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A study on serial estimation of serum albumin as a prognostic marker in critically ill patients

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Abstract
Aim: To analyse serum albumin as a prognostic marker in critically ill patients.
Material and methods: The present cross sectional study was conducted in the department of Medicine at Chhatrapati Shivaji Subharti Hospital, Subharti Medical College, Meerut, UP. A total of 100 patients were recruited. Detailed history was taken. Patients assessed clinically on day of admission to MICU. Routine investigations like Hb, WBC, platelet count, RFT, LFT, electrolytes and Serum albumin. Serum albumin level was measured on day 1,3,5,7 to MICU. Radiological investigations like X ray, USG, CT Scan were carried according to need without any cost to patient. Serum albumin was compared to parameters like death rate as mortality indicator, morbidity indicators, need for ventilator support and duration of hospital stay. The means and standard deviations of the measurements per group were used for statistical analysis (SPSS 22.00 for windows; SPSS inc, Chicago, USA).
Results: All the nonsurvivors have hypoalbuminemia on day three as compared to 48.75% of survivors with statistically significant difference as $p<0.05$. All the nonsurvivors have hypoalbuminemia on day five as compared to 40% of survivors with statistically significant difference as $p<0.05$. The total decline in serum albumin in the survivors from admission to day 7 is 0.87 g/dl. In nonsurvivors it is 1.04 g/dl over a period of 7 days. When mean albumin was compared statistically at different intervals, it was found to be statistically significant.
Conclusion: Early recognition of patients at high risk of poor outcome can prompt more aggressive management to improve their survival. Serum albumin is a cheap and cost effective and is routinely measured in all critically ill patients. Serial assessment of serum albumin provides useful prognostic information in critically ill patients.

Keywords: critically ill, albumin, hypoalbuminemia

Introduction

Critically ill (CI) patients are defined as those who because of dysfunction of one/more organs or sepsis are at increased risk of mortality [1, 2]. There are many antioxidants in extracellular fluids including albumin, which is known as one of the most potent antioxidants [3, 4]. Serum Albumin appears to be one such prognostic indicator. Its utility as a prognostic indicator has been studied in various contexts including critically ill patients [5].

The presence of critical illness is associated with hypoalbuminemia through a variety of mechanisms. Critical illness alters the distribution of albumin between the intravascular and extravascular compartments, affects the rate of albumin synthesis and increases albumin clearance and degradation. The rate of synthesis is also decreased in critical illness, and this is thought to be a result of the increase in gene transcription for the positive acute phase proteins such as C-reactive protein and decreased in the rate of transcription of albumin mRNA [6, 7].

Large cohort studies have failed to detect effects of albumin replacement on mortality; however, a variety of evidence suggests that specific groups studies may reap physiological and biochemical benefits [8]. Albumin administration does benefit critically ill patients, most notably by improving respiratory function and gas exchange, cardiovascular stability, neurologic status and fluid balance [9]. Morbidity outcomes in the group of patients with severe hypoalbuminemia are not clear. Product-associated morbidity was much lower in severely hypoalbuminemic subjects than in patients with albumin levels above 3.0 mg/L, suggesting a dose-dependent relationship [10].

In view of the above facts, this study intends to determine the acute changes in the serum albumin concentrations that occur following admission to the ICU and evaluate the role of serial serum albumin measurement as an independent prognostic indicator.

Material and Methods

The present cross sectional study was conducted in the department of Medicine at Chhatrapati Shivaji Subharti Hospital, Subharti Medical College, Meerut, UP. A total of 100 patients were recruited. Sample size was calculated by period prevalence in our MICU after applying exclusion and inclusion criterias and approved by registered statistician and ethics committee.

