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Original Article

Acute kidney injury in the pediatric intensive care unit at a tertiary care hospital of the Armed Forces: a cross-sectional observational study

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ABSTRACT

Background: Acute kidney injury (AKI) is shown to be the commonest complication in critically ill children admitted to the pediatric intensive care unit (PICU). Kidney Disease: Improving Global Outcomes (KDIGO) classification and definition are now used universally. We undertook prospective observational study to study the etiology and maximum stage of AKI as defined by KDIGO and its complications and outcomes.

Methods: All children admitted to the PICU were included in the study. The diagnosis of sepsis and multiorgan dysfunction syndrome (MODS) was made according to the standard international guidelines. The patients were followed up till discharge/death. All children were screened for AKI at admission and subsequently using serum creatinine measured by modified Jaffe's method and urine output measurement.

Results: A total of 197 children were admitted to the PICU. 38 (19.28%) developed AKI, and 6 (15.78%) developed stage III AKI. Malignancies, serious neurological and renal disorders, and postsurgery complications accounted for most of the cases with AKI. Six were admitted with primary renal condition. Sepsis with or without MODS was seen in 12 patients with AKI and in 8 without AKI. Twenty-one children with AKI and 3 children without AKI were exposed to nephrotoxic drugs. Twenty-three children with AKI required inotropic support. The average length of stay (ALOS) of children with AKI in the PICU was 9.86 days, whereas ALOS of children without AKI was 6.23 days. Eighteen children with AKI (47.36%) and 36 (21.38%) with no AKI died.

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Conclusions: AKI in children in the PICUs of referral hospitals in the armed forces have varied etiologies and presentations. These children require early identification and management with close monitoring to prevent long-term renal morbidity and mortality.

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Introduction

Acute kidney injury (AKI) has been shown to be the commonest complication in critically ill children admitted to the pediatric intensive care units (PICUs).¹ For ease of comparability, uniform definitions and classification for AKI in children and adults have been proposed by Kidney Disease: Improving Global Outcomes (KDIGO) as given in [Table 1](#). These are now used universally for the sake of uniformity.²

While the incidence of AKI in PICUs has been shown to vary between 30 and 50%,^{3,4} most children have early stages of AKI. These children may however deteriorate rapidly and show increase in the stage of AKI depending on the underlying disease, its severity, and various other factors. One-third of all children with AKI require renal replacement therapy (RRT).³ Also, AKI has been shown to be an independent risk factor for mortality.^{3,4} Keeping this in mind, 0 by 25 initiative was launched by the International Society of Nephrology (ISN) in 2013 with the aim of reducing the preventable deaths by AKI to nil by 2025.

Pediatric super specialties in the Armed Forces, as of date, can best be described being in a developing stage. Our center as of date has a 5-bed PICU with basic facilities for both conventional mechanical ventilation and noninvasive ventilation. Despite limited resources and infrastructure, the PICU team provides intensive care to critically ill children with various surgical and medical disorders. We conducted a prospective observational study in the children admitted to the PICU of our center to study the etiology of AKI, maximum stage of AKI as defined by KDIGO, complications, and outcomes.

The aim of the study was to determine and analyze the clinical profile, etiology, and outcome of critically ill children who developed AKI and to demonstrate association of risk factors and outcomes with AKI if any.

Material and methods

All children consecutively admitted to the PICU were included in the study. Written informed consent was obtained from either of the parents for inclusion in the study. The indications for admission to the PICU which were the inclusion criteria for our study were one or more of the following: children with altered sensorium with Glasgow Coma Scale (GCS) score <8, with respiratory distress requiring ventilatory support (noninvasive or invasive), with refractory seizures or status epilepticus, with shock requiring inotropic support, with fulminant hepatic failure, with stage III AKI as per KDIGO

classification, with severe cardiorespiratory illness, and in the immediate postoperative period after major surgery. This also included children with acute-on-chronic kidney disease with rise in serum creatinine $\geq 100\%$ of the patient's baseline or acute fall in urine output as per KDIGO criterion to study the causes and outcomes of AKI in these children. The diagnosis of sepsis and MODS was made according to the International Pediatric Sepsis Consensus guidelines.⁵ Hypertension was defined as >95th percentile blood pressure for age, height, and gender.⁶ The patients were followed up till discharge/death. Complete renal recovery was defined as normal serum creatinine with normal blood pressure and no proteinuria at discharge. Partial renal recovery was defined as elevated serum creatinine or persistent hypertension or proteinuria at discharge but with no requirement for RRT. Children with persisting requirement for RRT after discharge were classified as having no renal recovery.

