Study of Serum Albumin Levels in Hepatic Encephalopathy Patients Admitted in a Tertiary Care Hospital.

Abstract:

Background: Hepatic encephalopathy (HE) is a serious neuropsychiatric complication of chronic liver disease associated with significant morbidity and mortality. Serum albumin reflects hepatic synthetic function and possesses vital antioxidant, anti-inflammatory, and detoxifying properties. Hypoalbuminemia is extremely common in cirrhosis and may heavily influence the occurrence and severity of HE. This study aimed to evaluate the relationship between serum albumin levels and the clinical severity, complications, and mortality of hepatic encephalopathy.

Methods: A hospital-based prospective observational study was conducted at Muzaffarnagar Medical College over 18 months. A total of 100 adult patients (≥18 years) with overt hepatic encephalopathy were enrolled using purposive sampling. Patients were categorized into two groups based on serum albumin levels (< 3.5 g/dL and ≥ 3.5 g/dL). Demographic data, etiology, clinical complications, Child-Pugh class, and MELD scores were recorded and statistically analyzed.

Results: Hypoalbuminemia (< 3.5 g/dL) was highly prevalent, observed in 80% of the study population. Severe grades of HE (Grades II, III, and IV) were significantly more frequent in the low albumin group ($p = 0.0302$). Furthermore, complications such as ascites (70% vs. 30%, $p = 0.0009$) and upper gastrointestinal bleeding (46.25% vs. 20%, $p = 0.0327$) were significantly associated with low serum albumin. The low albumin cohort also presented with significantly higher mean MELD scores (22.85 vs. 17.75, $p = 0.0028$) and advanced Child-Pugh classifications ($p = 0.0403$). While in-hospital mortality was higher in the low albumin group (8.75% vs. 5%), this difference was not statistically significant ($p = 0.5803$).

Conclusion: Serum albumin levels below 3.5 g/dL are significantly associated with advanced grades of hepatic encephalopathy, higher MELD scores, and a greater incidence of cirrhosis-related complications like ascites and upper gastrointestinal bleeding.

Keywords: Hepatic Encephalopathy, Serum Albumin, Chronic Liver Disease, MELD Score, Hypoalbuminemia

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Introduction Hepatic encephalopathy (HE) is a complex neuropsychiatric syndrome that arises in patients with significant hepatic dysfunction, typically in the setting of advanced chronic liver disease (CLD) or portosystemic shunting. It manifests as a wide spectrum of cognitive and motor disturbances, ranging from subtle, covert cognitive changes to overt disorientation,

asterixis, stupor, and coma. In India, cirrhosis is a leading cause of liver-related hospital admissions, with alcohol-related liver disease and viral hepatitis being major etiologies. Patients frequently present late in the disease course, demonstrating advanced portal hypertension and multiple decompensating events, including HE.

Serum albumin, synthesized exclusively by hepatocytes, is an essential biomarker that reflects the liver's synthetic capacity. Beyond maintaining colloid oncotic pressure, albumin acts as a versatile transporter of endogenous ligands, shuttling long-chain fatty acids, bilirubin, hormones, and micronutrient metals. Importantly, it possesses robust antioxidant, anti-inflammatory, and detoxifying properties that help stabilize the endothelium. In the context of HE, where ammonia-induced astrocyte swelling, oxidative stress, and systemic inflammation drive brain dysfunction, albumin's neuroprotective properties are particularly relevant.

Hypoalbuminemia is highly prevalent in cirrhosis due to synthetic failure, poor nutritional status, and recurrent infections. Despite compelling evidence from Western cohorts regarding the prognostic importance of albumin, there is a distinct paucity of region-specific data from Indian tertiary care centers. Therefore, this study aimed to evaluate the relationship between serum albumin levels and the severity, associated complications, and in-hospital mortality of HE in patients admitted to a tertiary care hospital.

Materials & Methods This hospital-based prospective observational study was conducted at the Department of General Medicine at Muzaffarnagar Medical College, Muzaffarnagar (U.P.), over a period of 18 months. A total of 100 patients were enrolled using a purposive sampling technique.

The inclusion criteria mandated that patients be aged ≥ 18 years, diagnosed with overt hepatic encephalopathy at the time of admission, and provide written informed consent. Patients who received an albumin infusion prior to blood sampling, lacked serum albumin values, or had co-existing nephrotic syndrome or end-stage renal disease (CKD stage 5) requiring maintenance dialysis were excluded from the study.

