hepatorenal syndrome) were recorded.

Baseline investigations included:

- **Liver Function Tests**:

Serum bilirubin (vanadate oxidation method), ALT and AST (spectrophotometric method), serum albumin (bromocresol green method), and prothrombin time (automated coagulation analyzer).

- **Renal Function**: Serum creatinine (Jaffe method).
- **Ascitic Fluid Analysis**: Cytology, total protein, albumin, and SAAG.

- **Other Tests**:

Serum PTH (two-step immunochemical method), HBsAg and anti-HCV (ELISA), alpha-fetoprotein (quantitative immunochromatographic assay).

- **Imaging**: Abdominal ultrasonography.
- **Endoscopy**: Upper gastrointestinal tract endoscopy.

Serum 25-hydroxyvitamin D levels were measured using a chemiluminescence immunoassay (CLIA) on the Alinity ci machine. Grading of hepatic encephalopathy was performed according to WHC criteria, based on clinical and neuropsychological abnormalities.

**Data Processing and Analysis**

Data were collected using a structured questionnaire after obtaining informed consent from participants. The collected data were analyzed using SPSS (version 20.0).

- Quantitative variables were expressed as mean ± standard deviation (SD) or median (range), depending on distribution.
- Qualitative variables were analyzed using the chi-square test.
- Comparisons between case and control groups were performed using Student's t-test for continuous variables.
- The relationship between serum 25-hydroxyvitamin D levels and grades of hepatic encephalopathy was assessed using ANOVA.

A p-value < 0.05 was considered statistically significant.

## RESULTS

The age distribution of the study participants revealed that the mean age was 50.2 years with a standard deviation of 13.1 years, ranging from 20 to 72 years.

**Table I: Age distribution of the study group**

| Age Distribution | Mean | ±SD | min | -max |
|---|---|---|---|---|
| Age (Years) | 50. | 2±13.1 | 20 | -72 |

The study population comprised 34 male and 20 female participants, highlighting a higher prevalence of the condition among males compared to females within the sample.

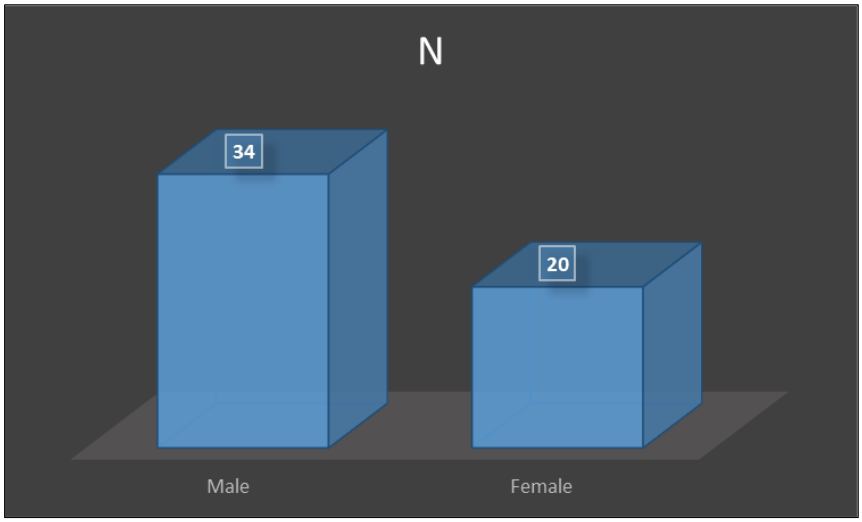


**Figure 1: Gender distribution of the study group**

Mean systolic BP was 108.7±12.6 mmHg, mean diastolic BP was 68.5±7.1 mmHg, mean Hb % was 10.1±2.0 g/dl, mean TC was (6.5±2.7)x109/L, mean platelet count was (142.3±76.0)x109/L, mean serum creatinine 0.9± 0.2 mg/dl, mean serum sodium was 132.9±6.1 mmol/L, mean serum potassium was 3.84±0.7 mmol/L, mean serum bilirubin 5.4±8.2 mg/dl, mean AST was 85.8±77 U/L, mean ALT was 55.3±38.2 U/L, mean prothrombin time was 18.9±4.4 sec, mean INR was 1.7±0.5, mean serum albumin was 2.5±0.5 g/dl, mean

serum 25- Hydroxyvitamin D was 10.1±4.8 (ng/ml), mean CP score 10.1±1.9 and mean MELD score 16.6±6.6.

