

Serum Serial Albumin as a Prognostic Marker in Critically III Patients

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Abstract

Introduction: Serum albumin (SA) is a useful marker of nutritional status of an individual. It serves as an indicator of overall clinical status in critically ill (CI) patients. Hypoalbuminemia is associated with increased mortality and morbidity in critical illness. It is a cheap and effective way to stratify the patients and take required emergency measures. The aim of the study is to determine the correlation between daily SA levels, mortality and clinical status of CI patients.

Materials and Methods: CI patients were defined as those who either had multi-organ dysfunction and/or sepsis and required intensive care. The patients with chronic liver and kidney disease were excluded from the study. Comparison and trend of SA over first 5 days of admission were studied among survivors (S) and non-survivors (NS) irrespective of diagnosis.

Observations: A significant difference ($P < 0.05$) was observed in the mean SA on day 3 between S and NS (2.89 and 2.55 g/dl, respectively). Among the S, those with higher mean SA on day 3 had shorter hospital stay (≤ 7 days, Group 1) compared to those with >7 days (Group 2) (mean SA 3.17 g/dl [2.54-3.78] and 2.77 g/dl [2.21-3.31], respectively) ($P < 0.05$). SA on day 1 (3.34 ± 0.68 g/dl) compared with SA on day 5 (3.77 ± 0.70 g/dl) in Group 1, showed an increasing trend which reached statistical significance ($P = 0.05$) whereas in Group 2, SA on day 1 when matched with SA on day 5, rise was in significant (3.14, 3.28 g/dl, $P > 0.05$, respectively). Those who recovered to higher SA value on day 5 had higher chances of survival (SA <2.5 g/dl - 70% mortality).

Conclusion: SA on day 3 correlated directly with higher mortality in CI patients. Day 3 SA and the level of change, during the hospital stay, had an impact on morbidity. Day 5 SA <2.5 g/dl served as a poor prognostic marker. SA thus serves as a simple but powerful prognostic tool for CI patients.

Key words: Critically ill, Day 3, Serum albumin, Survivor

INTRODUCTION

Albumin is the most abundant plasma protein and contributes to 55-60% of total protein of the body.¹ It is a useful marker of nutritional status of an individual. Besides maintaining colloidal osmotic pressure, it has important anti-inflammatory, antioxidant, ligand binding, and anticoagulant properties. It also helps in maintaining microvascular integrity.

Critically ill (CI) patients, i.e., those who because of dysfunction of one/more organs or sepsis are at increased risk of mortality.² It is important to identify the patients who are likely to have a poor outcome/increased complication rates so that aggressive management can be done.

Our scenario of resource-limited settings a good, simple, efficient, and cost-effective indicator is required to predict the risk of mortality and morbidity in such patients' albumin serves as an indicator of overall clinical status in CI patients. Albumin being a negative acute phase reactant, its concentration decreases often dramatically early in the course of illness and often does not increase till the recovery phase starts.³ Hypoalbuminemia is associated with increased mortality, increased hospital stay and higher complication rates.⁴⁻⁶ Each 10 g/L decrease in serum albumin (SA) concentration significantly increased

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mortality by 137%, morbidity by 89%, prolonged intensive care unit stay by 28%, hospital stay by 71%, and increased resource utilization by 66%.⁷

MATERIALS AND METHODS

This study was conducted in Netaji Subhash Chandra Bose Medical College, Jabalpur, Madhya Pradesh, India in 117 CI patients for the duration of 1 year 6 months.

Study Design

A cross-sectional observational study.

Inclusion Criteria

Patient willing to be a part of study.

Exclusion Criteria

Patient not willing, chronic liver failure, nephrotic syndrome, protein-losing enteropathy, chronic malnutrition.

The patients were investigated and complete blood counts, renal function tests (serum urea, serum creatinine, sodium potassium), and liver function tests (total protein, SA, serum bilirubin, aspartate aminotransferase, and alanine aminotransferase) were estimated. Serial SA for the first 5 days of admission was ascertained irrespective of diagnosis and correlation between serial trends of albumin and outcome/mortality was studied. Furthermore, the correlation of serial albumin estimation with the clinical status/morbidity of the subjects in terms in hospital stay, and ventilator requirements were studied.

Statistical analysis was performed using unpaired *t*-tests.

