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Incidence Of Acute Kidney Injury In Children Admitted To Pediatric Intensive Care Unit

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ABSTRACT

Background: Acute kidney injury (AKI) is a significant disorder of pediatric morbidity and mortality. **Objectives**: to know the incidence of acute kidney injury in children admitted to PICU, to identify the risk factors of AKI and to see the outcome of children affected with AKI.

Material & Methods: This Prospective, observational study was conducted among 250 children aged between 1 month-12 years, admitted in the Pediatric Intensive Care Unit in Government General Hospital; Siddhartha Medical College; Vijayawada

Results: Incidence of acute kidney injury is high in children who are severely sick, especially young children with shock, sepsis and those requiring mechanical ventilation. The presence of AKI resulted in increased mortality and morbidity. In most of the children with Acute kidney injury, the underlying cause is an extrarenal pathology like sepsis, shock, multi organ dysfunction

Conclusion: AKI remains a significant contributor to the morbidity and mortality of critically ill infants and children, especially those with multi-system organ failure. (83) AKI is associated with increased mortality and morbidity in critically ill children

Keywords: Acute kidney injury, Incidence, Risk factor, morbidity and mortality

Introduction: Acute kidney injury (AKI) is a significant disorder of pediatric morbidity and mortality. Survivors of AKI are at risk of compromised kidney reserves and residual abnormalities like proteinuria, hypertension, and chronic kidney disease (CKD). (1) The burden of AKI is quite variable in different regions of the world. An Indian study revealed an incidence of 25.1%. The annual rate of 0.8/100,000 population was reported from the United Kingdom and 0.39% from the USA. (2) Causes of AKI are classified as prerenal, intrinsic renal, and postrenal causes. Urolithiasis is the most frequent cause of AKI, followed by acute glomerulonephritis (GN) and severe dehydration. (2) These differences in epidemiology need to be identified to improve early identification and timely treatment. (3)

Acute kidney injury (AKI) (previously called acute renal failure) is characterized by a reversible increase in the blood concentration of creatinine and nitrogenous waste products and by the inability of the kidney to regulate fluid and electrolyte homeostasis appropriately". (4)

- Acute kidney injury is associated with severe morbidity and mortality in children.
- If not treated, AKI has a high risk of multiple organ failure and potentially death.

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- AKI affects 1 in 5 hospitalized patients, is associated with high expenditure resources leads to adverse outcomes.
- AKI is the cause of harmful short term consequences like more extended hospital stays, more significant disability after discharge. Higher risk of hospital mortality, adverse outcomes such as progression to CKD, development of cardiovascular diseases.
- Over the last 20yrs, significant efforts have been made to unveil better and characterize the mechanism and consequences of AKI.
- The burden of AKI is increasing in developing countries when compared to developed countries because of younger age and sepsis, shock.
- Besides, resource limitations in managing children who require renal replacement therapy add to the burden.
- In this review, we discuss the current knowledge about the incidence of the AKI.

.This study mainly focuses on to to know the incidence of acute kidney injury in children admitted to PICU, to identify the risk factors of AKI and to see the outcome of children affected with AKI

Materials & Methods: This Prospective, observational study was conducted among 250 children aged between 1 month-12 years, admitted in the Pediatric Intensive Care Unit in Government General Hospital; Siddhartha Medical College; Vijayawada who met inclusion criteria was taken up for study duration of the study period from January 2019 to November 2019. Permission for the study was obtained from the College authorities prior to commencement.

Inclusion criteria:

1. AGE: All children in the age group 1month – 12 yrs.
2. All children admitted in the Pediatric Intensive Care Unit; Government General Hospital; Vijayawada; in whom serum creatinine is done within 48hrs of illness.

