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Research paper

Study on the Prevalence of Hypoalbuminemia and their Clinical Outcome in Critically Ill Children Admitted to PICU in Tertiary Care Hospital

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Abstract
Introduction: *Hypoalbuminemia is a frequent and early biochemical derangement in critically ill-patients and is considered as a marker of disease severity and predictor of increased morbidity and mortality. The objective of the study is to evaluate prevalence of hypoalbuminemia and its association with disease severity and clinical outcome of illness in critically ill children.*

Methods: *A prospective observational study conducted at the PICU of Tertiary care Hospital. Children aged 1year to 12 years admitted to PICU were included. Serum albumin levels were estimated at the time of admission to PICU. Children who expired within 24 hours after ICU admission, children with hepatic or renal failure, and those who received albumin replacement before ICU admission were excluded. Pediatric risk of mortality III (PRISM-III) scoring system was used to assess the severity of illness at admission.*

Results: *The prevalence of hypoalbuminemia at admission was 38%. Mean serum albumin level in this study was 2.54 ± 0.38 g/dl. A lower s.albumin concentration correlated well with higher rates of complications such as ventilator dependency and development of new infections leading to longer length of PICU stay and higher mortality (31.5%). The mean length of PICU stay (8.6 ± 5.1; p<0.001) was statistically longer than those with normal albumin. A Strong negative correlation(r= -0.867) found between s.albumin level and the mortality rate.*

Conclusion: *Hypoalbuminemia at admission can be helpful for risk assessment and can be used as an outcome predictor in critically ill children.*

Keywords: *Critical ill children, Hypoalbuminemia, Mortality, PICU, PRISM III, S.Albumin.*

Introduction

Predicting the prognosis of patients admitted in intensive care unit (ICU) is important for evaluating the quality of ICU care and making decisions regarding further management[1]. The accurate methods of predicting outcomes of patients have been needed, therefore many scoring systems or parameters for predicting prognosis including mortality of patients have been proposed. The recently developed assessments based on physiologic variables have limitations as it requires many variables which are not possible to collect for all patients admitted to ICU[1]. Therefore, it is the need of the hour to identify noninvasive, simple, quick, accessible and easy means or parameters to predict the prognosis of the patients in ICU, especially for pediatric patients. The condition of

critically ill patients admitted to the ICU is vulnerable to oxidative stresses caused by reactive oxygen species, resulting in injuries to cells and tissues and activating extracellular antioxidant defense network consecutively[2,3]. There are many antioxidants in extracellular fluids including albumin, which is also known as one of the most potent antioxidants [3]

Albumin is a highly water soluble protein. It is synthesized in liver and forms about 60–70% of the total plasma proteins. It contributes to 80% of the colloidal osmotic pressure and thus, it plays a key role in the regulation of blood volume [4]. It constitutes up to two-third of total plasma protein, one-third of which is distributed in the intravascular space and two-third in the extravascular space. It is also involved in the binding and transport of various molecules including bilirubin, bile salts, hormones, micronutrients, and some drugs[5]. Several studies have also showed other functions of albumin such as antioxidant effects, inhibition of platelet aggregation, anti-inflammatory and anti-apoptotic effects[5]. Albumin is also considered as a negative acute phase reactant, and hypoalbuminemia is known to occur in infection and injury.

Hypoalbuminemia in this settings in adult patients is an independent predictor of mortality and is associated with poor outcomes in criticaliy ill adults[3,6,7]. Research on critically ill adult patients has shown that hypoalbuminaemia is a marker of disease severity and has been associated with prolonged ventilatory dependence and length of intensive care stay[8] thus serum albumin is considered as a predictor of increased morbidity and mortality. However, there is a paucity of data evaluating serum albumin levels and the incidence, significance and outcome of hypoalbuminemia in critically ill children admitted to intensive care unit (ICU) and only limited studies are available[9,10]. This study was conducted to evaluate prevalence of hypoalbuminemia in critically sick children admitted to pediatric ICU (PICU) and to examine its association with disease severity and its clinical outcome.

Aims and Objectives

1) To find out the frequency of occurrence of hypoalbuminemia
2) To evaluate the association between hypoalbuminemia and the outcome of illness
3) To evaluate whether hypoalbuminemia on admission is a marker of adverse outcome in this population in the Paediatric Intensive Care Unit (PICU).

Materials and Methods

This was a prospective, single-center, observational study conducted at the pediatric intensive care unit (PICU) of a tertiary care hospital over a period of 6 months from May 2019 to October 2019. The study protocol was approved by the Institutional Ethical Committee. A written informed consent was obtained from the parents before inclusion in the study.

Inclusion Criteria

All the patients admitted to the PICU from 1 year to 12 years of age. Admission to PICU was based on the decision of the treating consultant.

Exclusion Criteria

Subjects in whom hypoalbuminemia were expected to be attributable to a preexisting condition were excluded. These included:

1) Patients who had severe protein-energy malnutrition (PEM) (weight for height <-3 standard deviations).
2) Those with chronic diseases affecting the gastrointestinal system or liver or kidney (protein losing enteropathy, chronic liver disease, nephrotic syndrome, and end-stage renal disease).
3) Children with thermal burns and those who received fresh frozen plasma or whole blood or albumin within 4 weeks before admission in PICU were also excluded.