Data collection encompassed patient demographics, etiology of liver cirrhosis, and clinical presentation of complications, including ascites, acute upper gastrointestinal (UGI) bleeding, and infections. Routine biochemical workups included complete blood counts, comprehensive liver and kidney function tests, serum electrolytes, coagulation profiles, and viral markers (HBV, HCV). Hepatic encephalopathy was graded clinically utilizing the West Haven Criteria (WHC). Disease severity was further stratified using the Child-Pugh classification and Model for End-Stage Liver Disease (MELD) scores.

Statistical analysis was performed using SPSS Statistics for Windows, Version 22.0. Continuous variables were expressed as mean ± standard deviation, while categorical variables were expressed as frequencies and percentages. The Student’s t-test was utilized for continuous variables, and the Chi-square test was employed for categorical data. A p-value of < 0.05 was

considered statistically significant. The study was approved by the Institutional Ethics Committee (MMC/IEC/ No: 362/2024).

Results A total of 100 patients fulfilling the inclusion criteria were analyzed. The mean age of the participants was 55.19 ± 16.48 years. The cohort demonstrated a strong male predominance, comprising 84 males (84%) and 16 females (16%). Alcoholic liver disease was the most frequent etiology (53%), followed by viral hepatitis (26%), non-alcoholic steatohepatitis (NASH)/cryptogenic cirrhosis (18%), autoimmune liver disease (2%), and Wilson's disease (1%).

Hypoalbuminemia was exceedingly common; 80 participants (80%) presented with serum albumin < 3.5 g/dL, while only 20 participants (20%) had levels > 3.5 g/dL.

Table 1: Distribution of Serum Albumin Levels

Serum Albumin (g/dL)	Frequency	Percentage
< 3.5	80	80.00%
> 3.5	20	20.00%

The severity of HE was directly associated with lower serum albumin levels. Among patients with albumin < 3.5 g/dL, Grade II HE was the most frequent presentation (42.5%), followed by Grade III (30%) and Grade IV (17.5%). Conversely, 75% of patients in the > 3.5 g/dL group presented with milder Grade I or II HE. This difference was statistically significant (p = 0.0302).

Table 2: Hepatic Encephalopathy Grade According to Serum Albumin Levels

HE Grade	Serum Albumin < 3.5 g/dL	Serum Albumin > 3.5 g/dL
I	8 (10.00%)	7 (35.00%)
II	34 (42.50%)	8 (40.00%)

III	24 (30.00%)	4 (20.00%)
IV	14 (17.50%)	1 (5.00%)

p-value = 0.0302

Liver disease complications were heavily concentrated in the low-albumin group. Ascites was present in 70% of the low-albumin cohort, compared to just 30% in the higher albumin cohort (p = 0.0009). Upper gastrointestinal bleeding was noted in 46.25% of patients with albumin < 3.5 g/dL versus 20% in the > 3.5 g/dL group (p = 0.0327). The presence of concurrent infection/sepsis was high across both groups (77.5% vs. 85%) and did not show statistical significance based on the albumin threshold (p = 0.4614).

Laboratory investigations revealed that patients with serum albumin < 3.5 g/dL suffered from more significant physiological derangements. Mean hemoglobin was significantly lower (9.68 ± 1.32 g/dL vs. 10.51 ± 1.15 g/dL, p = 0.0105), and mean total bilirubin was significantly higher (3.68 ± 1.75 mg/dL vs. 2.52 ± 1.63 mg/dL, p = 0.0102) in the low-albumin group. Serum ammonia levels, however, did not differ significantly between the groups (p = 0.7848).

Table 3: Comparison of Laboratory Parameters by Serum Albumin Levels

Laboratory Parameters	**Serum Albumin < 3.5 g/dL (Mean ± SD)**	**Serum Albumin > 3.5 g/dL (Mean ± SD)**	**p-value**
Hemoglobin (g/dL)	9.68 ± 1.32	10.51 ± 1.15	0.0105
Total Bilirubin (mg/dL)	3.68 ± 1.75	2.52 ± 1.63	0.0102
ALT (U/L)	68.79 ± 23.37	66.40 ± 21.20	0.6688
AST (U/L)	85.11 ± 31.65	79.15 ± 26.39	0.4020
PT (sec)	5.60 ± 2.29	5.24 ± 1.96	0.4860
INR	1.87 ± 0.36	1.76 ± 0.28	0.1483
Sodium (mmol/L)	131.45 ± 5.83	132.55 ± 6.76	0.5191

