

**ASSOCIATION BETWEEN SERUM ALBUMIN AND THE SUCCESS OF FLUID
RESUSCITATION IN CHILDREN HOSPITALIZED IN CIPTO
MANGUNKUSUMO HOSPITAL BURN CENTER**

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ABSTRACT

Background : Burn injury has a great impact on mortality and morbidity in children. Significant loss of albumin (hypoalbuminemia) in burn patient often leads to serious complications. However, it is still unclear whether serum albumin has a role in the success of fluid resuscitation in children with burn injury.

Method : This is a retrospective cohort study based on medical record of children hospitalized with burn injury at Cipto Mangunkusumo Hospital Burn Centre from January 2012-March 2018. The subjects collected with the total sampling method.

Result : Most burn injury happen because of scalds, and have grade 2 burn injury with PELOD score<10. Almost all subjects was successfully resuscitated in the first 24 hour (95,1%). No association was found between the success of fluid resuscitation with either serum albumin [RR 1,175(95%CI 0,3-4,4) p=0,812], or with ureum, creatinin, lactate level, weight and the degree/extent of the burn injury.

Conclusion: The success rate of fluid resuscitation in pediatric burn injury was quite high in Cipto Mangunkusumo Hospital Burn Centre. No association was found between serum albumin and the success of fluid resuscitation during the first 24 hour period.

Keywords: *albumin, burn, pediatric, resuscitation*

Latar Belakang: Luka bakar pada pasien anak memiliki tingkat mortalitas dan morbiditas yang tinggi. Hilangnya albumin (hipoalbuminemia) secara signifikan pada pasien luka bakar seringkali menyebabkan komplikasi yang serius. Hingga saat ini masih belum diketahui secara pasti peran albumin serum dalam keberhasilan resusitasi cairan pada anak dengan luka bakar.

Metodologi : Studi kohort retrospektif dari data rekam medis pasien anak yang dirawat dengan luka bakar di Unit Luka Bakar Rumah Sakit Cipto Mangunkusumo bulan Januari 2012-Maret 2018. Sampel penelitian dikumpulkan dengan metode *total sampling*.

Hasil: Kasus terbanyak luka bakar disebabkan oleh air mendidih, dengan derajat 2 luka bakar dan skor PELOD <10. Hampir seluruh sampel berhasil diresusitasi pada 24 jam pertama (95,1%). Tidak ditemukan hubungan antara keberhasilan resusitasi cairan baik dengan albumin serum [RR 1,175(95%CI 0,3-4,4) p=0,812], ureum, kreatinin, kadar laktat, berat badan, dan derajat/luas luka bakar.

Kesimpulan: Tingkat keberhasilan resusitasi cairan pada anak dengan luka bakar di Unit Luka Bakar Rumah Sakit Cipto Mangunkusumo cukup tinggi. Tidak ditemukan hubungan antara albumin serum dan keberhasilan resusitasi cairan pada periode 24 jam pertama.

Keywords: *albumin, burn, pediatric, resuscitation*

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INTRODUCTION

Burn is an injury of skin and mucosa that cause loss of tissue because of contact to heat. Burn poses high morbidity and mortality among pediatric patients. In 2014, World Health Organization estimated 265.000 death annually due to burn.¹⁻³ Mortality of pediatric burn patients in Cipto Mangunkusumo Hospital (CMH) in 2012-2017 were 20.3%.⁴

Burn patients had abundant loss of albumin, thus having a risk to develop hypoalbuminemia. A significant hypoalbuminemia lead to tissue edema that would complicate as respiratory distress (lung edema), delayed wound healing, gastrointestinal malabsorption, and diarrhea as consequence of intestinal edema.⁵

In recent years, the uses of colloid in burn resuscitation were widely investigated. Cochrane systematic review concluded that mortality risk of patient receiving albumin transfusion were higher compared to control group.⁶ Otherwise, Pruitt et al reported "fluid creep" phenomena during burn resuscitation using crystalloid-based fluid.⁷

There were yet no study to investigate baseline albumin status of pediatric burn patients and its ability to predict resuscitation failure. In our hospital, Cipto Mangunkusumo Hospital (CMH) Jakarta, burn resuscitation protocol was using crystalloid-based fluid, but decision was made according to acute clinical condition. CMH is the top referral hospital in Indonesia in which 75% of its patients were referred from other healthcare facilities.⁴ This is the first study in Indonesia aimed to investigate baseline albumin level as predictor of burn resuscitation in pediatric patients.