Exclusion criteria:

1. Congenital kidney anomalies.
2. Known case of AKI or chronic kidney disease at admission.
3. Hospital stays for less than 24 hrs.
4. Serum creatinine not done at admission or 48hrs.
5. Post-operative surgery patients (cardiovascular, abdominal, neurological or orthopedic surgeries)

Sample Size Calculation: The incidence of AKI was estimated to be 5 - 30 % in PICU patients based on data in the literature. Assuming a variation of 7% from the actual incidence in PICU, i.e., absolute precision d= 0.07, and the chances of these to be at least 95 percent, the sample size was calculated as 250 subjects.

Parent informed consent was taken, information regarding the diagnosis, comorbidities, and the serial serum cr levels was recorded.

All subjects underwent serum creatinine measurement. 2 ml of intravenous blood was withdrawn and centrifuged at 3000 rpm for 10 min. Serum levels of creatinine were estimated on Cobas Integra-400 autoanalyzer by the modified Jaffe method, at admission, and after that every 24±6 h for three consecutive days in all children. Subsequently, the serum creatinine was done at daily intervals in children with AKI.

In those children without AKI, but having risk factors (features of dehydration, congestive heart failure or shock, new-onset sepsis), these levels were determined every 48±6 hr til discharged is confirmed.

Based on the AKIN criteria, Acute kidney injury was defined as abrupt (within 48 h) decrease in renal function with an increase in creatinine level. The illness was categorized as stage I (increase of creatinine by 0.3 mg/dL, or to 1.5-1.99 times

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baseline), stage II (addition to 2–2.99 times baseline) and stage III (increase to 3 times baseline, or 4 mg/dL with an acute rise of >0.5 mg/dL).

The urine output criterion was not taken for defining or staging AKI. Shock is confirmed in the presence of tachycardia, low volume pulses, cold peripheries, hypotension (blood pressure <-2 SD for that particular age and sex), or CFT >3 sec. Sepsis was said to be present if there is a systemic inflammatory response with suspected or proven infection.

The patients were evaluated to know the cause of AKI, its progression, and dialysis need. They were observed until discharge, and the outcome was examined about the maximal stage of AKI.

Statistical analysis: Data were analyzed using Medcalc software by student t-test and chi-square test and Microsoft excel Windows 7. Continuous data were expressed as mean ± SD and categorical variables as number (n %). The probability value (p-value) ≤ 0.05 was taken as statistically significant value. .

Result: For all the 250 children, serum creatine levels were done within 48hrs of illness and then repeated every consecutive day. Out of 250 children, 44 children were found to have acute kidney injury, and the remaining 206 NO AKI was found on monitoring serum creatinine levels.

Table 1: Comparison of RS in children with and without AKI

RS	AKI		NO AKI		Chi-square test	P-value
	No. of patients	Percentage	No. of patients	Percentage		
Yes	43	2.3	80	38.8	X^2=50.312	P<0.0001 HS
No	1	97.7	126	61.2		
Total	44	100.0	206	100.0		
HS: Highly significant						

Diagnosis of respiratory illness at admission includes Pneumonia, Asthma, and tuberculosis. The respiratory system was affected by 97.7% of the AKI case. It was altered in only 38.8% non- AKI cases. Thus the respiratory signs and symptoms are highly significant findings of AKI diagnosis. With p = <0.0001, i.e., most of the children with respiratory disease did have AKI. Table 1

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Table 2: Comparison of CNS in children with and without AKI.

CNS	AKI		NO AKI		Chi-square test	P-value
	No. of patients	Percentage	No. of patients	Percentage		
Yes	4	9.1	24	11.7	X^2=0.2388	P=0.6251 NS
No	40	90.9	182	88.3		
Total	44	100.0	206	100.0		
NS: Not significant						

Diagnosis of neurological illness at admission includes Meningitis, encephalitis, intracranial bleed, stroke. The central nervous system is affected by 9.1% of patients of the AKI group as compared to 11.7 % in the non-AKI group. Thus CNS involvement of AKI is not significant.

Table 3: Comparison of CVS in children with and without AKI.

