

Impact of albumin levels on clinical outcomes in children underwent abdominal surgery

Rismala Dewi, Freddy Guntur Mangapul Silitonga, Irawan Mangunatmadja

Abstract

Background Patients underwent abdominal surgery and had hypoalbuminemia were at risk of post-operative complications. The prognostic role of albumin levels in children with abdominal surgery remains unclear.

Objective To investigate the impact of albumin levels on clinical outcomes related to the complications in children with abdominal surgery.

Methods This was a retrospective cohort study on children aged 29 days to 18 years, who underwent abdominal surgery, had serum albumin levels measured at pre-operative and within 48 hours post-operatively, and hospitalized in Paediatric Intensive Care Unit of Dr. Cipto Mangunkusumo Hospital, Indonesia. The primary outcomes were post-operative complications (sepsis, surgical site infection, shock), length of stay in PICU, dehiscence, relaparotomy, and postoperative mortality.

Results This study recruited a total of 201 children. Pre- and post-operative serum albumin levels of ≤ 3.00 g/dL were found in 15.4% and 51.2%, respectively. Pre- and post-operative serum albumin levels of ≤ 3.00 g/dL were associated with higher risk of post-operative sepsis (RR 3.4; 95%CI 1.54 to 7.51) and relaparotomy (RR 3.84; 95%CI 1.28 to 1.49). The median of length of PICU stay was 4 days longer in children with pre-operative serum albumin levels ≤ 3.00 g/dL ($P < 0.001$).

Conclusion Hypoalbuminemia condition in children undergo abdominal surgery is associated with increased risk of post-operative sepsis, longer length of stay in PICU, and risk of relaparotomy. [Paediatr Indones. 2020;60:149-53; doi: <http://dx.doi.org/10.14238/pi60.3.2020.149-53>].

Keywords: hypoalbuminemia; clinical outcomes; abdominal surgery; pre- and postoperative

Systemic changes can be resulted from major surgery as body response to trauma.¹ Previous studies proved that compared to the pre-operative state, post-operative albumin level was significantly reduced.² Surgery causes the increment of capillary permeability which leads to albumin and plasma leakage, resulting in hypoalbuminemia.³ During laparotomy, 6-24% from total mass of circulating plasma protein is leaked to peritoneal cavity.⁴ Serum albumin level can be used to identify post-operative patients with high risk of morbidity and mortality.^{5,6} A study using multiple regression model found that first day of post-operative albumin level was independently associated with post-operative complications.⁶

Many studies found that albumin levels less than 3 g/dL were associated with post-operative complications.^{7,8} Albumin level less than 3.5 g/dL was associated with respiratory complications (pneumonia in 30 days post-operative, delayed ventilator weaning,

From the Department of Child Health, Universitas Indonesia Medical School/Dr. Cipto Mangunkusumo Hospital, Jakarta.

Corresponding author: Rismala Dewi, Department of Child Health, Universitas Indonesia Medical School/Dr.Cipto Mangunkusumo Hospital, Jalan Diponegoro no. 71, Jakarta, Indonesia 10430, Email: dewi22juli@gmail.com.

Submitted January 22, 2020. Accepted June 12, 2020.

and reintubation), surgical site infection, dehiscence, longer hospitalization period, and increasing one-year mortality risk.⁹⁻¹¹

Patients underwent abdominal surgery and had hypoalbuminemia were at risk of post-operative complications and higher risk of mortality.⁸⁻¹¹ However, the prognostic role of albumin level in children with abdominal surgery remains unclear. Therefore, we aim to investigate the impact of albumin levels on clinical outcomes related to the complications in children with abdominal surgery.

Methods

This was a retrospective cohort study conducted at Dr. Cipto Mangunkusumo Hospital, Jakarta, on children aged 29 days to 18 years who admitted in Paediatric Intensive Care Unit Dr. Cipto Mangunkusumo Hospital, between January 2015 and December 2017. Data were obtained from medical records. Inclusion criteria were subjects underwent laparotomy abdominal surgery and had serum albumin levels measured pre-operatively and within 48 hours post-operatively. Subjects with incomplete data were excluded. Independent variable was < 48 hours post-operative albumin level while the dependent variables included post-operative complications (sepsis, surgical site infection, shock), length of stay in PICU, dehiscence, relaparotomy, and post-operative mortality. Hypoalbuminemia was defined as serum albumin levels ≤ 3.00 g/dL. Association between serum albumin levels and clinical outcomes were analysed using Chi-square method for categorical data and Mann-Whitney for numerical data. This study had been approved by Research Ethics Committee, Universitas Indonesia Medical School.