METHOD

This is a retrospective cohort study aimed to investigate the association between serum albumin level and success rate of fluid resuscitation in paediatric burn patients. This study was conducted in CMH burn unit. Data were obtained from patient medical records. We included paediatric patients (<18 years old) that admitted to burn unit between January 2012 to March 2018. Inclusion criteria were admission of 24 hours after burn injury onset and received fluid resuscitation in CMH. Exclusion criteria were body weight > 30 kg, had inhalation trauma, chronic kidney disease, nephrotic syndrome, chronic liver disease, malnutrition, admission for wound and infection care, and incomplete medical record data.

Serum albumin, ureum, and creatinine level were measured before patient received resuscitation.⁸ Resuscitation endpoints were normal heart rate and blood pressure according to age and urine output > 1 mL/kg/hours.⁹⁻¹⁰ Resuscitation fluid volume calculation was using Parkland formula and given in the first 24 hours after burn injury onset.^{8,11} Normal albumin level in this study were 3.5 to 5.5 g/dL.

Continuous data were present as mean and standard deviation or median and minimum-maximum for not normally distributed data. Categorical data were presented as proportion or percentage. Bivariate analysis using cox-regression was done. Effects were measured using relative risk (RR) with 95% confidence interval. This study protocol had been approved by Research Ethic Committee, Faculty of Medicine Universitas Indonesia – CMH (280/UN2.F1/ETIK/2018).

RESULT

During 2012-2018, there were 225 child admitted to burn unit. Among 208 patients that fulfill inclusion criteria, 7 were excluded due to admitted for skin graft, 43 did not receive resuscitation, 17 did not undergo serum albumin examination, and 24 with body weight > 30 kg. The other 56 patients' medical records were incomplete, so that the final samples were 61 patients. Median age was 3 years old (7 months – 10 years). Most of burn injury occurred in patients < 4 years old (67,2%) and male (57,4%). About 80.1% patients have normal nutritional status. The most common etiology is scalds (burn due to hot/boiled water) as many as 78.7%. Around 68.9% patients have burn injury grade II or more severe. Baseline characteristics are shown in Table 1.

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Table 1. Subject baseline characteristics

| Characteristics | n | % |
|---|----|------|
| Age | | |
| 0- < 4 years old | 41 | 67.2 |
| 4- < 10 years old | 20 | 32.7 |
| Gender | | |
| Male | 35 | 57.4 |
| Female | 26 | 42.6 |
| Nutritional status | | |
| Normal | 49 | 80.3 |
| Undernutrition | 9 | 14.7 |
| Overweight/Obese | 3 | 4.9 |
| Etiology of Burn Injury | | |
| Fire | 13 | 21.3 |
| Scalds | 48 | 78.7 |
| Grade | | |
| II | 42 | 68.9 |
| II-III | 19 | 31.1 |
| Pelod score 2 | | |
| < 10 | 55 | 88.5 |
| ≥10 | 6 | 9.8 |
| Time from onset to resuscitation | | |
| ≤ 8 hours | 29 | 47.5 |
| > 8-24 hours | 32 | 52.5 |
| Burn total body surface area | | |
| 10-20% | 30 | 49 |
| > 20% | 31 | 51 |
| Resuscitation outcome | | |
| Success | 58 | 95.1 |
| Fail | 3 | 4.9 |

Mean albumin level at admission was 3.1 (\pm 0.8) g/dL. Mean ureum level in 24 hours was 25.1 (\pm 10.1) mg/dL. Mean creatinine level was 0.4 (\pm 0.1) mg/dL while lactate level was 2.5 mmol/L, as shown in Table 2.

Table 2. Baseline laboratory results before 24 hours of onset

| Variable | N | Mean (DS) |
|--------------------|----|--------------------|
| Albumin (g/dL) | 61 | 3,1 (\pm 0.8) |
| Ureum (mg/dL) | 40 | 25,1 (\pm 10.1) |
| Creatinine (mg/dL) | 40 | 0,4 (\pm 0.1) |
| Lactate (mmol/L) | 33 | 2,5 (\pm 1.1) |

Pediatric patient received resuscitation was relatively similar in this period. In 2012, there were 40% patients resuscitated while it increased to 65.79% in 2017 (Table 3).