CVS	AKI		NO AKI		Chi-square test	P-value
	No. of patients	Percentage	No. of patients	Percentage		
Yes	3	6.8	12	5.8	X^2=0.06338	P=0.8012 NS
No	41	93.2	194	94.2		
Total	44	100.0	206	100.0		
NS: Not significant						

Diagnosis of heart disease at admission includes Cyanotic or Acyanotic heart disease in heart failure, acquired heart diseases like rheumatic heart disease, infective endocarditis. The cardio-vascular involvement of AKI is not significant. Of the AKI patient group, only three patients had CVS signs and symptoms. Whereas 12 patients of the control group showed CVS involvement.

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Table 4: Comparison of RENAL in children with and without AKI.

RENAL	AKI		NO AKI		Chi square test	P value
	No. of patients	Percentage	No. of patients	Percentage		
Yes	3	6.8	9	4.4	X^2=0.4760	P=0.4903
No	41	93.2	197	95.6		NS
Total	44	100	206	100.0		
NS: Not significant						

Diagnosis of renal disease at admission includes nephrotic syndrome, glomerulonephritis, and obstructive uropathy. The renal pathology and involvement were present in 3 AKI cases only. It indicates the prevalence of prerenal and postrenal etiology of AKI. In the control group as well, the renal pathology was reported in only 9 out of 206 cohorts. Thus, renal pathology is not significant in pediatric patients.

Sepsis is also a known etiology of AKI and was present in 13 cases of AKI group and 24 patients of the non-AKI group. The number of cases with sepsis was highly significant.

Table 5: Comparison of SEPSIS in children with and without AKI.

SEPSIS	AKI		NO AKI		Chi square test	P value
	No. of patients	Percentage	No. of patients	Percentage		
Yes	13	29.5	24	11.7	X^2=9.207	P=0.0024 HS
No	31	70.5	182	88.3		
Total	44	100.0	206	100.0		
HS: Highly significant						

Diagnosis of malignancies includes hematological malignancies like ALL, AML, neuroblastoma. The incidence of malignancy was nil in both groups. There was no case of malignancy in both AKI as well as the non-AKI group.

Mechanical ventilation was required in 25 (56.8%) with AKI and 3 (1.5%) children without AKI, which was found to be statistically highly significant in the AKI group ($p = < 0.0001$).

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Table 6: Comparison of MORTALITY in children with and without AKI.

MORTALITY	AKI		NO AKI		Chi square test	P value
	No. of patients	Percentage	No. of patients	Percentage		
Yes	13	29.5	17	8.3	X^2=15.655	P<0.0001 HS
No	31	70.5	189	91.7		
Total	44	100.0	206	100.0		
HS: Highly significant						

Mortality in children with AKI 13 (29.5%) and without AKI 17 (8.3%) was noted and was found to be significantly higher in children with AKI.

Incidence of AKI: Out of 250 children admitted to PICU who were included in the study, 44 were found to have AKI, out of which

Stage I --- 38 (85.7%), Stage II --- 5 (11.4%), Stage III --- 1 (2.9%)

Thus the incidence of Acute Kidney Injury in children admitted to the pediatric intensive care unit was found to be **17.6%**

Out of **250** children admitted in PICU, **44** were found to have Acute Kidney Injury. Out of which, **38** children were in AKI stage I, **five** children in AKI stage II, and **1** in AKI stage III.

Out of the **38** children with AKI stage I, **5** progressed to AKI stage II and out of them, one child further progressed to AKI stage III.

Out of the 38 children with AKI stage 1, 6 children progressed to AKI stage II, and out of the remaining 32 children, 23 children recovered entirely with the return of serum creatinine levels to normal, and without persistent hypertension or urinary abnormalities.

And out of 9 children who did not have a complete recovery, one child had persistent hypertension, one child had persistent urinary abnormalities, and two children had persistently elevated serum creatinine levels, and the other four children died.

Out of the six children who progressed from stage I to stage II, three children expired, one child had a persistent urinary abnormality, and one child had persistently elevated serum creatinine. One child progressed from stage II to stage III. The one child in AKI stage III, expired

Out of the 38 children with AKI, 32 children survived, of which 23 (72%) children had a complete recovery, 9 (28%) children had a partial recovery, and deaths were 13 (28.57%).

