

The Influence of Albumin Level in Critically Ill Children to Length of Stay and Mortality in Paediatric Intensive Care Unit

Gema Nazri Yanni^{1*}, Munar Lubis², Muhammad Ali³

¹Department of Child Health, Universitas Sumatera Utara, Medan, Indonesia; ²?; ³?

Abstract

Citation: Yanni GN, Lubis M, Ali M. The Influence of Albumin Level in Critically Ill Children to Length of Stay and Mortality in Paediatric Intensive Care Unit. Open Access Maced J Med Sci. <https://doi.org/10.3889/oamjms.2019.445>

Keywords: Albumin level; Critically ill children; Hypoalbuminemia; Length of stay; Mortality

***Correspondence:** Gema Nazri Yanni. Department of Child Health, Universitas Sumatera Utara, Medan, Indonesia. E-mail: gema.nazri.yanni@gmail.com

Received: 14-Aug-2019; **Revised:** 15-Sep-2019; **Accepted:** 16-Sep-2019; **Online first:** 14-Oct-2019

Copyright: © 2019 Gema Nazri Yanni, Munar Lubis, Muhammad Ali. This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (CC BY-NC 4.0)

Funding: This research did not receive any financial support

Competing Interests: The authors have declared that no competing interests exist

BACKGROUND: The use of albumin in the critical care setting is a very controversial issue. Low serum albumin concentration in critical illness is associated with a poor outcome.

AIM: We aimed to evaluate the influence of albumin level in critically ill children to the length of stay and mortality in the Pediatric Intensive Care Unit (PICU) Haji Adam Malik General Hospital, Medan, Indonesia.

METHODS: The study used an observational method with a cross-sectional design. The population of the study was all patients with major postoperative surgery and critically ill that admitted to the PICU at Haji Adam Malik Hospital from the period of June 2008 to September 2008. The albumin level of the subjects was determined on the first day admitted.

RESULTS: The group with hypoalbuminemia (< 3 g/dL) was given albumin supplementation according to a protocol in the PICU. The group with hypoalbuminemia have an average length of stay 7.6 days (9.7%) and mortality of 12 subjects (36.4%). The group with normal albumin level have 4.7 days (5.0%) and mortality 13 subjects (37.1%). There was no significant effect of albumin level to mortality.

CONCLUSION: Albumin level did not affect the length of stay and mortality in PICU.

Introduction

Albumin is a protein produced in the liver which plays a role in blood oncotic pressure. Besides, in colloid osmotic pressure, albumin also works as a transport molecule for bilirubin, fatty acids, and medications [1].

The role of albumin in critical illness is not fully understood. There are significant differences in the role of albumin between healthy and critically ill children. Low serum albumin concentrations in critically ill patients are associated with poor outcomes [2], [3], [4]. In healthy individuals, albumin act to maintain Colloid Osmotic Pressure (COP) but is less correlated in critically ill individuals [4]. Patient with a critical illness has a low COP. Among 200 patients,

those with critical illness had a COP of 19.1 mmHg. Low colloid osmotic pressure correlates with high morbidity and mortality in critically ill patients. The COP of 15 mmHg is associated with a 50% life expectancy. Administration of albumin supplementation will increase COP and prevent fatal complications such as pulmonary oedema, which in turn, develop into respiratory failure [3], [4].

The osmotic pressure can be directly measured using oncometers or Van't Hoff equation: $\text{osmotic pressure} = n \times (c / M) \times RT$, where n = number of particles in the substrate ($n = 1$ for plasma proteins), c / M = molar concentration of the substrate, R = constant of 0.082, T = absolute temperature [5].

Based on a descriptive study of 134 children with critical illness in the pediatric intensive care unit (PICU), the incidence of hypoalbuminemia before admission was 57% and may increase to 76% in the

first 24 hours [6].

Hypoalbuminemia often occurs in critical illness. The causes of hypoalbuminemia are complex and affected by various mechanisms such as the imbalance between albumin production and destruction, increased capillary permeability, and altered intravascular and extravascular albumin distribution [2], [4].

The relationship between hypoalbuminemia and poor outcomes has motivated clinicians to provide exogenous albumin in patients with hypoalbuminemia. Although hypoalbuminemia directly leads to a poor outcome, there is still controversy about this [4].

Material and Methods

This study used an observational method with a cross-sectional design. The study was conducted at Haji Adam Malik General Hospital from June 2008 to September 2008.

The subjects of the study were all patients admitted to PICU at Haji Adam Malik General Hospital, Medan, Indonesia, from the period of June 2008 to September 2008. The subjects were taken with the purposive sampling method.

