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Research Article

INCIDENCE, RISK FACTORS, AND OUTCOME OF ACUTE KIDNEY INJURY AMONG CHILDREN IN PEDIATRIC INTENSIVE CARE UNIT IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Objective: The study aimed to study the incidence, risk factors, outcome, and disease pattern of acute kidney injury (AKI) among children admitted in the pediatric intensive care unit (PICU).

Methods: The present study was a prospective study done to study the incidence, risk factors, and outcome of AKI among children of the age group 1 month–12 years admitted in PICU at a tertiary care hospital.

Results: A total of 480 PICU admissions were recruited, of which 276 children met the inclusion criteria. Of these, AKI was diagnosed in 119 children (50.4%) using pediatric risk, injury, failure, loss, and end-stage renal disease criteria, and the remaining 117 children were classified as non-AKI. The majority of children (63%) were in the age group of 5–12 years, and the male-to-female ratio was 1.2:1. From this study, it was recorded that the pathogenesis of AKI could be attributed to acute glomerulonephritis (AGN) (85%), sepsis (74%), and others like snake bite, diarrhea, poisoning cases, scorpion sting, diabetic ketoacidosis, heart failure, and unclassified causes with observable numbers. The most common offender is shock (91.4%) with vasopressor support (85.4%). Out of 82 children on inotropic support, 46 were on adrenaline. It was observed that the majority of children (93.5%) developed AKI during the course in hospital. The mortality rates were 64.7% and 24.5% among AKI and non-AKI patients. The mean duration of hospital stays among children without AKI was 5 days.

Conclusion: The presence of AKI is associated with longer PICU and hospital stay, with higher mortality imposing a significant burden to health-care system.

Keywords: Children, Acute kidney injury, Incidence, Risk factors.

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INTRODUCTION

Acute kidney injury (AKI) is common in critically ill children and is a common encounter in our day-to-day intensive care practice. Studies have revealed that mortality from AKI is as high as 30–40% in the pediatric critically ill population [1]. Furthermore, more concerning is that a proportion of patients with insult of AKI might progress to chronic kidney disease (CKD) [1]. Much of the available data on the clinical course of patients with AKI is from western literature. Compared to that, reports from our country are scanty. However, the incidence and risk factors of AKI in our country may be different from western countries, so there is a need to study the most common diseases and conditions causing AKI, which can help in detecting AKI at the earliest and in developing strategies for prevention and treatment of AKI [2].

The etiology and management of AKI differ between developing and developed countries and also within the country, from one hospital to another, location, level of expertise, and resources available at the center. Furthermore, as in adults, AKI carries a significant risk for the late development of CKD in surviving children [3]. Further, reliable epidemiological data from developing countries regarding AKI in children are lacking [4].

AKI can be defined as the abrupt loss of kidney function, leading to a decrease in glomerular filtration rate and impaired control of acid-base, electrolyte, and fluid balance. The term AKI has replaced acute renal failure as it emphasis that renal dysfunction encompasses a spectrum of disease severity rather than a single discrete entity. AKI is a common problem in children admitted to hospital, especially among those requiring intensive care, and it is an independent risk factor for increased mortality and severe morbidity [5].

It has been found that about two million people die due to AKI annually, and mortality increases when there is a decline in renal function after admission in the intensive care unit [6]. This entity refers to the continuum of kidney insult that starts long before sufficient loss of excretory kidney function can be sensed. Hence, this condition is a significant diagnostic and therapeutic challenge for clinicians. Moreover, there is no specific treatment developed so far that can reduce AKI or speed up the recovery.

The incidence of AKI is highly varied, and its pattern in different countries is affected by various factors, namely, definitions, ethnic groups, etiology, and economic conditions. AKI has been reported to be on the rise in both developing and developed countries, and it is independently associated with increased mortality and morbidity in children and adults with the subsequent development of renal dysfunction [1,3,5]. Therefore, our present study aims to study the incidence, risk factors, and outcome of AKI among children of age group 1 month–12 years admitted in our pediatric intensive care unit (PICU) so as to throw light on the disease pattern in our region.

METHODS

It is a cross-sectional observational study. This study was conducted in the Department of Pediatrics, a tertiary care teaching hospital at Central District of Tamil Nadu. After Institutional Ethics Committee clearance and getting written informed assent from the parents, the study was

initiated among children of ages 1 month–12 years, who were admitted in PICU fulfilling inclusion criteria.

