MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.36478/makrjms.2024.9.668.674

Study of Incidence of Acute Kidney Injury in Patients Admitted in PICU for Various Causes

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ABSTRACT

Acute Kidney Injury has been reported to be on rise in both developing and developed countries and it is independently associated with increased mortality and morbidity in children with subsequent development of renal dysfunction. Present study was aimed to study incidence of Acute Kidney Injury in patients admitted in PICU for various causes. This was a prospective observational study conducted under in children within the age group of 2 month to 12 years with length of stay for at least >72 hours in PICU, developed AKI. In this study 131 children developed AKI according to KIDGO criteria giving an incidence of 38.1%. In this study mean age of AKI patient admitted was 3.18±3.11 years. Gender distribution in AKI patient was male 51.9% and female was 48.1%. In present study out of 331 children most common diagnosis at admission to PICU in AKI patients was encephalitis (47.9%), LRTI (21%) and sepsis (18.3%) followed by, severe dehydration (12%), Severe Anemia (7%), complicated malaria (3.1%), Nephrotic Syndrome (0.8%), DKA (0.8%), liver disease (0.8%), were the remaining. As per KDIGO 44 (45.8%) patients were in stage 1, 28 (29.2%) were in stage 2 and 24 (25.0%) were in stage 3. Of 131 patients 32 (18.3%) required inotrope, 11 (45.8%) were discharged, 12 (50%) expired, 1(4.2%) went LAMA, p-value=<0.001 which considered highly significant. Total 33 (12.2%) patients who were ventilated, 11 (68.75%) went expired, discharged, 5 (31.2%), p-value=<0.001 which considered highly significant. Mechanical ventilator and Inotropes were the factors which were more likely to predict mortality in AKI with Odds ratio of 46.2 and 27.0 respectively. The incidence of acute kidney injury among critically ill children admitted to PICU was 38.1%. The commonest etiology for patients with acute kidney injury was AES (47.9%) followed by LRTI (21%) and sepsis (18.3%).

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Key Words
Acute kidney injury, critically ill children, PICU, AES, inotrope support, mechanical ventilation

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Received: 25 August 2024
Accepted: 01 September 2024
Published: 30 September 2024

Citation: Vikas Anand and G. Surendiran, 2024. Study of Incidence of Acute Kidney Injury in Patients Admitted in PICU for Various Causes. Res. J. Med. Sci., 18: 668-674, doi: 10.36478/makrjms. 2024.9.668.674

INTRODUCTION

Acute Kidney Injury has been reported to be on rise in both developing and developed countries and it is independently associated with increased mortality and morbidity in children with subsequent development of renal dysfunction[1,2]. The incidence of AKI was fourfold higher in critically ill patients (36.1%) compared to non-critically ill patient (09%)[2]. The incidence of AKI is found to be 5% in hospitalized patients and 30% in PICU. In a prospective study done in southern India it was found that the incidence of AKI was 25.1% in critically ill children with 27.8% in patients requiring RRT[2]. The mortality rate in severe AKI is almost 50%, depending on the type of AKI and comorbidities of the patient. In the Madrid study, patients with ATN had a mortality rate of 60%, whereas those with prerenal or postrenal disease had a 35% mortality rate[3]. Most deaths are not caused by the AKI itself but rather by the underlying disease or complications. In the Madrid data, 60% of deaths were caused by the primary disease and the remaining 40% were caused by cardiopulmonary failure or infection[4]. AKI is not merely a marker of illness. There is a need to decrease the growing burden of Acute Kidney Injury and its complications globally. Present study was aimed to study incidence of Acute Kidney Injury in patients admitted in PICU for various causes.

MATERIALS AND METHODS

This was a prospective observational study conducted under the department of Paediatric, Uttar Pradesh University of Medical Sciences Saifai, Etawah, UP. The study was conducted between the period of January 2019-June 2020. Study was approved by institutional ethical committee.

Inclusion Criteria:

- All children within the age group of 2 month to 12 years with length of stay for at least >72 hours in PICU, developed AKI, parents willing to participate in present study.

Exclusion Criteria:

- Parents not giving consent.
- Patients with known primary kidney disease at the time of admission.
- PICU stay <72 hours.
- Patient admitted in PICU for surgical reasons.
- Patient admitted in PICU and refer to higher center for various causes before 72 hours.

