Incidence and Outcome of Acute Kidney Injury in Hospitalised Children

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ABSTRACT

Introduction: Acute kidney injury (AKI) is common in hospitalised children with adverse short and long term outcomes. Detection of the incidence, etiological profile and outcome of AKI is important for starting preventive and therapeutic modalities. This study aimed to determine the incidence, etiology and short term outcome of AKI at a tertiary centre in Eastern Nepal.

Methods: A prospective observational study was conducted in children from two months to 14 years of age admitted in paediatric wards and paediatric intensive care unit (PICU) of a tertiary centre of Eastern Nepal. AKI was defined according to pRIFLE criteria.

Results: From May 2015 to March 2016, 942 patients enrolled in Paediatric wards and PICU were evaluated. The overall incidence of AKI was found to be 5.9% and 18.23% in patients admitted in PICU. AKI was commonest among cases having infectious etiology compromising 73.2% (n = 41), 17.85% (n = 10) due to primary renal disease, 5.35% (n = 3) secondary to congenital heart disease, and 3.57% due to other causes. Among AKI patients, 55.4% (n = 31) required inotropic support, 33.9% (n = 19) required mechanical ventilation while 5.36% (n = 3) underwent dialysis. Out of 56 AKI patients 71.4% (n = 40) had improved clinical outcome and 28.6% (n = 16) expired. Patient with AKI had significant longer duration of hospital stay as compared to non AKI (Seven days vs. three days, $p < 0.001$). Mortality was high among AKI patients on injury and failure stage ($p = 0.003$) and those requiring mechanical ventilation and inotropic support ($p < 0.001$).

Conclusions: The incidence of AKI was found to be high in paediatric patients. Presence of AKI increased the duration of hospital stay and mortality in hospitalised children often requiring mechanical ventilation and inotropic support.

Keywords: AKI; Incidence; Outcome; Mortality

INTRODUCTION

Acute kidney injury (AKI) is associated with significant morbidity and mortality in hospitalised children.[1,2] Studies of AKI in paediatric 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.[2-4] About 5% of all patients admitted to hospitals and 30% of those admitted to intensive care units develop AKI and frequently need renal replacement therapy.[5]

Rates of AKI in the hospital and paediatric intensive care unit (PICU) appear to have increased due to increasing use of more invasive management and severe illness of critically ill children.[6,7] Single - centre studies from the 1980s and 1990s report haemolytic uremic syndrome (HUS), other primary renal causes, sepsis, and burns as the most prevalent causes leading to AKI in children. The latest studies reveal a dramatic shift in the epidemiology of AKI, with the most common causes being renal ischaemia, nephrotoxin use and sepsis.[8-10] In 2004, a standardised AKI consensus definition was proposed by the Acute Dialysis Quality Initiative, namely, the RIFLE criteria (Risk, Injury, Failure, Loss, End-Stage Renal Disease).[11] The adult-derived RIFLE definition was modified, applied and validated in paediatric patients and renamed the paediatric RIFLE (pRIFLE) criteria.[6] Patients with RIFLE class R were indeed at high risk of progression to class I or class F.[12] Despite significant improvements in therapeutics, the mortality and morbidity associated with AKI remain high.[13-16]

In developing countries like ours we have limited data about incidence of AKI in hospitalised children. Detection of the incidence, etiological profile and outcome of AKI is important for starting preventive and therapeutic modalities. The aim of this study is to identify incidence of AKI in hospitalised children, common etiologies and short term outcome in our setup.

METHODS

This prospective observational study was carried out from May 2015 to March 2016 in Paediatric wards and PICU of BPKIHS, Dharan, Nepal, in children from two months to 14 years. The study was approved by Institutional review board of BPKIHS. 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 pRIFLE criteria. All the children who were diagnosed as AKI were included in the study after taking informed consent from the parents. The patients excluded were those children who had chronic kidney disease, congenital renal anomalies, who had been admitted for less than 24 hours and who did not give consent.

The predesigned screening proforma included SIRS / sepsis, shock, dehydration, congestive cardiac failure and use of nephrotoxic agent as risk factor for development of AKI. Urine output was measured in patients admitted in Paediatric wards who were at risk of AKI and those admitted in PICU. Serum level of creatinine was estimated by auto-analyser by modified Jaffes method at admission thereafter every 24 hr for critically ill children. In patients, who were not critically ill but having risk factors, the level was determined at admission and every 48 hour till resolution of primary illness.

