Incidence and Outcome of Acute Kidney Injury In Hospitalized Children

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Abstract

Background: Acute kidney injury (AKI) is now increasingly common in hospitalized children with adverse short and long term outcomes. The objective of this study is to know the incidence, etiology and short term outcome of AKI in developing nation.

Methods: This prospective observational study is done in pediatric wards and pediatric intensive care unit (PICU) of tertiary center of eastern Nepal, between age group 2 months to 14 years. AKI is defined according to pRIFLE criteria.

Results: From May 2015 to March 2016 942 patient enrolled in Pediatric wards and PICU are evaluated. The incidence of AKI was 5.9% and 21.76% in PICU. AKI was commonest among cases having infectious etiology compromising 73.2% (n=41), 16.1%(n=9) due to primary renal disease , 5.35%(n=3) secondary to congenital heart disease, and 5.35% due to other causes. Inotropes was required in 55.4% (n=31) cases, nineteen(33.9%)required mechanical ventilator while 3 (5.36%) underwent hemodialysis. Out of 56 AKI patients 71.4% (n=40) improved and 28.6% (n=16) expired. Patient with AKI had significant longer duration of hospital stay as compared to Non AKI (7 day vs 3 days , P< 0.001). Mortality was high in AKI patient who required mechanical ventilation, inotropes (p<0.001) and AKI Injury and Failure stage(p=0.003) .

Conclusion: The incidence of AKI is high in pediatric patients. Patients with AKI increases the duration of hospital stay and mortality is more in patients requiring mechanical ventilation and inotropes.

Background

Acute kidney injury (AKI) is associated with significant morbidity and mortality in hospitalized children (1). Studies of AKI in pediatric patients show that the causes and incidence of AKI depend on country's level of development, the hospital's level of complexity and the definitions used. About 5% of all patients admitted to hospitals and 30% of those admitted to intensive care units develop acute kidney injury (AKI) and frequently need renal replacement therapy(2). Hospital and pediatric intensive care unit (PICU)-acquired pediatric AKI (pAKI) rates appear to have increased due to increasing use of more invasive management and higher illness severity of critically ill children(3). Single-center studies from the 1980s and 1990s report hemolytic uremic syndrome (HUS), other primary renal causes, sepsis, and burns as the most prevalent causes leading to pAKI where as latest studies reveal a dramatic shift in the epidemiology of pAKI, with the most common causes being renal ischemia, nephrotoxin use, and sepsis(4). Recently a standardized AKI consensus definition and staging was proposed by the Acute Dialysis Quality Initiative, namely, the RIFLE criteria (Risk, Injury, Failure, Loss, End-Stage Renal Disease). Patients with RIFLE class R were indeed at high risk of progression to class I or class F(5,7,8). Despite significant improvements in therapeutics, the mortality and morbidity associated with AKI remain high (6). In developing countries like ours we have limited data about incidence of AKI in hospitalized children. There is marked paucity of

reports about etiology behind development of AKI as well as its outcome. Detection of the incidence, etiological profile and outcome of AKI is important for starting preventive and therapeutic modalities(7).

Methods

This prospective observational study was carried out from May 2015 to March 2016 in Pediatric wards and PICU of B.P. Koirala Institute of Health Sciences, Dharan, Nepal, in children from 2 months to 14 years. The patients excluded were (i)children with chronic kidney disease(II) congenital renal anomaly (iii) known AKI at admission. The study is approved by Institutional review board of BPKIHS. Informed assent was taken from parents. Confidentiality of data was made.

Children admitted in paediatric ward or PICU were screened for the presence of AKI by using a predesigned screening form during a one year period, according to the criteria of the pRIFLE. Urine output was measured on patients who were on risk of AKI and those admitted in intensive care unit. The predesigned screening proforma included SIRS/sepsis, shock, dehydration, CCF and use of nephrotoxic agent as risk factor for development of AKI. Serum level of creatinine was estimated by autoanalyzer by modified Jaffes method at admission thereafter every 24 hr for critically ill children. In patient, who were not critically ill but having risk factor the level were determined at admission and every 48 hour till resolution.

The mean eCCl was taken as 120ml/min/1.73m$^{2.}$ Patient having AKI were labelled as Risk, Injury, or Failure based on eGFR or urine output criteria whichever was severe according to pRIFLE scale. The progression of AKI was recorded along with treatment received during the management. eGFR (ml/min/1.73m^2)was calculated by Schwartz formulas as shown(9).

eGFR= k * length(cm)/serum creatinine(mg/dl)

This study considered 95% confidence interval and 80% power for sample size estimation. According to literature review the incidence of AKI is 4-6%, taking incidence as 5% the sample size came out to be 860.

All the data collected were entered in MS excel and SPSS version 11.5 and used for data analysis. Descriptive analysis: Percentage (%), Proportion, Mean, Median, Standard Deviation, Interquartile range, Range were calculated along with Graphical and tabular presentation were made. Chi square test was applied to find out significant association between categorical data and. Mann-Whitney U test was applied for comparing nonparametric numerical data with categorical data. Kruskal-Wallis H test was applied for comparing hospital days according to pRIFLE scale. p value less than 0.05 was considered statistically significant.

