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Risk factors of Acute Kidney Injury and outcome of children affected with AKI

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ABSTRACT:

Background: The etiology of AKI in children varies in developed and developing countries. in the former, AKI follows major surgeries, complications associated with malignancies, and the use of nephrotoxic drugs. **Objectives**: 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: The minimum age at enrollment was one month to 12 years of age. The comparison between the two groups based on gender was not significant (P=0.1873). None of the patients in the non-AKI group required dialysis, but in the AKI group, of the 44cases, nine case needed dialysis. The number of dialysis is highly significant, with P<0.001. CNS involvement of AKI is not significant. The hepatic pathology as cause or effect was less prevalent and was reported in only three patients of both AKI and non-AKI groups. Shock is one of the known causative factors for the development of AKI.

Conclusion: In most of the children with Acute kidney injury, the underlying cause is an extrarenal pathology like sepsis, shock, multi organ dysfunction.

Keywords: Acute kidney injury, Incidence, Risk factor, outcome

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)

In 2004, due to the lack of a consistent definition, the Acute Dialysis Quality Initiative group drafted the RIFLE criteria, establishing a multidimensional, staged definition. (4) The RIFLE criteria have been redrafted three times so far. In the first modification, the Pediatric RIFLE (pRIFLE) standards, adapted the RIFLE criteria for use in children. In the second modification, the definition evolved with the AKI Network (AKIN) approaches. It expanded the diagnosis of AKI to include

patients who experienced a ≥0.3-mg/dl increase in serum creatinine in 48 hours. The latest modification involved, the Kidney Disease Improving Global Outcomes (KDIGO) classification system, harmonized RIFLE, AKIN, and pRIFLE. (5)

AKI is defined as a reduction in glomerular filtration rate (GFR), which is manifested as an elevated or a rise in serum creatinine from baseline. Generally, the most commonly used laboratory finding to make the diagnosis of AKI is elevated (or a surge in) serum creatinine).

So, serum creatinine is often a delayed and imprecise test as it reflects GFR in individuals at steady-state with stable kidney function, and does not accurately reflect the GFR in a patient whose renal function is changing. Despite the limitations, elevated or a rise in serum creatinine remains the most commonly used test to know the diagnosis of AKI in children.

The inability of serum creatinine to accurately reflect kidney function has been especially problematic for clinical research in pediatric AKI. This has resulted in the use of > 35 definitions of AKI in clinical studies, ranging from changes in serum creatinine to dialysis requirement. Because of the lack of a consensus definition, comparisons among studies are severe, resulting in a wide range of quoted epidemiology, morbidity, and mortality rates in the pediatric AKI literature. (5) Standardized and tested definitions for pediatric AKI include the Pediatric Risk, Injury, Failure, Loss, and pRIFLE, and KDIGO classifications. It is recommended that the KDIGO AKI definition and staging is used to guide clinical care. (5,6)

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

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 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 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).

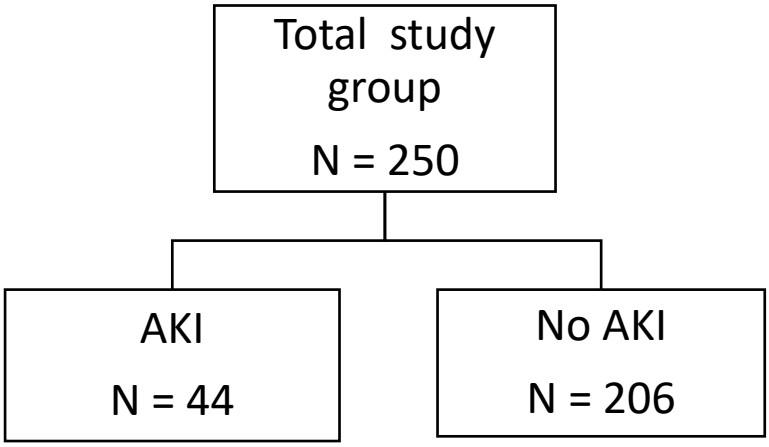
The urine output criterion was not taken for defining or staging AKI. Shock is confirmed in the presence of tachycardia, low volume pulses, cold peripheries, hypotension (blood pressure <-2 SD for that particular age and sex), or CFT >3 sec. Sepsis was said to be present if there is a systemic inflammatory 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: 44 children were found to have acute kidney injury, and the remaining 206 NO AKI was found on monitoring serum creatinine levels.

FLOW CHART: Number of children with and without AKI



The minimum age at enrollment was one month to 12 years of age. The study has included a total of 44 AKI cases up to 49 months of age. In the control group, a total of 206 non-AKI pediatric cases were enrolled.

