International Journal of Medical and Health Research
ISSN: 2454-9142
Received: 28-05-2019; Accepted: 30-06-2019
www.medicalsciencejournal.com
Volume 5; Issue 8; August 2019; Page No. 235-239

Incidence and aetiology of acute kidney injury among hospitalized children in northern India: A prospective, observational study

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Abstract
Objectives: To determine the incidence, aetiology and outcome of acute kidney injury (AKI) in hospitalized patients aged 1 month to 15 years.
Methods: Conducted among patients diagnosed with AKI (defined according to the Acute Kidney Injury Network criteria), admitted in the pediatric wards and the pediatric intensive care unit (PICU) of a tertiary hospital in northern India. Incidence of AKI (based on the serum creatinine criteria proposed by the AKI Network) and clinico-etiological profile of AKI was studied.
Results: The incidence of AKI was 5.6 % in the pediatric wards and 27% in the PICU. AKI occurred in association with infections (58.9 %), acute glomerulonephritis (16.6 %), envenomations (4.1%), cardiac disease (3.7 %), and haemolytic uremic syndrome (3.3 %). Pneumonia constituted 28.9 % of the infections. Renal replacement therapy (RRT) was required in 19.3 % of patients; mortality was 13.6 %. A significant proportion of children had partial renal recovery at discharge.
Conclusions: The incidence of AKI is high in the patient population, including the non-critically ill children. AKI continues to be associated with adverse outcomes.

Keywords: Acute kidney injury, Hospitalized children, Incidence, Clinico-etiological profile

Introduction
Acute kidney injury (AKI) is an important medical condition encountered in hospitalized pediatric patients often associated with adverse short- and long term outcomes [1, 2]. Clinical manifestations of acute kidney injury (AKI) range from subtle changes in glomerular filtration rate (GFR) to symptomatic end-organ failure. Mortality rates in critically ill children with AKI ranges from 9% and 67% and most of these AKI are due to acute tubular necrosis (ATN) that is secondary to hypovolemia, sepsis or the use of nephrotoxic agents [3]. However, there are only limited epidemiologic studies on pediatric acute kidney injury (AKI). Given the limited data available on the clinic-epidemilogical profile of pediatric AKI, differing spectrum of peditric AKI in developing nation than developed ones and the fallacies of retrospective studies, this prospective, observational study was conducted in tertiary level teaching hospital of northern India to determine the incidence and clinic-epidemilogical profile of pediatric AKI.

Materials and Methods
This prospective observational study was conducted in upgraded department of paediatrics of Patna Medical College & Hospital (PMCH), in Patna, Bihar, India, during the period from 1st January 2018 to 31st December 2018.

Aim & Objective: The primary objective of this study was to estimate the incidence of AKI {as defined by the Acute Kidney Injury Network (AKIN) classification} in hospitalized pediatric patients from age 1 mo to 15 y of age. The secondary objectives were to study the clinico-etiological profile of AKI among these children.

Study population: All patients in the age group of 1 month to 15 years, admitted to pediatric wards or pediatric Intensive Care Unit (PICU) were included in the study.

Exclusion criteria: Patients with CKD Stage V (estimated glomerular filtration rate <15 mL/min/1.73m^2), bilirubin level >5 mg/dL, hospital stay of less than 24 hours or having serum creatinine not done at admission or at 24 hours were excluded from study.
Patients were classified as (critically ill) if they were admitted to the PICU, required mechanical ventilation or vasopressor support (need for dopamine and/or dobutamine at a dose exceeding 10 µg/kg/minute, and/or adrenaline at any dose for management of hypotension, had impaired level of consciousness (Glasgow coma scale <7) or had uncontrolled or poorly controlled seizures. Patients who did not meet these criteria were considered not critically ill.

Serum creatinine assessment: Serum creatinine estimation was done of all patients enrolled in this study, during time of admission. Serum creatinine estimation was done by modified Jaffe method [5] using autoanalyzer. Repeat serum creatinine estimation was done every 24±4 hours for 3 consecutive days and then daily till discharge from the hospital. In subjects
If there was a rise in serum creatinine, re-classification and progression to maximum AKI stage during hospital stay was recorded. AKI was diagnosed and staged based on AKIN classification [4].