The patients who were noticed with pre-existing renal disease, CKD, nephritic syndrome, a bilirubin level more than 5 mg/dL, a hospital stay of <48 h, and serum creatinine not done at admission were excluded from the study. Serum creatinine levels were measured on admission into the PICU and repeated every 24±6 h for 5 days in all children who were enrolled in the study.

All the patients were catheterized and urine output was monitored every 8th hour according to pediatric risk, injury, failure, loss, and end-stage renal disease (pRIFLE) criteria. Using pRIFLE criteria, which are based on a rise in serum creatinine, decreased urine output, and estimated creatinine clearance, children were classified as AKI developed either at admission or during the course in hospital and monitored until the outcome. The baseline creatinine value was taken as the age-appropriate creatinine value. Those who did not meet pRIFLE criteria were classified as non-AKI, and alternate-day serum creatinine levels were monitored. Children were then followed up until discharge or death; demographic details such as age, gender, clinical features, underlying etiology, and details regarding interventions were collected and analyzed.

Data were entered using Excel, and analysis was performed using Stata version 14. Continuous variables were expressed as mean (SD), and categorical variables were expressed as a proportion. The main outcome incidence was expressed as proportion with a 95% CI. A chi-square test is used to assess the association between two categorical variables. A t-test, or ANOVA, was used to assess the association between two continuous variables. $p<0.05$ was considered to be statistically significant.

RESULTS

In this study, a total of 480 children who were admitted in PICU were identified, and out of them, 276 (57.5%) children met the inclusion criteria. Among them, only 236 (85.5%) children were included in this study. Of these, AKI was diagnosed in 119 children (50.4%) using pRIFLE criteria, and the remaining 117 (49.6%) children were classified as non-AKI (Fig. 1). The demographic details, clinical course, and outcome details were noted. The data collected were statistically analyzed.

The majority of children (63%) in the age group of 5–2 years developed AKI, followed by 34% of children in the age group 1–5 years, and the remaining 22% among age group <1 year developed AKI (Table 1). This age group determination was not statistically significant. The gender analysis of AKI children showed not much variations where 59 (49.6%) were males and 60 (50.4%) were females, and the p-value determination was not statistically significant (0.086).

The pediatric patients included in this study were admitted in PICU for various clinical complications, where AKI was developed and noticed. Among them, 85% of children with AGN developed AKI, followed by sepsis (74%), diabetes ketocidosis (66.7%), diphtheria (66.7%), snake bite (65.5%), congenital heart disease (CHD)/congestive cardiac failure (58.8%), scorpion sting (46.2%), diarrhea (45%), poisoning (7.1%), and others (17.4%). Among children who developed AKI, sepsis constitutes a major proportion, and the details are depicted in Table 2.

Shock was present in 81 children enrolled in the study; among them, 91.4% (74) of children developed AKI during the course of the illness. There were 48 children with respiratory distress from underlying causes such as pulmonary edema, pleural effusion, empyema, bronchopneumonia, pneumothorax, and ARDS. Of these, 64.6% (31) of children developed AKI (Table 3). Out of a total of 51 children with seizures of infectious, inflammation, and toxin-induced etiology, only 41.2% (21) developed AKI. Totally, 108 children in the study were admitted in altered sensorium, out of which 68.5% (74) had AKI.

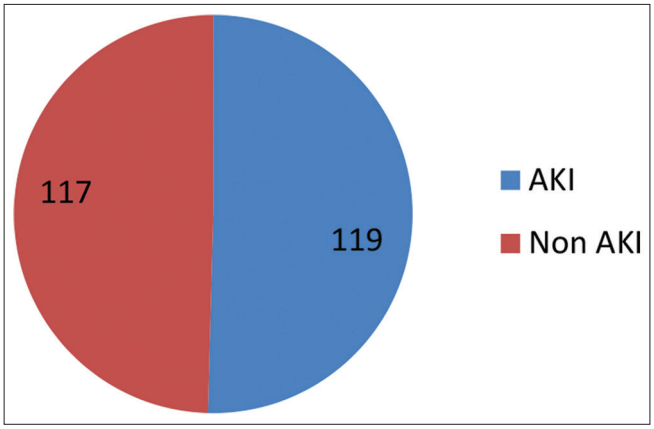

Fig. 1: Incidence of acute kidney injury among children admitted in pediatric intensive care unit (n=236)