Table 3. Pediatric burn patients received resuscitation

| Year | Total patients | Received resuscitation | Percentage |
|------|----------------|------------------------|------------|
| 2012 | 35 | 14 | 40.00 |
| 2013 | 39 | 16 | 41.02 |
| 2014 | 39 | 20 | 51.28 |
| 2015 | 33 | 18 | 54.54 |
| 2016 | 33 | 14 | 42.42 |
| 2017 | 38 | 25 | 65.79 |

Patients that resuscitated early (under 8 hours after burn onset) were having 0.14 risk of resuscitation failure compared to patients resuscitated in 8-24 hours, but statistically insignificant. It also undetermined whether it was a risk or a protective factor due to its broad confidence interval (Table 4).

Table 4. Correlation of resuscitation time to outcomes

| Time from onset to resuscitation | Fluid resuscitation | | RR | 95% CI | p |
|----------------------------------|---------------------|-------------|-----------|-----------|-----------|
| | Succeed | Failed n(%) | | | |
| \leq 8 hours | n(%) 26 (44,8) | 3 (100) | 0,14 | 0 - 1.51 | 0,367 |
| > 8-24 hours | 32 (55,2) | 0 (0) | reference | reference | reference |

As seen in Table 5, we found no statistically significant difference between serum albumin level of patient having successful and failure of resuscitation (3.1 vs 3.2 g/dL). Similar result was also found in ureum level (2.3 vs 2.1 mg/dL), creatinine level (0.4 vs 0.39 mg/dL), and lactate (2.3 vs 1.0 mmol/L). Although patient with failure of resuscitation have higher burn area, it was not statistically significant.

Table 5.Correlation between laboratory parameters and resuscitation outcome

| Laboratory parameters (n) | Fluid resuscitation | | RR | 95% CI | p |
|----------------------------|---------------------|--------------------|-------|-----------|-------|
| | Succeed (mean (SD)) | Failed (mean (SD)) | | | |
| Albumin (n=61) g/dL | 3,1 (±0,8) | 3,2 (±0,9) | 1,175 | 0,3-4,4 | 0,812 |
| Ureum (n=40) mg/dL | 2,3 (±11,9) | 2,1 (±11,3) | 1,034 | 0,8-1,2 | 0,667 |
| Creatinine (n=40) mg/dL | 0,4 (±0,15) | 0,39 (±0,2) | 1,844 | 0-9,4 | 0,927 |
| Lactat (n=33) mmol/L | 2,3 (±1,04) | 1 (±0,4) | 0,006 | 0-52,2 | 0,271 |
| Total burn area (n=61) | 23,7 (±13,22) | 33 (±5,29) | 1,044 | 0,96-1,12 | 0,256 |

DISCUSSION

During the study period, there were 33.800 pediatric patients and 859 burn patients hospitalized, so that its prevalence was 0.6% among pediatric patients and 24.2% among burn patient. Proportion of patients received resuscitation in the first 24 hours was 73.1% in CMH. This was far higher than in Indonesian population data (7.8%), since CMH is a national referral hospital.¹²

In our study, population of child age 0-4 years old was the majority of burn patients, since those are period of active learning and exploration in child.¹³ In this period, a child tends to explore new things, such as puts her/his hand on boiled water or even throws liquid on the table.¹⁴

Most of burn patients were have normal nutritional status, similar to previous study.³ The most common burn severity was grade II (68.9%) in which the injury extends from epidermis to deep dermis. Rashid et al reported that 72.6% pediatric burn patients were also grade II.¹⁶

All patients included in this study received fluid resuscitation in the first 24 hours. Early resuscitation is associated to ebb phase which would favor the prognosis. Organ impairment in burn injury, such as acute kidney injury, could be prevented by adequate fluid resuscitation.¹⁷ Critical period of renal ischemic time was between 8 and 48 hours after injury.¹⁸ Otherwise, our study did not demonstrate difference in outcome between resuscitation under 8 hours and 8-24 hours. Adequate resuscitation is the first step to protect organ damage, mainly renal and thus further reduce mortality.¹⁹

Our study used 3 criteria to indicate a successful resuscitation: urine output >1 mL/kg/hours, normal heart rate and blood pressure according to age.⁹

In neonatal patients, endpoint of resuscitation was slightly differed, consist of response to tactile stimulation, adequate capillary refill time, heart rate below 180x/minute, systolic blood pressure 60-80 mmHg, and urine output more than 1 mL/kg/hours. We do not evaluate response to tactile stimulation due to unavailable data in medical records. Urine output target in our study was 1 mL/kg/hours, similar to Romanowski et al, except for patient > 30 kg which its target was 0.5 mL/kg/hours in that study. Fluid adjustment was then made based on urine output. Successful rate of resuscitation in our study was 95.1%. Three subject which have failed resuscitation was caused by septic shock. This result showed that burn resuscitation in CMH was adequate and monitored closely.

