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Original Research Article

Incidence and etiology of acute kidney injury in children admitted to PICU using pRIFLE criteria

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ABSTRACT

Background: Acute kidney injury is a common problem highly associated with hospitalization. Acute Kidney Injury (AKI) is associated with severe morbidity and mortality especially in children. Lack of consensus definition has been major limitation in improving outcomes. This study tries to address the need of limited data on pediatric AKI. Detection of the incidence, etiological profile and outcome of AKI is important for the initiation of preventive and therapeutic strategies, identifying patients early to avoid renal replacement therapy.
Methods: This prospective observational study was conducted in the pediatric intensive care unit (PICU) of tertiary hospital (GMC Srinagar) between January 2015 to December 2016.This is the only prospective study conducted in this hospital, all other studies conducted here and other higher centers were retrospective. Serum creatinine level was estimated on all patients on admission and alternate days till discharge from Pediatric Intensive Care Unit (PICU). Urine output was recorded. Estimated Creatinine- Clearance (eCrCL) was calculated using Schwartz formula. AKI diagnosis and staging was based on pRIFLE (pediatric RIFLE) criteria. eCrCl criteria was used to diagnose and stage AKI. Maximal stage that the patient progressed during the stay in PICU was assigned the stage for that case.
Results: Of total 500 cases, 480 cases met inclusion criteria. Of them, the incidence of AKI was 154 (32.1%). Stage 'Risk (R)', 'Injury (I)' and 'Failure (F)' constituted 93(60.38%), 46 (29.8%) and15 (9.74%) respectively. Maximum AKI occurred in <1 year (30.5%). Infections were commonest etiology. Amongst infections sepsis (30.5%) was most common, followed by acute gastroenteritis (20.7%) and pneumonia (16.9%). Hypotension, nephrotoxic drugs, sepsis, need for mechanical ventilation were significant ($p<0.001$) risk factors for AKI. Pre-renal causes constituted 68% and intrinsic renal 32%.
Conclusions: The incidence of AKI is high among critically ill children. AKI continues to be associated with adverse outcomes. pRIFLE staging system provides early identification and stratification of AKI. Infections are leading etiology of AKI in children.

Keywords: Acute kidney injury, pRIFLE, PICU

INTRODUCTION

Acute kidney injury previously called acute renal failure is associated with severe morbidity and mortality, especially in children.[1] It is characterized by a reversible increase in the blood concentration of creatinine and nitrogenous waste products and by the inability of the kidney to appropriately regulate fluid and electrolyte homeostasis.[2] If left untreated, the condition has a high risk of multiple organ failure and potentially death. Patients who suffer from AKI may have subsequent renal dysfunction after original injury. Children are more susceptible for this dysfunction.[3] Acute kidney injury

(AKI) affects one in five hospitalized patients, is associated with high expenditure of resources, and leads to the adverse outcomes.[4] AKI is the cause of harmful short term consequences like longer hospital stays, greater disability after discharge and greater risk of in hospital mortality as well as adverse long term outcomes such as progression to chronic kidney disease, development of cardiovascular disease and increased risk of long term mortality.[5] Over the last 20 years great efforts have been made to better unveil and characterize the mechanisms and consequences of AKI. Acute Dialysis Quality Initiative Group (ADQI) proposed RIFLE criteria (Risk, Injury, Failure, Loss of function, End stage renal disease) criteria for defining AKI; later modified in children as pRIFLE (pediatric RIFLE) and have been followed by the Acute Kidney Injury Network (AKIN) and the 'Kidney Disease Improving Global Outcomes' (KDIGO) classifications.[6] These tools have provided more robust knowledge on the epidemiology and outcomes of AKI, especially for the critically ill patient.

A new potential pathway for earlier recognition and better outcome prediction has been opened up by research on more sensitive and specific markers. In addition, the pathogenesis of AKI, namely the role of the immune system, is now less elusive and this knowledge may help further categories AKI and discover new treatment tools. In this review we discuss the current knowledge on the incidence and etiology of AKI.

