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ORIGINAL RESEARCH

Patient Profile, Risk Factors and Short-Term Outcome of Children with Acute Kidney Injury: Experience of a Tertiary Care Centre

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ABSTRACT

Background: Acute kidney injury (AKI) is defined as an abrupt onset of renal dysfunction resulting from injurious endogenous or exogenous processes characterized by a decrease in glomerular filtration rate (GFR). AKI is a common complication in critically ill children and an early diagnosis and prompt treatment is important for better outcome as the condition is potentially reversible in early stages. **Methods:** This prospective observational study was conducted over 2 years from April 2022 to March 2024 at PICU of a tertiary care hospital, PMCH Patna, Bihar, India including critically ill children of age group >2 months <15 years. Children were diagnosed as AKI and its severity categorized, either at admission or subsequently during the hospital stay based on pRIFLE criteria. Clinical variables and outcome were documented to identify the number, timings, risk factors and outcome of AKI. **Result:** Mean age of the study group was 3.71±2.31 years. Mean weight was 13.4±3.79 Kg. Males (45) outnumbered females (34) with a male: female ratio of 1.3:1. Incidence of AKI was 21.3 (n=79) per 100 cases of PICU admission. Most (55.7%) of these cases were in risk category and only 21.5% reached failure stage. 66 of 79 patients (83.6%) children suffered from AKI within 24 hours of admission while 74 (93.7%) had AKI within 72 hours of admission to our PICU. Children who suffered from AKI had lower mean age & a significantly higher PRISM score at admission. Comparison of PRISM score in the pRIFLE subclasses showed that patients with a more severe pRIFLE subclass also had a higher average PRISM III score. In multivariate regression analysis only lower mean age, sepsis, shock, MODS and a higher PRISM score at admission were found to significantly contribute to the occurrence of AKI. Total days of PICU and hospital stay were significantly higher in patients with AKI as compared to non-AKI patients. **Conclusion:** AKI is a significant problem in critically ill children. Most of such children suffer from AKI by 72 hours of PICU admission. Lower age, higher PRISM score, sepsis, shock and MODS were independent risk factors for AKI. Though AKI alone doesn't lead to increased mortality, it does lead to significantly longer PICU and hospital stay, thereby burdening our already overwhelmed healthcare system. The higher is the severity of AKI, more is the mortality as well as length of PICU and hospital stay.

Key words: Acute kidney injury, mortality, risk actors, Paediatric intensive care unit, pRIFLE.

INTRODUCTION

Acute kidney injury (AKI) which was formerly also called as acute renal failure (ARF), is a clinical syndrome where acute deterioration in renal function results in the inability of the kidneys to maintain fluid and electrolyte homeostasis in body. It is considered as an abrupt onset of renal dysfunction resulting from injury by endogenous or exogenous processes characterized by a decrease in glomerular filtration rate (GFR) & an increase in serum creatinine1. AKI is a common entity in sick children, more so in critically ill children admitted to the paediatric intensive care unit (PICU) and is a significant contributor to morbidity and mortality2,3. Though serum creatinine is used as a pointer for kidney damage, it is not sensitive for early detection of AKI as its rise commomnly occurs only when kidneys are already damaged significantly. Thus, the most critical part in early identification and management of AKI in phase of reversibility is missed when the chances of a good

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recovery is significantly higher than later stages.4 Urine output is also considered a sensitive marker for kidney function and marker for tubular injury, but it also has some drawbacks as the relationship between urine output, GFR and tubular injury is complex. In situations such as hypotension and volume depletion due to any cause, urine output decreases despite normal tubular function. Similarly, in non-oliguric renal failure, urine output can remain normal even in the presence of significant tubular damage. GFR estimation is the best accepted overall index of assessment of kidney function which can be calculated at bedside easily by modified Schwartz formula. Researchers established that paediatric modification of RIFLE criteria (pRIFLE, table 1) is a useful tool to detect AKI & its severity early in sick children5.

AKI tends to occur early in the course of PICU stay (commonly within 7 days of admission) and children who do not suffer from AKI in the first week are less likely to get it later.6 Similarly, children who do not have improvement in their renal function within 24-48 hours of admission to PICU are at a high risk of requiring subsequent renal replacement therapy. However, there is paucity of data regarding AKI in Indian children. Extrapolation of results of western researchers to developing countries may not be valid as the patient profile and aetiology can be greatly different at times.7 As a result, there is pressing need to study AKI in Indian children so that strategies for its early detection, timely intervention and prevention as well can be developed. It can be interpreted that no or little improvement even after identification and treatment in many cases means that patients often hadn't received essential care before it was too late. Most of the Indian studies were retrospective in design which might have distorted the results, so we aimed to prospectively determine the occurrence and determinants of AKI in critically ill Indian children admitted to the PICU of a tertiary care hospital.

