Original Research Article

Hypoalbuminemia in critically sick children

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ABSTRACT

Background: Hypoalbuminemia at admission is a common finding in patients admitted to the Paediatric Intensive Care Unit (PICU) and may predict morbidity and mortality.

Methods: Patients of age more than 1 year and less than 12 years diagnosed with hypoalbuminemia on the grounds of the inclusion criteria who were admitted in the Paediatric Intensive Care Unit (PICU) were enrolled in the study as 'cases' and patients with normal levels of serum albumin and otherwise similar characteristics to cases were included in the study as 'controls'. Detailed clinical examination and required investigations were done. Above collected information was utilized to select two groups for the study i.e., those with hypoalbuminemia and others with no hypoalbuminemia. Both these groups were further followed up till discharge or death and the outcome in terms of morbidity and mortality was noted.

Results: Incidences of MODS and degree of severity of illness as judged by PRISM III score in cases and control showed that, a lower serum albumin concentration correlated well with higher rates of complications such as ventilator dependence and development of new infections leading longer stay in the critical care unit. The mean length of PICU stay in cases group was statistically longer than in the control group. Although we did not observe a difference in fatal outcome in patients managed with either Human Albumin or Fresh Frozen Plasma compared to those managed conservatively in this study, we did observe a decreased mean length of PICU stay and rate of complications in the patients treated with either Human Albumin or Fresh Frozen Plasma, thus achieving a faster rate of recovery with lesser rate of complications and thus alleviating the morbidity, though still not being able to affect the overall mortality.

Conclusions: Hypoalbuminemia at admission was a predictive factor of poor outcome in critically ill children. It is associated with a higher mortality, a longer length of stay in the PICU, as well as longer ventilator use.

Keywords: Clinical outcomes, Critically ill children, Hypoalbuminemia, Prediction factor

INTRODUCTION

Serum albumin plays an essential role by maintaining intravascular oncotic pressure and facilitating the transport of many hormones, drugs and bioactive elements in blood circulation. Furthermore, several previous studies showed other functions of albumin such as antioxidant effects, inhibition of platelet aggregation, anti-inflammatory and anti-apoptotic effects.[1] Hypoalbuminemia is commonly found in patients with heart failure, liver cirrhosis, nephrotic syndrome, severe malnutrition, thermal injuries and protein-losing enteropathy. In critically ill patients, their blood albumin level might be low due to a decrease in synthesis by the liver, an increase in albumin degradation and/or a loss due to capillary leakage during a period of inflammation and infection.[2-4] In adults with critical illness, hypoalbuminemia is clearly associated with poor clinical outcomes.[5] A meta-analytical study showed that the presence of hypoalbuminemia is connected with a higher mortality rate, length of intensive care stay, as well as

overall hospital stay, along with duration of ventilator use. It has been estimated that each 10 g/L decrease in serum albumin will result in a mortality increase of about 137%.[5] However, there is a paucity of studies in the paediatric population, and which show conflicting results. Our goal in this Hospital-based prospective study was i) to investigate the frequency of occurrence of hypoalbuminemia ii) to examine the association between hypoalbuminemia and the outcome of illness iii) to evaluate whether hypoalbuminemia on admission is a marker of adverse outcome in this population in the Paediatric Intensive Care Unit (PICU) iv) whether correction of albumin by Human Albumin infusion or FFP helps in decreasing the morbidity or mortality of the sick child.

METHODS

A hospital based nested case control observational study done in Paediatric Intensive Care Unit at tertiary care hospital. The study population comprised of 80 cases (patients with hypoalbuminemia) and 80 controls (patients with normoalbuminemia).

At the time of initial evaluation, a through history (including history regarding birth, dietary history, family history, past and current treatment history) was entered in the pre-set questionnaire and detailed examination of each child including anthropometry (weight, height, BSA, according to Indian Association of Paediatrics classification) was done. Serum albumin monitoring, complete blood counts, blood urea nitrogen and serum creatinine and fasting blood glucose according to a predesigned proforma with a chest radiograph (postero-anterior or antero-posterior views); electrocardiogram; arterial blood gas analysis and serum electrolyte measurement as needed. Above collected information was utilized to select 2 groups for the study i.e., those with hypoalbuminemia (defined as cases) and others with no hypoalbuminemia (defined as controls). Both these groups were further followed up till discharge and records of treatment given in cases (Albumin or Fresh Frozen Plasma) was recorded. The outcome in terms of morbidity and mortality was noted.

RESULTS

This was a Hospital-based Nested case control observational study amongst the patients admitted to the Paediatric Intensive Care Unit of our hospital with 80 patients with hypoalbuminemia as cases and 80 cases without the same as controls.

In this study authors received a gender distribution equitable to the local populace with the mean age of presentation being 6 - 6.5 years of age. The Patient's disease severity (Paediatric Risk of Mortality [PRISM] score) was calculated and recorded as shown in Table 1. The cases and controls had a comparable PRISM III score, calculated at admission.