Results

During 3 year-period time, there were 231 children underwent laparotomy, but only 201 subjects were eligible. Most common indications of laparotomy were intraabdominal tumours (16.5%), followed by choledochal cysts (14.5%), adhesiolysis (14.5%), biliary atresia (14.5%), and perforated appendicitis (7.9%). Subjects' characteristics are listed in **Table 1**.

Pre-operative and post-operative hypoalbuminemia were identified in 15.4% and 51.2% of subjects, respectively.

Both pre-operative and post-operative hypoalbuminemia were associated with higher risk of post-operative sepsis, but neither with surgical site infection nor dehiscence. Pre-operative hypoalbuminemia were associated with relaparotomy (**Table 2**). The median for length of stay in PICU was four days longer in subjects with pre-operative hypalbuminemia (**Table 3**).

Table 1. Demographic characteristic of study subject

Characteristics	N=201
Gender, n(%)	
Boys	93 (44.63)
Girls	108 (53.7)
Age, n(%)	
0-5 years	137 (68.2)
5-10 years	25 (12.4)
10-15 years	27 (13.4)
15-18 years	12 (6.0)
Nutritional status, n(%)	
Normal-overweight-obese	110 (54.7)
Wasted	62 (30.8)
Severely wasted	29 (14.4)
Type of surgery, n(%)	
Emergency	34 (16.9)
Elective	167 (83.1)
Pre-operative albumin level, n(%)	
≤ 3.00 g/dL	31 (15.4)
>3.00 g/dL	170 (84.6)
Post-operative albumin level, n(%)	
≤ 3.00 g/dL	103 (51.2)
>3.00 g/dL	98 (48.8)
Pre-operative albumin transfusion, n(%)	
Yes	27 (13.4)
No	0
Post-operative albumin transfusion, n(%)	
Yes	18 (8.9)
No	9 (4.5)
Surgical site infection, n(%)	
Yes	8 (3.9)
No	193 (96.1)
Dehiscence, n(%)	
Yes	8 (3.9)
No	193 (96.1)
Relaparotomy, n(%)	
Yes	16 (7.9)
No	185 (92.1)
Mortality, n(%)	
Yes	14 (6.9)
No	187 (93.1)

Table 2. Association between albumin level and clinical outcomes after laparotomy procedures.

Outcomes/parameter	Sepsis			Surgical site infection			Dehiscence			Relaparotomy		
	Yes	No	RR (95%CI)	Yes	No	RR (95%CI)	Yes	No	RR (95%CI)	Yes	No	RR (95%CI)
Pre-operative albumin level												
≤ 3.0 g/dL	19	12	3.4 (1.54 to 7.51)	2	29	1.88 (0.36 to 9.70)	1	30	0.77 (0.09 to 6.54)	6	25	3.84 (1.28 to 11.49)
> 3.0 g/dL	54	116	P=0.002	4	164	P=0.357	7	163	P=1.000	10	160	P=0.021
Pre-operative albumin level												
≤ 3.0 g/dL	48	55	2.55 (1.40 to 4.63)	7	96	7.07 (0.85 to 58.58)	6	7	2.96 (0.58 to 15.08)	11	92	2.22 (0.74 to 6.65)
> 3.0 g/dL	25	73	P=0.002	1	97	P=0.066	2	96	P=0.280	5	93	P=0.114

RR=relative risk; CI=confidence interval

Table 3. Median length of stay in PICU based on albumin levels

Outcomes	Albumin level, g/dL		P value
	≤ 3.0	> 3.0	
Median length of stay (range), days			
Pre-operative	8 (2-33)	4 (1-64)	<0.001
Post-operative	5 (1-64)	4 (1-38)	0.025

Mortality rate among subjects with pre-operative serum albumin level of ≤ 3.00 g/dL was 19.2%, while those with albumin >3.00 g/dL had mortality rate of 5.6%. A Kaplan Meier curve showed a better survival in subject with normal albumin compared to those with pre-operative hypoalbuminemia, despite a $P=0.254$ from Log Rank (Mantel-Cox) with $\alpha=0.05$.