Table 1: The modified paediatric version of the rifle criteria (pRIFLE).

Category	Estimated creatinine clearance(ml/min/1.73m2)	Urine output
Risk (R)	Decrease by 25%	< 0.5 mL/kg/hr for 8 h
Injury (I)	Decrease by 50%	< 0.5 mL/kg/hr for 16 h
Failure (F)	Decrease by 75% or < 35 mL/min/1.73 m2	< 0.3 mL/kg/hr for 24 hr or anuric for 12 hours
Loss (L)	Loss of renal function > 4 weeks	
End stage (E)	End stage renal disease	

Aim and Objectives

To study AKI in sick children admitted to the PICU in terms of incidence, severity, risk actors and short-term outcome.

MATERIALS AND METHODS

Study setting: P.I.C.U of department of Pediatrics P.M.C.H Patna, Bihar, India

Study duration: 2 years, from April 2022 to March 2024.

Study design: hospital based prospective observational study.

Inclusion criteria: Sick children of age >2 months to <15 years admitted to PICU & staying for >24 hours.

Exclusion criteria: Children with eGFR below 15 ml per minute per 1.73 m2 of body surface area, known cases of chronic kidney disease, patient on dialysis or recipient of kidney transplant were excluded.

Data Collection: After obtaining written informed consent from the guardians, cases were enrolled in this study. Data regarding baseline characteristics, demographic variables, primary illness, detailed relevant history, clinical examination findings, admission diagnosis and investigation reports were recorded in a structured proforma. Serum creatinine was estimated by modified Jaffe method and estimated creatinine clearance (eCCl) was calculated as per modified Schwartz formula. Renal clearance value of 120 ml/min/1.73 m2 was considered as reference. Further work up (lab investigations &/or radiological examinations) were done as per clinical scenario and any such relevant additional information was recorded. AKI was defined and categorized based on pRIFLE criteria (either at admission or subsequently during the hospital stay) and the maximum pRIFLE stage reached during PICU stay was considered as the final AKI stage. Special focus was given on extracting information about the primary disease or condition, PRISM score[8], use of nephrotoxic drugs, mechanical ventilation, renal replacement therapy, mortality and total length of PICU and hospital stay.

Statistical analysis: Pertaining data was first entered in Microsoft excel and subsequently analysed by SPSS version 20 software. Dichotomous variables were analysed by Chi-Square test. Continuous variables were compared by t-test. p value less than 0.05 was considered significant.

RESULT

Mean age of the study group was 3.71±2.31 years. Mean weight was 13.4±3.79 Kg. Males (45) outnumbered females (34) with a male: female ratio of 1.3:1. Incidence of AKI was 21.3 (n=79) per 100 cases of PICU admission. As shown in Table 2 below, most (55.7%) of these cases were in risk category and only 21.5% reached failure stage. We got only 3 cases in renal loss 2 in end stage renal disease category.

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Table 2: AKI cases according to degree of severity as per pRIFLE classification.

AKI severity	Number (n=79)	Percentage
Risk category	44	55.7%
Injury category	17	21.5%
Failure category	13	16.4%
Loss	3	3.8%
End stage renal disease	2	2.5%

Time of occurrence of AKI: 66 of 79 patients (83.6%) children suffered from AKI within 24 hours of PICU admission while 74 (93.7%) had AKI within 72 hours of admission to our PICU. The maximum time for presentation of AKI was 9 days in our study.

Baseline characteristics: On comparing the two cohorts, we found that those children who suffered from AKI had lower mean age & a significantly higher PRISM score at admission.

Table 3: Comparison of baseline characteristics of patients in AKI and non-AKI groups

Characteristic	Children with AKI, n=79	Children without AKI, n=312	p value
Age, mean (SD)	3.71 (2.31)	5.38 (2.95)	0.01
Male gender	45; 56.9%	189; 60.6%	0.49
PRISM score, Mean (SD)	6.39 (4.31)	4.17 (3.65)	0.01

AKI and primary condition at admission: Among the children with AKI, 48(60.7%) had infectious etiology. Pneumonia constituted 24% (n=19) & tropical febrile illnesses (dengue, malaria) constituted 8.8% (n=7) of all AKI patients. Sepsis (without localizing signs) was seen in 11 (13.9%) cases. Overall, 14 cases (17.7%) had a positive blood culture: Staphylococcus aureus (2), Streptococcus pneumoniae (4). Pseudomonas aeruginosa (2), Escherichia coli (2), Klebsiella pneumoniae (3), Enterococcus species (1). Diagnoses with sepsis, shock or pneumonia at PICU admission was significantly more common in patients with AKI.