Discussion: In our study, the incidence of acute kidney injury according to Acute Kidney Injury Network criteria in children admitted to PICU was 17.6%. And the risk factors of AKI were sepsis and shock, as the incidence of AKI was significantly higher in children with sepsis and shock.

In our study, among 250 PICU admissions, 17.6% of patients developed AKI. Laoprasopwattana *et al.* (5) reported an incidence of 0.9% among children in Thailand with respiratory and liver failure, along with significant bleeding.

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Several forms of renal involvement have been identified in patients with dengue, including elevation of the serum creatinine level, AKI, acute tubular necrosis, hemolytic uremic syndrome, proteinuria, glomerulopathy, and nephrotic syndrome. (6) Of the total 19 cases of dengue in our study, one patient developed AKI.

In our study, renal pathology and involvement were present in 3 AKI cases only. It indicates the prevalence of prerenal and postrenal etiology of AKI. In the control group as well, the renal pathology was shown in only 9 out of 206 cohort. Escobar *et al.* (7) analyzed the etiology of AKI in children at a tertiary hospital and reported that the need for dialysis itself contributed to mortality. Because of the hypercatabolic state of malarial AKI, hemodialysis or PD should be immediately performed in a situation of the rapid increase in creatinine concentration. PD is less practical but feasible in developing countries. (8)

In the case of AKI, fluid or metabolic imbalance often requires the initiation of RRT. (74) In the past, the documented mortality rates for children requiring dialysis ranged anywhere from 35% to 73%. (9) During our study, none of the patients in the non-AKI group required dialysis, but in the AKI group, of the 44 cases, nine case needed dialysis. The number of dialyses is highly significant, with $P<0.0001$.

Mechanical ventilation was required in 25 (56.8%) with AKI and 3 (1.5%) children without AKI in our study. In critically ill children, the incidence of AKI is higher and increases their mortality rate, especially in infants. In children, higher mortality is associated with multi-organ system dysfunction and the requirement of mechanical ventilation.

In this study, the incidence of shock was 31.8% and was highly significant. The control group, however, had a low prevalence of trauma (9.2%). Sepsis has been a consistent risk factor in 78% of cases of AKI across neonatal populations with associated morbidity and mortality. (12) Mathur et al. described AKI secondary to meningitis, disseminated intravascular coagulation, and septic shock in low birth weight neonates. (13)

In the study conducted by Sandra marital et al. 2013, 28, the incidence of AKI in critically ill children was 4.4%, and the mortality rate was 44% in children with AKI using criteria. It also identified the need for dialysis as an independent risk factor for AKI. The cause was extrarenal in 72%, and primary kidney pathology in 27.2% of the cases, and sepsis was the most common cause of acute kidney injury.

In the present study, AKIN criteria were used for staging AKI, and extrarenal conditions constitute about 91.4%, a significant part of etiology, and the remaining 8.6% by primary kidney pathology. Sepsis and shock were the most common risk factors for AKI.

Mehta *et al*. (14) found that younger age, shock, sepsis, and need for mechanical ventilation were independent risk factors for AKI in their cohort. Bailey *et al*. found that thrombocytopenia, higher age, hypotension, hypoxemia, and coagulopathy were independent predictors for the development of AKI.

Overall, AKI remains a significant contributor to the morbidity and mortality of critically ill infants and children, especially those with multi-system organ failure. (15) Regardless of the baseline serum creatinine (BSc) used, AKI is associated with increased mortality and morbidity in critically ill children.

Conclusion: Incidence of acute kidney injury is high in children who are severely sick, especially young children with shock, sepsis and those requiring mechanical ventilation. The presence of AKI resulted in increased mortality and morbidity. In most of the children with Acute kidney injury, the underlying cause is an extrarenal pathology like sepsis, shock, multi organ dysfunction.

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