Primary system involvement (neurologic, respiratory, cardiac, hematologic and generalized sepsis without specific organ system involvement) was noted as shown in Table 2. Most common condition was Nervous system condition in cases and acute febrile illness (AFI) in controls. There was no significant difference in system affected between two groups.

Table 1: Baseline characteristics and disease severity (PRISM score).

Variables	Cases	Controls	P value
Serum albumin (g/dl)	2.5±0.5	4.3±0.6	<0.001
Age in years	6.5±3.6	6±3.3	0.346
Sex ratio (male: female)	1.35	1.10	0.525
Prism score	28.3±12.9	27.7±19.7	0.842

Table 2: System wise involvement in cases and controls.

System affected	Group			
	Cases		Controls	
	Count	%	Count	%
AFI	23	28.7%	20	25.0%
NS	24	30.0%	17	21.2%
CVS	14	17.5%	12	15.0%
RS	8	10.0%	14	17.5%
Renal	7	8.8%	10	12.5%
Hematology	4	5.0%	7	8.8%

$\chi 2 = 4.542$, df = 5, p = 0.474

Mean serum albumin in cases at admission was 2.5±0.5 and in controls was 4.3±0.6. There was significant difference in serum albumin levels between two groups at admission. At day 3 increase in serum albumin levels were observed among cases (Table 3).

Table 3: Serum albumin levels (gm/dL) comparison between two groups on admission and at day 3.

Serum albumin on admission	Group				P value
	Cases		Controls		
	Mean	SD	Mean	SD	<0.001*
	2.5	0.5	4.3	0.6	

Among cases 26.2% had pedal oedema and 23.8% had Anasarca, among controls 16.2% had pedal oedema and 2.5% had Anasarca. This difference in pedal oedema and Anasarca was statistically significant (Table 4).

Among cases 25% were given albumin and 63.7% were given fresh frozen plasma. An equitable increase in level of serum albumin was noted in patients managed with either Human Albumin or Fresh Frozen Plasma, hence both the modalities can be used alternatively for correction of albumin (Table 5).

Table 4: Edema comparison between two groups.

Edema	Group			
	Cases		Controls	
	Count	%	Count	%
Absent	40	50	65	81.2
Pedal edema	21	26.2	13	16.2
Anasarca	19	23.8	2	2.5

$\chi^2 = 21.59$, df = 2, p <0.001

Mean serum albumin in cases treated at admission was 2.47±0.6, among cases managed conservatively was 2.9±0.6. There was significant difference in serum albumin levels between these groups at admission. At day 3 increase in serum albumin levels were observed among cases treated and those managed conservatively. A significant increase was noted in the treated cases.

Table 5: Serum albumin levels (gm/dL) comparison between the groups.

Group	Group			
	Cases		Controls	
	Count	Mean±SD	Count	Mean±SD
Case treated	71	2.47±0.6	71	2.72±0.6
Case not treated	9	2.9±0.6	9	2.97±0.6

Table 6: Treatment among cases.

Treatment	Group	
	Cases	
	Count	%
Albumin	20	25.0%
Fresh Frozen Plasma	51	63.7%
No	9	11.2%

Among cases 25% were given albumin and 63.7% were given fresh frozen plasma (Table 6).

Although authors did not observe a difference in fatal outcome in patients managed with either Human Albumin or Fresh Frozen Plasma compared to those managed conservatively, authors did observe a decreased mean length of PICU stay and rate of complications in the patients treated with either Human Albumin or Fresh Frozen Plasma, thus achieving a faster rate of recovery with lesser rate of complications thus alleviating the morbidity, although still not being able to affect the overall mortality (Table 7).

Mean length of PICU stay among cases was 7.8±5.1 days and among controls was 5.1±3.2. This difference in length of stay between cases and controls was statistically significant i.e. the patients who were managed conservatively had a longer stay (Table 8).

Table 8: Length of PICU stay (in days) between two groups.

Length of PICU stay	Group				P value
	Cases		Controls		
	Mean	SD	Mean	SD	
	7.8	5.1	5.1	3.2	<0.001*

Among cases 32.5% died and 67.5% survived, similarly among controls 25% of them died and 75% survived. There was no significant difference in outcome between two groups (Table 9).

Table 9: Comparison of outcome between two groups.

Outcome	Group			
	Cases		Controls	
	Count	%	Count	%
Death	26	32.5%	20	25.0%
Survived	54	67.5%	60	75.0%

$\chi^2 = 0.112$, df = 1, p <738

Table 10: Comparison of outcome between three groups.

Comparison of outcome		Groups					
		Cases treated with albumin		Case treated with Fresh Frozen Plasma		Cases managed conservatively	
		Count	%	Count	%	Count	%
Outcome	Death	7	35.0%	19	37.3%	2	22.23
	Survived	13	65.0%	32	62.7%	7	77.78

Among cases treated with Albumin 35% died and 65% survived, among cases treated with FFP 37.3% died and 62.7% survived and similarly among controls 35% of them died and 65% survived. There was no significant difference in outcome between three groups (Table 10).

