Section: Miscellaneous

Original Research Article

HYPOALBUMINEMIA AS A PREDICTOR OF MORBIDITY IN SEVERE TRAUMATIC BRAIN INJURY PATIENTS: A RETROSPECTIVE STUDY

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ABSTRAC

Background: Traumatic brain injury (TBI) has been a leading cause of death, morbidity and disability all over the world. Various serum markers have been studied to establish a correlation to the outcome of TBI patients like IL-6, serum albumin, pre-albumin levels, S-100 B protein and other glial markers.

Materials and Methods: A retrospective study was conducted on 110 patients admitted to Dayanand Medical College and Hospital, Ludhiana, from 2018 to 2019. The participants were patients with severe traumatic brain injury. Serum albumin levels were measured on admission (Day 1) and patient's outcome was determined at the time of discharge using the Glasgow Outcome Score (GOS). Serum albumin levels at admission were correlated with the duration of hospital stay, total stay in intensive care unit (ICU) and length of ventilator support required. Complications, if any were noted.

Results: 78 out of 110 patients had an unfavourable outcome; of which 78.2% had hypoalbuminemia and 21.8% had normal albumin levels at the time of admission. Among 32 patients with a favourable outcome, 75% had normal albumin levels, while 25% had hypoalbuminemia. Patients with hypoalbuminemia had a mean hospital stay of 17.03 ± 2.56 days, in contrast to patients with normal serum albumin levels who had a hospital stay of 14.10 ± 1.85 days. Hypoalbuminemia patients had a mean ICU stay of 6.94 ± 1.53 days as compared to patients with normal serum albumin levels who had a mean ICU stay of 5.56 ± 1.25 days. Mean duration of mechanical ventilation was 5.17 days in hypoalbuminemic patients and 4 days in patients with normal serum albumin. Complications were observed in 37.68% of patients with hypoalbuminemia, compared to 17.07% of those with normal serum albumin levels.

Conclusion: The strong association between hypoalbuminemia and the increased need for surgical intervention in TBI patients suggests that serum albumin levels can serve as a valuable prognostic indicator in these cases.

Keywords: Hypoalbuminemia Albumin, favourable, unfavourable, traumatic brain injury, Outcome, Intensive Care Unit.

INTRODUCTION

Traumatic brain injury remains a serious concern and one of the leading causes of morbidity and mortality, particularly among young adults.[1] An uncertainty exists about the likely outcome after traumatic brain injury (TBI).[2] It still remains impossible to say with certainty what will be the future course of events in an individual patient. But intensive research in the last two decades has made it possible to predict more

confidently about the likely outcome and also to consider prognosis in terms of probabilities rather than prophecies.[3]

TBI is a significant public health problem worldwide and is predicted to surpass many diseases as a major cause of death and disability There is some data to indicate that the majority of TBI cases (60%) are as a result of road traffic incidents (RTI), followed by falls (20-30%), and violence (10%). In addition to being a major cause of mortality, injuries are also associated with increased disability and morbidity. India leads rest of the world in fatalities due to road accidents.[4]

Even if people survive, the concomitant physical disabilities, long-term cognitive and psychological damage pose a major threat. With the subsequent secondary damage setting insidiously, the pathological sequel warrants a multidisciplinary approach for management along with longer period of stay in the ICU setting. It takes a heavy toll on both financial status of the patients and the hospital's available resources. In order to mitigate the misery of the patients and to judiciously allocate the hospital resources, it becomes mandatory to predict the favourable outcome earlier in order to take decision whether to continue aggressive therapeutic measures or not.[5]

Serum albumin is one of the negative acute phase reactants and its level tends to fall in the plasma as a result of injury or infection independent of the nutritional status.[6] Many studies have highlighted the role of albumin as a prognostic marker in life threatening illnesses, various types of cancer such as colorectal, lung and breast cancer.[7] It has also been studied to determine the clinical outcome following cardiac surgery.[8] Du Chen, Long Ba, et al. studied the use of serum albumin along with pre-albumin to predict the poor outcome in TBI and observed that serum albumin serves as a better marker.[9]