Table 1: Age-wise analysis of AKI versus non-AKI children

Age groups	AKI versus non-AKI frequency		p-value
	AKI (n=119)	Non AKI (n=117)	
Below 1 year (n=58)	22 (18.5)	36 (30.8)	0.082
1–5 years (n=65)	34 (28.6)	31 (26.5)	
5–12 years (n=113)	63 (52.9)	50 (42.7)	

AKI: Acute kidney injury

Table 2: Incidence of AKI in various diseases

Diseases	AKI (n=119)	Non-AKI (n=117)
Acute glomerulonephritis (n=20)	17 (85)	3 (15)
Diabetes ketoacidosis (n=9)	6 (66.7)	3 (33.3)
Diarrhea (n=11)	5 (45.5)	6 (54.5)
Diphtheria (n=6)	4 (66.7)	2 (33.3)
Poisoning (n=14)	1 (7.1)	13 (92.9)
Scorpion sting (n=13)	6 (46.1)	7 (53.9)
Sepsis (n=54)	40 (74.1)	14 (25.9)
Snake bite (n=29)	19 (65.5)	10 (34.5)

AKI: Acute kidney injury

Table 3: Risk factors associated with AKI

Risk factors	Total cases (n=236)	AKI patients (n=119)	p-value
Altering sensorium	108	74 (68.5)	0.000
Respiratory distress	48	31 (64.6)	0.028
Seizures	51	21 (41.2)	0.136
Shock	81	74 (91.4)	0.000

AKI: Acute kidney injury

Out of 46 children who are exposed to nephrotoxic drugs during treatment of underlying disease, 80.4% (37) of the children developed AKI. Among 82 children who were on inotropic support, 85.4% (70) of children developed AKI. In addition, 61 (78.2%) children who were required ventilatory support (n=78) had AKI (Fig. 2).

In this study, out of 82 children on inotropic support, 46 children were on adrenaline. Out of which, the majority of children (93.5%) developed AKI during the course in hospital. Almost all children who were treated with combined adrenaline and noradrenaline for refractory shock (n=12) had developed AKI. Only 25% and 50% of children treated with nor adrenaline (n=4) and dobutamine (n=20), respectively, developed AKI (Fig. 3).

Among the 119 cases that developed AKI, 36 children were with AKI on admission, and the remaining 83 children developed AKI during

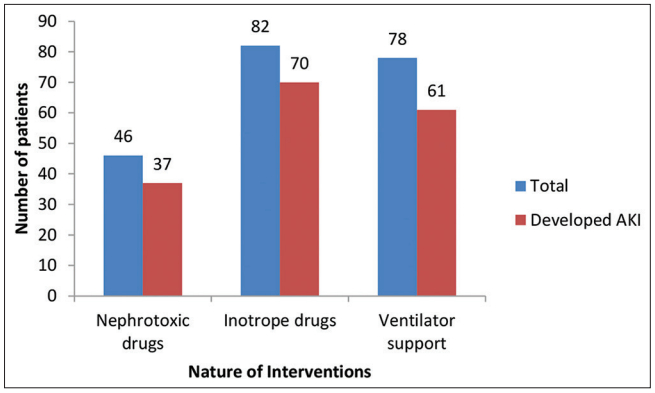

Fig. 2: Intervention in pediatric intensive care unit associated with acute kidney injury

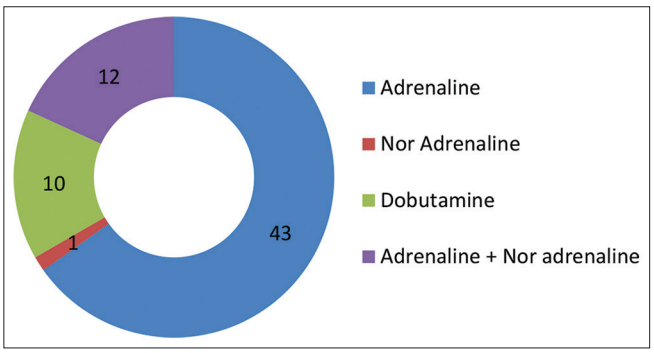

Fig. 3: Effect of inotrope on acute kidney injury

the course in hospital. It was observed that there was decreased urine output and increased serum creatinine values. Comparatively, AKI patients showed higher variations than non-AKI patients. The mean urine output and serum creatinine values were done and compared (Table 4).