Study was explained to parents in local language and written informed consent was taken. PICU admission based on American Academy of Pediatrics Committee on hospital care and section on critical care admission guidelines for the pediatric intensive care unit excluding surgical indications[5]. After written and informed consent from parents proper history, General and systemic examination was done and recorded on pre design study Performa. Anthropometry was done in all admitted patient based on WHO classification till 05 years and BMI in patient >05 years. At the time of admission during intra-venous line access blood sample was taken for routine investigation like complete blood count (CBC), general blood picture (GBP), Serum Electrolyte, random blood sugar (RBS), Liver function test and kidney function test (KFT) in all patient. Other investigation was done according to the need. KFT (Including Serum Urea and Serum creatinine) was done in every patient at the time of admission and daily till it gets normalized. If during treatment patient have clinical feature of AKI like decreased urine output and Edema then serum urea and serum creatinine was measured again and if it was found deranged then it was measured daily till it get normalized then weekly and at time of discharged. Urine output measured and recorded as ml/kg/hour daily in every patient. Serum levels of creatinine was estimated on (ELITech-SLECTRA) auto analyzer by calorimetric Jaffe kinetic method, at the time of admission and was measured again daily for 3 days and at the time of discharge from PICU. Diagnosis and staging of AKI was done on Kidney Disease Improving Global Outcomes (KDIGO) criteria, either serum creatinine or urine output was used to diagnose and stage AKI[6]. Specific investigation likes CSF, Blood culture, Malaria, Widal, Dengue and Radiological investigations like X-Ray, MRI, CT scan will be done on the nature of the disease. AKI were managed as per departments standard operative protocols. Course during admission and outcome were noted. Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi-square test or Fisher exact test as applicable. $P<0.5$ was considered as statistically significant.

RESULTS AND DISCUSSIONS

In this study after 356 consecutive admissions in PICU, 343 patients enrolled after fulfilling inclusion criteria patients admitted to PICU were screened for AKI, in which 131 children developed AKI according to KIDGO criteria giving an incidence of 38.1%. In this study mean age of AKI patient admitted was 3.18±3.11 years. Gender distribution in AKI patient was male 51.9% and female was 48.1%. immunization status in AKI was 52.7%, 16% and 31.3%. Immunized, partial Immunized and Non-immunized respectively. Nutritional status in AKI was 3.1%, 16.7%, 31.2% and 49% of normal, mild moderate and severely malnourished respectively.

Table 1: General Characteristic in AKI Patients

Characteristic	N	Percentage
Age (mean±SD)	3.18 ± 3.11	
2 months to 1 year	48	36.6%
>1 to 5 years	54	41.2%
>5 to 10 years	25	19.1%
>10 years	4	3.1%
Sex		
Male	**68**	**51.9%**
Female	63	48.1%
Immunization status		
Immunized	69	52.7%
Partial immunized	21	16.0%
Non-immunized	41	31.3%
Malnutrition		
Normal	3	3.1%
Mild	16	16.7%
Moderate	30	31.2%
Severe	47	49.0%

Table 2: Nutritional Status in AKI Patients

	Age intervals				
Malnutrition	**2 months to 1 year**	**>1yrs to 5 years**	**>5 yrs to 10 years**	**>10 years**	**Total**
Normal	15 (27.2%)	10 (20.4%)	8 (40.0%)	5 (71.4%)	(38 29 %)
Mild	6 (10.9%)	9 (18.3%)	1 (5%)	0	16 (12.2 %)
Moderate	9 (16.3%)	8 (16.3%)	11(55.0%)	2 (28.5%)	30 (22.9 %)
Severe	25 (45.4%)	22 (44.8%)	0	0	47 (35.8 %)
Total	55 (100.0%)	49 (100.0%)	20 (100.0%)	7 (100.0%)	131 (100.0 %)

p-value=<0.001

Table 3: Etiology of Acute Kidney Injury

	Age intervals				
	2 months to 1 year	**>1 yr to 5 years**	**>5 to 10 years**	**>10 years**	**Total**
Encephalitis	16 (47.9%)	17 (31.5%)	11 (44%)	2 (50%)	53 (40.6%)
LRTI	11 (22.9%)	11 (20%)	5 (20%)	1 (25%)	28 (21%)
Sepsis	4 (8.3%)	16 (29.6%)	4 (16%)	0	24 (18.3%)
Severe dehydration with AGE	5 (10.4%)	4 (7.4%)	2 (8%)	1 (25%)	12 (9.2%)
Severe anemia	3 (6.2%)	3 (5.6%)	1 (4%)	0	7 (5.3%)
Complicated malaria	1 (2.1%)	2 (3.7%)	1 (4.0%)	0	4 (3.1%)
DKA	0	1 (1.9%)	0	0	1 (0.8%)
Nephrotic syndrome	0	0	1 (4%)	0	1 (0.8%)
Liver disease	1 (2.1%)	0	0	0	1 (0.8%)
Total	48 (100%)	54 (100%)	25 (100%)	4 (100%)	131 (100%)