Table 1: Definition and classification of AKI [4]

Definition of Acute Kidney Injury

An abrupt (within 48 h) reduction in kidney function defined as an absolute increase in serum creatinine of more than or equal to 0.3 mg/dl, an increase in serum creatinine of more than or equal to 1.5-fold from baseline, or a reduction in urine output (documented oliguria of less than 0.5 ml/kg/ h for more than 6 h)

Classification/Staging System for Acute Kidney Injury

Stage	Serum creatinine criteria	Urine output criteria
1	Increase in serum creatinine of more than or equal to 0.3 mg/dl or increase to more than or equal to 1.5- to 2-fold from baseline	Less than 0.5 ml/kg per hour for more than 6 h
2	Increase in serum creatinine to more than 2- to 3-fold from baseline	Less than 0.5 ml/kg per hour for more than 12 h
3	Increase in serum creatinine to more than 3-fold from baseline or serum creatinine of more than or equal to 4.0 mg/dl with an acute increase of at least 0.5 mg/dl	Less than 0.3 ml/kg per hour for 24 h or anuria for 12 h

On a pre-designed proforma patients' demographic details, information regarding co-morbid condition, relevant history and examination findings, were documented. The patients were evaluated to ascertain the etiology of AKI, its progression and need for dialysis. The etiology of AKI, need for RRT and short term outcomes (complete renal recovery, partial renal recovery), were recorded

Result

Overall 8200 children were assessed for eligibility, out of which 200 were excluded for reasons such as <48 hrs of hospital stay, stage 5 CKD etc. Finally 8000 children were included in the study, of which 7600 children were admitted in the pediatric wards; and 400 in the PICU (Fig. 1). Out of these 7600 children admitted in pediatric ward, 425 children had AKI, giving an incidence of 5.6 %. However 27% (n=108) of patients admitted in PICU had AKI.

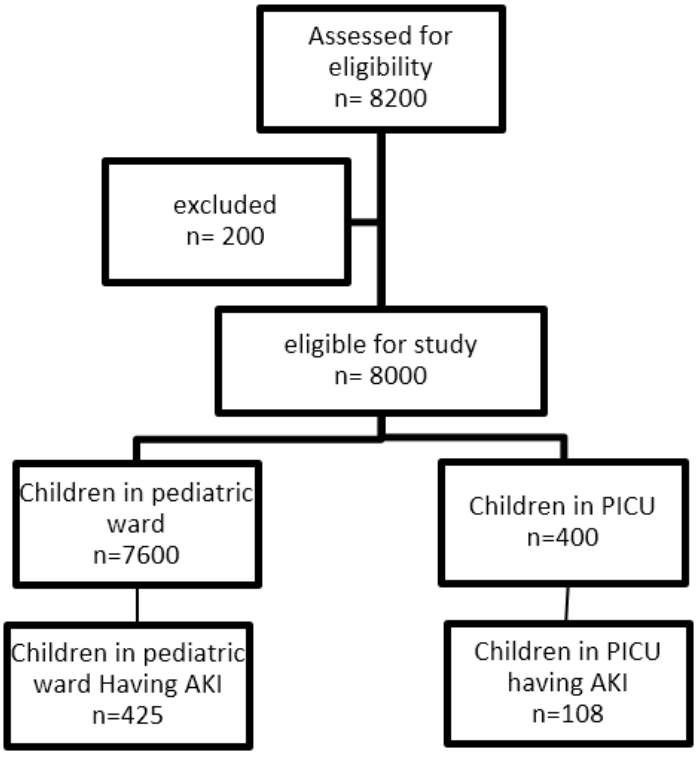

Fig 1

The median serum creatinine level at the time of admission was 1.6 mg/dl (interquartile range 0.9–1.9). 76.9 % (n=410) of cases, had AKI at time of admission itself while 23.1% (n=123) developed AKI during hospital stay.