Inclusion Criteria: Critically ill Patients [failure of one or more organs/system or depend on survival from advanced instruments of monitoring and therapy] admitted in MICU and subjects with age of 18 yrs and above were included in the study

Exclusion Criteria: Surgically Ill [Post-Operative Nephrotic/ Nephritic Syndrome], cirrhosis of liver, malnutrition,

protein losing enteropathy, patient who have not given informed consent were excluded from the study.
Methodology: Written informed consent was taken from each patient/relative of patient (if pt was not in state to give consent) and study explained. Patients were selected on basis of inclusion and exclusion criterias. Detailed history was taken. Patients assessed clinically on day of admission to MICU. Routine investigations like Hb, WBC, platelet count, RFT, LFT, electrolytes and Serum albumin. Serum albumin level was measured on day 1,3,5,7 to MICU. Radiological investigations like X ray, USG, CT Scan were carried according to need without any cost to patient. Serum albumin was compared to following parameters:
A] Death rate [as mortality indicator]
B] Morbidity indicators;
1] Need for ventilator support.
2] Duration of hospital stay.

Statistical analysis
Data so collected was tabulated in an excel sheet, under the guidance of statistician. The means and standard deviations of the measurements per group were used for statistical analysis (SPSS 22.00 for windows; SPSS inc, Chicago, USA). Difference between two groups was determined using student t-test as well as chi square test and the level of significance was set at $p < 0.05$.

Results
Out of 100 subjects, 80 survived while 20 were expired. In our study 59% of the subjects were males and 41% were females. Mortality was reported more among 60% and 40% of the males and females respectively. When mortality was compared according to mortality, it was found to be statistically insignificant.
The mean age of study population was 55.81 years (±20.16 years).The mean age in survivors was 46.48 years (± 21.24 years) with range of 19–85 years. The mean age in non survivors was 62.19 years (±13.57 years) with range of 28–86 years. There was a significant difference ($p = 0.03$) between the two groups indicating a higher age at admission for non-survivors (table 1).

Table 1: Age distribution among the study groups

Age (in years)	Survivors		Non survivors		Total	
	N	%	N	%	N	%
<30	24	30	1	5	25	25
31-40	10	12.5	1	5	11	11
41-50	8	10	2	10	10	10
51-60	7	8.75	5	25	12	12
61-70	17	21.25	6	30	23	23
>70	14	17.5	5	25	19	19
Total	80	100	20	100	100	100
Chi Square	7.19					
p value	0.03*					

*: statistically significant

Out of the 100 cases in study group, largest number of patients were with neurological disorders, comprising 33 cases (33%). In the survivor group, 55% patients have normal serum albumin levels on admission as compared to just 10% in the nonsurvivor group, suggesting hypoalbuminemia at admission indicates a poorer prognosis in terms of increased mortality.

Table 2: Serum Albumin levels in two groups on day one

Serum Albumin (g/dl)	Survivors		Non survivors		Total	
	N	%	N	%	N	%
<3.5	44	55	18	90	62	62
>3.5	36	45	2	10	38	38
Chi Square	16.89					
p value	<0.01*					

*: statistically significant

All the nonsurvivors have hypoalbuminemia on day three as compared to 48.75% of survivors with statistically significant difference as $p<0.05$. All the nonsurvivors have hypoalbuminemia on day five as compared to 40% of survivors with statistically significant difference as $p<0.05$ (table 3).

Table 3: Serum Albumin levels in two groups on day three

Serum Albumin (g/dl): Day 3	Survivors		Non survivors		Total	
	N	%	N	%	N	%
<3.5	39	48.75	20	100	59	59
>3.5	41	51.25	0	0	41	41
Chi Square	14.38					
p value	<0.01*					
Serum Albumin (g/dl): Day 5	Survivors		Non survivors		Total	
	N	%	N	%	N	%
<3.5	32	40	20	100	52	52
>3.5	48	60	0	0	48	48
Chi Square	23.92					
p value	<0.01*					
Serum Albumin (g/dl): Day 7	Survivors		Non survivors		Total	
	N	%	N	%	N	%
<3.5	30	37.5	20	100	50	50
>3.5	50	62.5	0	0	50	50
Chi Square	18.53					
p value	<0.01*					

*: statistically significant

The total decline in serum albumin in the survivors from admission to day 7 is 0.87 g/dl. In nonsurvivors it is 1.04 g/dl over a period of 7 days. When mean albumin was compared statistically at different intervals, it was found to be statistically significant (table 4). The results show that there is a steady fall in serum albumin in both groups. However the fall in nonsurvivors is more steep than survivors. Our study indicates that the strongest predictor of outcome of the patient is serum albumin on day three with highest odds ratio. Outcome of the patient is poorly correlated with serum albumin level on day one which has the lowest odds ratio.