Discussion

This study found that children with pre- and post-operative serum albumin level of ≤ 3.00 g/dL had higher risk of post-operative sepsis compared to those with normal serum albumin levels. This result was similar with a previous study that found albumin level was inversely proportional to post-operative sepsis.¹² In this study, we were not able to show any associations between pre- and post-operative serum albumin levels with surgical site infection and dehiscence. This results were not accordance with the results of a previous study that found 24% of post-laparotomy patients who had dehiscence were hypoalbuminemia.¹³ Hypoproteinaemia contributed in inflammation phase elongation, fibroplasia disruption, collagen proliferation and synthesis, neo-angiogenesis, and wound remodelling. Other factors, i.e. anemia, nutritional status, presence of other diseases, degree of wound contamination, surgery urgency, surgical site infection, non-proper surgery preparation, and surgery

timing, also affected the presence of dehiscence.^{13,14} In 8 subjects in this study who had dehiscence, we identified the contributing factors were malnutrition, burst abdomen, and haemophilia with inhibitors that disrupted wound healing phase since coagulation until remodelling phase.

Pre-operative serum albumin level of ≤ 3.00 g/dL was associated to higher risk of relaparotomy. A previous study showed that hypoalbuminemia was a risk factor for relaparotomy. From all patients underwent laparotomy, 54% were found hypoalbuminemia with mean albumin level of 3.4 g/dL. As much as 71% of all patients underwent relaparotomy due to anastomosis dehiscence and 66% from patients underwent relaparotomy due to burst abdomen were found to have hypoalbuminemia.¹⁵

In this study, the lower the albumin level (either pre- or post-operatively), the longer hospitalization period was found. This results were in accordance with study by Hennessey *et al.*¹⁶ that showed hypoalbuminemia was associated significantly with longer hospitalization period compared to those with normal serum albumin levels (19.5 days *vs.* 12 days). Another study found that patients with albumin level between 3.0 and 3.4 g/dL had 2 (95% CI 1.83 to 2.34) days longer median post-operative hospitalization period compared to those with albumin level >3.4 g/dL.¹⁷ A study in adults in Thailand showed that patients with non-hypoalbuminemic had significantly shorter length of hospital stay [6.8 (SD

2.6) days] compared to those with albumin level of < 3.5 g/dL [(9.6 (SD 4.7) days)].¹⁸

The lower albumin level also associated with higher mortality rate. Subjects with post-operative serum albumin level \leq 3.00 g/dL had mortality rate of 19.2%. The cause of mortality in all subjects was septic shock. A study found mortality rate of 40%, with mortality risk of 9%, 29%, 67%, and 83% in patients with hyperalbuminemia (>4.5 g/dL), normal serum albumin levels (3.5-4.5g/dL), moderate hypoalbuminemia (2.5-3.5 g/dL), and severe hypoalbuminemia (<2.5 g/dL), respectively.¹⁹

No significant difference was found in mortality rate among post-operative serum albumin levels of \leq 3.00 g/dL compared to those with albumin of >3.00 g/dL. This was explained by three subjects with malignancies and one subject with hemophilia in the albumin > 3.00 g/dL subjects group, which showed that albumin level was not the only factors affecting mortality in these subjects. Mortality in this study was caused by pre-operative septic shock that aggravating malignancies existed. Hemophilia with inhibitor also affected coagulation phase as the initial process of wound healing. Blood losses were also predicted to play a role in mortality.²⁰

Limitations of this study included the bias that could be happened due to incomplete data in medical records. Serum albumin levels sometimes were not measured because of patient's condition, i.e. emergency situation for surgery. This condition made subjects were excluded from the study. Protocol for albumin transfusion also differed during the study period due to the National Health System regulation regarding to albumin transfusion.

In conclusion, hypoalbuminemia is associated with increased risk of post-operative sepsis, longer length of stay in PICU, and risk of relaparotomy.

Conflict of Interest

None declared.