AKI stage 1, stage 2 and stage 3 were detected in 236 (44.3%), 205 (38.5 %) and 92(17.2%) of AKI patients initially. 19 patients from stage 1 progressed to stage 2, while 5 progressed to stage 3. Similarly, 11 patients progressed from stage 2 to stage 3. Finally, the maximum stages of AKI were stage 1 in 212 (39.8 %), stage 2 in 213 (40%) and stage 3 in 108 (20.2 %) (Table 2). (The AKI stages mentioned hereafter refer to the maximum stages reached during hospital stay).

Table 2: Incidence of AKI, according to stages

AKI stages	Initially n (%)	Finally n (%)
Stage 1	236 (44.3%)	212 (39.8 %)
Stage 2	205 (38.5 %)	213 (40%)
Stage 3	92 (17.2%)	108 (20.2 %)

The median age of the patients with AKI was 46 months (range 1–176 months), and 303 (56.8%) of these total 533 AKI cases were boy. The median age of children admitted to PICU (17 months; range 1–164) was lesser than those in the wards (46 mo; range 1–176) ($p < 0.05$). Children admitted to the PICU and wards were however, comparable with regard to sex or length of hospital stay (8.7 d vs. 9.8d, $p > 0.05$).

Infection was most common {58.9% (n=314)} factor associated with AKI and pneumonia constituted 28.9% of all infections associated with AKI (Table 3). Diarrhoea was 2nd most common infection (14%) associate with AKI. Sepsis (without localizing signs) was diagnosed in 37 children, 18 of which were culture positive. Organisms isolated were Escherischia coli (7 cases), Klebsiella pneumonia (5 cases), Pseudomonas aeruginosa (3 cases) and Streptococcus pneumonia (3 cases).After infection, acute glomerulonephritis was most commonly (16.6%) associated condition with AKI.

Table 3: Clinical conditions associated with AKI

Clinical Conditions	N (%)	
Infection	314 (58.9)	
Pneumonia	91 (17)	
Sepsis (without localizing signs)	37 (7)	Culture Positive 18
		Culture Negative 19
Acute watery diarrhea (non-cholera)	44 (8.2)	
Cholera	03 (0.5)	
Dengue hemorrhagic fever/Dengue shock syndrome	42 (7.8)	
Meningoencephalitis	27 (5)	
Enteric fever	14 (2.6)	
Urinary tract infection	11 (2)	
Scrub typhus	8 (1.5)	
Tuberculosis	17 (3.1)	
Cellulitis	6 (1.1)	
Empyema	5 (0.9)	
Malaria	4 (0.7)	
Leptospirosis	3 (0.5)	
Suppurative parotitis	2 (0.37)	
Acute Glomerulonephritis	89 (16.6)	
Acute posts treptococcal GN	79 (14.8)	
Rapidly progressive glomerulonephritis (RPGN)	10 (1.8)	
Envenomations	22 (4.1)	
Snake envenomation	8 (1.5)	
Scorpion envenomation	13 (2.4)	
Wasp envenomation	1 (0.18)	
HUS	18 (3.3)	
D+ HUS	12 (2.2)	
D-HUS	6(1.1)	
Drugs	13 (2.4)	
Underlying cardiac disease (congestive heart failure)	20 (3.7)	
Myocarditis/Dilated cardiomyopathy	9 (1.6)	
Congenital heart disease	7 (1.3)	
Rheumatic heart disease	4 (0.7)	
Underlying renal disease	27 (5)	
Nephrotic syndrome	8 (1.5)	
Focal sclerosing glomerulosclerosis (FSGS)	4 (0.7)	
Posterior urethral valve (PUV)	6 (1.1)	
Chronic glomerulonephritis	7 (1.3)	
Nephrolithiasis	2 (0.3)	
Others	30 (5.6)	
Total	533	

Total of 73 patients died giving the mortality rate of 13.6 %. Mortality in AKI stage 1, stage 2 and stage 3 was 24 (11.3 %), 22 (10.3 %) and 27 (25 %) respectively.

Mortality was 3 in PSGN, 1 in diarrhea and highest in pneumonia (26 %, n=19). Mortality in infants was 31.7 %, while it was 12.7 % above infancy ($p < 0.05$).