Table:1 Comparison of Age (Months) in children with and without AKI

Age(Months)	AKI		NO AKI	
	No. of patients	Percentage	No. of patients	Percentage
< 10	9	20.5	45	21.8
10 – 19	9	20.5	28	13.6
20 – 29	17	38.6	22	10.7
30 – 39	4	9.1	35	17.0
40 – 49	5	11.4	26	12.6
50 – 59	0	0	4	1.9
60 – 69	0	0	8	3.9
70 – 79	0	0	9	4.4
80 – 89	0	0	9	4.4
90 – 99	0	0	3	1.5
100+	0	0	17	8.3
Total	44	100.0	206	100.0

Among the AKI group, 18 female and 26 male patients, whereas in the non-AKI group, 109 female and 97 male patients participated. The comparison between the two groups based on gender was not significant (P=0.1873).

Table 2: Comparison of Gender in children with and without AKI

Gender	**AKI**		**NO AKI**		**Chi square test**	**P value**
	No. of patients	**Percentage**	**No. of patients**	**Percentage**		
Female	18	40.9	109	52.9	X^2=1.739	P=0.1873 NS
Male	26	59.1	97	47.1		
Total	44	100.0	206	100.0		
NS: Not significant						

None of the patients in the non-AKI group required dialysis, but in the AKI group, of the 44cases, nine case needed dialysis. The number of dialysis is highly significant, with P<0.001.

Table 3: Comparison of DIALYSIS in children with and without AKI

DIAYLIS	AKI		NO AKI		Chi square test	P value
	No. of patients	Percentage	No. of patients	Percentage		
Yes	9	20.5	0	0	X^2=43.710	P<0.0001 HS
No	35	79.5	206	100.0		
Total	44	100.0	206	100.0		
HS: Highly 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. Similar to renal, the hepatic pathology as cause or effect was less prevalent and was reported in only three patients of both AKI and non-AKI groups. Diagnosis of liver disease at admission includes hepatic encephalopathy, liver failure, and cirrhosis of the liver.

Table 4: Comparison of LIVER in children with and without AKI

LIVER	AKI		NO AKI		Chi square test	P value
	No. of patients	Percentage	No. of patients	Percentage		
Yes	3	6.8	3	1.5	X^2=4.450	P=0.0349 Sign
No	41	93.2	203	98.6		
Total	44	100.0	206	100.0		

Shock is one of the known causative factors for the development of AKI. Diagnosis of shock at admission includes trauma secondary to dehydration, illness, septic shock. In the study group, its incidence was 31.8% and was highly significant. The control group, however, had a low prevalence of trauma (9.2%).

Table 5: Comparison of SHOCK in children with and without AKI

SHOCK	AKI		NO AKI		Chi-square test	P-value
	No. of patients	Percentage	No. of patients	Percentage		
Yes	14	31.8	19	9.2	X^2=16.155	P<0.0001 HS
No	30	68.2	187	90.8		
Total	44	100.0	206	100.0		
HS: Highly significant						

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: 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.* (7) reported an incidence of 0.9% among children in Thailand with respiratory and liver failure, along with significant bleeding.

In our study, 8 cases of malaria were enrolled in the control group, and no evidence of malaria with AKI complication has come across. The occurrence of AKI in severe *falciparum* malaria is common in Southeast Asia and the Indian subcontinent. The precise mechanism of renal involvement is not known. Still, several hypotheses, including mechanical obstruction by the infected RBC, immune-mediated glomerular pathology, fluid loss, decreased oral intake, and alterations in the renal microcirculation, have been proposed. (8) In children, parasite sequestration in renal vessels is less frequent, but still occurs, and may potentially contribute to AKI. (9) Acute kidney injury, nephrotic syndrome (NS), and chronic kidney failure (CKF) were the predominant clinical patterns of kidney disease in hospitalized HIV positive children, and the mortality is high. (10) HIV- positive status has a significant impact on their treatment and quality of life and needs intervention even during the early stages of renal diseases. (11) While none of the AKI diagnosed children had HIV, only one case had HIV in the control group in our study.

In the case of AKI, fluid or metabolic imbalance often requires the initiation of RRT. (12) In the past, the documented mortality rates for children requiring dialysis ranged anywhere from 35% to 73%. (12) 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 $P<0.0001$.

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. (13) Mathur et al. described AKI secondary to meningitis, disseminated intravascular coagulation, and septic shock in low birth weight neonates. (14) Hypotension associated with systemic inflammation has a direct impact on the kidneys in addition to direct microvasculature damage. (15)

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. The diagnosis was based on the reduction of the glomerular filtration rate, which in turn depends on the increase of plasma creatinine.

Longer duration of stay and prolonged mechanical ventilation in critically ill children are risk factors for increased mortality was seen in a two-center retrospective cohort study. (6) Hence, the RIFLE classification is beneficial for predicting in-hospital mortality. (16) The pediatric patients with AKI were found to have a higher mortality rate as compared to those without AKI (73.4% vs. 58.7%).

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. (17) Mathur et al. described AKI secondary to meningitis, disseminated intravascular coagulation, and septic shock in low birth weight neonates. (18)

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.

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

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