Funding Acknowledgement

The authors received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

References

1. Alberti LR, Petroianu A, Zac RI, Andrade Jr. JCCG. The effect of surgical procedures on serum albumin concentration. *Chirurgia*. 1990;103:39-43. PMID: 18459495.
2. Mahkovic-Hergouth K, Kompan L. Is replacement of albumin in major abdominal surgery useful? *J Clin Anesth*. 2011;23:42-6. DOI: 10.1016/j.jclinane.2010.06.007.
3. Bold J. Use of albumin. *Br J Anaesth*. 2010;104:276-84. DOI: 10.1093/bja/aep393.
4. Nielsen OM. Sequential changes in circulating total protein and albumin masses after abdominal vascular surgery. *Ann Surg*. 1985;202:231-4. DOI: 10.1097/00000658-198508000-00014.
5. Garg T, Chen LY, Kim PH, Zhao PT, Herr HW, Donat SM. Preoperative serum albumin is associated with mortality and complications after radical cystectomy. *Br J Urol Int*. 2014;113:918-23. DOI: 10.1111/bju.12405.
6. Gibbs J, Cull W, Henderson W, Daley J, Hur K, Khuri S. Preoperative serum albumin level as a predictor of operative mortality and morbidity. *Arch Surg*. 1999;134:36-42. DOI: 10.1001/archsurg.134.1.36.
7. Goh SL, De Silva RP, Dhital K, Gett RM. Is low serum albumin associated with postoperative complications in patients undergoing oesophagectomy for oesophageal malignancies. *Interact Cardiovasc Thorac Surg*. 2015;20:107-13. DOI: 10.1093/icvts/ivu324.
8. Liu X, Wu X, Zhou C, Hu T, Ke J, Chen Y, et al. Preoperative hypoalbuminemia is associated with an increased risk for intraabdominal septic complications after primary anastomosis for Crohn's disease. *Gastroenterol Report*. 2017;5:298-304. DOI:10.1093/gastro/gox002.
9. Bohl DD, Shen MR, Kayupov E, Della Valle CG. Hypoalbuminemia independently predicts surgical site infection, pneumonia, length of stay, and readmission after total joint arthroplasty. *J Arthroplasty*. 2016;31:15-21. DOI: 10.1186/s12893-016-0186-6.
10. Khan R, Qadar M, Maqsood SU, Kashif MA, Hussain MZ, Afzal M. Tension sutures in closure of midline laparotomy-avoidance of wound dehiscence. *Pak Armed Forces Med J*. 2017;67:S74-7.
11. Kougias P, Salami AC, Sharath S, Garcia A, Pathak A. Preoperative albumin levels and major postoperative complications after elective abdominal aortic aneurysm repair. *J Vascular Surg*. 2016;63:170-1s.
12. Sun JK, Sun F, Wang X, Yuan ST, Zheng SY, Mu XW. Risk factors and prognosis of hypoalbuminemia in surgical septic patients. *Peer J*. 2015;3:1-14. DOI: 10.7717/peerj.1267.

13. Ramneesh G, Sheerin S, Surinder S, Bir S. A prospective study of predictors for post laparotomy abdominal wound dehiscence. *J Clin Diagn Res.* 2014;8:80-3. DOI: 10.7860/JCDR/2014/7348.3921.
14. Walming C, Angenete E, Block M, Bock D, Gessler B, Haglund E. Retrospective review of risk factors for surgical wound dehiscence and incisional hernia. *BMC Surg.* 2017;17:19-24. DOI: 10.1186/s12893-017-0207-0.
15. Krishna A, Shivaramgowda S, Kumar A, Manjunath S. Relaparotomy – the surgeons nightmare. *Indian J Surg.* 2018;80:1-6. DOI: DOI: 10.1007/s12262-018-1823-3.
16. Hennessey DB, Burke JP, Ni Donochu T, Conor S, Winter DC, Kenneth M. Preoperative hypoalbuminemia is an independent risk factor for the development of surgical site infection following gastrointestinal surgery: a multiinstitutional study. *Ann Surg.* 2010;252:325-9. DOI: 10.1097/SLA.0b013e3181e9819a.
17. Moghadamyeghaneh Z, Hwang G, Hanna MH, Phelan MJ, Carmichael JC, Mills SD, *et al.* Even modest hypoalbuminemia affects outcomes of colorectal surgery patients. *Am J Surg.* 2015;210:276-84. DOI: 10.1016/j.amjsurg.2014.12.038.
18. Lohsiriwat V, Chinswangwatanakul V, Lohsiriwat S, Akaraviputh T, Boonnuch W, Methasade A, *et al.* Hypoalbuminemia is a predictor of delayed postoperative bowel function and poor surgical outcomes in right-sided colon cancer patients. *Asia Pac J Clin Nutr.* 2007;16:213–17.
19. Akirov A, Masri-Iraqi H, Atamna A, Shimon I. Low albumin levels are associated with mortality risk in hospitalized patients. *Am J Med.* 2017;130: 11-9. DOI: 10.1016/j.amjmed.2017.07.020.
20. Hoffman M. The influence of hemophilia on wound healing. *Blood.* 2009; 114: 1-21. DOI: 10.1182/blood.V114.22.SCI-21.SCI-21.