The inclusion criteria included major post-operative surgery and critically ill, while the exclusion criteria included multiple congenital anomalies, post-operative surgery patient with length of stay less than 24 hours, burn patient and those who refuse to take part in the study.

The variables being studied include 1) albumin level in the first day admitted; 2) length of stay; 3) mortality; and 4) type of cases, with classification surgery or non-surgery case.

Before the research was carried out, ethical clearance was sought and approved by the Ethics Committee of Universitas Sumatera Utara Medical Faculty.

Results

From this study, of 68 subjects in the PICU, there were 33 patients with hypoalbuminemia (48.5%) and 35 (51.4%) with normal albumin level. From the two groups, the mean albumin level was 3.05 g/dL (0.749), with the lowest levels of 1.5 g/dL and the highest at 4.7 g/dL. The mean albumin level was 2.33 g/dL in hypoalbuminemia group and 3.62 g/dL in normal albumin group with $P = 0.001$ (Table 1).

Table 1: The characteristics of subjects in both study groups

Parameter	Hypoalbuminemia (n = 33)	Normal albumin (n = 35)
Albumin level (g/dL), mean (SD)	2.33 (0.40)	3.61 (0.44)
Gender, n (%)		
Male	23 (69.7)	24 (68.6)
Female	10 (30.3)	11 (31.4)
Age (months) mean (SD)	53.3 (49.9)	53.1 (48.8)
Weight (Kg) mean (SD)	15.6 (13.13)	14.8 (9.55)
Eid index, n (%)		
< 70	9 (27.3)	11 (31.4)
70-80	3 (9.10)	7 (20.0)
80-90	6 (18.2)	7 (20.0)
90-110	10 (30.3)	7 (20.0)
110-120	3 (9.10)	2 (5.70)
> 120	2 (6.10)	1 (2.90)
Type of cases, n (%)		
Surgical	21 (63.6)	19 (54.3)
Non-surgical	12 (36.4)	16 (45.7)

This study showed that there was a higher proportion of male than female. In the hypoalbuminemia group, the proportion of male patients was 69.7%, and female patients were 30.3%, whereas in the normal albumin group, the number of male patients was 68.6% and female patients were 31.4%.

Furthermore, the mean age, weight, and nutritional status, in this case, were assessed by EID index and type of case (surgical or non-surgical) between the two groups did not show significant differences.

In this study (Table 2), we also found that the hypoalbuminemia group needs longer treatment (7.6 days) compared to the normal albumin group (4.7 days).

Table 2: The relationship between albumin levels and length of stay and mortality

Parameter	Hypo- albuminemia (n = 33)	Normal albumin (n = 35)	P
Length of stay (days); mean (SD)	7.6 (9.77)	4.7 (5.0)	0.134
Mortality, n (%)			
Yes	12 (36.4)	13 (37.1)	0.947
No	21 (63.6)	22 (62.9)	

This is different from the results of this study where the patients were not distinguished whether as surgical and non-surgical cases, and it was found that there was higher mortality in the normal albumin group (37.1%) than the hypoalbuminemia group (36.4%) although both were not significantly different.

Table 3: The results of multivariate analysis of length of stay

Variable	B	P	95% CI
Albumin level	-3.502	0.049	-6.984; -0.020
Type of cases	6.424	0.001	-2.838; 10.010
Nutritional status	-0.146	0.808	-1.339; 1.047

In this study (Table 3 and Table 4), nutritional status had no significant association with length of stay and mortality, but the types of cases, whether surgical or non-surgical had a significant association with length of stay and mortality ($P = 0.001$). From Table 3, the results of multivariate analysis showed that the variables with the greatest contribution to the length of stay were the types of cases.

Table 4: The results of the multivariate analysis of mortality

Variable	B	P	95% CI
Albumin level	0.371	0.540	0.442; 4.775
Type of cases	-2.093	0.001	0.038; 0.403
Nutritional status		0.816	
(1)	-6.73	0.621	0.035; 7.338
(2)	-2.38	0.758	0.174; 3.578
(3)	-0.378	0.654	0.110; 3.577
(4)	0.677	0.450	0.340; 11.40
(5)	0.734	0.430	0.205; 3.511
(6)	2.331	0.322	0.123; 4.712

Discussion

Albumin has several physiological functions and has been used extensively in the field of anaesthesia and intensive care as indicated. After more than 60 years of clinical research, administration of albumin is still questionable. In critically ill patients, several pathophysiological processes such as infection, trauma, or major surgery result in an inflammatory process that eventually releases mediators such as cytokines and leukocyte activation. This will result in disruption of endothelial function, increased microvascular permeability, and extravasation of fluid (including albumin) to the tissue. Acute-phase proteins, produced by the liver, are the sign of inflammation that is used to evaluate the relationship between hypoalbuminemia and poor outcomes [7], [8].

