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Incidence and Risk Factors for Acute Kidney Injury in PICU of Dr. Mohammad Hoesin Hospital Palembang

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ABSTRACT

Introduction. Acute kidney injury (AKI) is a heterogeneous group of conditions characterized by a sudden decrease in the glomerular filtration rate, manifested by an increase in serum creatinine or oliguria. In the Pediatric Intensive Care Unit (PICU), AKI is one of the most common conditions found. Several factors, including age, infection, sepsis, shock, heart disease, mechanical ventilation, and multiple organ failure cause the increase in the incidence of AKI in children. This study aimed to determine the incidence and risk factors for AKI in critically ill children in the PICU of Dr. Mohammad Hoesin Hospital Palembang. **Methods.** This study was an observational analytic with a cross-sectional design. This study used secondary data based on the medical records of patients treated at the PICU. Critically ill children aged 1-18 years who were treated at the PICU of Dr. Mohammad Hoesin Hospital Palembang in the period of 1 January 2020 to 31 December 2021 were included while existing kidney dysfunction before being admitted to PICU and not fulfilled medical records were excluded to the study**. Results.** AKI incidence in PICU was 46.7%. There were significant risk factors for AKI which are age (p 0.025), sepsis (p 0.019), shock (p 0.002), mechanical ventilation used (p 0.043), nephrotoxic drugs (p 0.039), and fluid overload (p 0.039). **Conclusion.** This study found that age, sepsis, shock, mechanical ventilation, nephrotoxic drugs, and fluid overload, were significant risk factors for the incidence of AKI in critically ill children in PICU.

1. Introduction

Acute kidney injury (AKI) is a group of heterogeneous conditions characterized by a sudden decrease in glomerular filtration rate, which manifests with increased serum creatinine or oliguria, and is classified by stage and etiology.[1] For decades, AKI has been known as one of the factors influencing the prognosis of critical patients.[2]

The incidence rate of AKI is 20-50% in the Intensive Care Room (ICU). In the Paediatric Intensive Care Unit (PICU), AKI is one of the most common conditions.[3] Based on a study by Louzada and Ferreira in 2021, the incidence rate of AKI in the PICU population was 12.6%, similar to the incidence rate obtained in other reports 4-26.9%.[4] In Indonesia, research conducted by Nilawati in 2012 showed the incidence of AKI in PICU was 16.77% from 149 patients. This figure is quite high, so it is necessary to detect AKI earlier by checking the glomerular filtration rate and monitoring urine output.[5] The increase in the incidence of AKI in children is due to several factors, including age, infection, sepsis, shock, heart disease, mechanical ventilation, multiple organ failure, hypoxia, and coagulopathy.[6]

There has been no research and data directly on the incidence and risk factors of AKI in pediatric patients of PICU Dr. Mohammad Hoesin Hospital. Identification of risk factors for AKI in children can promote diagnosis and management quickly and precisely so that it is expected to reduce the incidence and decrease the morbidity and mortality of AKI in critically ill children. Therefore, this study aims to determine the incidence rate and risk factors for acute kidney injury in pediatric patients of PICU Dr. Mohammad Hoesin Hospital Palembang.

2. Methods

The study design of this research is observational analytics with a cross-sectional study design. This study used secondary data based on the patient's medical record. The samples in this study were pediatric patients treated at the PICU of Dr. Mohammad Hoesin Hospital Palembang who met the inclusion and exclusion criteria in the period January 1, 2020 to December 31, 2021. The sampling

technique is quota sampling with a sample of 90 patients. The data obtained were then analyzed with the SPSS program.

3. Results

There were 42 patients diagnosed with AKI out of a total of 90 critically ill children treated in the PICU. Based on this, it was found that the incidence of AKI in PICU of Dr. Mohammad Hoesin Hospital Palembangin 2020–2021 was 46.7%. The time of admission of patients to the diagnosis of AKI was most found on the first day in 33.34% of patients, and the longest onset was in 9th day.

Table 1 illustrates that from a total of 42 patients diagnosed with AKI, the degree of AKI based on pRIFLE criteria most common was stage risk in 17 patients (40.48%), followed by stage failure which was found in 16 patients (38.09%).

Of the total 90 patients in this study, 54 patients (60%) of patients aged <5 years, with more patients were found to be female (55.6%) compared to patients who were male (44.4%). In this study, 46 (51.1%) patients had sepsis, and 40 (44.4%) patients had shock. As many as 79 (87.8%) patients were on mechanical ventilators during their treatment in the PICU. This study also found as many as 76 (84.4%) patients had history of taking nephrotoxic drugs during or before admit to PICU. Types of nephrotoxic drugs found in this study include beta lactam antibiotics (75%), furosemide (17.1%), mannitol (10.52%), aminoglycosides (7.89%), spironolactone (5.26%), rifampicin (3.94%), and cyclosporine (2.63%).