Table 4: Complaints in AKI

	Age intervals								
	2 months to 1 year		**>1 years to 5 years**		**>5 years to 10 years**		**>10 years**		
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**p-value**
General complaints									
Fever	46	95.8%	48	88.9%	24	96%	3	75%	0.270
Swelling	2	4.2%	1	1.9 %	1	4%	1	25%	0.140
Yellow discoloration of body	0	0%	1	1.9 %	0		0		0.697
Progressive pallor	2	4.2%	1	1.9 %	0		0		0.687
Rashes	2	4.2%	3	5.6 %	0		1	25%	0.161
Abdominal complaints									
Abdominal pain	0	.0%	9	16.7%	2	8.0%	1	25.0%	0.021
Vomiting	14	29.2%	16	29.6%	7	28.0%	0	.0%	0.649
Loose stool	16	33.3%	10	18.5%	1	4.0%	0	.0%	0.017
CNS complaints									
Convulsion	11	22.9%	17	31.5%	13	52.0%	2	50.0%	0.076
Altered sensorium	5	10.4%	15	27.8%	15	60.0%	1	25.0%	<0.001
Weakness of body	1	2.1%	1	1.9%	0	.0%	0	.0%	0.900
Respiratory complaints									
Cough	15	31.2%	12	22.2%	2	8.0%	0	.0%	0.096
Decreased feeding	8	16.7%	4	7.4%	1	4.0%	0	.0%	0.236
Fast breathing	9	18.8%	12	22.2%	3	12.0%	0	.0%	0.548

Table 5: Staging of AKI

Stage	N	Percentage
Stage I	76	58.0%
Stage II	35	26.7%
Stage III	20	15.3%

Table 6: Inotrope Support and its Outcome

	Outcome			
Inotropes	**Discharged**	**Lama**	**Expired**	**Total**
N	99 (90%)	4 (80%)	4 (25%)	107 (81.7%)
Y	11 (10%)	1 (20%)	12 (75%)	24 (18.3%)
Total	110 (100%)	5 (100%)	16 (100%)	131 (100%)

Table 7: Mechanical Ventilation and its Outcome

	Outcome			
Ventilator	**Discharged**	**Lama**	**Expired**	**Total**
No	105 (95.5%)	5 (100%)	5 (31.2%)	115 (87.8%)
Yes	5 (4.5%)	0	11 (68.8%)	16 (12.2%)
Total	110 (100%)	5 (100%)	16 (100%)	131 (100%)

Table 8: Univariate Analysis of Outcome (Expired vs Survived)

Parameters	Expired	Survived	OR (95% CI)	p-value
Age				
0-4 years	7(43.8%)	41(37.3%)	ref	
4-7 years	4(25.0%)	45(40.9%)	1.921 (0.524-7.043)	0.325
7-10 years	4(25.0%)	21(19.1%)	.896 (0.236-3.411)	0.872
>10 years	1(6.2%)	3(2.7%)	.512 (0.046-5.651)	0.585
Gender				
Male	8(50.0%)	56(50.9%)	ref	
Female	8(50.0%)	54(49.1%)	0.964 (0.338-2.752)	0.946
AKI (KDIGO Staging)				
Stage I	9(56.2%)	64(58.2%)	ref	
Stage II	3(18.8%)	31(28.2%)	1.453 (0.367- 5.749)	0.594
Stage III	4(25.0%)	15(13.6%)	0.527 (0.143-1.945)	0.337
Ventilator				
No	5(31.2%)	105(95.5%)	ref	<0.001
Yes	11(68.8%)	5(4.5%)	46.20 (11.54-184.84)	
Inotropes				
No	4(25.0%)	99(90.0%)	ref	<0.001
Yes	12(75.0%)	11(10.0%)	27.00 (7.42-98.25)	