Among those who had AKI, 50.4% of children were in the stage of injury, 39.4% were in risk, and the remaining 10% were in failure (Table 5). No children were recorded for loss of function or end-stage. Out of a total of 119 children with AKI, 24.4% of children were showed underlying comorbidities. Underlying comorbidities found among children with AKI were severe acute malnutrition, Type 1 diabetes mellitus, CHD and dilated cardiomyopathy, cerebral palsy, and Down's syndrome (Table 5).

Among 119 children with AKI, the mortality and recovery rates were 64.7% and 35.3%, respectively. The majority of children without AKI recovered (78.6%), and the mortality rate was 21.4% (Fig. 4).

DISCUSSION

AKI is a frequently encountered complication associated with critical illness in our day-to-day practice in the PICU. This could either be the cause of hospitalization or a complication of illness in severely ill children admitted in an intensive care unit. By the literature and from our everyday practice, we can infer that early identification and managing AKI are the keys. Furthermore, more concerning is that a proportion of patients with an insult of AKI might progress to CKD [1].

Hence, timely identification and management could be lifesaving. Serum creatinine measurement and monitoring are being employed to assess kidney function. pRIFLE criteria for grading AKI for the pediatric population are used. Among the 236 children, 119 were diagnosed to have AKI, thus showing an incidence of 50.4%.

A landmark trial – an assessment of worldwide AKI, renal angina, and epidemiology study was done involving patients admitted to the PICU

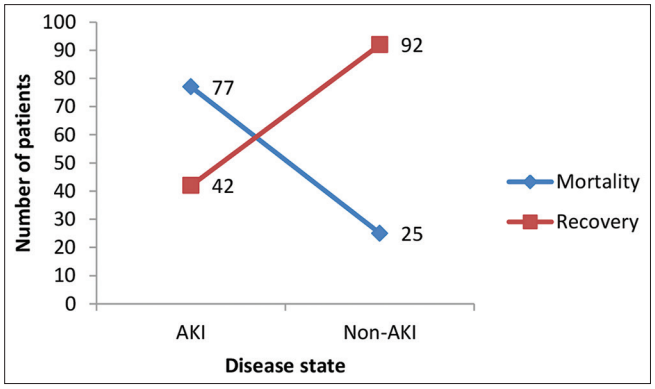

Fig. 4: Mortality versus recovery rates

Table 4: Mean urine output and serum creatinine

Patients	Urine output (mL/kg/h)			Serum creatinine (mg/dL)		
	Day 1	Day 2	Day 3	Day 1	Day 2	Day 3
AKI	1.1	0.5	0.3	0.6	1.5	1.9
Non-AKI	1.9	1.7	1.8	0.31	0.32	0.34

AKI: Acute kidney injury

Table 5: Various stages, hospital stay, comorbidities, and dialysis requirements of acute kidney injury patients

Various stages (n=119)		Hospital stay	Comorbidities (n=29)	
Risk	47 (39.5)	9 days	Severe acute malnutrition	11 (38)
Injury	60 (50.4)	10 days		
Failure	12 (10.1)	7 days	Type 1 diabetes mellitus	5 (17.2)
Requirement of dialysis				
Required	40 (33.6)		Congenital heart diseases	7 (24.1)
Not required	79 (66.4)			
			Dilated cardiomyopathy	3 (10.3)
			Cerebral palsy	2 (6.9)
			Down's syndrome	1 (3.5)

to define the incremental risk of death and complications associated with severe AKI. This was done among 4683 pediatric patients over a period of 3 consecutive months who were admitted to the PICU. It was reported that AKI developed in 26.9% of patients within 7 days of PICU admission [7], where the incidence was low when compared to the present study.

The reference studies reported an incidence of AKI of 51.1% [8] and 25.1% [9] using pRIFLE criteria, which is very close to our observation. However, the sample size varies; anyhow, both studies analyzed the data by percentage calculation only. While comparing our findings with the Indian studies, it showed the incidence of 38.1% [10] and 42.9% [2]. In another study analyzing the intensive care unit stay, 60.2% [11] and 65% [12] developed AKI, and it is considered the higher reported incidence, whereas the lower incidences included 26.9% of patients [7].