Results

During the study period 942 patients admitted in pediatric ward and PICU fulfilled the criteria and were evaluated. Out of 942 patient 56 patient develop AKI according to pRIFLE criteria accounting for 5.9%.

Among 170 patient admitted in PICU during the period 21.76% (n=37) developed AKI according to pRIFLE criteria. The median age of presentation of AKI was 90 months (IQR 8.25, 141) and range of 2-168 months. Among the AKI cases 51.8 %(n=29) were of male gender and rest were female. Among the patient with AKI 57.14% (n=32) had dyelectrolytemia. Hyperkalemia was present in 41.07%(n=23) hyponatremia in 25% (n=14) and hypernatremia in 7.14% (n=4) of cases. Hypertension was present in14.28% of cases (n=8).

Among these AKI cases 30.4% (n=17) met Risk criteria, 35.7% (n=20) met Injury and 33.9% (n=19) met Failure criteria. AKI was present among 15.1%(n=42) cases having SIRS,32.3%(n=31) cases having shock, 28.3%(n=17) having dehydration and 9.3%(n=4) cases having CCF.

AKI was commonest among cases having infectious etiology compromising 73.2% (n=41), 16.1% (n=9) due to primary renal disease, 5.35%(n=3) secondary to congenital heart disease, and 5.35% due to other causes.

Table 1: Etiological diagnosis of AKI

Diagnosis	No of patient (%)
Infections	**41(73.2%)**
Meningoencephalitis	14
Sepsis	12
Acute gastroenteritis with dehydration	8
Severe pneumonia	2
Septic arthritis	2
Bronchiolitis	1
Leptospirosis	1
Necrotizing Fasciitis	1
Renal	**9(16.1%)**
PIGN	5
Nephrotic syndrome	3
Henoch Scholein purpura	1
Cardiac	**3(5.35%)**
Congenital heart disease with CCF	3
Others	**3(5.35%)**
Meningomyelocele repair with dehydration	1
Burn	1
Obstructed uropathy	1

Out of 56 AKI patients 71.4% (n=40) improved and 28.6% (n=16) expired. Thirty seven children (66%) children with AKI needed PICU. Patient with AKI had longer duration of hospital stay(7 days, IQR 1-4 days, range 1-16) as compared to patient without AK(3days IQR 2-5 days, range 2-5 days) which is statistically significant($p<0.001$), whereas PICU stay among AKI and Non AKI cases was not statistically significant as shown in table 2.

Table 2: Hospital stay among AKI and Non AKI patient

	Median day (IQR), Range		P value
	AKI	Non AKI	
Total days	7(4-10),1-16	3(2-5),1-28	**<0.001$**
Ward days	7(4-9),2-12	3(2-5),1-28	**<0.001$**
PICU days	3(1-5),1-10	2(2-4),1-17	0.085$

$: Mann-Whitney U test

Among the AKI patient who were in Risk according to pRIFLE all improved while 10 patients at Injury and 6 patients with Failure expired which is statistically significant as shown in table no 3.

Table 3: pRIFLE stage at diagnosis vs outcome

pRIFLE stage	Outcome		P value
	Improved (%)	Expired (%)	
Risk	17 (100)	0 (0)	**0.003****
Injury	10 (50)	10 (50)	
Failure	13 (68.43)	6 (31.57)	

**: Chi-square test

Mortality was high in AKI patient who required mechanical ventilation and inotropes which was statistically significant. Renal replacement therapy was provided to 3 patient (2 peritoneal dialysis and 1 hemodialysis) who were in failure. Two of the patients who went RRT were expired.

Table 4: Intervention done among AKI patient vs outcome.

Intervention done	Outcome		p value
	Improved	Expired	
Normal saline bolus	30	16	**0.027****
Furosemide	15	4	0.372**
Inotropes	15	16	**<0.001****
Transfusion	8	7	0.070**
Mechanical ventilation	3	16	**<0.001****
Renal replacement therapy	1	2	

**: Chi- square test

Among the 56 AKI patient 40 patient who patient who improved, 35 patient showed complete recovery while 5 had incomplete recovery having abnormal creatinine.

The need of mechanical ventilation, Inotropes , PICU admission was higher in AKI injury and failure group which is statistically significant.

Table 5: Outcome of AKI among Risk,Injury and Failure.

Characteristics				P value
	Risk	Injury	Failure	
Mechanical ventilation	0	12	7	**<0.001****
Need of Inotropes	5	15	11	**0.02****
Need of PICU	6	16	15	**0.006****
Total days Median(IQR),Range	7(4,10),2-13	7(4.25,10),1-16	9(4,12),1-15	0.763#
Ward day Median(IQR),Range	5(4,8.5),2-10	5(4.75,7.5),2-12	8(5.75,10),3-12	0.124#
PICU day Median(IQR),Range	2.5(2,3.5),2-5	4(3,5),1-10	2(1,5),1-6	0.118#

**: Chi-square test, #: Kruskal wallis test

Discussion

This prospective study showed incidence of AKI as 5.9% of hospitalized children and 21.76% among PICU children. Literature vary greatly on incidence of pediatric AKI and difficult to compare. Most of study were conducted on critically ill patient and utilized AKIN criteria to define AKI(10). Among the AKI cases 30.4 %(n=17) met Risk criteria, 35.7 % (n=19) met injury and 35.7% (n=20) met Failure criteria at the time of diagnosis of AKI. In our study patient who met Risk criteria was low, this may due to urine output was measured on those with predefined risk factor and those admitted to PICU, which may miss patient who were in Risk stage.