All children were screened for AKI at admission using serum creatinine measured by modified Jaffe's method and urine output measurement. Children admitted to the PICU with a primary renal condition were also included in the study. The urine output was measured by catheterization of the urinary bladder in children in shock and/or with poor GCS score and by direct measurement of the volume per void in other children. Urine output was measured by diaper weight every 4 h in infants and younger children who were not toilet trained. The clinical details, underlying etiology, comorbid conditions, and treatment details including use of nephrotoxic drugs and need for vasopressors and ventilation were recorded in a predesigned proforma. Blood gas analysis and serum sodium and potassium levels were also measured in all patients at admission and repeated along with renal function tests as indicated clinically. The outcomes at discharge including mortality in both the groups, i.e., group 1 with AKI and group 2 without AKI, were also recorded. The difference between the two groups, if any, was then analyzed for exposure to nephrotoxic drugs, need for inotropic support and ventilation, average length of stay, and mortality by paired t test using SSPS software.

Results

A total of 197 children were admitted to our PICU from May 2017 to April 2018 (one calendar year). Thirty-eight (19.28%) developed AKI, and of them, 6 (15.78%) developed stage III AKI. The baseline characteristics of children with AKI with their underlying disease during their stay at PICU are as given in [Table 2](#). Underlying etiology, maximum stage of AKI, and outcomes in children admitted in the PICU with

Table 1 – Staging of AKI as per KDIGO.

Stage of AKI	Serum creatinine	Urine output
1	1.5–1.9 times the baseline or ≥ 0.3 mg/dl increase	<0.5 ml/kg/h for 6–12 h
2	≥ 2 –2.9 times the baseline	<0.5 ml/kg/h for >12 h
3	>3 times the baseline or >4 mg/dl or patient initiated on any form of renal replacement therapy	<0.3 ml/kg/h for ≥ 24 h or anuria ≥ 12 h

AKI, acute kidney injury; KDIGO, Kidney Disease: Improving Global Outcomes.

AKI are as shown in Table 3. Fig. 1 gives a pictorial description of the distribution of the underlying etiologies of AKI. Children with malignancies, with serious neurological and renal disorders, as well as having undergone complex surgeries accounted for most of our cases who developed AKI. Six children were admitted with a primary renal condition including one child with atypical hemolytic uremic syndrome, one with rapidly proliferative glomerulonephritis, and two children with nephrotic syndrome with peritonitis and septic shock.

Sepsis with or without multiorgan dysfunction syndrome (MODS) was seen in 12 patients with AKI and in 8 without AKI (p value < 0.001).

Exposure to nephrotoxic drugs including antibiotics such as vancomycin or amikacin was seen in 18 children with stage I and II AKI and in 3 children with stage III AKI, and one child received streptomycin along with vancomycin. As compared to this in the group that did not develop AKI, 42 of 159 received nephrotoxic drugs (p value = 0.03).

Inotropic support was required by 22 of 38 children with AKI. Of these, 20 had stage I and II and III had stage III AKI. Only 12 of 159 children without AKI required inotropic support (p value < 0.001).

Children with AKI had a mean or average length of stay (ALOS) of 9.86 days in the PICU, whereas children who did not have AKI had a mean stay in the PICU of 6.23 days.

In children with AKI 1 and 2, 15 had mortality, 3 children with stage III AKI died during the course of their illness (47.36%), and 36 (21.38%) children with no AKI expired during PICU admission.

Discussion

AKI has been defined as rise in creatinine to ≥ 0.3 mg/dl within 48 h, increase to >1.5 times the baseline value, or urine output < 0.5 mL/kg/hr.² AKI has been shown to be associated with increased mortality and greater morbidity.^{3,4} Various studies have brought out that children with AKI have longer

average stay in hospitals, prolonged intensive care unit (ICU) admission, greater need for mechanical ventilation, and greater mortality.^{7,8} Also, even a small increase in creatinine from the baseline has been shown to predict the development of AKI, especially in children who undergo complex cardiac surgeries.⁹

Data on AKI from large multicentric pediatric studies have been lacking so far. In the Assessment of Worldwide AKI in Pediatrics, Renal Angina and Epidemiology (AWARE) trial conducted recently, 4683 critically ill children from 32 PICUs across Asia, Australia, Europe, and North America were included. In this trial, 26.9% of children developed AKI and 11.6% patients had severe AKI. They demonstrated that severe AKI increased the risk of mortality by day 28 and 11.0% of children with severe AKI died as compared with 2.5% in those without severe AKI (P < 0.001). Severe AKI was also found to be associated with increased use of mechanical ventilation and RRT.¹⁰

The data on epidemiology of pediatric AKI among Indian children in general and specifically among those admitted to PICUs in the armed forces hospitals remain scarce.

Our study describes the etiology of AKI, maximum stage of AKI as defined by KDIGO, and complications and outcomes in children admitted to the PICU of a tertiary care hospital of the Armed Forces. AKI was seen in children of all age groups from early neonatal period to adolescence, although the etiologies were different. We found a slight male preponderance. This has been brought out in earlier studies also, although it is not clear whether this is truly a function of the disease epidemiology or because of cultural mores, especially in the Indian population. The incidence of AKI in our study was 19.28%, with stage III AKI in 15.78% of these children, which is comparable to earlier studies.^{11,12}

We found that children with AKI had a significantly greater exposure to nephrotoxic drugs. The children who developed AKI also had a significantly higher rate of inotropic drug use than those children with no AKI. Children with AKI were also shown to have significantly higher incidence of MODS. This has been reported in earlier studies also.^{7,8,10}

Table 2 – Baseline characteristics of children admitted to the PICU with AKI.