Although the incidences of MODS and degree of severity of illness as judged by PRISM III was similar in the two groups at admission, a lower serum albumin concentration correlated well with higher rates of complications such as ventilator dependence and

development of new infections leading longer stay in the critical care unit. The mean length of PICU stay in cases group was statistically longer than in the control group. Similar to previous studies, this study found significant association between low serum albumin levels and in-hospital stay.

DISCUSSION

Hypoalbuminemia is a frequent occurrence in critically ill patients, with spontaneous normalisation of values often only occurring late in the recovery phase of the disease.[6] The aetiology of hypoalbuminemia in critical illness is complex and may involve a number of mechanisms such as an imbalance between albumin synthesis and degradation, increased capillary leakage, and altered intravascular and tissue albumin distribution.[6] A low serum albumin concentration may be associated with a poor outcome independent of the underlying disease process.[6]

In present study the mean albumin levels at admission of cases was 2.5 g/dL and controls were 4.3 g/dL. The prevalence of hypoalbuminaemia on admission in critically ill children from previous studies is about 33-57%.[7-9] This might reflect the differences in the study population and the definition of hypoalbuminaemia. Tiwari et al, defined hypoalbuminaemia as a serum albumin level lower than 2.5 g dL-1 while Durward et al, defined it as lower than 3.3 g dL-1.[10,11] In order, to give greater weight to all these studies, a clear definition of hypoalbuminaemia in paediatric patients should be made. Due to this limitation, the true prevalence of hypoalbuminaemia is difficult to compare directly.

According to the meta-analytical study there is a strong association between patients with hypoalbuminaemia and high mortality rates in adult intensive care units (ICUs) while the studies in PICUs show conflicting outcomes.[5] The mortality rate in hospitals showed no statistically significant difference between the hypoalbuminaemia and nonhypoalbuminaemia groups in the studies by Tiwari et al, and Durward et al.[10,11] However, Horowitz et al, reported that the survival rate of hypoalbuminemic patients is significantly less than patients with normal serum albumin.[7] But in present study patients with hypoalbuminemia had more fatal outcome.

A low serum albumin concentration correlates with increased length of stay in the intensive care unit (ICU) and with complication rates, such as ventilator dependency and the development of new infection.[4] In present study the mean Length of PICU stay of cases was 7.8 days and controls were 5.1. In the studies of Horowitz et al, (cases - 8.08 days, controls - 4.41 days) and Kittisakmontri et al, (cases - 8.6 days, controls - 6.7 days) the mean Length of PICU stay were similar to present study, however Tiwari et al (cases - 10.5 days, controls - 9.1 days) noted a significantly longer Length of PICU stay.[7,8,10] Thus the mean Length of PICU stay in our study

was comparable to Kittisakmontri et al, and Horowitz et al.[7,8]

Hypoalbuminemia is a predictor of increased mortality and morbidity in ICU patients. Non-survivors of critical illness have lower serum albumin concentrations than survivors. In present study 32.5% of the cases and 25% of the controls had suffered a fatal outcome. There was a significant difference in outcome between the two groups. In the study of Tiwari et al 10 (cases - 23.9%, controls - 19.8%) a similar pattern of fatal outcome was noted.

CONCLUSION

The incidence of pedal oedema and anasarca were significantly higher in hypoalbuminemic patients (cases) in our study, which is comparable with the known literature. The most common condition associated with hypoalbuminemia in our study was nervous system involvement which could be attributed to hypoalbuminemia, which confers neuroprotective effect to CNS as has been collaborated by previous studies. The use of PRISM III score as severity scoring system helped us better prognosticate the patients as regards to severity of their illness with consequently better triaging, utilisation of resources and appropriate treatment to improve the outcome. A low serum albumin concentration correlated well with rates of complications such as ventilator dependence and development of new infections leading longer stay in the critical care unit. The mean length of PICU stay in hypoalbuminemic patients was statistically longer than normoalbuminemic patients. The comparison of PICU stay in our study and in the previous studies in both the groups of patients was comparable.

Significant difference in fatal outcome was noted with normoalbuminemic patients having fared better. An increase in level of serum albumin was noted in patients treated with either Human Albumin or Fresh Frozen Plasma, hence both the modalities can be used alternatively for correction of albumin. Although we did not observe a difference in fatal outcome in patients managed with either Human Albumin or Fresh Frozen Plasma compared to those managed conservatively in this study, we did observe a decreased mean length of PICU stay and rate of complications in the patients treated with either Human Albumin or Fresh Frozen Plasma. Thus, concluding that replacement of albumin is very likely to improve serum albumin levels, significantly decrease the morbidity but may not reduce the mortality. Hence, authors advocate the cautious use of these agents under the watchful eye of the treating physician.

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