Serum albumin level done within first 24 hour of admission was considered as admission albumin level. Hypoalbuminemia was defined as serum albumin level <3.5 g/dl. Baseline data collected were age, sex, weight, height, diagnosis categorized by organ system, length of hospital stay, length of

PICU stay, and receipt of ventilator support and outcome. Pediatric risk of mortality 3 (PRISM III) scoring system was used to assess the severity of illness at admission. PRISM III scoring system offers better triaging, which is comparable to PIM 2 (Paediatric Index of Mortality), but does not over-predict the death rate like PIM 2.

Subjects were divided into two groups according to their albumin level as hypoalbuminemia group (hypoalbuminemia subjects) and normoalbuminemic group (subjects with normal albumin level). Children who were discharged against medical advice were excluded from the analysis of outcome and duration of hospital stay. All the data analyses were conducted using the SPSS version 20.0. Mortality risk was computed using Pearson's Chi-square test.

Results

The study population included 100 subjects out of 140 subjects admitted to PICU during the study period. 40 children were excluded (Fig. 1). The mean age of the study population was 6.5 years. Hypoalbuminemia was present on admission in 38%. The mean serum albumin level of studied population was 2.54 ± 0.38 g/dl in hypoalbuminemic group and 4.1 ± 0.6g /dL in normoalbuminemic group (p <0.001) . The patient's disease severity (Paediatric Risk of Mortality [PRISM] score) was calculated at admission and recorded as shown in Table 1. Patients with hypoalbuminemia on admission had higher PRISM Score (13.6 ±9.9 vs 8.8 ±8.2, p value 0.002). The diagnostic categories of the patients are given in Table 2. Primary system involvement (neurologic, respiratory, cardiac, hematologic and generalized sepsis without specific organ system involvement) was noted. It was observed that most commonly Nervous system was affected. There was no significant difference in system affected between two groups.
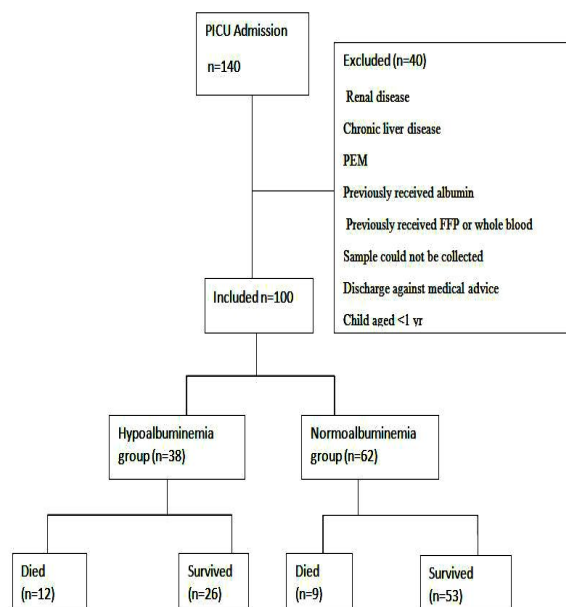

Figure 1: Flow chart of study subject admitted to pediatric intensive care unit

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

Variables	Hypoalbumin emic group (n=38)	Normoalbumi nemic group (n=62)	P value
Serum albumin (g/dl)	2.54 ±0.38	4.1 ± 0.6	< 0.001
Age in years	6.4 ±3.6	6 ±3.5	0.346
Sex ratio (male : female)	1.4	1.6	0.521
Weight (in kg)	14.2±2.3	14.7±2.5	0.497
PRISM score	13.6 ±9.9	8.8 ±8.2	0.002

Table 2: Primary System wise involvement:

System affected	Hypoalbuminemic group (n=38)		Normoalbuminemic group (n=62)	
	No.of patient	Percent (%)	No.of patient	Percent (%)
CNS	14	34.4	15	23.8
Sepsis without focus	11	29.3	13	19.0
Respiratory	08	22.4	23	38.0
CVS	03	8.6	9	14.2
Haematology	02	5.1	2	4.7

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

Serum albumin on admission	Hypoalbuminemic group (n=38)		Normoalbuminemic group (n=62)		P value
	Mean	SD	Mean	SD	< 0.001
	2.54	0.38	4.10	0.6	

Longer duration of PICU stay was observed in children with hypoalbuminemia compared to children with normal albumin levels. Mean length of PICU stay among hypoalbuminemia group was 8.6 ± 5.1 days and among normoalbuminemia group was 5.5±3.2 days. This difference in length of stay between the two groups was statistically significant.

Table 4: Length of PICU stay (in days) between two groups.