Though serum albumin levels are known to fall in the first few days following head injury, hypoalbuminemia at admission has, so far, not been studied in detail.[10] A few studies have demonstrated hypoalbuminemia in mild, moderate and severe head injury at admission. Mean admission serum albumin level showed a positive correlation with GCS at admission. The elevation of IL-6 likely corresponds with the increasing severity of injury. Many studies have suggested serum albumin to be a valuable prognostic indicator in critically ill patients and not necessarily a marker of only nutritional status.[11]

Given the limited availability of clinically established biomarkers for head injury severity, it is essential to investigate each potential marker in relation to neurological outcomes. Thus, the aim of our study was to study the role of serum albumin as a marker for predicting prognosis in terms of ICU stay, duration of ventilatory support, total stay in hospital along with any complications that were faced. Also to study the relation between serum albumin levels in surgically and non-surgically managed patients admitted with severe traumatic brain injury.

MATERIALS AND METHODS

A retrospective study was conducted on patients admitted to the emergency and trauma centre of Dayanand Medical College and Hospital, Ludhiana, from 2018 to 2019. The participants were individuals with severe traumatic brain injury, characterised by a Glasgow Coma Score (GCS) of 8 or below.

Inclusion Criteria of the study

1. Patients with severe head injury (GCS ≤ 8)
2. Head injury confirmed through CT or MRI

Exclusion Criteria of the study

1. Patients below 18 years or above 65 years of age.
2. Patients with polytrauma.
3. Patients with pre-existing hepatic disease, chronic renal failure or cardiopulmonary conditions.

Neurological and radiological assessments of all the patients were done using a non-contrast CT scan of the head. Upon admission, serum albumin levels were recorded and an appropriate treatment plan was formulated based on clinical evaluation and imaging. Patients received care in the neuro-intensive care unit and neurosurgery ward. Ventilatory and inotropic support were initiated as deemed necessary.

Serum albumin levels were measured on admission (Day 1) and The patient's outcome was determined at the time of discharge using the Glasgow Outcome Score (GOS). Patients were classified into two groups: Unfavourable outcome (GOS scores 1, 2, and 3) and Favourable outcome (GOS scores 4 and 5). Serum albumin levels at admission were correlated with the duration of hospital stay, intensive care unit (ICU) stay, length of ventilator support required, and any complications if encountered.

Treatment strategies were made according to clinical and radiological findings. Decision regarding surgical or non-surgical management were made accordingly.

Glasgow Outcome Scale (GOS)

Score Term Definition

1. Dead- No life.
2. Vegetative state- Unaware of self and environment.
3. Severe disability- Unable to live independently.
4. Moderate disability- Able to live independently.
5. Mild disability- Able to return to work/school.

Ethical approval for the study was obtained from the respective institutional ethics committee.

Statistical Analysis

Data was analysed using descriptive statistics and frequency distribution methods. Mean values were presented as Mean ± SD, and categorical data was represented as counts (n, %). The Student's t-test and Chi-square test were applied, considering a p-value of ≤ 0.05 as statistically significant. The analysis was performed using Intercooled Stata 9.2 statistical.

RESULTS

A total of 110 head injury patients aged 10 to 65 years were studied. Most of them were in the 31-40 years old age group. Of the 110 patients,77.3% were male and 22.7% were female. In our study, 69 out of 110 patients had serum albumin levels below 3.5 g/dL, while 41 had levels of 3.5 g/dL or higher. [Table 1]. A favourable outcome was observed in 29.1% patients, while 70.9% had an unfavourable outcome. Complications occurred in 30% of cases which included infections, cardiac issues and renal complications; while 70% patients had no complications.

Table 1: Demographic Profile of Patients under study.