**Table II: Baseline characteristics of the study group**

| Baseline characteristics | Mean | ±SD | min | -max |
|---|---|---|---|---|
| SBP (mmHg) | | 108.7±12.6 | | 90-140 |
| DBP (mmHg) | | 68.5±7.1 | | 60-80 |
| Hb% (g/dl) | 10.1 | ±2.0 | 4.30 | -14.2 |
| TC (x$10^9$/L) | 6. | 5±2.7 | 2 | .0-13.5 |
| Platelet count (x$10^9$/L) | 142.3 | ±76.0 | 35 | -380 |
| S. Creatinine (mg/dl) | 0. | 9±0.2 | 0.46 | -1.26 |
| S. Sodium (mmol/L) | 132.9 | ±6.1 | 118 | -146 |
| S. Potassium (mmol/L) | 3.8 | 4±0.7 | 2 | .2-5.3 |
| S. Bilirubin (mg/dl) | 5. | 4±8.2 | 0.3 | -43 |
| AST | 85.8± | 77.0 | | 12-464 |
| ALT (U/L) | 55.3 | ±38.2 | 15 | -222 |
| Prothrombin time (Sec) | 18.9 | ±4.4 | 12.1 | -32.8 |
| INR | 1.7 | ±0.5 | 1.0 | -3.3 |
| Serum albumin (g/dl) | 2.5 | ±0.5 | | 1.5-3.5 |
| S. 25-Hydroxyvitamin D (ng/ml) | 10.1 | ±4.8 | 3.5 | 22.7 |
| CP score | 10.1 | ±1.9 | | 6-14 |
| MELD score | 16.6 | ±6.6 | 6 | -35 |

Table III shows lab parameters of the patients, it was observed that mean serum bilirubin was found 8.2±10.5 mg/dl in cases and 2.7±3.6 mg/dl in control group. Mean serum prothrombin time was 20.5±4.8 seconds in case and 17.3±3.4 seconds in control group. Mean INR was 1.9±0.5 in case and 1.5±0.5 in control group. Mean Child-Pugh score was 11.3±1.5 in case and 8.9±1.5 in control group. Mean MELD score was 19.7±6.7 in case and 13.6±5.1 in control group. Mean serum 25-Hydroxyvitamin D was 6.6±2.1 ng/ml in case and 13.6 ±4.2 mg/L in control group. These all were statistically significant ($p<0.05$) between the groups. But Hb%, WBC count, platelet count, serum potassium, serum AST, serum ALT, albumin were not statistically significant ($p>0.05$) between the groups.

**Table III: Distribution of the study patients by lab parameters (n=54)**

| Lab parameters | Case (cirrh with encep) (n=27) | | Control (cirrh without ence) (n=27) | | P value |
|---|---|---|---|---|---|
| | Mean | ±SD | Mean | ±SD | |
| Hb% (g/dl) | | 10.1±2.1 | 10.0 | ±2.0 | 0.864$^{ns}$ |
| TC (x$10^9$/L) | 6. | 4±2.8 | 6. | 6±2.6 | 0.820$^{ns}$ |
| Platelet count (x$10^9$/L) | 137.2 | ±69.7 | 147.3 | ±82.8 | 0.628$^{ns}$ |
| S. Creatinine (mg/dl) | 0.9 | ±0.2 | 0.9 | ±0.2 | 0.635$^{ns}$ |
| S. Sodium (mmol/L) | 132. | 0±6.8 | 133.7 | ±5.2 | 0.319$^{ns}$ |
| S. Potassium (mmol/L) | 3.9 | ±0.6 | 3.7 | ±0.8 | 0.552$^{ns}$ |
| S. Bilirubin (mg/dl) | 8.2 | ±10.5 | 2.7 | ±3.6 | 0.001$^{s*}$ |
| AST (U/L) | 87.3 | ±54.0 | 84.3 | ±95.8 | 0.889$^{ns}$ |
| ALT (U/L) | 62.7 | ±35.8 | 47.9 | ±39.7 | 0.157$^{ns}$ |
| Prothrombin time (Sec) | 20.5 | ±4.8 | 17.3 | ±3.4 | 0.007$^{s}$ |
| INR | 2.0 | ±0.5 | 1. | 5±0.5 | 0.007$^{s}$ |
| Serum albumin (g/dl) | 2.5 | ±0.5 | 2.5 | ±0.5 | 0.977$^{ns}$ |
| S.25-Hydroxyvitamin-D (ng/ml) | | 6.6±2.1 | 13.6±4.2 | | <0.0001$^{s}$ |

Cirr –cirrhosis, enc -encephalopathy

Table IV shows relation of serum 25-Hydroxyvitamin D level and cirrhosis without encephalopathy and with different grades of encephalopathy of the patients, it was observed that, among the patients, 27 patients were without encephalopathy whose serum 25-Hydroxyvitamin D level mean 13.6ng/ml, 9 patients were in grade 1 encephalopathy whose mean value 8.6ng/ml,12 patient were grade 2 whose mean value 6.5ng/ml, 4 patients were in grade 3 whose mean value 3.9ng/ml and 2 patients were in grade 4 whose mean value 3.5ng/ml. The difference was statistically significant ($p<0.0001$).