This study did not find significant difference of baseline serum albumin between success and failed resuscitation group. This results was supported by previous study that colloid administration in the first 24 hours is not beneficial.²⁰ Colloid administration in burn resuscitation is still debatable, although Parkland formula was actually designed for resuscitation using crystalloid, such as Ringer Lactate.⁸ A Cochrane systematic review also reported that albumin administration increase mortality among burn injury patients compared to placebo.⁶ On the other hand, experts said that fluid creep theory was strong enough to support consideration of colloid use in burn injury resuscitation.^{8, 16, 21, 22} In recent years, there were changing trends of colloid use, from Fresh Frozen Plasma (FFP) to albumin due to safety reason (infection and risk of acute lung injury).^{16, 23-26} FFP also reserved for patient with acute bleeding or coagulopathy.²⁷

In our study, none of the patients received colloid during resuscitation in the first 24 hours. A study using radioisotope demonstrated that in early phase of burn injury (first 24 hours), plasma expansion was not related to type of fluid administered. Capillary integrity and intravascular oncotic pressure had not much alteration so that colloid administration was not useful in this phase. In contrast, colloid administration increased risk of lung edema, mostly during 8-12 hours after burn onset. Non burned tissue were relatively less to developed edema due to internal mechanism that prevent plasma protein leakage, but not for burned tissue. Other study hypothesized that colloid administration would reduce total fluid volume, but a strong evidence from randomized clinical trial is needed.²⁸⁻²⁹

There were yet no multicenter nor longitudinal study on albumin use in pediatric resuscitation. A retrospective study by Faraklas et al use albumin 5% in one third of total fluid resuscitation and use intake to output (IO) ratio for resuscitation monitoring. This ratio will correct fluid balance into the baseline level by administering albumin, and no significant complication were reported.¹¹ Previously, albumin was also investigated in pediatric patients with burn injury more than 15% TBSA. This study reported less crystalloid volume, but it has low sample size (n = 23) so that a larger study were needed in the future.³⁰

Melinyshyn et al⁸ use albumin 5% in burn resuscitation, but did not demonstrate difference in duration of mechanical ventilation, wound healing, length of stay, nor survival rate. Albumin supplementation also has been proven to be not beneficial in a randomized controlled trial by Greenhalgh et al, while it increases the cost.³¹ Albumin supplementation also have various results in resuscitation of nonburn injury pediatric patients.³²

This study did not show significant difference in baseline albumin level between patient with succeed or failed resuscitation. Although mean albumin level was below standard level (<3.5 g/dL), it was still clinically sufficient since it was not categorized as hypoalbuminemia (<2.5 g/dL). This low albumin levels were not an indication of albumin transfusion and expected to increase to normal level at day 7-10 after burn injury.^{5, 31} This would be supported by adequate nutritional status in our study subjects (80.3%). Even without albumin transfusion, most of our patient have successfully resuscitated.

CONCLUSION

Proportion of burn injury patients received fluid resuscitation in the first 24 hours in CMH is 71.7%. Most of pediatric burn patients were < 4 years old, have burn grade II with total surface area >20%. Time from onset to resuscitation were between 8-24 hours, with baseline albumin level 3.1 g/dL and lactate level 2.5 mmol/L. In our study, no statistically significant difference between baseline serum albumin level and success of resuscitation in the first 24 hours was found.

Further Consideration

Parent education is needed to prevent burn injury in especially in children below 4 years old. Parents are needed to be educated about possible cause of burn, burn first aid, and the awareness to bring children to emergency department after occurrence of burn injury as soon as possible. Although we did not found the association between serum albumin and the success of fluid resuscitation in our population, further study in burn patients with low albumin serum level is needed to find its resuscitation outcome and to assess appropriate timing of albumin transfusion as indicated.

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