	Number of cases	Percentage
Age (31-40 years)	30	27.3%
Gender Male Female	 85 25	 77.3% 22.7%
Outcome Favourable Unfavourable	 32 78	 29.1% 70.9%
Complications No Yes	 77 33	 70% 30%
Serum Albumin (Day1) Hypoalbuminemia Normalalbuminemia	 69 41	 62.7% 37.3%
Management Conservative (C) Surgical (SU)	 39 71	 35.5% 64.5%

Our study found no statistically significant difference between patient outcome and age distribution and gender.

Our study, [Table 2] depicts that mean serum total protein was 6.0 ± 0.09 in the favourable group and 5.95 ± 0.09 in the unfavourable group. 78 out of 110 patients had an unfavourable outcome; of which 78.2% had hypoalbuminemia and 21.8% had normal albumin levels at the time of admission. Among 32 patients with a favourable outcome, 75% had normal albumin levels, while 25% had hypoalbuminemia. The mean serum albumin at admission was significantly higher in the favourable outcome group (3.54 ± 0.08) compared to the unfavourable outcome group (3.42 ± 0.08). Statistical analysis showed a significant correlation between admission serum albumin levels to discharge or death outcomes.

Table 2: Characteristics According to Neurological Outcomes

	Unfavourable (n=78) Mean /SD / Total Percentage	Favourable (n=32) Mean /SD / Total Percentage	p-value
Total Serum Protein (TSP) on Admission	5.95 0.09	6.05 0.09	0.00
Serum Albumin on Day 1 (S.ALB D1) Hypo Normal	 6178.2% 1721.8%	 825% 24 75%	0.000
Mean Serum Albumin on Day 1 (S.ALB D1)	3.42 0.08	3.54 0.08	0.000

P<0.001highly significant

In our study, patients with serum albumin levels <3.5 g/dL (hypoalbuminemia) had a mean hospital stay of 17.03 ± 2.56 days, with a median of 17 days and a range of 10–24 days. In contrast, patients with normal serum albumin levels had a mean hospital stay of 14.10 ± 1.85 days, median of 14 days ranging from 10 to 18 days. Statistical analysis revealed a significant correlation between serum albumin levels and hospital stay ($p < 0.001$) [Table 3].

Our study depicted that patients with serum albumin levels <3.5 g/dL (hypoalbuminemia) had a mean ICU stay of 6.94 ± 1.53 days, with a median of 7 days and a range of 4–11 days. Patients with normal serum albumin levels had a mean ICU stay of 5.56 ± 1.25 days, median of 6 days ranging from 3 to 8 days. Statistical analysis showed a significant correlation between serum albumin levels and ICU stay ($p < 0.001$) [Table 3].

In patients having serum albumin levels < 3.5 g/dl (hypoalbuminemia), mean duration of mechanical ventilation was 5.17 ± 1.36 days with median of 5 days and a range of 2-8 days. Among the patients

with normal mean serum albumin mean duration of mechanical ventilation was 4 ± 1.025 days with a median of 4 days and range of 2-6 days. On statistical analysis the correlation between mean serum albumin and duration of mechanical ventilation was found to be statistically significant (p<0.001). [Table 3]

Table 3: Co-relation with hospital stay, ICU stay and Ventilatory support

Days of hospital stay	**Hypoalbuminemia (n=69)**		**Normalbuminemia (n=41)**		**t**	**p-value**
	Mean	**SD**	**Mean**	**SD**		
Mean	17.03	2.561	14.10	1.855	6.395	0.000
Median	17.00		14.00			
Min-Max	10	24	10	18		
	Hypoalbuminemia (n=69)		Normalbuminemia (n=41)		t	p-value
Intensive Care Unit (ICU) Stay Days	Mean	SD	Mean	SD		
Mean	6.94	1.533	5.56	1.246	4.886	0.000
Median	7.00		6.00			
Min-Max	4	11	3	8		
	Hypoalbuminemia (n=69)		Normalbuminemia (n=41)		t	p-value
Ventilatory Support Days	Mean	SD	Mean	SD		
Mean	5.17	1.361	4.00	1.025	4.774	0.000
Median	5.00		4.00			
Min-Max	2	8	2	6		

SD-Standard Deviation p<0.001 highly significant

Complications were observed in 37.68% of patients with hypoalbuminemia, compared to 17.07% of those with normal serum albumin levels. The complication rate was significantly higher in the hypoalbuminemia group (p = 0.0225). Additionally, 38.5% of patients with an unfavourable outcome experienced complication. Whereas, only 9.4% of those with a favourable outcome had complications, with this difference being statistically significant (p = 0.003) [Table 4a&4b].