Potassium (mmol/L)	4.31 ± 0.74	4.23 ± 0.57	0.5990
Serum Albumin (g/dL)	2.54 ± 0.41	3.74 ± 0.20	< 0.0001
Serum Ammonia (µmol/L)	115.95 ± 28.06	117.70 ± 23.93	0.7848

Disease severity scoring indexes corroborated the clinical and laboratory data. A higher proportion of patients in the low-albumin group belonged to Child-Pugh Class B (42.5%) and Class C (38.75%), whereas Class A predominated in the > 3.5 g/dL cohort (45%) ($p = 0.0403$). Correspondingly, the mean MELD score was significantly higher among patients with hypoalbuminemia (22.85 ± 6.17) compared to those with higher albumin levels (17.75 ± 6.09, $p = 0.0028$).

Despite higher morbidity indicators, the overall in-hospital mortality was 8%, comprising 7 cases (8.75%) in the < 3.5 g/dL group and 1 case (5%) in the > 3.5 g/dL group. This difference did not reach statistical significance ($p = 0.5803$).

Discussion The present study was undertaken to comprehensively evaluate the clinical significance of serum albumin levels in patients admitted with hepatic encephalopathy. The demographic distribution reflected a mean age of 55.19 years with a significant male preponderance (84%). This aligns closely with findings by Rauf et al. (66% males) and Riggio et al. (67% males), emphasizing the demographic trends typical of cirrhosis populations globally. Alcoholic liver disease was the paramount etiological factor (53%), reflecting the growing public health impact of alcohol consumption in India, an observation supported by Rauf et al. and Riggio et al., who also cited alcohol and viral hepatitis as the principal drivers of decompensated liver disease.

Hypoalbuminemia (< 3.5 g/dL) was universally prevalent, affecting 80% of the cohort. Albumin's role in maintaining oncotic pressure and acting as a robust systemic antioxidant makes it critical to mitigating the neurotoxic mechanisms of HE, such as ammonia-induced astrocytic swelling. The current data conclusively demonstrates that patients with lower albumin experience more severe encephalopathy (Grades II-IV) compared to those with preserved albumin levels ($p = 0.0302$). Kaji et al. correspondingly highlighted that low serum albumin is heavily associated with impaired cognitive function and can serve as a vital marker for HE onset.

Furthermore, patients in the hypoalbuminemic cohort suffered from higher rates of portal hypertension complications, exhibiting significantly greater incidences of ascites (70%, $p = 0.0009$) and upper gastrointestinal bleeding (46.25%, $p = 0.0327$). The relationship between albumin and advanced disease was strongly validated through severity scores. The mean

MELD score was significantly elevated in the low-albumin cohort (22.85 vs. 17.75, p = 0.0028), and a significantly larger proportion of these patients fell into Child-Pugh Classes B and C.

Laboratory correlations further reinforced the state of advanced hepatic failure in the < 3.5 g/dL group, marked by significantly lower hemoglobin (p = 0.0105) and elevated total bilirubin (p = 0.0102). These exact findings were mirrored in a large-scale study by Bai et al., which also documented that low albumin tightly correlated with lower hemoglobin, higher bilirubin, and prolonged prothrombin times.

While in-hospital mortality trended higher in the low albumin group (8.75% vs. 5%), statistical significance was not reached (p = 0.5803), likely owing to the study's relatively small sample size and short-term, hospital-based focus. Nonetheless, these findings definitively position serum albumin not merely as a marker of nutritional status, but as a crucial prognostic indicator for disease severity, complication rates, and the degree of neurological impairment in hepatic encephalopathy.

Conclusion Hypoalbuminemia is a predominant and clinically critical feature in patients presenting with hepatic encephalopathy. The present study demonstrates that serum albumin levels below 3.5 g/dL are significantly associated with more severe grades of HE, higher frequencies of ascites and gastrointestinal bleeding, and more advanced liver failure as indicated by elevated Child-Pugh and MELD scores. Routine measurement of serum albumin serves as an accessible, vital tool for risk stratification, enabling clinicians to identify patients at a high risk of life-threatening complications and guide timely therapeutic interventions in tertiary care settings.

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