A study observed an incidence of 56.9% among female children and commented that female gender is an independent risk factor for the development of AKI [2]. Another study revealed that there is no correlation between age and gender in the development of AKI [11]. Controversially, the observation of males outnumbered (70%) is more than females in developing AKI [13]. This study observed the incidence of female children more (56.6%), but this data were statistically insignificant; thus, further extensive study with an increased sample size and the involvement of multiple study centers is required. This

variation was due to the regional variation in patient characteristics and presentations.

In this study, we could see that the pathogenesis of AKI could be more attributed to sepsis (74%), and acute glomerulonephritis (85%). Literature observed, sick patients were more likely to develop AKI, and those with sequential organ failure assessment (SOFA) scores >9 were more likely to develop AKI. Furthermore, it was commented that sepsis and cardiovascular causes resulted in a high incidence of AKI [11]. Another regional study showed that the precipitating causes for renal failure were acute gastroenteritis (85%), underlying renal pathology (43%), proven sepsis (22%), and suspected sepsis (22%) [13]. Although the present study has taken sepsis as a single entity, the proportion of sepsis leading to AKI was high compared to the previous study.

Another study depicted that glomerulonephritis and snake bite were the two most important causes of AKI in children, making up 70% of all cases of their study population [14]. While sepsis, glomerulonephritis, hemolytic uremic syndrome, and acute tubular necrosis predominate in developing countries, these have been replaced by hemato-oncologic complications and pulmonary failure as causes of AKI in the West [15]. Another study on AKI among pediatric patients concluded that sepsis is the leading cause of acute renal failure in the pediatric population [16].

The Indian studies observed that the incidence of AKI in common tropical acute febrile illnesses such as scrub typhus, falciparum malaria, enteric fever, dengue, and leptospirosis is 41.1% [17]. However, in this study, it had reported very few cases of tropical illness and they were categorized under unclassified causes. Differently, another study denoted that 40% of diphtheria children were complicated by AKI [18], and this could be explained by the regional profile of cases reporting to the hospitals.

We have observed diabetic ketoacidosis complicating AKI in 66.7% of the children, and the outcome was compared with other studies [2,13,19,20]. Envenomation by a snake bite complicating AKI is an important entity. Although we reported an incidence of 65.5%, similar studies in the southern part of India had only three cases of snake envenomation complicating AKI [14,19]. The varying nature of the incidence could be due to the difference in the number of children attending hospital services with snake bites.

Risk factors, including shock (91.36%), are the most common offender, followed by vasopressor support (85.36%). Literature suggesting the development of AKI has reported that septicemia, multiple organ dysfunction syndrome, nephrotoxic drug usage, vasopressor support, and mechanical ventilation were significantly associated with the development of AKI [2,10,16,19].

Out of 82 children on inotropic support, 46 were on adrenaline. Out of which, the majority of children (93.5%) developed AKI during the course in hospital and around 64.6% of patients with respiratory distress due to varied etiology have led to AKI. Thus, many studies have also documented that hospital stays play a key role in AKI and related risk factors [13,21,22].

In this study, 68.5% presented with altered sensorium, as supported by many studies [3,23]. The history of the usage of nephrotoxic drugs has increased the risk of renal injury [3,9]. The mortality was observed among 64.7% AKI and 24.5% non-AKI children, where these data are highly variable [3,10,19,22]. Furthermore, it was commented that AKI was independently associated with a longer PICU stay and required mechanical ventilation [8,19].

CONCLUSION

A higher incidence of AKI is found in children admitted in PICU. The majority of children with underlying sepsis, acute glomerulonephritis, snake bites, and diabetes ketoacidosis contribute to the development of AKI. The major risk factors for developing AKI are those children with shock requiring mechanical ventilation, on vasopressor support, especially adrenaline and combined adrenaline and noradrenaline support, and those exposed to nephrotoxic drugs. These risk factors support in early identification of AKI.

The presence of AKI is associated with longer PICU and hospital stays, with higher mortality imposing a significant burden to health-care system. As per the 0 by 25 (0 cases by the year 2025) initiative, nobody should die of preventable and treatable AKI. It is now evident that for AKI, early identification and timely management are the keys. Future studies should throw light on the effects of AKI on long-term renal and non-renal outcomes at our region.

CONFLICTS OF INTEREST

None.

AUTHORS' CONTRIBUTION

Raja M – Formal analysis, partial supervision, validation, and primary corrections; Sivaprasath P – Conceptualization, formal analysis, project administration, and final drafting; and Dhivya P – Partial conceptualization, data collection and curation, investigation, methodology, primary data analysis, and initial drafting.

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