16 patients were of mild malnourished, 30 patients were of moderate malnourished, 47 were severely malnourished and 38 patients were normal. Above age of 5 years, BMI between-2 to-3 SD were taken as mild to moderate grade malnourished and BMI>-3 SD was considered as severe malnourished. In age group of 2 months to 1 years, out of 55 patients 6, 9 and 25 were mild, moderate and severely malnourished respectively and 15 patients were normal. Among age group >1 years to 5 years, out of 49 patients 9,8 and 22 were mild, moderate and severely malnourished respectively. In age group >5-10 years, out of 20 patients 1 and 11 were mild and moderate malnourished respectively and 8 were normal. Among age group >10 years out of 7 patients 2 were moderate malnourished and 5 were normal, which shows highly significant with value p-value=<0.001. In present study out of 331 children most common diagnosis at admission to PICU in AKI patients was encephalitis (47.9%), LRTI (21%) and sepsis (18.3%) followed by, severe dehydration (12%), Severe Anemia (7%), complicated malaria (3.1%), Nephrotic Syndrome (0.8%), DKA (0.8%), liver disease (0.8%), were the remaining. Among encephalitis in AKI patients out of 53 patients 17 (26.4%) were in age group of >1 years to 5 years, in sepsis 16 out of 24 (29.6%) were in age group of >1 years to 5 years. In present study general complaints in AKI patient admitted in which shows most common clinical presentation in patient admitted in PICU was fever. other clinical presentation was pallor followed by progressive pallor, Swelling, lymphadenopathy and rashes was present. In present study systemic complaints in AKI patients admitted in PICU out of 131 AKI patients who were admitted in our institute in PICU had significant complaints of abdominal pain with (p<0.021), loose stool with (p=0.017) as abdominal complaints which shows significant p value. In present study systemic complaints in AKI patients admitted in PICU out of 131 AKI patients who were admitted in our institute in PICU had significant complaints of altered sensorium with (p<0.001) as CNS complaints. In present study, systemic complaints in AKI patients admitted in PICU out of 131 AKI patients who were admitted in our institute in PICU had respiratory complaints cough and fast breathing and all other complaints, had no significant for the Aki patients. As per KDIGO 44 (45.8%) patients were in stage 1, 28(29.2%) were in stage 2 and 24(25.0%) were in stage 3. Of 131 patients 32 (18.3%) required inotrope, 11 (45.8%) were discharged, 12(50%) expired, 1(4.2%) went LAMA, p-value=<0.001 which considered highly significant. Total 33(12.2%) patients who were ventilated, 11 (68.75%) went expired, discharged, 5(31.2%), p-value=<0.001 which considered highly significant. Mechanical ventilator and Inotropes were the factors which were more likely to predict mortality in AKI with Odds ratio of 46.2 and 27.0 respectively. About two million people die due to AKI annually and the mortality increases when there is decline in the renal function, after the admissions in the intensive care unit[8]. This entity refers to the continuum of kidney insult that starts long before sufficient loss of excretory kidney function can be sensed. Detection of incidence, etiological profile and outcome of AKI is important for commencement of preventive and therapeutic strategies, identifying patients early to avoid renal replacement therapy and for improved clinical decision making. For many years, vasomotor disturbances and ischemic injury were the main focus of attention in the study of etiology of acute kidney injury[8,9]. Since then, growing knowledge on the mechanisms of acute

