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RESEARCH ARTICLE

RISK FACTORS AND OUTCOME OF ACUTE KIDNEY INJURY IN CHILDREN ADMITTED TO THE PEDIATRIC INTENSIVE CARE UNIT

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ABSTRACT

Background: Acute kidney injury (AKI) is a common and serious complication in children admitted to the Pediatric Intensive Care Unit (PICU). The primary objective of our study was to estimate the incidence of AKI in children admitted to PICU. Secondary objective was to study the etiology ,short term outcome and determine the predictors of fatality in children with AKI. **Methods**: This was a prospective, cross sectional study conducted in children aged 1month to 18 years in the Pediatric Intensive Care Unit of Amrita Institute Of Medical Science, Kochi from Nov 2015 to Oct 2017 based on Acute Kidney Injury Network Criteria(AKIN). **Results**: The incidence of AKI was 18% .59.3% of the AKI patients were ≤5year of age. Most common cause for AKI was due to infections(87%) mainly sepsis(42.7%). 88.9% children had pre renal, 9.3% had renal and 1.9% had post renal type of AKI.40.7% were in stage 1,13% in stage2 and 46.3% in stage 3 based on AKIN criteria. 42.6% had complete recovery, 16.7% had partial recovery and death in 40.7% patients. 25.9% of AKI patients required dialysis. Children with AKI (7.85 ± 4.917) had prolonged PICU stay when compared with Non AKI group (4.28 ± 2.920 days) with p value: <0.001. AKI was associated with increased mortality (40.7%, $p < 0.001$). 43.8% of children with prerenal AKI and 77.3% children in stage 3 had the highest mortality (P value <0.001). Predictors of fatality were presence of Hypertension and the need for Ventilation (P-value < 0.05). **Conclusions**: It was concluded that the incidence of AKI was 18%. Most common etiology was Sepsis (42.5%) Children with AKI had prolonged PICU stay. AKI was associated with increased mortality ($p < 0.001$).Need for Ventilation was found to be a significant risk factor for developing AKI (p <0.001).Predictors of fatality were Hypertension and the need for Ventilation.

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INTRODUCTION

Acute kidney injury (AKI) in the pediatric patient is an important problem, particularly in critically ill children requiring admission to the Pediatric Intensive Care Unit (PICU).This is one of the most common conditions seen in the PICU where we come across AKI in patients either on admission to the PICU or as a complication during the course. Studies have shown that AKI is independently associated with poor outcome (Plötz *et al*., 2005). AKI (previously called acute renal failure) refers to an abrupt decrease in kidney function, resulting in the retention of urea and other nitrogenous waste products and in the dysregulation of extracellular volume and electrolytes. The incidence rate of AKI in pediatrics globally is not actually known (Lameire, 2006; Lameire, 2006; Lameire *et al*., 2005).

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Mortality rates in critically ill children with AKI are high, ranging between 9% and 67% (Palmieri, 2009; Kendirli, 2007) and is increased if complicated by multiorgan failure, organ transplantation and acute respiratory distress syndrome (Askenazi, 2011; Basu, 2011). The major limitation in improving the outcomes from AKI was mainly due to a lack of a consensus definition. In 2002, the consensus group of nephrologists and intensive care specialists proposed replacing ARF with new, strictly defined term AKI. RIFLE, AKIN, pRIFLE criteria has been put forward by them and now there is consensus in AKI definition. These criteria have been evaluated in many studies of critically ill AKI adults; however few are published in pediatrics (Kavaz *et al*., 2012). Most of the pediatric studies based on acute kidney injury are limited to the developed countries and are based on retrospective analysis of records (Palmieri, 2009). Hence detection of incidence, etiological profile and outcome of acute kidney injury are important for commencement of preventive and therapeutic strategies (Rama, 2015). As there are limited data on the risk factors, clinical profile,morbidity

and mortality of children with AKI in India our aim was to study the incidence , etiology , risk factors and outcome including predictors of fatality of acute kidney injury in children admitted to the PICU of Amrita institute of medical sciences Kochi.

METHODOLOGY

Materials and Methods: This is a prospective, cross sectional study conducted in the Pediatric Intensive Care Unit of Amrita Institute of Medical Sciences, Kochi from November 2015 to October 2017. The study protocol was approved by institutional ethics committee. Based on the literature, the incidence rate reported was 25.1%, with a relative precision 20% and 95% confidence level, the minimum sample size was 300.

Inclusion criteria: All patients within the age group of 1 month to 18 years admitted to the PICU from November 2015 to October 2017 were included in the study. Children with AKI were staged according to AKIN criteria (Mehta , 2007).

Exclusion Criteria: All newborns, patients with known kidney disease and postoperative patients.