**Table IV: Distribution of the study patients by serum 25-Hydroxyvitamin D level and encephalopathy grades. (n=54)**

| Grade of enceph | Case, n=27 | | Control, n=27 | | P value |
|---|---|---|---|---|---|
| | n | Mean±SD | n | Mean±SD | |
| No enceph | 0 | 0 | 27 | 13.6±4.2 | <0.0001[s] |
| Grade 1 | 9 | 8.6±0.7 | 0 | 0 | |
| Grade 1 | 4 | 3.9±0.9 | 0 | 0 | |
| Grade 3 | 4 | 3.9±0.9 | 0 | 0 | |
| Grade 4 | 2 | 3.5±0.0 | 0 | 0 | |

## DISCUSSION

This study explored the clinical characteristics and laboratory parameters of cirrhotic patients with and without hepatic encephalopathy (HE), along with the association of serum 25-Hydroxyvitamin D levels across different grades of encephalopathy. The mean age of participants in this study was 50.2 years, which aligns with findings from other studies conducted on cirrhosis patients globally, where middle-aged individuals are commonly affected. Similar to studies reported that the male predominance in the study group, comprising 63% males, suggests that cirrhosis and its complications, including HE, may be more prevalent in males, potentially due to higher exposure to risk factors such as alcohol use and viral hepatitis [12].

The mean serum 25-Hydroxyvitamin D level was significantly lower in cirrhotic patients with HE compared to those without HE, with a striking decrease observed in advanced grades of HE. These findings are consistent with research that highlights a progressive decline in vitamin D levels with increasing severity of liver dysfunction. The study demonstrated a mean serum vitamin D level of 6.6 ng/ml in cases with HE and 13.6 ng/ml in controls, a pattern also observed in similar studies, suggesting a possible role of vitamin D deficiency in the pathophysiology of HE.

Interestingly, no significant difference was observed in other parameters such as hemoglobin levels, white blood cell counts, and platelet counts between the two groups. However, parameters like serum bilirubin, prothrombin time, INR, and Child-Pugh scores were significantly higher in HE cases, which is consistent with the well-established association of these markers with liver disease severity. The findings regarding the MELD score also corroborate with previous studies, showing significantly elevated scores in patients with HE compared to controls [13, 14].

A notable finding of this study was the relationship between vitamin D levels and grades of encephalopathy. As the grade of encephalopathy advanced, the vitamin D levels decreased significantly, with the lowest levels observed in Grade 4 HE (3.5 ng/ml). This trend supports the hypothesis that vitamin D deficiency may exacerbate hepatic dysfunction and contribute to the worsening of HE. Such findings have been echoed in studies by Bajaj *et al*., who reported similar trends in vitamin D insufficiency among cirrhotic patients with HE.

Contrasting findings were observed regarding liver enzyme levels, where AST and ALT levels did not show significant variation between cases and controls. This contrasts with some studies that reported higher enzyme levels in advanced liver disease, indicating variability in enzyme release patterns depending on the underlying etiology of cirrhosis [14, 15].

Overall, this study reinforces the critical role of vitamin D in liver health and its potential association with HE severity. While the findings align with most studies conducted in similar populations, some variations may be attributed to differences in sample sizes, geographic settings, and etiologies of cirrhosis. Future studies with larger sample sizes and longitudinal designs are recommended to further explore the causal relationship and potential therapeutic implications of vitamin D in cirrhotic patients with HE.

## CONCLUSION

This study highlights the significant association between vitamin D deficiency and the severity of hepatic encephalopathy (HE) in cirrhotic patients. The findings reveal that serum 25-Hydroxyvitamin D levels decrease progressively with higher grades of encephalopathy, suggesting its potential role in the pathophysiology of HE. Cirrhotic patients with HE demonstrated significantly higher serum bilirubin, prothrombin time, INR, Child-Pugh, and MELD scores compared to those without HE, reflecting greater liver dysfunction. These results underscore the need for further research to investigate the role of vitamin D supplementation as a therapeutic strategy in managing HE and improving outcomes in cirrhotic patients.

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