Table 4: Comparison of diagnosis at admission between children in AKI and non-AKI groups

Diagnosis	AKI group: n (%)	Non-AKI group: n (%)	p value
Sepsis	11 (13.9%)	17 (5.4%)	0.03
Shock	17 (21.5%)	31 (9.9%)	0.03
Dengue	5 (6.3%)	21(6.7%)	0.83
Malaria	1 (1.2%)	17(5.4%)	0.51
Pneumonia	19 (24%)	41(13.1%)	0.03
Cardiac disease	6 (7.6%)	31 (9.9%)	0.81
Acute Encephalitis syndrome	5 (6.3%)	53 (16.9%)	0.09
Gastroenteritis	4 (5.1%)	14 (4.5%)	0.43
Liver failure	8 (10.1%)	34 (10.9%)	0.92
Meningoencephalitis	4 (5.1%)	24 (7.7%)	0.85
Poisoning	2 (2.5%)	27 (8.6%)	0.37
Malignancy	2 (2.5%)	19 (6.1%)	0.29

AKI in relation to PRISM score at admission: Comparison of PRISM score in the pRIFLE subclasses showed that patients with a more severe pRIFLE subclass also had a higher average PRISM III score.

Table 5: pRIFLE subclass and mean PRISM score of patients with AKI:

pRIFLE subclass	PRISM score: Mean (SD)
Risk (R)	4.82 (2.44)
Injury (I)	6.03 (3.62)
Failure (F)	7.19 (3.79)
Loss (L)	7.93 (4.06)
End stage renal disease (E)	8.3 (4.39)
Non-AKI Group	4.17 (3.65)

Risk factors for AKI: Univariate analysis was performed to identify risk factors for AKI and it was found that lower mean age, shock, sepsis, CHF, coagulopathy, MODS, Mechanical ventilation and use of nephrotoxic drugs were found to be more commonly associated with AKI in univariate analysis. However, in multivariate

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regression analysis only lower mean age, sepsis, shock, MODS and a higher PRISM score at admission were found to significantly contribute to the occurrence of AKI in these children.

Table 6: Risk factors for occurrence of AKI (univariate analysis)

Risk Factors	AKI group	Non- AKI group	p value
Mean age	3.71 (2.31)	5.38 (2.95)	0.01
Shock	17 (21.5%)	31 (9.9%)	0.03
Sepsis	11 (13.9%)	17 (5.4%)	0.03
Congestive Cardiac failure	13(16.5%)	21(6.7%)	0.04
Coagulopathy	17(21.5%)	16(5.1)	0.01
MODS	31(39.2%)	61(19.5%)	0.02
Mechanical Ventilation	33(41.8%)	56(17.9%)	0.01
Nephrotoxic drugs	21 (26.6%)	34 (10.9%)	0.04
PRISM score: Mean (SD)	6.39 (4.31)	4.17 (3.65)	0.001

Duration of specialized care and mortality: Total days of PICU and hospital stay were significantly higher in patients with AKI as compared to non-AKI patients. Though patients with AKI were more likely to need mechanical ventilation (P =0.01), duration of ventilation was comparable between AKI and non-AKI groups. Also, there was no significant difference in mortality between the two groups.

Table 7: Duration of mechanical ventilation, length of PICU stay, length of hospitalization and mortality in AKI and Non-AKI groups

Variable	AKI group	Non-AKI group	p value
Days on Mechanical ventilation: Mean (SD)	6.92 (2.37)	7.43 (2.29)	0.20
Days of PICU stay: Mean (SD)	7.23 (3.67)	5.14 (2.85)	0.01
Days of Hospital stay: Mean (SD)	12.83 (3.91)	10.9 (3.07)	0.02
Mortality	19 (24.6%)	54 (17.3%)	0.20

Renal recovery: Children who had abnormal serum creatinine at the time of shifting out of PICU were followed up for renal recovery in ward and in subsequent follow up visits post discharge. 51 (85%) out of the surviving 60 patients with AKI had complete renal recovery before discharge. Amongst these 9 patients with non-normalization of serum creatinine, 1 died, 5 developed chronic kidney disease and 2 had normalization of serum creatinine during follow-up visits by 1 month after discharge. 1 such child didn't turn up for follow up and hence his final status couldn't be ascertained.