The percentage of fluid overload <5% was more common in patients (74.4%) compared to the percentage of fluid overload ≥5% (25.6%) with the highest value of 15.7%. Neoplasms (24.4%) were the most common underlying disease for patients treated in the PICU in this study. The most common type of neoplasm is leukemia, which is found in 31.8% of the neoplasm patients.

Table 1. Characteristics of pediatric patients of PICU Dr. Mohammad Hoesin Hospital Palembang (N=90)

Characteristics	n	%
AKI staging (n=42)		
Risk	17	40,48
Injury	9	21,43
Failure	16	38,09
Loss	0	0,0
End Stage Renal Disease	0	0,0
Age		
<5 years	54	60,0
≥5 years	36	40,0
Sex		
Male	40	44,4
Female	50	55,6
Sepsis		
Yes	46	51,1
No	44	48,9
Shock		
Yes	40	44,4
No	50	55,6
Mechanical Ventilation		
Yes	79	87,8
No	11	12,2
Nephrotoxic drugs		
Yes	76	84,4
No	14	15,6
Fluid Overload		
≥5%	23	25,6
<5%	67	74,4
Underlying organ disease		
Respiratory system	19	21,1
Neurologic system	14	15,6
Endocrine and metabolic system	4	4,4
Cardiovascular system	21	23,3
Neoplasm	22	24,4
Gastrointestinal system	6	6,7
External injury	3	3,3
Integumen system	1	1,1

The relationship between risk factors and the incidence of AKI in pediatric patients admitted to the PICU is presented in Table 2. Based on the hypothesis tests that have been done, it was found that risk factors for age (PR 2.671, p 0.025), sepsis (PR 2.747, p 0.019), shock (PR 3.946, p 0.002), ventilator use (PR 4.615, p 0.043), nephrotoxic drugs (PR 3.865, p 0.039), and fluid overload (PR 2.778, p 0.039) had a statistically significant association with the incidence of AKI in this study.

Table 2. The association between risk factors and incidence of AKI in pediatric patients of PICU Dr. Mohammad Hoesin Hospital Palembang

Risk factors	N	AKI (n=42)		Not AKI (n=48)		PR	*p-value**
		n	%	n	%		
Age							
<5 years	54	20	22,2	34	37,8	2,671	0,025
≥5 years	36	22	24,4	14	15,6		
Sex							
Male	40	18	20,0	22	24,4	1,128	0,777
Female	50	24	26,7	26	28,9		
Sepsis							
Yes	46	27	30,0	19	21,1	2,747	0,019
No	44	15	16,7	29	32,2		
Shock							
Yes	40	26	28,9	14	15,6	3,946	0,002
No	50	16	17,8	34	37,8		
Mechanical ventilation							
Yes	79	40	44,4	39	43,3	4,615	0,043
No	11	2	2,2	9	10,0		
Nephrotoxic drugs							
Yes	76	39	43,3	3	3,3	3,865	0,039
No	14	3	40,5	11	12,2		
Fluid Overload							
≥5%	23	15	16,7	8	8,9	2,778	0,039
<5%	67	27	30,0	40	44,4		

* Chi-square test

4. Discussion

The incidence of AKI was found in 42 (46.7%) of the 90 patients treated in the PICU. Similar incidence rate was found in Nguyen and Devarajan's study where the incidence of AKI in PICU patients was 30 to 50%.[7] Naik et al also reported incidence rate of AKI in PICU was 40.9%.[6] This result is higher than in Nilawati's study which reported an AKI incidence of 16.7%.[5] The higher incidence might due to monitoring of patients' daily urine output which was not carried out in previous study. The uses of pRIFLE criteria based on urine output has a high sensitivity compared to its specificity, so the detection of AKI is higher.[8]

This study found significant association between age and the incidence of AKI (PR 2.671, *p* 0.025). Naik et al also showed significant association between lower age and the incidence of AKI (OR 0.85, 95% CI 0.78 -0.94, *p* 0.001).[6] Retrospective research conducted by Zan et al also reported significant association between age and AKI in PICU.[9] Similar results that AKI is more prevalent at younger age were shown in the studies conducted by Mehta et al (*p* 0.002) and Jiang et al (*p* <0.001).[10,11] This is due to immature compensatory mechanisms in younger children, including poor ability to concentrate urine.[12]

This study found no significant association between gender and incidence of AKI. Similar results were obtained in study of Jiang and Zan.[9,11] Different results showed by study conducted by Güzel that there is a higher incidence of AKI in males. They suggest that there is association with androgens that contribute to hemodynamic disorders and the development of damage to the kidneys.[13] The absence of a significant association between gender and AKI in this study might due to the number of female patients found in this study more than men, in contrast to other studies which were generally dominated by male patients.