The etiology of AKI in children varies in developed and developing countries. Infectious etiology comprised 73.2% (n=41) cases, AKI due to primary renal disease was 16.1% (n=9), 5.35% due to congenital heart disease and 5.35% due to other causes in our study. Among the Infectious etiology meningoencephalitis was commonest (n=14,25%), followed by sepsis (n=12, 21.4%) and acute

gastroenteritis (n=8, 14.3%). Esezober et al 2014 (11)found sepsis (41.8%); primary kidney disease (29.7%) and malaria (13.2%) were causes of AKI . In Mondal et al(12) Infectious etiology comprised 55.4% of cases, glomerulonephritis constituted 16.9%, 4.8% of underlying cardiac disease, 4.2% of envenomation, 6% of underlying renal disease,2.4% cases of HUS and 7.8% of other cases.

The mortality in AKI in children too has been reported to

vary widely from 16 % to 43.8 % [4,8,10,16–19

According to literature the mortality of AKI varied from 14.5 to 37% with more mortality in critically ill patient(2,12,13). In our study mortality among AKI patient was 28.6 %(n=16). None of patient in Risk expired,50%(n=10) expired who were diagnosed in Injury and 31.57% (n=6) expired among Failure stage(p value 0.003). In Soler et al Mortality was significantly higher in the AKI-IF group when compared to the no-AKI-R group (16.7% v 6.25% p=0.03).

Mortality is high among patient who require mechanical ventilation (p< 0.001), Inotropic support (p<0.001) and those in AKI IF group(p=0.03) which is statistically significant similar to studies done by Akrian et al(5). Among 56 AKI, 3 (5.36%) patient had underwent renal replacement therapy. All patients who had undergone RRT were in Failure (15.8%) according to pRIFLE stage. Patient with AKI required prolonged duration of hospital stay as compared to patient who did not develop AKI (p value <0.001), though the duration of PICU was increased among AKI it wasn't statistically significant. In our study the Median duration of hospital stay among AKI patient was 7 days (IQR 4-10), (range 1-16). In Poonam et al(12) The median duration of hospital stay was 9 (6-13) days for patients with AKI compared to 7 (5-10) days for those without AKI (P=0.02). Here total hospital length of stay was lower than other studies because mortality among cases which were in Injury or Failure was high. Though the hospital LOS increased from Risk to Injury and failure it wasn't statistically significant (p value 0.763). The length of stay also differed due to etiology of AKI. In our study patients with acute gastroenteritis who develop Injury and Failure, improved more quickly after correction of dehydration and length of stay was short.

The present study has some limitations. Only short term outcomes of study subjects were examined. Children with AKI may have long term residual renal injury. Neonates and infants upto 2 months were excluded in this study since their susceptibility and etiology of AKI is considerably different from older infants and children. Urine output criteria for defining AKI were used only in the critically ill patient, and having predefined risk factor may have led to under-reporting in the incidence of AKI. A potential limitation of our study is that it assumed a baseline creatinine clearance (eCCl) of 120 mL/min/1.73 m2 for all patients, as the baseline creatinine levels were unknown for most patients.

Conclusion

This prospective study provides data on the incidence of AKI in hospitalized children. Incidence of AKI is high in pediatric patient including non-critically ill children and associated with risk factors shock, sepsis and dehydration. Infectious etiology was the commonest cause of AKI followed by primary renal disease.

They had longer duration of hospital stay and mortality was high among AKI patient who need mechanical ventilation, inotropes and AKI Injury and Failure.

Abbreviations

AKI : Acute Kidney Injury

AKIN : Acute kidney Injury Network

ATN : Acute tubular necrosis

CCF : Congestive cardiac failure

CKD : Chronic kidney disease

eCCl : estimated creatinine clearance

ESRD : End stage renal disease

GFR : Glomerular filtration rate

HUS : Hemolytic uremic syndrome

IQR : Inter quartile range

LOS : Length of stay

pAKI : Pediatric Acute Kidney Injury

PD : Peritoneal dialysis

PICU : Pediatric Intensive Care Unit

PIGN : Post infectious glomerulonephritis

RIFLE : Risk, Injury, Failure, Loss, End stage

RRT : Renal Replacement Therapy

SCr : Serum creatinine

SIRS : Systemic Inflammatory Response Syndrome

pRIFLE: pediatric Risk Injury Failure Loss End stage

IQR: Interquartile Range

Declarations

1. Ethical approval: Institutional review committee, BPKIHS
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