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Original Article

Acute kidney injury and mortality in critically ill children

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Abstract

Background Mortality from acute kidney injury (AKI) can be as high as 60% in critically ill children. This high mortality rate is influenced by the severity of primary diseases, organ dysfunction, and the stage of acute kidney injury.

Objective To assess for an association between AKI and mortality in critically ill children hospitalized in the pediatric intensive care unit (PICU).

Methods A cross-sectional study was conducted from April to July 2012. All patients aged 1 month to 18 years who were hospitalized in the PICU for more than 24 hours were included. Urine output and serum creatinine levels were evaluated daily. Patients were categorized according to the pediatric risk, injury, failure, loss, and end stage renal disease (pRIFLE) criteria. Chi square, Fisher's exact, Mann-Whitney U, and Kruskal-Wallis tests were used to assess for an association between AKI, mortality, pediatric logistic organ dysfunction (PELOD) score, and length of PICU stay. A P value of <0.05 was considered as statistically significant.

Results During the study period, 57 children were admitted, consisting of 25 (43.9%) females and 32 (56.1%) males, with a median age of 43 months. The prevalance of AKI was 31.5% (18/57) and classified into stages: risk 13/18, injury 3/18, and failure 2/18. The mortality rate for AKI was 16.7%. There was no association between AKI and mortality (P=0.592). The PELOD scores were found to be similar among patients (SD 11.32 vs. SD 12.23; P=0.830), and there was no association between AKI and length of PICU stay (P=0.819).

Conclusion There is no association between AKI and mortality in critically ill children admitted in PICU. **[Paediatr Indones. 2014;54:251-5.]**

Keywords: *acute kidney injury, critically ill, mortality*

Acute kidney injury (AKI) is characterized by a reversible increase in the blood concentrations of creatinine and nitrogenous waste products, and by the kidney's inability to appropriately regulate fluid and electrolyte homeostasis.[1] A modified version of the RIFLE criteria for pediatric patients was developed (pRIFLE) due to the lack of a standardized definition of AKI in children. The pRIFLE criteria are based on a decrease in estimated creatinine clearance (eCCI), whereas the urine output is based on body weight. In their cohort, 82% of the 150 enrolled patients developed AKI in accordance with the pRIFLE criteria, mainly in the initial week of admission.[2]

In pediatric patients, the main causes of AKI are sepsis, nephrotoxic drugs, and renal ischemia in critically ill patients.[1,3] Sepsis, especially septic shock, is one of the main causes of AKI. The prevalence of AKI caused by sepsis ranges from 9% to 40%, has a poor prognosis, and is associated with a 70% mortality

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rate.[4,5] The mortality from AKI is as high as 60% in critically ill children. This high mortality rate is influenced by the severity of the primary diseases, organ dysfunction, and stage of acute kidney injury.[6]

Considering the close association between severely ill patients and AKI, the quantification of ICU patient disease severity is mandatory. In pediatrics, the commonly used prognostic indicators are the pediatric risk index score for mortality (PRISM), PELOD, and pediatric index of mortality (PIM).[7-9] The aim of this study was to assess for an association between AKI and mortality in critically ill children.

Methods

A cross-sectional study was conducted between April and July 2012 in PICU patients at the Haji Adam Malik Hospital, Medan. The inclusion criteria were all patients older than 29 days and younger than 18 years, with a > 24 hour length of PICU stay. Patients with a history of previous renal diseases were excluded. Informed consent was obtained from subjects' parents or guardians after explanation of the study was given.

Purposive sampling was done on patients who met the inclusion criteria. Subjects were followed during their stay in the PICU, and their data collected daily according to the approved protocol. Patients were categorized according to mortality risk rate prognosis by admission (using the PELOD score), degree of kidney injury (pRIFLE) during the hospitalization, length of PICU stay in days, and outcomes (either discharge or death). For the PELOD score, six organ systems (neurologic, cardiovascular, renal, respiratory, hematologic, and hepatic) were considered, each with up to 3 variables (total of 12 variables). Each variable was assigned points (0, 1, 10, or 20) based on the level of severity.

For kidney injury categorization (pRIFLE), urine output and serum creatinine were analyzed daily (**Table 1**). The estimated creatinine clearance was calculated according to the Schwartz formula for glomerular filtration rate (GFR): $eGFR = k \times L/S_{cr}$, where eGFR is the estimated GFR in mL/minute/1.73 m^2, L is height in centimeters, S_{cr} is serum creatinine in mg/dL, and k is an empirical constant determined by comparing the L/S_{cr} ratio against measured GFR. The value of k is 0.45 for term infants throughout the first year of life, 0.55 for children and adolescent girls, and 0.7 for adolescent boys.

Data were analyzed using *SPSS version 18.0*. The quantitative variables were expressed as means and standard deviations. The categorical variables were described by their absolute (n) and relative (%) frequencies. The association between acute kidney injury and mortality in critically ill children was analyzed by appropriate tests (Chi square, Fisher's exact, Mann-Whitney U, and Kruskal Wallis tests). The significance level was accepted as $P<0.05$. This study was approved by the Ethics Committee of the University of North Sumatra Medical School.

Results

During the study period, 72 children were admitted to the PICU. A total of 57 patients met the inclusion criteria and were eligible for analysis. Of the 57 patients in this study, 56.1% were males. Thirty-nine patients did not develop AKI and served as controls while 18 patients (31.5%) developed AKI as defined by pRIFLE criteria. There were no statistically significant differences in the baseline demographic characteristics between patients with and without AKI. The mortality rate was 3/18 in AKI patients and 6/39 (15.4%) in non-AKI patients (**Table 2**).