Sepsis was known as risk factors of AKI. This study found significant association between sepsis and the incidence of AKI in PICU (PR 2.747, *p* 0.019). Similar results were found in the study of Naik et al and Mehta et al, where there were significant association between sepsis and AKI (*p* <0.001).[6,10]

At least three mechanisms in sepsis that can cause AKI are inflammation, microcirculation dysfunction, and metabolic reprogramming. The inflammatory response is the primary defense mechanism of the host against invading pathogens. During sepsis, inflammatory mediators are released into the intravascular compartment. These molecules attach

to receptors, such as toll-like receptors. Renal tubular epithelial cells express toll-like receptors, especially TLR2 and TLR4. When exposed to damage or pathogens filtered through the glomerulus, renal tubular epithelial cells will exhibit increased oxidative stress, production of reactive oxygen species, and mitochondrial injury. In addition, renal tubular epithelial cells initiate paracrine signals to neighbored cells to be deactivated in an effort to minimize cell death.[14]

Significant association between shock and the incidence of AKI was found in this study (PR 3.946, *p* 0.002). This is in line with the research of Naik et al which found a significant association between shock and AKI in pediatric patients admitted to the PICU (*p* <0.001).[6] Mehta et al also reported significant association between shock and the incidence of AKI (*p* <0.001).[10]

Shock leads to a decrease in renal perfusion (pre-renal), which then provokes inflammatory and metabolic changes in the epithelium of the renal tubules. Ischemia that occurs in shock causes circulating heme to produce reactive oxygen species and oxidative stress in the kidneys. This triggers a cascade that causes apoptosis, resulting in AKI.[15]

Significant association between mechanical ventilation and the incidence of AKI in PICU (PR 4.615, *p* 0.043) was found in this study. This is in line with the research of Naik et al and Mehta et al, where significant relationship was found between the use of mechanical ventilation and AKI in the PICU. .[6,10] Ventilators can trigger AKI due to hemodynamic changes that interfere with renal perfusion, neurohumoral-mediated changes in the intra-renal bloodstream, and systemic inflammatory mediators produced by ventilator induced lung injury (VILI).[16]

There is an inverse relationship between CPAP levels and kidney function, where mechanical ventilation induces 'circulatory stress' which can be identified with decreased kidney function. Positive pressure ventilation can cause decreased cardiac output by impeding venous backflow. In addition, neurohumoral mediators released during mechanical ventilation also alter renal blood flow from the cortex to the medulla leading to sodium reabsorption and decreased GFR. Sodium reabsorption requires high oxygen utilization, so mechanical ventilation can decrease oxygen perfusion through hemodynamic effects.[16]

Significant association between the use of nephrotoxic drugs and the incidence of AKI was found in this study (PR 3.865, *p* 0.039). Similar results was found in the studies of Zan et al and Jiang et al (*p* < 0.001).[9,11] Some drugs cause acute tubular injury in hosts at risk due to toxicity and congenital dysfunctions of renal handling. Drug-induced acute interstitial nephritis also occurs when drugs elicit a T-cell-mediated immune response that promotes tubulointerstitial inflammation. The third pathway of renal injury results from insolubility of drugs in the urine leading to their intratubular precipitation as crystals with an associated inflammatory response. Pseudo-AKI caused by drugs that inhibit tubular creatinine secretion as well as hemodynamic causes of elevated serum creatinine should be considered in patient evaluation.[17]

Fluid overload is a condition where there is a positive fluid balance in patients which is usually caused by excessive fluid administration. Cumulative fluid balance is calculated based on total fluid input minus total fluid output in the first 24 hours the patient is admitted to the PICU, divided by body weight at admission.[18]

Twenty five percent patients in this study have fluid overload ≥5% and significantly associated with AKI (PR 2.778, *p* 0.039). Similar results was found in the study of Zan et al that there was a significant relationship between fluid overload >2% and AKI in PICU (*p* <0.001).[9] According to research by Li et al, early fluid overload (first 24 hours of treatment in the PICU) ≥5% is a risk factor for AKI (OR 1.34, *p* <0.001). A threshold of 5% FO is equivalent to a positive fluid balance of 50 mL/kg, is recommended as the limit for higher risk of AKI in at-risk patients requiring mechanical ventilation and one or more vasoactive agents.[18]

Fluid overload causes endothelial dysfunction due to inflammation and ischemic-perfusion injury, causing glycocalyx damage and capillary leakage. Capillary leakage leads to interstitial edema, then at the same time, due to a significant loss of volume to the interstitial compartment, a reduction in circulating intravascular volume occurs. This then leads to decreased renal perfusion and further leads to AKI.[19]

5. Conclusion

This study concluded that there were association between age, sepsis, shock, mechanical ventilation, nephrotoxic drugs, and fluid overload on the incidence of AKI in critically ill children in PICU.

6. Acknowledgements

None

7. References

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