Baseline characteristics	With AKI, n = 38	Without AKI, n = 159	P value
Age (range/mean)	09 days–168 months (mean = 32.52 months)	07 days–162 months (mean = 32.34 months)	
Gender (M %)	22 (57.89%)	81 (50.94%)	0.4
Nephrotoxic drugs	17 (44.73%)	42 (26.41%)	0.03
Inotropic support	22 (59.45%)	12 (7.54%)	<0.001
MODS	12 (32.43%)	8 (5.03%)	<0.001

AKI, acute kidney injury; PICU, pediatric intensive care unit.

Table 3 – Underlying etiology, maximum stage of AKI, and outcomes in children admitted to the PICU with AKI.

Underlying etiology		n	Maximum stage of AKI		Outcomes
1	Hematolymphoid or solid organ malignancy with MODS	All	n = 4	Stage I, n = 4	Mortality, n = 5
		Ewing sarcoma	n = 1	Stage II & III, n = 3	Complete recovery, n = 2
		Osteosarcoma and neuroblastoma	n = 1		
			n = 1		
2	Children with primary renal disorder	aHUS	1	Stage III, n = 3	Complete recovery, n = 4
		RPGN	1	Stage I, n = 3	CKD, n = 2
		Single kidney with grade V VUR with pyelonephritis (AKI on CKD)	1		
		NS with peritonitis and septic shock	2		
		TA with bilateral RAS	1		
3	Postoperative (major surgery) with sepsis ± MODS	11		Stage I, n = 3	Mortality, n = 6
				Stage II, n = 3	Complete recovery, n = 5
				Stage III, n = 2	
4	Severe neurological disorders	7		Stage I, n = 4	Mortality, n = 3
				Stage II, n = 2	Complete recovery, n = 4
				Stage III, n = 1	
5	Others (n = 7)	VSD with CCF with pneumonia	3	Stage I, n = 3	Mortality, n = 2
		Severe acute respiratory infection	2	Stage II, n = 3	Complete recovery, n = 5
		Acute severe bronchial asthma	2	Stage III, n = 1	

aHUS, atypical hemolytic uremic syndrome; AKI, acute kidney injury; CCF, congestive cardiac failure; CKD, chronic kidney disease; MODS, multiorgan dysfunction syndrome; NS, nephrotic syndrome; PICU, pediatric intensive care unit; RAS, renal artery stenosis; RPGN, rapidly progressive glomerulonephritis; TA, Takayasu aortoarteritis; VSD, ventricular septal defect; VUR, vesicoureteral reflux

In our study, the commonest etiology associated with AKI was MODS secondary to hematolymphoid malignancies or severe neurological involvement. This reflects the overall profile of children admitted to the PICU at our center which is the referral center for most of the peripheral hospitals from the Southern states and is akin to the data from the PICU of superspecialty centers in India and abroad^{10,13}. We did not have cardiac cases with AKI in the postoperative period as children with congenital heart diseases requiring surgical management are managed at another specialized cardiothoracic center with its own ICU.

In a study from South India, however, the authors found that the predominant conditions associated with AKI were infections, postinfectious glomerulonephritis (PIGN), envenomations and Hemolytic Uremic Syndrome (HUS).¹⁴ In another study from a government tertiary care hospital from

Pakistan, AKI was reported to be most frequent due to primary renal disorders including PIGN, obstructive urolithiasis, and crescentic GN, highlighting the regional and ethnic variations in etiologies of AKI.¹⁵

It is also now clear that even if the children with AKI show complete renal recovery, they have significantly higher incidence of residual renal abnormalities including proteinuria and hypertension.^{16,17}

In the Translational Research Investigating Biomarker Endpoints (TRIBE AKI) study, 131 children were followed up for 5 years with postoperative AKI in 57 of them. At follow-up, 22 children (17%) had hypertension, whereas 9 (8%), 13 (13%), and 1 (1%) had microalbuminuria, an estimated Glomerular filtration rate (eGFR) less than 90 mL/min/1.73 m², and an eGFR less than 60 mL/min/1.73 m², respectively. Twenty-one children (18%) had chronic kidney disease.¹⁸

Fig. 1 – Underlying etiologies in children with AKI. AKI, acute kidney injury.

Keeping this in mind, we plan to keep all children who were diagnosed to have AKI during their PICU stay on close follow-up, and they will be periodically checked for proteinuria, hypertension, and renal parameters even after complete renal recovery.

Our study has some obvious limitations. We have included data from a single center over last one year only. This may not reflect the complete picture of pediatric AKI encountered by the pediatricians in the Armed Forces Medical Services (AFMS) hospitals. The strength of the study is that it brings forth an unreported snapshot of AKI in our tertiary care hospitals and gives us the baseline etiological data along with the outcomes of children with AKI which will help us plan further studies as well as intervention modalities.

Conflicts of interest

The authors have none to declare.

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