A prospective study of routine nutritional laboratory parameters examined less than 24 hours in 105 severely ill children in intensive care unit found a prevalence of hypomagnesaemia 20%, hypertriglyceridemia 25%, uremia 30%, and hypoalbuminemia 52% [9].

Hypoalbuminemia is a marker of morbidity and mortality in children with a critical illness. A retrospective study comparing groups of patients with hypoalbuminemia and groups with normal albumin levels in patients in the PICU showed that in the hypoalbuminemia group, the length of stay in PICU was longer (8.1 days) compared to those with normal albumin levels (4.4 days). The hypoalbuminemia group has a lower life expectancy and a higher rate of organ failure [10].

A study of cardiac and non-cardiac surgery patients and kidney impairment found that hypoalbuminemia was a predictor of poor outcome, where each 10 g/dL decrease in serum albumin would increase the mortality odds by 137%, morbidity by 89%, length of stay in the intensive care unit and hospital care by 28% and 71%, respectively [11].

Hypoalbuminemia is the result of a combination of inflammation and inadequate caloric input in patients with chronic renal failure. Inflammation and malnutrition will reduce the synthesis and increase protein catabolism which may

reduce albumin concentration [12].

Transcapillary albumin excretion increased by 300% in patients with septic shock and by 100% after cardiac surgery. In septic patients, transcapillary changes will occur if appropriate treatment is administered. With increased albumin flow through the capillary membrane, there is an increase in lymphatic return to the intravascular space. Albumin movement during major surgery shows a decrease in lymphatic flow and albumin concentration in the lymphatic vessels. Measurements of total circulation and albumin exchange showed a 30% reduction with major surgery (Nicholson, 2000). In a prospective study, serum albumin was shown as a predictor of the outcome of postoperative patients [13].

A Cochrane Collaboration study concluded that there is no evidence which showed that albumin reduces mortality in patients with hypovolemia compared to cheaper alternatives such as normal saline and in critically ill patients with burns or hypoalbuminemia [14].

In this study, according to the intensive care unit protocol, all patients in the hypoalbuminemia group received albumin substitution as needed. Hypoalbuminemia is a frequent phenomenon in critical illness. Treatment focuses on the main causes of hypoalbuminemia rather than administering albumin. The results of several meta-analyses of albumin administration in hospitalised patients were inconsistent [15].

The role of albumin in critically ill patients is not supported by scientific evidence. Hypoalbuminemia correction does not have a significant advantage; treatment is aimed at basic diseases to treat hypoalbuminemia [13]. Albumin is recommended according to the appropriate indications for patients in the intensive care unit [8].

Intravenous albumin is appropriate for patients with cirrhosis with ascites, kidney failure, and hepatorenal syndrome awaiting liver transplantation. In patients with nephrotic syndrome who do not respond to standard therapy, severe symptomatic hypovolemia, administration of intravenous albumin and diuretics might be considered [16]. From an in-vitro study of sepsis patients, it was shown that albumin administration did not affect vascular permeability. The administration of 200 ml of 20% albumin was not significant in reducing microvascular protein leakage [17]. From a review of a randomised clinical study, administering low dose hyperoncotic albumin for hypovolemic resuscitation has several advantages such as reducing morbidity, renal impairment, and oedema [18].

Addition of albumin in parenteral nutrition solutions is also not recommended. It is said that fatal complications may occur compared to its benefits. Possible complications include infection, incompatibility, and chemical and physical instability

[19]. It was stated that the administration of albumin would cause a decrease in life expectancy in patients with critical illness [20]. This is in contrast to a study of a meta-analysis of randomised controlled trials that did not find the effect of albumin on mortality [21].

The study also found no difference between the hypoalbuminemia and normal albumin groups to mortality ($P = 0.947$). Based on previous studies and based on the results of our study, albumin levels do not affect the length of stay and mortality of patients in the intensive care unit.

In this study, there was no effect of albumin levels on the length of stay and mortality of patients in the pediatric intensive care unit. The type of cases has a significant association in the length of stay and mortality.

Acknowledgements

Authors thanks and expresses appreciation to the Department of Child Health, Faculty of Medicine, University of Sumatera Utara, Haji Adam Malik General Hospital.