Table 4: Comparison of mean albumin at different intervals among survivors and non-survivors

Serum Albumin (g/dl)	Survivors		Non survivors		p value
	Mean	SD	Mean	SD	
Day 1	3.48	0.53	3.02	0.26	0.008*
Day 3	3.11	0.48	2.72	0.21	0.003*
Day 5	2.82	0.37	2.28	0.28	0.003*
Day 7	2.61	0.39	1.98	0.24	<0.01*

*: statistically significant

In the study group, the mean duration of mechanical ventilation was 9.3 days (± 2.9 days). The average number of days survivors were on mechanical ventilation was 8.6

days (± 2.3 days) and in non survivors, this duration was 10.1 days (± 2.6 days). The duration of mechanical ventilation was significantly more (p = 0.02) in non survivors. The average duration of hospital stay was significantly longer (p = 0.007) in survivors as compared to non-survivors (table 5).

Table 5: No. of days of ventilation, ICU and Hospital stay in two groups

No. of days of ventilation	Survivors		Non survivors		Total	
	N	%	N	%	N	%
5-7	38	47.5	7	35	45	45
8-10	29	36.25	5	25	34	34
11-13	12	15	6	30	18	18
>13	1	1.25	2	10	3	3
Chi Square	8.74					
p value	0.02*					
No. of days of ICU stay	Survivors		Non survivors		Total	
	N	%	N	%	N	%
5-7	6	7.5	0	0	6	6
8-10	36	45	2	10	38	38
11-13	25	31.25	9	45	34	34
>13	13	16.25	9	45	22	22
Chi Square	9.78					
p value	0.009*					
No. of days of Hospital stay	Survivors		Non survivors		Total	
	N	%	N	%	N	%
5-10	8	10	2	10	10	10
11-15	41	51.25	16	80	57	38
16-20	19	23.75	1	5	20	34
>20	12	15	1	5	13	22
Chi Square	10.51					
p value	0.007*					

*: statistically significant

Discussion

Patients who are admitted in Intensive Care Unit (I.C.U.) are at an increased risk of mortality due to the severity of their illness. It is thus, important to identify the patients at the time of admission who are likely to have a poor outcome, so that such patients can be managed aggressively. Serum Albumin appears to be one such prognostic indicator. Its utility as a prognostic indicator has been studied in various contexts including critically ill patients. This study intends to determine the acute changes in the serum albumin concentrations that occur following admission to the ICU and evaluate the role of serial serum albumin measurement as an independent prognostic indicator.

In our study out of 100 critically ill subjects, 80 survived while 20 were expired. In a study by Sanket Mahajan *et al.* [11], 31 patients (62%) were discharged from the hospital (survivors) and 19 patients (38%) expired in the hospital (non survivors). Similarly Dubois *et al.* [12] concluded that hypoalbuminemia was a potent dose-dependent independent predictor of poor outcome in terms of mortality, morbidity and prolonged hospital stay. Young Suh Kim *et al.* [14] in their study showed that serum albumin level in the survival group is higher than that in the non-survival group (3.4 g/dl [interquartile range, 3 to 3.8 g/dl] vs. 2.9 g/dl [interquartile range, 2.3 to 3.4 g/dl], P < 0.001).

Mortality was reported more among 60% and 40% of the males and females respectively with statistically insignificant difference. The present study shows that males are more likely to suffer from a critical illness than females. Sanket Mahajan *et al.* [11] in their study revealed that amongst survivors (31), 22 (71%) were males and 9 (29%) were females. In non survivors (19), 15 (78.9 %) were males and 4 (21.1 %) were females which is similar to our study. In one study, this was found to be 59.3% males and 38.7% females [15]. This is comparable to our study population.