kidney injury have shown that though important, ischemic-reperfusion injury is only one of the mechanisms causing acute kidney injury[7]. Acute kidney injury is a common complication associated with critical illness in children which either is a cause of hospitalization or a complication of illness in severely ill children admitted in an intensive care unit. It is prevalent in both developing and developed countries causing increased morbidity and mortality. Prevention by early recognition and intervention at different levels (individual, community and hospital) may help to improve outcome. The importance of serial creatinine measurements and careful monitoring of the urine output particularly in the high-risk groups needs to be recognized. The newer definitions define early acute kidney injury as a small rise in creatinine or a drop in urine output-if treated early, acute kidney disease may be prevented, along with the long-term consequence of chronic kidney disease. A global strategy to decrease the burden of acute kidney injury needs to be developed[10]. During the study period there were a total of 343 consecutive admissions to PICU. A total of 131 children were diagnosed with acute kidney injury. In present study mean age was 3.18±3.11 years, majority of these children were in the age group of >1 year to 5 years (41.2%) followed by the age group 2 months to 1 years (36.6%). A study by Al-Jaboor[11] reported the median age of children with acute kidney injury in a PICU admitting children between 1-14 years to be 5.4 years. In our county study by Krishnamurthy[2] found the median age of patients with acute kidney injury was 21 months (range 1-144 months)., there were 53.7% boys. In the Agarwal[12] study 19/54 (35%) belonged to the 1-5-year group. In present study, amongst children with acute kidney injury, males and females ratio were almost equal (51.9% vs 48.0%). In other study on 92 children, though retrospective by Agarwal[12] males predominated 54/38-70%). Keenswijk[13] also reported more male children to have acute kidney injury. The incidence of acute kidney injury in the present study were assessed by serum creatinine and KDIGO definition criteria were applied. In a prospective multicentric study in 30 ICU settings of 28 tertiary centers performed by Jiang Li[14] incidence of acute kidney injury was found to be 38.4%. In another retrospective study by Sutherland[15] with a huge study population of 14,795 study population over a period of 5 years acute kidney injury was reported in 37.3%. The overall incidence of acute kidney injury in this study population was 38.1% (131/343) based on serum creatinine. In a prospective study by Krishnamurthy[2] in southern population of India, the incidence was 25.1% while Mehta[16] reported a much higher incidence of 45.1%. Luo[14] Found that the incidence of acute kidney injury was 38.4%. In another study by Xiong[17] reported the incidence of acute kidney injury to be 3.9/1000 admissions. Keenswijk[13] in his retrospective cohort study reported the incidence to be much higher at 5.9/1000 children. The children who were admitted in PICU during the study period were grouped according to their presenting diagnosis. Children most common diagnosis at admission to PICU in acute kidney injury patients was AES (acute encephalitis syndrome) (47.9%), LRTI (lower respiratory tract infection) (21%) and sepsis (18.3%) followed by, severe dehydration (12%), severe anemia (7%), complicated malaria (3.1%), nephrotic syndrome (0.8%), DKA (diabetic ketoacidosis) (0.8%), liver disease (0.8%), were the remaining. Previous studies show sepsis, glomerulonephritis and HUS as predominant etiologies in developing countries, which have been replaced by haemato-oncological complications and pulmonary failure as causes of acute kidney injury in west[2,18]. In present study AES, pneumonia and sepsis accounted for majority of all infections. Increased risk of developing acute kidney injury has been mentioned with pneumonia, but seems to have been under-reported in children[19]. In a prospective study from Scotland, out of 1241 adults with pneumonia, 18% had acute kidney injury. In the study by Shweta Naik[20] sepsis, bronchopneumonia, status epilepticus, gastroenteritis and renal pathologies were identified as significant causes of acute kidney injury. In the study by Sriram Krishnamurthy[2]., pneumonia accounted for about 66.7% as a cause of acute kidney injury. Other significant causes found to be associated with acute kidney injury were sepsis, meningoencephalitis in that study. In a study by Garuda Rama[21] the most common associated etiology with acute kidney injury was sepsis. 7 cases of snake envenomation and 4 cases of scorpion sting were reported in the study to be associated with acute kidney injury which is a common problem in some parts of India. In present study Univariate analysis was performed to analyze the parameters i.e. need for Mechanical ventilator and Inotropes, which were significantly influencing mortality and outcome. In the multivariate model, requirement of mechanical ventilation was found to be an independent predictor of mortality. In a study by Sriram Krishnamurthy[2] they observed that the predictors of mortality on univariate analysis were. Age <10 months, shock and requirement of mechanical ventilation while metabolic acidosis did not predict mortality. In the multivariate model, requirement of mechanical ventilation was found to be an independent predictor of fatality. Mehta[16] found that shock was the only independent predictor of mortality[10]. Age below 2 years, shock, fluid overload, need for mechanical ventilation, multi-organ failure and late referral predicted poor outcomes in a study of Ghani[22] from Kuwait. In present study similar

predictor as in present study mean age was 3.18 with standard deviation of±3.11 and the risk increases as the age decreases in children in present study, majority of these children were in the age group of >1 year to 5 years (41.2%) followed by the age group 2 months-1 years (36.6%). In this study we had significant sample size as we found most of other studies had similar sample size. Enough sample size in this study which makes this study more valid. In contrast to other study which were mostly retrospective, our study is prospective study. Apart from that we did serial measurement of kidney function test on day 0, day 1 and day 3 which further increases sensitivity of our study. Limitations of present study were, non-availability of actual base line serum creatinine values of our patients. Accurate urine output measurement was again a limitation. It was a single center observational study. Therefore, only associations can be shown and no absolute causality. Only hospital mortality has been calculated. The postoperative cases, trauma cases, surgical cases were not been included.

CONCLUSION

The incidence of acute kidney injury among critically ill children admitted to PICU was 38.1%. Mortality rate was 19.7% in critically ill patients with acute kidney injury had partial renal recovery at the time of discharge. The commonest etiology for patients with acute kidney injury was AES (47.9%) followed by LRTI (21%) and sepsis (18.3%). 24/131 (18.3%) patients who required inotrope support and 16/131(12.2%) were on mechanical ventilation. Patient on mechanical ventilation had poor outcome with 68.8% expired and 31.2% discharged. The occurrence of shock, use of inotrope support and ventilation had a highly significant (p=<0.01) association with the risk of developing acute kidney injury. Overall, outcome of acute kidney injury patients was 110 (84%) discharged, 5 (3.8%) took LAMA, 16 (12.2%) expired.

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