The overall mortality of children admitted in the PICU during the study period was 36.7 %. Those with AKI had a mortality of 47.3 %, while those without AKI had a mortality of 34.2 % ($p < 0.05$).

385 (83.7 % of survivors) children with AKI had complete renal recovery, while 75 (16.3 % of survivors) had partial renal recovery at discharge.

In AKI stage 1, 178 (83.9) had complete renal recovery, while 10 (4.7 %) had partial renal recovery at discharge. In AKI stage 2, the corresponding figures were 163 (76.5 %) and 28 (13.1%) respectively. In AKI stage 3, these figures were 44(54.3 %) and 37 (45.7 %), respectively.

Table 4: Outcome in AKI, according to stage, n (%)

	Complete recovery	Partial recovery	Need for RRT	Mortality
Stage 1 n=212	178 (83.9)	10 (4.7)	20 (9.4)	24 (11.3)
Stage 2 n=213	163 (76.5)	28 (13.1)	35 (16.4)	22 (10.3)
Stage 3 n=108	44 (40.7)	37 (34.2)	48 (44.4)	27 (25)
Total n=533	385 (72.2)	75 (14)	103 (19.3)	73 (13.6)

Complications and co-morbidities included shock 211(55.2 %) children, severe metabolic acidosis 153 (28.7 %), hyperkalemia 105 (19.7 %), encephalopathy 103 (19.3 %), hypertension 95 (17.8 %), hyponatremia 93 (17.5%), thrombocytopenia 84(15.7 %), hypernatremia 38 (7.1 %). 109 (28.5 %) children required mechanical ventilation and 103 (19.3 %) required renal replacement therapy {60(58.2%) peritoneal dialysis & 43 (41.8 %) haemodialysis}. The mortality among children requiring RRT was higher as compared to children not requiring RRT (35.7 % vs. 18.6 %, $p < 0.05$). Requirement of RRT was not affected by age.

Discussion

The overall incidence of AKI, using the AKIN criteria, was 6.6% in our study population. The incidence was around five times higher, in critically ill patients (27%) compared to non-critically ill patients (5.6%). Most patients with AKI at the time of presentation were in Stage 1(n=236, 44.3%) however, finally during course of treatment number of patients in both stage 1 and 2 were nearly equivalent. In recent prospective studies from India, the incidence of AKI has ranged from 5% to 16.6% in non-critically ill children [6-9] and 15% to 53.2% in critically ill children [6-7, 9-10]. The incidence of AKI in our study (5.6% in non-critically ill and 27% in critically ill) was similar to studies in children both from developed as well as developing countries [6-10] including reports from India.

Most patients with AKI, at the time of admission, in our study were in Stage 1 (44.3%) followed by Stage 2 (38.5%) and stage 3 (17.2%).This observation was similar to other studies [7, 9, 11].

Most common condition associated with AKI was found to be infection (n=314, 58.9%), followed by PSGN, envenomations and HUS. Pneumonia was most common (n=91, 17%) infection associated with AKI, followed by Sepsis (without localizing signs), Acute watery diarrhea (non-cholera), Dengue hemorrhagic fever/Dengue shock syndrome and meningoencephalitis. These findings were consistent with those in other studies from the developing countries [12-16]. Renal replacement therapy is required in almost 6%–45% of critically sick patients [6, 7, 9, 17] which is consistent with 19.3% of the AKI patients requiring RRT in this study.

Complete renal recovery was observed in majority of patients with AKI [385 (72.2%)], similar to other studies [6, 9, 11, 18]. Risk for mortality was significantly higher in Stage 3 AKI patients, $P < 0.001$. Our study confirms that AKI is an independent risk factor for mortality [2, 9, 17].

Mortality figures of 13.6% among AKI patients in the present study were comparable to previous reports of 9% to 67% [9]. The mortality in this study was lower than some of the studies from India [6, 7] and some developed countries [19].

Limitations

Being a tertiary level referral hospital reported incidence might be higher than that in normal population.

Conclusion

Incidence of AKI is high in hospitalized children; even among non-critically ill children. And AKI continues to be associated with adverse outcomes, including high mortality and partial renal recovery. Infection is one of the most common condition associated with AKI.

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