In the survivor group, 55% patients have normal serum albumin levels on admission as compared to just 10% in the nonsurvivor group, suggesting hypoalbuminemia at admission indicates a poorer prognosis in terms of increased mortality. Mahajan S*et al.* [11] revealed similar findings in their study. They reported that, in the survivor group, 45.2% patients have normal serum albumin levels on admission as compared to just 10.5% in the non-survivor group, suggesting hypoalbuminemia at admission indicates a poorer prognosis in terms of increased mortality. More non-survivors were hypoalbuminemic at admission than survivors suggesting that a low serum albumin at admission indicates a poor prognosis. One study reports survivors had higher admission albumin (2.57 g/dl vs 2.10 g/dl, p<0.005) than non-survivors [16]. Another study reports similar findings with survivors having higher mean albumin concentration (18.3 ± 4.6 g.L-1) compared to non survivors (15.7 ± 5.1 g.L-1) (p < 0.05) [14].

All the nonsurvivors have hypoalbuminemia on day three as compared to 48.75% of survivors with statistically significant difference as p<0.05 in our study. All the nonsurvivors have hypoalbuminemia on day five as compared to 40% of survivors with statistically significant difference as p<0.05. On day seven, all the nonsurvivors have hypoalbuminemia as compared to 37.55% of survivors with statistically significant difference as p<0.05 in our study. One study reports day three levels as 2.9 g/dl (± 0.6 g/dl) which are similar to our studies [14]. All the non-survivors were still hypoalbuminemic as compared to survivors where now, 83.9% of patients were hypoalbuminemic as reported by Mahajan S *et al.* [11].

Our study indicates that the strongest predictor of outcome of the patient is serum albumin on day three. Outcome of the patient is poorly correlated with serum albumin level on day one. One study reports day five albumin levels to be the strongest predictor of mortality. This difference is noted because of the method of analysis of data and the use of different kind of statistical test to predict the outcome.

In the present study, the average duration for which patient were in ICU was significantly higher (p = 0.009) in non survivors as compared to survivors. Mahajan S *et al.* [11] in their study revealed similar results. One study reports length of ICU stay for mechanically ventilated patients to be 11.2 days (± 13.7 days) [14]. This difference is noted presumably because of a larger sample size, i.e. 5183 patients in the study versus 50 patients in our study. One another study reports a significant 28% increase in odds for prolonged ICU stay per 10g/L decrement in serum albumin [4]. This explains the longer ICU stay of non survivors in our study population since they have lower serum albumin levels at all times as compared to survivors.

The average duration of hospital stay was significantly longer (p = 0.007) in survivors as compared to non-survivors in the present study. In a study by Sanket Mahajan76, the average duration of hospital stay was significantly longer (p=0.0136) in survivors. One cohort study reports a significant hypoalbuminemia related increase of 71% in odds of prolonged hospital stay [4]. However, the broad inclusion criteria adopted in the study

and a larger sample size of 2, 91,443 patients have made a significant difference in the observations. One study reports an average of 22.5 days (± 23.7 days) as length of stay in hospital for mechanically ventilated patients [15]. This difference is observed because of a larger sample size of 5183 patients included in the study.

This study has some limitations. First, it is a single-center, observational study with small sample size. Therefore further studies with larger sample size might be needed in a multicenter setting.

Conclusion

Critically ill patients have higher mortality rates. Early recognition of patients at high risk of poor outcome can prompt more aggressive management to improve their survival. Serum albumin is a cheap and cost effective and is routinely measured in all critically ill patients. Serial assessment of serum albumin provides useful prognostic information in critically ill patients. Serum albumin on day 3 correlated directly with higher mortality in CI patients. Serum albumin thus serves as a simple but powerful prognostic tool for critically ill patients.

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