RESULTS

- Among the cohort of CI patients studies 80 (68.4%) were male and 37 (31.6%) females. The majority of the subjects belonged to age group of 15-30 years, i.e., out of total 117 patients around 42% were 15-30 years old.
- The majority of the CI patients had neurological diagnosis (32%) followed by cardiovascular and respiratory involvement (20% each). The rest had involvement of other organ systems.
- Out of total 117 patients, 70 patients (59.8%) recovered from critical illness and 47 patients (40.17%) succumbed to their illness. 30 males (37.5%) and 17 females (45.9%) died during the course of illness.
- It was seen that the mean value of SA on day 1 in survivors (S) was 3.21 ± 0.60 g/dl, while in non-survivors (NS), it was 3.06 ± 0.54 g/dl. The serial trend of albumin among S showed a fall till day 2 followed

by a consistent rise from day 3 onward. The mean SA on day 5 in S was 3.43 ± 0.64 g/dl.

The fall on day 2 as well as the rise on subsequent days (day 3 and day 5) was significant ($P < 0.05$).

Among NS the mean SA values showed a significant fall till day 4 (2.44 ± 0.45), followed by a paradoxical small inconsistent rise on day 5 with the day 5 value being 2.46 ± 0.52 g/dl (Table 1).

The S were divided on the basis of in-hospital stay into two groups (Figure 1).

- Group 1- Those with in hospital stay of <7 days
- Group 2 – Those with in hospital stay >7 days.

Serial albumin levels and the rate of change of albumin in the two groups were compared. Out of total 70 patients who survived 33% belonged to Group 1 and 67 % belonged to Group 2.

- The serial albumin in both the groups showed a fall till day 2 followed by a rise from day 3 onward. The mean fall in SA on day 2 in Group 1 was less as compared to Group 2 (0.34 vs. 0.49 g/dl). Furthermore, there was more marked rise in SA in Group 1 on day 5 taking day 1 as baseline compared to Group 2 (0.43 vs. 0.14 g/dl).

The admission day mean SA of Group 1 was more than the Group 2 (3.34 ± 0.68 / 3.14 ± 0.56); however, the difference was not significant ($P > 0.05$).

Table 1: Comparative mean SA

Days	Mean albumin		<i>P</i> value
	S (n=70)	NS (n=47)	
Day 1	3.21 ± 0.60	3.06 ± 0.54	>0.05
Day 2	2.76 ± 0.67	2.61 ± 0.50	>0.05
Day 3	2.89 ± 0.60	2.55 ± 0.53	<0.05
Day 4	3.17 ± 0.63	2.44 ± 0.45	<0.05
Day 5	3.43 ± 0.64	2.46 ± 0.52	<0.05

SA: Serum albumin, S: Survivors, NS: Non-survivors

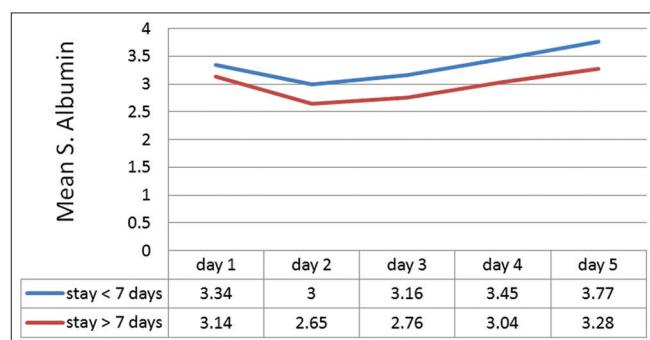


Figure 1: Serum albumin in survivors

It was seen that the Group 1 patients had a higher mean SA on day 3 (3.16 ± 0.62) compared to those with Group 2 (2.76 ± 0.55) with a $P < 0.05$.

- In terms of ventilator requirements by S 21 patients (30%) required ventilator support (Group A), while 49 patients (70%) did not require ventilatory support (Group B) (Figure 2).

Both the Groups A and B patient showed a fall in SA till day 2 followed by a rise. On comparing SA on daily basis (day 1-5), no significant difference was found between the two groups ($P > 0.05$).

- On comparing day 5 albumin between S and NS, it was found that those who recovered to higher mean albumin value on day 5 had higher chances of survival. As the mean albumin level increased so did the survival rate. Those who has albumin >3.5 g/dl on day 5 100% survival was seen (Table 2).

DISCUSSION

SA and Outcome (Mortality)

- On comparing serial albumin over first 5 days of admission between S and NS, it was seen that day 1 SA value of S, 3.21 ± 0.60 g/dl was marginally higher than NS (3.06 ± 0.54), though the difference was statistically not significant ($P > 0.05$).

In a study by Nirmala *et al.* (2015), marginally higher SA was found in S versus NS on day 1 (3.46 ± 0.25 vs. 3.44 ± 0.30), but the difference was statistically not significant.