Technical Information: Following an informed parental consent, clinical history and examination were taken, comorbidities were noted, and relevant data regarding investigations were collected for all children admitted to PICU. Serum levels of creatinine were estimated at admission and at daily intervals in PICU patients till discharge from PICU. Urine output was measured and recorded as ml/kg/hour. Diagnosis and staging of AKI was based on AKIN definition & classification. Either serum creatinine or urine output was used to diagnose and stage AKI.

The incidence of AKI in PICU was calculated as number of patients developing AKI of the total admissions to PICU during the study period. The patients with AKI were followed up till discharge/death. They were evaluated to ascertain the etiology of AKI, its progression, need for dialysis and the short term outcome in relation to stage of AKI. Serum creatinine levels of those with AKI were done at the time of discharge from hospital to record their recovery status. Complete recovery was defined as normal blood pressure and normal serum creatinine for age (0.2-0.4mg/dL for infants; 0.3-0.7 mg/dL for 1-12 yr; 0.5-1.0 mg/dL for 13-18 yr). Partial recovery was the presence of hypertension, or elevated serum creatinine. Patients requiring maintenance dialysis were classified as dialysis dependent.

Statistics: Statistical analysis was done using IBM SPSS 20. (SPSS Inc, Chicago, USA). For all the continuous variables, the results were either given in Mean ± SD, and for categorical variables as percentage. To study the stastical significance of the association of categorical variables, Chi Square test was applied. To compare the mean difference of numerical variables with groups, independent two sample 't' test was applied for parametric data and Mann Whitney U test for non parametric data. For finding the stastically significant risk factors, binary logistic regression was applied. A P-value < 0.05 was considered as statistically significant.

RESULTS

Of the 300 people studied ,54 children had AKI with an incidence of 18%.The mean age among the AKI group was 5.337± 5.2331years .57.4% of children were boys and 42.6% girls . Age distribution among children with AKI is shown in table 1

Table 1: Age distribution in AKI

Group	Frequency	Percentage
≤5 years	32	59.3
6-10 years	9	16.7
>10 years	13	24.1

Etiology of children with AKI were infections (87%), drugs (3.7%), poisoning(1.9%), Nephrotic syndrome (3.1%), renal tubular acidosis (2.4%) and hemolytic uremic syndrome (1.9%).Most common infections are shown in table 2. Among infections sepsis accounted for the maximum number of children with AKI

Table 2. Common Infections associated with AKI

Group	Frequency	Percentage
ADD	8	17.0
Pneumonia	14	29.7
Dengue fever	1	2.1
Sepsis	20	42.5
Encephalitis	3	6.38
UTI	1	2.1

Type of renal injury and Staging based on AKIN criteria is shown in tables 3 and 4

Table 3. Type of AKI

Group	Frequency	Percentage
Pre renal	48	88.9
Renal	5	9.3
Post renal	1	1.9

Table 4. AKI Staging based on AKIN criteria

Stage	Frequency	Percentage
Stage 1	22	40.7
Stage 2	7	13.0
Stage 3	25	46.3

Complete recovery was seen in 42.6% , partial recovery in 16.7% and death in 40.7% of the children with AKI. . 25.9% children with AKI required dialysis. The need for ventilation was high in AKI group with p value of <0.001(table 5).

Table 5. Requirement of Ventilation

Ventilation	Non AKI		AKI		P value	OR(CI)
	n	%	n	%		
Yes	11	4.5	19	34.2	<0.001**	11.597(5.092-26.414)
No	235	95.5	35	64.8		

Children in AKI group (7.85 ± 4.917days) had prolonged PICU stay when compared with Non AKI group (4.28 ± 2.920 days)(p value: <0.001). Multivariate logistic regression was done to find the risk factors of AKI. Need for ventilation had 3 times more risk for developing AKI (p value<0.001). Mortality among children with AKI (40.7%) was high when compared with Non AKI group (6.9%) (table 6).

Table 6. Mortality among AKI and Non AKI group

Death	Non AKI		AKI		P value	OR(CI)
	n	%	n	%		
Yes	17	6.9	22	40.7	<0.001**	9.261(4.449-
No	229	93.1	32	59.3		19.227)

Table 7. Comparison of incidence and mortality in the present and previous studies

Study	Year	Sample Size	Criteria	Incidence	Mortality
Present	2017	300	AKIN	18%	40.7%
T.S.Prabhakar[13]	2012	200	AKIN	17.5%	28.57%
Krishnamurthy *et al*[16].	2011	215	AKIN	25.1%	17.5%
Mehta *et al*.[17]	2008	108	AKIN	36.1%	37%
Bailey *et al*.[14]	2007	985	AKIN	4.5%	12%
Schneider *et al*.[15]	2010	3396	RIFLE	10%	30.32%