Of the 18 AKI patients, 17 out of 18 were diagnosed with AKI on the first day. In this study, AKI patients were classified into risk, injury and failure groups comprising of 13, 3, and 2 subjects, respectively (**Table 3**).

Table 1. Pediatric RIFLE criteria[2]

AKI classification	eCCl	Urine output
Risk	eCCl decrease by 25%	<0.5 mL/kg/h for 8 h
Injury	eCCl decrease by 50%	<0.5 mL/kg/h for 16 h
Failure	eCCl decrease by 75% or <35 mL/min/1.73 m^2	<0.5 mL/kg/h for 24 h or anuric for 12 h

eCCl= estimated creatinine clearence

Table 2. Characteristics of subjects

Characteristics	AKI (n = 18)	No AKI (n = 39)
Mean age (SD), months	52.3 (63.34)	77.8 (64.46)
Gender, n		
Male	13	19
Female	5	20
Mechanical ventilation, n		
Yes	3	19
No	15	20
PELOD score, n		
< 10	9	21
10 – 19	3	5
≥ 20	6	13
Mortality, n		
Yes	3	6
No	15	33
Primary diseases, n		
Neurology	2	15
Cardiovascular	2	3
Nephrology	0	1
Respiratory	1	6
Gastroenterology	4	0
Burn victim	1	0
Post-surgery	8	14

Table 3. Characteristics of acute kidney injury patients

Characteristics	n=18
pRIFLE criteria	
Risk	13
Injury	3
Failure	2
Onset, hours	
<24	17
≥24	1
Duration, hours	
<48	14
≥48	4

Table 4. Association between AKI and mortality

AKI	Mortality		P value
	Yes n	No n	
AKI (n=57)			
Yes	3	15	0.592
No	6	33	
pRIFLE criteria (n=18)			
Risk	2	11	0.783
Injury	1	2	0.484
Failure	0	2	NA

There was no association noted between AKI and mortality in our setting (P=0.592). There was also no correlation between pRIFLE criteria and mortality rate (**Table 4**).

Table 5 shows that there was no significant difference in PELOD scores between AKI and non-AKI patients (P=0.830), nor were there significant PELOD score differences between the pRIFLE groups. We also noted that AKI had no association with the length of PICU stay of these critically ill children (**Table 6**).

Table 5. Mean PELOD score in AKI

	PELOD score	P value
AKI patients, mean (SD)	10.2 (11.32)	0.830
Non-AKI patients, mean (SD)	10.3 (12.23)	
pRIFLE criteria		
Risk, mean (SD)	8.5 (11.28)	0.516
Injury, mean (SD)	13.6 (15.18)	
Failure, mean (SD)	16.5 (6.36)	

Table 6. Association between AKI and length of PICU stay

	Length of stay		
	≤7 days n	>7 days n	P value
AKI			
Yes	13	5	0.819
No	27	12	
pRIFLE criteria			
Risk	9	4	0.996
Injury	2	1	0.931
Failure	2	0	NA

Discussion

AKI has a catastrophic impact and is common in critically ill patients. It may be multifactorial in etiology. AKI may progress to renal failure, preventing the kidneys from performing their most important role, homeostasis.[10]

The incidence of AKI in our study was 31.5%, similar to the incidence in Brazil (30.6%).[10] Other studies reported incidences of 82% in the USA,[2] and 58% in the Netherlands.[11] With regards to AKI staging, we found that 13/18 of patients were in the risk stage, 3/18 in the injury stage, and 2/18 in the failure stage. The stage distribution was different

in Brazil, with 39.1% in the risk stage, 39.1% in the injury stage, and 21.8% in the failure stage.[10] Another study from the USA also found risk as the main stage of AKI with 48.8%, 26%, and 25.2%, respectively.[2] These differences may be explained by the differing populations studied, and by differing ICU characteristics.

With regards to mortality, several studies have clearly shown that any degree of AKI is an indicator of poor prognosis for critically ill patients.[11-16] A cohort study in Brazil identified a ten-fold higher mortality rate in patients with any stage of AKI.[10] Another study in the Netherlands also found a higher mortality rate in the AKI group compared to the non-AKI group (25% vs. 5%, respectively; $P<0.05$).[11] In contrast, we found no difference in occurrence of mortality between AKI and non AKI patients ($P=0.592$), similar to a study in the USA.[2]

The mean PELOD scores in our study were similar in AKI and non AKI groups ($P=0.830$). A study in the Netherlands using PIM II and PRISM scores also found no difference between the prognostic scores in patients with and without AKI.[17] However, studies from Brazil and the USA using PIM II scores found higher mean and median PIM II scores in the AKI groups.[2,10]

Past studies that used RIFLE criteria showed that the mean length of ICU stay increased as AKI severity progressed. A study in the USA noted a trend for the AKI group to stay longer in the ICU, and concluded that AKI was an independent factor for increased risk of longer hospital stay.[2] However, we found no difference between AKI and non AKI patients regarding the length of PICU stay ($P=0.819$). Similarly, a Dutch study showed no statistically significant differences between the control and AKI groups with regards to length of ICU stay.[11]

There were some limitations in our study. We had a relatively small sample size and this was a single center study, which may have led to bias due to specific environmental characteristics in the population. Additionally, other biases may have been present due to the heterogeneous distribution of some clinical features (age, severity ill scores, or mechanical ventilation).

In conclusion, there is no association between AKI and mortality in critically ill children admitted in PICU.

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