References

- North I. Principles of critical care: Fluid therapy and blood product, 2nd edn. Philadelphia: McGraw- Hill: 1999:39-40.
- AL-Khafaji A, Webb AR. Should albumin be used to correct hypoalbuminemia in the critically ill? No. TATM. 2003; 5(4):392-6. <https://doi.org/10.1111/j.1778-428X.2003.tb00179.x>
- Dubois MJ, Vincent JL. Use of albumin in the intensive care unit. TATM. 2002; 4(3):80-4. <https://doi.org/10.1111/j.1778-428X.2002.tb00066.x>
- Nicholson JP, Wolmarans MR, Park GR. The role of albumin in critical illness. Br J Anaesth. 2000; 85(4):599-610. <https://doi.org/10.1093/bja/85.4.599> PMID:11064620
- Brandis K. Fluid physiology, 2008. <http://www.AnaesthesiaMCQ.com>. Accessed November 14, 2008.
- Durward A, Mayer A, Skellett S, Taylor D, Hanna S, Tibby SM, Murdoch IA. Hypoalbuminaemia in critically ill children: incidence, prognosis, and influence on the anion gap. J Arc Dis Child. 2003; 88:419-22. <https://doi.org/10.1136/adc.88.5.419> PMID:12716714 PMID:PMC1719575
- Jain RK, Chakravorty N, Chakravorty D, et.al. Albumin: an overview of its place in current clinical practice. Indian J. Anaesth. 2004; 48(6):433-8.
- Boldt J. The good, the bad, and the ugly: should we completely banish human albumin from our intensive care units? Anesth Analg. 2000; 91(4):887-95. <https://doi.org/10.1097/0000539-200010000-00022> PMID:11004043
- Hulst JM, Goudoever JB, Zimmermann LJ, et.al. The role of initial monitoring of routine biochemical nutritional markers in critically ill children. J Nutr Biochem. 2006; 17(1):57-62. <https://doi.org/10.1016/j.jnutbio.2005.05.006> PMID:16111880
- Horowitz IN, Tai K. Hypoalbuminemia in critically ill. Arch Pediatr Adolesc Med. 2007; 161:1048-52. <https://doi.org/10.1001/archpedi.161.11.1048> PMID:17984406
- Vincent JL, Dubois MJ, Navickis RJ, Wilkes MM. Hypoalbuminemia in acute illness: is there a rationale for intervention? Annals of Surgery. 2003; 237(3):319-34. <https://doi.org/10.1097/01.SLA.0000055547.93484.87> PMID:12616115 PMID:PMC1514323
- Don BR, Kaysent G. Serum albumin: relation to inflammation and nutrition. Seminars in dialysis. 2004; 17(6):432-7. <https://doi.org/10.1111/j.0894-0959.2004.17603.x> PMID:15660573
- Gibbs J, Cull W, Henderson W, Daley J, Hur K, Khuri SF. Preoperative serum albumin level as a predictor of operative mortality and morbidity. Arch Surg. 1999; 134(1):36-42. <https://doi.org/10.1001/archsurg.134.1.36> PMID:9927128
- Alderson P, Bunn F, Li Wan Po A, et al. Human albumin solution for resuscitation and volume expansion in critically ill patients (review). The Cochrane Collaboration. The Cochrane Library. 2008; 2:1-24.
- Finfer S, Bellomo R, Myburgh J. Efficacy of albumin in critically ill patients. BMJ. 2003; 326:559-60. <https://doi.org/10.1136/bmj.326.7389.559> PMID:12637372 PMID:PMC1125456
- Bernheim J. Efficacy of intravenous albumin administration in hypoalbuminemic patients: why and when. IMAJ. 2005; 7(2):113-5.
- Margarson MP, Soni NC. Effects of albumin supplementation on microvascular permeability in septic patients. J Appl Physiol. 2002; 92(5):2139-45. <https://doi.org/10.1152/japplphysiol.00201.2001> PMID:11960967
- Jacob M, Chappell, Conzen P, et.al. Small-volume resuscitation with hyperoncotic albumin: a systematic review of randomized clinical trials. Crit Care. 2008; 12:1-13. <https://doi.org/10.1186/cc6812> PMID:18318896 PMID:PMC2447554
- Lester LR, Crill CM, Hak EB. Should adding albumin to parenteral nutrient solutions be considered an unsafe practice? Am J Health-Syst Pharm. 2006; 6:1-8.
- Vincent JL, Sakr Y, Reinhart K, Sprung CL, Gerlach H, Ranieri VM. Is albumin administration in the acutely ill associated with increased mortality? Results of the SOAP study. Crit Care. 2005; 9(6):745-54. <https://doi.org/10.1186/cc3895> PMID:16356223 PMID:PMC1414048
- Wilkes M, Navickie R. Patient survival after human albumin administration a meta-analysis of randomized controlled trials. Ann Intern Med. 2001; 135:149-64. <https://doi.org/10.7326/0003-4819-135-3-200108070-00007> PMID:11487482