Mortality was more in prerenal type (47.9%) when compared with renal and post renal type of AKI. Children with stage3 AKI (77.3%) had highest mortality (P value is 0.001) when compared with stage 1(13.6%) and stage 2 (9.1%).Most common cause for death was due to sepsis (100%) followed by bronchopneumonia and acute diarrheal disease. There was 100% survival rate in all other conditions. Multivariate logistic regression was done to find out the predictors of fatality. Logistic regression indicates two significant predictors of fatality–Hypertension and the need for Ventilation (P-value < 0.05).Children with hypertension had 7.5 times and children who required ventilation had 5 times more risk for death in AKI

DISCUSSION

AKI is associated with severe morbidity and mortality in children. Incidence detection, etiological profile and outcome of AKI is important for commencement of preventive and therapeutic strategies. The incidence of AKI in our PICU was 18%.This was comparable to previous Indian study by T S Prabhakar *et al*. (2015) where incidence was 17.5%. However the incidence rate was high when compared to other studies done in developed countries such as Bailey *et al* (4.5%) and Schneider *et al*. (2010) (10%) (Table-7). The etiology of AKI varies from developed and developing countries. Infections mainly sepsis predominate in developing countries while these are replaced by major surgery, haemato-oncological complications, nephrotoxic drugs and pulmonary failure as cause of AKI in developed countries. In our study too infections contributed majority of AKI cases. Amongst infections sepsis was the most common etiology for developing AKI, followed by pneumonia and acute diarrhoeal disease. This was similar to both Krishnamurthy *et al*. (2013) and Mehta *et al* study (2012). Prerenal type of AKI accounted for 88.9% of AKI. This is different from other previous studies such as Krishnamurthy *et al*. and Mehta *et al*. The difference may be due to the exclusion criteria in the present study. AKI Stage 1, 2, 3 were diagnosed in 22 (40.7%), 7 (13%) and 25 (46.3%) of AKI patients. Maximum number of AKI patients were in Stage 3. This was comparable to Krishnamurthy *et al*., where the maximum number of AKI patients were in Stage 3. Complete recovery was recorded in 54.5% of children with AKI where as in Krishnamurthy *et al*. study, complete recovery was seen in 82.5% of AKI survivors .Dialysis was done in 25.9% of AKI patients.

This was high when compared with Krishnamurthy *et al*. study were dialysis was done in 14.5% of AKI patients and 15.1% in Mehta *et al*. Study. Risk factors associated with AKI was associated with need for ventilation. Ventilation was 3times more likely to exhibit Acute kidney than Control.This was comparable with Mehta *et al*. study where besides the need for ventilation, young age and sepsis were also risk factors for AKI. The duration of PICU stay was 7.85 ± 4.917 days in AKI group compared to 4.28 ± 2.920 days in Non AKI group ($p < 0.001$). This was comparable to Mehta *et al*. study, were the mean duration was 9 days and 7 days in AKI and Non AKI group. Both the studies support the fact that in the presence of AKI, the PICU and Hospital stay increases. Mortality was high in AKI patients acoounting for 40.7%, when compared to previous studies such as Krishnamurthy *et al*. and Mehta *et al* where the mortality rates were 17.5% and 37% respectively. In the present study, mortality was 77.3% in Stage 3. This is comparable to Mehta *et al*. study, where the risk of mortality was higher in patients with AKI Stage 2 and Stage 3.The common cause of mortality was sepsis (100%).In Krishnamoorthy *et al* the common cause was pneumonia followed by sepsis. In the present study, need for ventilation and hypertension were found to be the predictors of fatality in AKI patients($p < 0.001$). In Krishnamurthy *et al*. study, besides need for ventilation, age, sepsis, severe metabolic acidosis, encephalopathy, shock and need for dialysis were also considered as the predictors of Mortality.

Limitations

Limitations of our study is that there was no followup after discharge to know the impact of AKI on long term renal function. Neonates were excluded in this study due to their susceptibility and etiology of AKI is different from older children and infants

Conclusion

It was concluded that the incidence of AKI was 18%.59.3% of the AKI patients were ≤5year of age and Boys constituted 57.4%.Most common etiology was Sepsis (42.5%).Children with AKI had prolonged PICU stay. AKI was associated with increased mortality ($p < 0.001$). Children with sepsis accounts for 100% mortality. Stage 3 had the highest mortality (77.3%). Prenal AKI accounts for the highest moratlity. This is the one condition which is reversible, if diagnosed at an earlier stage and managed with adequate fluid resuscitation. .Need for Ventilation was found to be a significant risk factor for developing AKI ($p <0.001$) among children in the PICU. Predictors of fatality were Hypertension and the need for Ventilation in children with AKI ($p < 0.001$).

Recommendations

Follow up of patients with acute kidney injury after discharge is necessary for assessment of long term complications. Larger multi centered studies are further required for a clearer understanding of the outcomes of acute kidney injury which would allow optimization of follow-up strategies.

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