The baseline eCCl was taken as 120 ml/min/1.73m^2 assuming normal renal function. Patients 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 modified Schwartz formula as shown.[17] eGFR = k × length (cm) / serum creatinine (mg/dl), where k is 0.413

Patients were investigated as per clinical decision. Sepsis was defined as presence of SIRS with suspected or proven infection. SIRS was defined as two of the four criteria, one of which was abnormal temperature or abnormal leukocyte count:

1. Core temp > 101.3^{0}F (38.5^{0}C)
2. Mean heart rate > 2 SD above normal for age in absence of external stimuli
3. Respiratory rate > 2 SD above normal for age or need of mechanical ventilation
4. Leucocyte count > 12,000 or < 4000/mm^3

Shock was defined as presence of tachycardia, feeble pulses, cool peripheries, hypotension (blood

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	10 (17.85%)
• PIGN	5
• Nephrotic syndrome	3
• Henoch Scholein purpura	1
• Obstructed uropathy(Urethral stone)	1
Cardiac	3 (5.35%)
• Congenital heart disease with CCF	3
Others	2 (3.57%)
• Meningomyelocele repair with dehydration	1
• Burn	1

pressure < - 2 SD for age and sex) or capillary refill time > 3 seconds. Dehydration was defined as presence of any two of following:- a) Lethargic / restless or irritable b) Sunken eyes c) Not able to drink or drink eagerly d) Skin pinch goes slowly. Congestive cardiac failure was diagnosed clinically by the presence of tachycardia, tachypnea, hepatomegaly, edema, basal crepts or cardiac enlargement. Use of nephrotoxic agent was defined as use of any agent which can aberrant renal function due to purposeful or accidental exposure. Such agents included use of aminoglycoside, vancomycin, acyclovir and amphotericin. Other etiological diagnoses were based on standard definitions.

Indication for PICU admission included one or more of the following: impaired consciousness (GCS < 7, signs of raised ICP, respiratory failure, poorly controlled seizures, requiring inotropic support, requirement of RRT). Complete recovery was defined as normal urine output and blood pressure and normal serum creatinine for age (0.2 - 0.4 mg/dL for infants; 0.3 - 0.7 mg/dL for 1 - 12 year; 0.5 - 1.0 mg/dL for > 12 years). This study considered 95% confidence interval and 80% power for sample size estimation. According to literature review the incidence of AKI was 4 - 6%, taking incidence as 5% the sample size was calculated to be 860.

Table 2. pRIFLE stage at diagnosis vs outcome

pRIFLE stage	Outcome		P value
	Improved (%)	Expired (%)	
Risk (n = 17)	17 (100)	0 (0)	0.003**
Injury (n = 20)	10 (50)	10 (50)	
Failure (19)	13 (68.43)	6 (31.57)	

***: Chi-square test*

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 and 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 Paediatric wards and PICU fulfilled the criteria and were evaluated. Out of 942 patients 56 developed AKI according to pRIFLE criteria accounting for 5.9%. Among 170 patients initially admitted in PICU during the period, 18.23% (31) developed AKI according to pRIFLE criteria. Six patients admitted in ward later were shifted to PICU after development of AKI. The median age of presentation of AKI was 90 months (IQR 8.25, 141) and range of two - 168 months. Among the AKI cases 51.8% (29) were of male gender. Among the patients with AKI, 57.14% (32) had dyselectrolytemia. Hyperkalemia was present in 41.07% (23), hyponatremia in 25% (14) and hypernatremia in 7.14% (Four). Metabolic acidosis

Table 3. Outcome of AKI among Risk, Injury and Failure

Characteristic	Risk (n = 17)	Injury (n = 20)	Failure (n = 19)	p value
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*

(Ph < 7.2) was seen in 21.4% (12) and 14.28% (Eight) had hypertension. Among all AKI cases, 16.1% (Nine) cases fulfilled urine output criteria only, 33.9% (19) fulfilled only eGFR criteria and 50% (28) fulfilled both.

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. Out of 56 AKI patients 71.4% (40) improved and 28.6% (16) expired. Thirty seven (66%) children withAKI needed PICU care. Mortality was high in AKI patients who were in Injury / Failure stage and those who required mechanical ventilation and inotropes (table 2 and 3). Initiation of renal

Table 5. 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**
Blood transfusion	8	7	0.070**
Mechanical ventilation	3	16	< 0.001**

Table 4. Hospital stay days among AKI and Non AKI patient

Hospital stay days	Median day (IQR), Range		p value
	AKI (n = 56)	Non AKI (n = 886)	
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

replacement therapy (RRT) was required in five patients who were in Failure stage. Since two of the parents refused RRT due to poor clinical condition, three of them received RRT (Two peritoneal dialysis and one haemodialysis). Two of the patients who went RRT and two patients who denied RRT expired. Patients with AKI had longer duration of hospital stay as compared to patients without AKI (table 4).