Relation between AKI category, duration of treatment & mortality: As expected, with increasing severity of AKI, there was increase in the duration of PICU stay as well as hospitalization. Similarly, when mortality was studied, there was a progressive and significant increase in mortality with increasing pRIFLE class i.e. 6.8% for risk, 29.4% for injury, and 61.5% for failure patients (P <0.05 for trend).

Table 8: Relation between pRIFLE class, length of PICU stay, length of hospitalization & mortality

AKI class	Median duration of PICU stay	Median duration of hospitalization	Mortality
RISK	4 (range 3-7)	7 (range 5-9)	3/44 (6.8%)
INJURY	5(range 3-8)	8(range 5-12)	5/17 (29.4%)
FAILURE	9(range 7-12)	12 (range 9-16)	8/13 (61.5%)
Non-AKI	6 (range 3-9)	10(range 7-13)	54(17.3%)

DISCUSSION

The present study was conducted in PICU of a tertiary care level teaching hospital with the objective to study AKI in detail among critically ill paediatric patients. Various researchers have reported incidence of AKI ranging widely from quite low to high (5-70%).[9,10] In their work from northern India, Mehta et al.[11] reported 36.1% incidence of AKI in the critically ill children. Such variability can be partly explained by the variable definitions of AKI incorporated in the studies. Zappitelli et al[12] showed that taking baseline eCCl of 120 ml/min (instead of 100ml/min) and using baseline estimated creatinine clearance (instead of changes in serum creatinine), more patients were diagnosed as having AKI. Here, we have used the pRIFLE criteria using changes in eCCl as the defining criteria and assumed the baseline eCCl to be 120 ml/min. This may have led to a relatively higher incidence of AKI in the present study.

In our study, nearly 84% children had AKI at admission while 94% developed AKI within 72 hours, similar to the study by Bailey et al.[13] This supports the observation that children develop their maximum number of organ failures early in the intensive care unit (ICU) course, unlike the observation in adult patients who develop organ dysfunction late and

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frequently one after the other. Most (55%) of the AKI cases were in risk category and only 16.4% reached failure stage. This highlights that most children have a potentially reversible cause of AKI and hence early diagnosis and intervention can lead to a better outcome in children with AKI.

Various researchers have described different risk factors for development of AKI in critically ill children. However, there can be no generalization due to the heterogenicity of the definition incorporated and the population studied. While sepsis, glomerulonephritis, HUS and acute tubular necrosis are the major cause in developing countries, these are replaced by haemato-oncologic complications and pulmonary failure in the west. In the present study, we found that lower mean age, sepsis, shock, MODS and a higher PRISM score at admission were found to significantly contribute to the development of AKI. This can be attributed to the fact that sicker children have higher chances of organ injury. This was also evident by our finding that patients with a more severe pRIFLE subclass also had a higher average PRISM III score.

Though some studies have shown that AKI is associated with increased mortality, some have negated this finding[14]. Although crude mortality seemed to be higher in AKI group, this wasn't significant statistically. As expected, a significant trend of higher mortality with higher AKI stage was found. Similarly, with increasing severity of AKI, there was increase in the duration of PICU stay as well as hospitalization. Children who survived their illness had excellent renal recovery in our study. This can be partly explained by the early diagnosis and prompt treatment of the primary condition that had led to AKI.

CONCLUSION

AKI is a significant problem in critically ill children affecting nearly 21% of the sick children admitted to PICU. Most of such children suffer from AKI by 72 hours of PICU admission. Lower age, higher PRISM score, sepsis, shock and MODS are independent risk factors for AKI. Though AKI alone doesn't lead to increased mortality in PICU, it does lead to significantly longer PICU and hospital stay, making it a major burden on our already overwhelmed healthcare system. Higher is the severity of AKI, more is the mortality as well as length of PICU and hospital stay.

Limitation: First limitation is that ours is a single-centre study. Secondly, we classified patients by pRIFLE criteria, which used a change in eCCL, and if baseline creatinine was unavailable, the patients were assumed to have a normal baseline eCCL of 120 ml/min/1.73 m2. Whereas, Acute Kidney Injury Network (AKIN) group proposed refinements to the pRIFLE classification to use change in serum creatinine instead of change in eCCL.

Conflict of Interest: none

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