Length of PICU stay (days)	Hypoalbuminemic group		Normoalbuminemic group		P value
	Mean	SD	Mean	SD	< 0.001
	8.6	5.1	5.5	3.2	

The need for ventilatory support was significantly higher in children with hypoalbuminemia (42%; 16 of 38) as compared to children with normal albumin levels (20.5%; 14 of 62) (p=0.003). The mean number of days in ventilator among the Hypoalbuminemic group was 7.1±6.8 and among the Normoalbuminemic group was 4.2±3.2. This difference in between the two groups was found to be statistically significant. (p<0.001)

Table 5: Recipients of ventilatory support

Number mechanically ventilated	Hypoalbuminemic group (n=38)		Normoalbuminemic group (n=62)		P value
	No. of patient	Percentage	No. of patient	Percentage	0.003
	16	42	14	20.5	

Table 6: Length of ventilation in days

Number of days in ventilator	Hypoalbuminemic group (n=38)		Normoalbuminemic group (n=6\2)		P value
	Mean	SD	Mean	SD	<0.001
	7.1	6.8	4.2	3.2	

Finally, when considering the outcome, children with hypoalbuminemia had a mortality rate of 31.5% (12 of 38) which was 2.2 times greater than the normal albumin level group, i.e., 14.5% (9 of 62). The mean serum albumin in expired children was 2.59±0.79 g/dL, compared to 3.54±0.82 g/dL in survivors (p=0.002). A strong negative correlation was found between serum albumin levels and the mortality rate. (r= -0.867)

Table 7: Comparison of outcome between two groups

Outcome	Hypoalbuminemic group (n=38)		Normoalbuminemic group (n=62)	
Died	12	31.5	9	14.5
Survived	26	68.4	53	85.4

Table 8: Correlation between hypoalbuminemia and mortality

Hypoalbuminemia	Mortality	P value	Correlation (r)
36	12	0.002	-0.867

Discussion

Hypoalbuminemia is frequently associated with early biochemical derangement in critically ill-patients. It is commonly attributed to either decreased synthesis or increased loss. Diversion of synthetic capacity to other proteins (acute-phase reactants) is another cause of hypoalbuminemia in critically ill patients. Inflammatory disorders can accelerate the catabolism of albumin while simultaneously decreasing its production[9,11]. Critical illness, dramatically increases capillary permeability and alters albumin exchange between intravascular and extravascular compartments, thereby altering the rate of synthesis and degradation of albumin[12]. A low serum albumin concentration may also be associated with poor outcome independent of the underlying disease process[4].

We found hypoalbuminemia in about one-third of patients, which is consistent with data of Horowitz and Tai[9] and Tiwari et al[13]. The mean serum albumin in our study population (2.54 g/dL, SD 0.38) is almost similar to other Indian pediatric studies[13,14]. The prevalence of hypoalbuminaemia on admission in critically ill children from previous studies is about 33-57%.[9,13,14,15,16,17] . 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 while Durward et al, defined it as lower than 3.3 g dL-1.10,11. Thus, a clear definition of hypoalbuminaemia in paediatric patients should be made in order to give greater weightage to all these studies. Due to this limitation, the true prevalence of hypoalbuminaemia is difficult

to compare directly in pediatric patient. In present study we found hypoalbuminemia in 38% of the children admitted to PICU.

Murray et al. established that serum albumin level was associated with longer ICU and hospital stay in sick patients[18]. In our study, hypoalbuminemic patients had prolonged PICU stay, high incidence of respiratory failure requiring mechanical ventilator, prolonged ventilatory support, and higher mean number of mortality. These results are largely consistent with findings by Horowitz and Tai[9], Durward et al.[10], Tiwari et al[13], Golhar ST et al[14] and Kumar et al[17].

Despite the fact that hypoalbuminemia is an independent predictor of morbidity and mortality, there is no definite evidence to support the use of albumin to treat hypoalbuminemia or hypovolaemia in critically ill patients [3,19,20].The use of albumin infusion as a treatment for hypoalbuminemia , therefore, remains a subject of ongoing debate and several evidenced-based reviews[3,4,20]. In SAFE study, use of albumin replacement as a volume expander for the critically ill-adults with hypotension did not result in decreased mortality or morbidity[20].Although hypoalbuminemia was present in 38% of the study subjects; albumin infusion was not given to any of the study subjects as it is very expensive and economically not feasible. Thus, a further and widened based studies are needed for indication of albumin infusion in critically ill children with hypoalbuminemia.

Conclusion

Hypoalbuminemia is common in patients admitted to our PICU and is an independent predictor of increased mortality and morbidity in ICU patients. A low serum albumin concentration correlated well with rates of complications such as ventilator dependence and longer stay in the critical care unit and higher mortality. Thus, hypoalbuminemia at admission can be helpful for risk assessment and therefore can be used as an outcome predictor in critically ill children admitted to PICU.

Limitations

1) Short duration of study period
2) No clear definition of hypoalbuminaemia in paediatric patients. Hence, the true prevalence of hypoalbuminaemia is difficult to compare directly.
3) Albumin infusion not given to any of the study subject due to its high cost
4) Any new infection which might have developed during prolonged ventilation could not be ruled out.

Acknowledgement

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