Table 4a: Association between Serum Albumin and complications

		Serum Albumin-MEAN		**Total**	**P value**
		1)Normal (n=41)	**2)Hypo albuminemia (n=69)**		
COMPLICATIONS	Yes	7 (17.07%)	26(37.68%)	33	0.025
	No	34(82.9%)	43(62.31%)	77	
Total		41	69		

P<0.05 significant

Table 4b: Association between complications and outcome

		Outcome (GOS) on discharge(F/UF)				**Total**	**Chi-square value**	**p-value**
		F (n=32)		**UF (n=78)**				
Complications	No	29	90.6%	48	61.5%	77	9.141	0.003
	Yes	3	9.4%	30	38.5%	33		

P<0.05 significant

Among the 110 patients in our study, 71 (64.5%) underwent surgical intervention, while 39 (35.5%) were managed conservatively. The mean serum albumin level in the conservative group was 3.49± 0.1 mg/dL, while it was significantly lower in the surgical group at 3.43 ± 0.09 mg/dL (p = 0.001) [Table 5].

Table 5: Mean Serum Albumin in Conservative and Surgical Groups

Management	Conservative (n=39)		Surgical (n=71)		t	p-value
S.ALB D1	Mean	SD	Mean	SD		
Mean	3.49	0.10	3.43	0.09	3.374	0.001
Median	3.50		3.41			
Min-Max	3-4.0		3-4.0			

S ALB D1- Serum Albumin on Day 1, p=0.001 highly significant

DISCUSSION

Assessing long-term neurological outcome after severe traumatic brain injury is difficult and often characterized by uncertainty.[12] Serum albumin level is correlated with outcome in various clinical situations. Albumin has multiple physiologic properties that could be beneficial in brain injury. The Lund therapy for elevated intracranial pressure uses albumin as part of its protocol and demonstrates favourable outcome.[13] The objective of this study was to analyze the role of serum albumin as a predictor of prognosis and outcome in terms of ICU stay, duration of ventilatory support, total stay in hospital, complications and comparison between surgically and non-surgically managed patients admitted with severe traumatic brain injury.

In our study, among 78 patients with an unfavourable outcome, 78.2% had hypoalbuminemia while 21.8% had normal albumin levels at admission (D1). Of the 32 patients with a favourable outcome, 75% had normal albumin levels, and 25% had hypoalbuminemia. A statistically significant correlation was found between hypoalbuminemia and unfavourable outcomes. These findings align with studies by various authors. Dhandapani et al. reported that 62% of patients with hypoalbuminemia at admission had an unfavourable outcome at three months, compared to 18% with normal albumin levels ($p < 0.001$).[14] Similarly, Pandey et al. found that 76% of patients with an unfavourable outcome had hypoalbuminemia while only 32% in the favourable group had low albumin levels.[15] Du Chen et al. also demonstrated that in TBI patients with serum albumin ≥3.5 g/dL, the proportion of unfavourable outcomes was significantly reduced.[9]