- The serial trend of albumin among S showed a fall till day 2 followed by a consistent rise from day 3 onward. The mean SA on day 5 (3.43 ± 0.64) was higher than

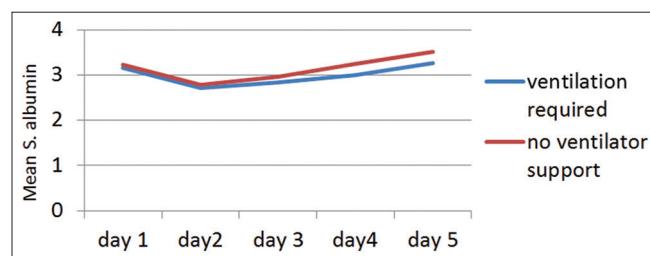


Figure 2: Ventilatory requirements

Table 2: Day 5 SA and outcome

SA (g/dl)	Outcome (%)		Total (%)
	S	NS	
<2.5	4 (30.7)	9 (69.3)	13 (100)
2.5-3	9 (75)	3 (25)	12 (100)
3.0-3.5	24 (88.5)	3 (11.1)	27 (100)
>3.5	30 (100)	0 (0)	30 (100)

SA: Serum albumin, S: Survivors, NS: Non-survivors

the day 1 value. The fall on day 2 as well as the rise on subsequent days (day 3 and 5) was significant ($P < 0.05$).

- Among NS the mean SA values showed a significant fall till day 4 (2.44 ± 0.45), followed by a paradoxical small inconsistent rise on day 5 with the day 5 value (2.46 ± 0.52) being less than the day 1 value (3.06 ± 0.54).
- Mean SA on day 3 in NS was much less than that in S group and the difference was statistically significant ($P < 0.05$). The mean SA level between S and NS on day 4 and 5 was also significant though the sample size was lesser due to deaths between day 4 and 5.

Study by Nirmala *et al.* (2015) showed a fall in SA on day 3 was strongly associated with mortality among patients with CI (S - 3.46 ± 0.29 /NS - 2.83 ± 0.51).

Mahajan *et al.* (2015) also reported strongest predictor of the outcome of patients is SA on day 3 (S - 3.04 ± 0.51 /NS - 2.75 ± 0.22).

SA and Duration of Stay of S (Morbidity)

- The serial albumin in both Groups 1 and 2 showed a fall till day 2 followed by a rise from day 3 onwards. Also in Group 1 mean SA on day 1 (3.34 ± 0.68) when matched with SA on day 5 (3.77 ± 0.70), rise almost reached significance level ($P = 0.05$), while in Group 2, it was not significant ($3.14, 3.28, P > 0.05$).
- The mean SA on day 3 was significantly lower in those with in hospital stay >7 days as compared to those with in hospital stay <7 days. Thus, hypoalbuminemia at day 3 correlates with a longer in hospital stay.
- A steeper fall in SA and a slow rise was seen in patients with in hospital stay >7 days, whereas lesser and gradual fall and higher rise was seen in those with in hospital stay <7 days. Thus, the rapidity of fall and rise of SA correlates with in hospital stay of S.

In a study by Santosh *et al.* (2016), SA in S having complication and with prolonged stay (>21 days) was significantly low ($P < 0.05$).

Dubois *et al.* concluded that hypoalbuminemia was a potent dose-dependent independent predictor of poor outcome in terms of mortality, morbidity and prolonged hospital stay.

SA and Ventilatory Requirements

The mean SA levels in those who required ventilation was comparable to those who did not require ventilation. Therefore, SA levels cannot be taken as an indicator of ventilator requirements in critical illness.

Santosh *et al.* (2016) reported that SA in S with requirement of ventilation was significantly low.

Day 5 SA and Outcome

- Those who recovered to higher mean albumin value on day 5 had higher chances of survival. No mortality was seen in subjects who has SA value of >3.5 g/dl on day 5. While SA <2.5 g/dl had mortality rate of 70%. Thus, SA value of 2.5 g/dl on day 5 can be taken as prognostic marker of poor outcome while those who recovered to mean value of >3.0 g/dl have a far better prognosis in terms of mortality.
- Blunt *et al.* (1998) showed that NS were late embryogenesis abundant able to recover from minimum albumin concentration than S.

Patients ability to recover to a higher albumin level could then conceivably taken as an indicator of recover from systemic insult and thus be used to predict long-term outcome.

CONCLUSION

CI patients have higher mortality rates. Early recognition of patients at high risk of poor outcome can prompt more aggressive management to improve their survival. SA is a cheap and cost effective and is routinely measured in all CI

patients. Serial assessment of SA provides useful prognostic information in CI patients.

SA on day 3 correlated directly with higher mortality in CI patients. SA on day 3 and the level of change, during the hospital stay, had an impact on morbidity. Day 5 SA <2.5 mg/dl served as a poor prognostic marker. SA thus serves as a simple but powerful prognostic tool for CI patients.

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