Among 56 AKI patients, 40 improved, 35 showed complete recovery while five had incomplete recovery having abnormal creatinine. The need of mechanical ventilation, inotropes, PICU admission was higher in AKI injury and failure group which was found to be statistically significant.

DISCUSSION

This prospective study showed overall incidence of AKI as 5.9% among hospitalised children and 18.23% among PICU admission. Literature vary greatly on incidence of paediatric AKI and difficult to compare. Most of the studies were conducted on critically ill patients and utilised AKIN criteria to define AKI.[18] In a study done in southern India the incidence of AKI was 5.2% in the paediatric wards and 25.1 % in the PICU.[5] The variation in the use of different criteria for diagnosing AKI may have resulted in a vast difference in the prevalence of AKI among children.

The etiology of AKI in children varies in developed and developing countries. While sepsis, acute glomerulonephritis (AGN), HUS and ATN predominate in developing countries, these have

been replaced by hemato-oncologic complications, post surgery, nephrotoxic drug and pulmonary failure as causes of AKI in the west. Studies done in India by Krishnamurthy et al showed AKI occurred in association with infections (55.4%), AGN (16.9%), cardiac disease (4.8%), envenomations (4.2%) and HUS (3.6%). Pneumonia constituted the commonest infection (26.1%) followed by tropical febrile illnesses (15.6 %) in their study.[5] Esezober et al. found sepsis (41.8%); primary kidney disease (29.7%) and malaria (13.2%) were causes of AKI in 2014.[19] In a retrospective study done by Malla et al in Nepal, among nine (3.9%) cases of AKI, infectious and prerenal AKI accompany the most with 33% due to diarrhoeal dehydration, 22% due to septicemia, 22% secondary to PIGN and 11% secondary to hepatorenal failure and posterior urethral valve.[20] Similarly in another study from Nepal, Bhatta et al. found 25 (3.9%) children with AKI of whom 14 / 25 (56%) cases of HUS, 4 / 25 (16%) cases of ATN of which two (50%) were due to AGE and two (50%) wasp sting, PSGN 2 / 25 (8%) and one sepsis (4%).[22] Meningoencephalitis was the commonest (25%) infectious cause followed by sepsis in our study. Since meningoencephalitis is common in Eastern part of Nepal and often require PICU admission, these patients are at risk of developing AKI due to SIRS, dehydration and secondary to use of nephrotoxic agents. Among the AKI cases 30.4% (17) met risk criteria, 35.7% (19) met injury and 35.7% (20) met failure criteria at the time of diagnosis. In our study patients who met risk criteria were less as compared to other studies. This variation may have been present in our study as urine output was measured only on those with predefined risk factors and those admitted to PICU.

According to literature, the mortality of AKI varied from 14.5 to 37% with more mortality in critically ill patient.[21,22] We found mortality as 28.6% (16). All patients in risk stage improved and mortality was high in injury and failure stage (p value 0.003). In Soler et al.'s study, mortality was significantly higher in the AKI-Injury failure group when compared to the no-AKI-Risk group (16.7% vs 6.25% p = 0.03).[23] We noted that mortality was high among patient who required mechanical ventilation, inotropic support and those in AKI IF group similar to other studies studies.[6] Among 56 children with AKI, five (8.92%) patients needed initiation of RRT but only three (5.36%) patients underwent RRT (Two PD and one HD). In prospective studies done in India by Nawaz et al and Krishnamurthy et al, dialysis was required in 6.6% (PD = Eight; HD = Two) and 14.5% of patients (PD = 11, HD = 13) respectively.[24,25]

Patients with AKI required prolonged duration of hospital stay as compared to patients 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 patients was seven days (IQR 4 - 10), (Range 1 - 16). Though the hospital LOS increased from risk to injury and failure it wasn't statistically significant (p value 0.763). The PICU length of stay also differed from other studies because in our study, patients with AGE who developed injury and failure improved more quickly after correction of dehydration. Mortality was high among AKI IF stage. RRT was provided to only three patients who were in failure and those with financial constraint and limited beds availability in PICU were transferred early to ward after stabilisation.

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 up to two 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 m^2 for all patients, as the baseline creatinine levels were not known for most patients. Although our study has some limitations, it is expected to provide knowledge in regards to AKI in Eastern Nepal and lead further larger studies in the field.

CONCLUSIONS

This prospective study provides data on the incidence of AKI in hospitalised children. Incidence of AKI was high in paediatric patients including non-critically ill children. 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 patients who were in injury and failure stage and often requiring mechanical ventilation and inotropic support.

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