In our study, patients with serum albumin levels <3.5 g/dL (hypoalbuminemia) had a mean hospital stay of 17.03 ± 2.56 days, with a median of 17 days and a range of 10–24 days. In contrast, patients with normal serum albumin levels had a mean hospital stay of 14.10 ± 1.85 days, median of 14 days ranging from 10 to 18 days. Statistical analysis revealed a significant correlation between serum albumin levels and hospital stay ($p<0.001$). Regarding ICU stay, patients with hypoalbuminemia had a mean duration of 6.94 ± 1.53 days, with a median of 7 days and a range of 4–11 days. Patients with normal serum albumin levels had a mean ICU stay of 5.56 ± 1.25 days, median of 6 days ranging from 3 to 8 days. This correlation was also statistically significant ($p<0.001$). Bernard F et al. reported that patients in the favourable group spent an average of 7 days in the ICU, compared to 11 days in the unfavourable group. They also observed that hypoalbuminemia persisted longer in patients with extended ICU stays.[13] Similarly, Pandey et al. found a significant difference in neuro-ICU stay duration, with a mean of 8.08 ± 3.008 days for hypoalbuminemic patients and 3.84 ± 2.433 days for those with normal albumin levels ($p<0.001$).[15] In terms of mechanical ventilation, hypoalbuminemic patients had a mean duration of 5.17 ± 1.36 days, with a median of 5 days and a range of 2–8 days, while patients with normal serum albumin levels had a mean of 4 ± 1.025 days, median of 4 days ranging from 2 to 6 days. Statistical analysis confirmed a significant correlation ($p<0.001$). Bernard F et al. found that the favourable group spent an average of 4 days on mechanical ventilation, compared to 9 days in the unfavourable group ($p<0.001$).[13] Pandey et al. also observed a statistically significant difference ($p=0.011$) in mechanical ventilation duration between hypoalbuminemic (5.92 ± 3.008 days) and normoalbuminemic (3.50 ± 2.433 days) patients.[15]

Overall, our findings align with previous studies, indicating that hypoalbuminemia is a reliable predictor of hospital stay, ICU stay and mechanical ventilation duration. Recognizing this relationship can help optimize critical care resource management. Hypoalbuminemia has been linked to a higher risk of complications, including surgical site infections, respiratory and urinary tract infections, wound dehiscence and CSF leaks. It has also been linked to systemic issues affecting the heart, liver and kidneys. In our study, complications occurred in 37.68% patients with hypoalbuminemia, compared to 17.07% with normal serum albumin. This shows a significantly higher complication rate in the hypoalbuminemia group ($p = 0.0225$). Additionally,

38.5% patients with an unfavourable outcome experienced complications, whereas only 9.4% with a favourable outcome had complications which is a statistically significant difference (p = 0.003). Pandey et al. reported a higher incidence of infections and delayed wound healing in the unfavourable group (14.9%) compared to the favourable group (8.5%), though this difference was not statistically significant (p = 0.201).[15]

Among the 110 patients in our study, 71 (64.5%) underwent surgical intervention, while 39 (35.5%) were managed conservatively. The mean serum albumin level in the conservative group was 3.49 ± 0.1 mg/dL, while it was significantly lower in the surgical group at 3.43 ± 0.09 mg/dL (p = 0.001). Dhandapani et al. reported that 36% of patients undergoing surgery had a ≥15% fall in serum albumin at three weeks, compared to 25% in the non-surgical group.[14]

Surgery is a physically demanding process that triggers various physiological and biochemical changes in the body. Several preoperative and perioperative measures can help minimize surgical stress and improve outcomes. Our study highlights that identifying patients at higher risk of surgical stress can be done using a simple and cost-effective test—serum albumin estimation. The strong association between hypoalbuminemia and increased need for surgical intervention in TBI patients suggests that serum albumin levels can serve as a valuable prognostic indicator in these cases.

CONCLUSION

Serum albumin levels are a valuable prognostic marker in critically ill patients. It predicts the nutritional status along with potential outcome of the patient after trauma and surgery. Head trauma is one of the major cause of morbidity, mortality and disability in a patient. Sequelae to head trauma is long term cognitive and psychological damage. It is important for doctors to prognosticate patient of TBI early in the course of treatment so as to predict the outcome of patient in future. This study aimed to identify a cost-effective and widely available biomarker for prognosticating the outcome of severe TBI cases. Based on our findings, serum albumin proves to be a valuable prognostic tool to predict the duration of icu stay, ventilatory support requirement along with total hospital stay. It can also be used to predict the outcome of the patient after surgery for severe traumatic brain injury.

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