The spectrum and burden of AKI in developing countries may be different from that of developed countries.[7] The patients from developing countries are younger, infection associated AKI is more common and a significant proportion may have already developed AKI at the time of hospitalization. In addition, resource limitations in managing children who require renal replacement therapy add to the burden.[7,8]

Most of the studies in AKI are based on adult population. The incidence and clinico-etiological profile of AKI varies from adults to children. Of the pediatric studies on incidence of AKI, many are limited to developed countries and often retrospective.[9] Hence limited data availability on clinical profile of pediatric AKI from Indian children, fallacies of retrospective studies, and regional variations in the profile of AKI makes it compelling to study incidence, etiology and outcome of AKI in pediatric patients and current study tries to address this.

METHODS

This was a Prospective and observational study conducted at Government Medical College Srinagar. All patients within the age group of 1 month to 18 years admitted to Pediatric Intensive Care Unit (PICU) in between January 2015 to Dec 2016 were included in the study. Patients with known kidney disease and post-operative cases were excluded from the study. The study was approved by the Institute Ethics Committee. Informed consent was taken from parents of all participants. Detailed clinical history and examination was done, co-morbidities were noted, and relevant data regarding investigations was collected for all children admitted to PICU. Serum creatinine levels were estimated by modified Jaffe method, which is quick, simple, reliable and inexpensive method of creatinine estimation.[10] Serum creatinine was estimated on all patients admitted to PICU on the day of admission and on alternate days till discharge from PICU. Serum creatinine was repeated frequently in children who develop shock, sepsis, need for ventilation, inotropes or diuretics. Creatinine estimation was done at daily intervals in those patients with AKI. Estimated creatinine clearance (eCrCL) was calculated using Schwartz formula.[11] Age related creatinine clearance was taken as the baseline CrCl. Urine output was measured and recorded as ml/kg/hour. Only patients who were catheterized were considered for urine output.

Diagnosis and staging of AKI was based on Pediatric RIFLE definition and classification. eCrCl was used to diagnose and stage AKI. Shock was defined in presence of tachycardia, feeble pulses, cool peripheries, hypotension (blood pressure <-2 Standard deviation (SD) for age and sex) or capillary filling time >3 seconds. Sepsis was the presence of systemic inflammatory response syndrome with suspected or proven infection.[12] The diagnosis of pre-renal vs. renal was decided based on clinical diagnosis and supported by progressively increasing serum creatinine values, even after 48 hours of admission and appropriate fluid therapy (Table 1).

Estimated GFR for children is calculated using Schwartz formula:

eCrCL = K x Height/Sr. creatinine

K = 0.45 for infants 1 to 52 weeks old
K = 0.55 for children 1 to 13 years old
K = 0.55 for adolescent females 13-18 years old
K = 0.7 for adolescent males 13-18 years old.

The maximal stage that the patient progressed during the stay in PICU was assigned the final stage for that case. The patients were evaluated to ascertain the etiology of AKI and its progression and were followed until discharge.

Statistical analysis

The incidence of AKI in children was approximately 5% among non-critically ill and 30% in critically ill according to Basu and Askenazi et al.[4,12] In order to estimate these incidence rates at 95% confidence, and precision of 2.5% for the non-critically ill and 9% for critically ill, the minimum required sample sizes were 304 and 104, respectively (Formula used is n=z21-α/2

P(1-P)/€2 where z = 95% power and 5% level of significance (1.96), P is the incidence, €= Absolute precision).The admissions to our PICU in previous year were well above the minimum required sample. Hence all the cases in the study period were considered.

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean±SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. Multivariate Logistic regression analysis was done to assess the risk factors for the development of AKI.

Statistical software

The statistical software namely SAS 9.2, SPSS 17.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

Table 1: Classification/staging system of AKI.

Estimated creatinine clearance		Urine output
Risk	Decrease by 25%	<0.5ml/kg/hr for 8hrs
Injury	Decrease by 50%	<0.5ml/kg/hr for 16hrs
Failure	Decrease by 75% OR eCrCl <35ml/min/1.73m^2	<0.3ml/kg/hr for 24 hours or Anuric for 12 hours.
Loss	Persistence of failure>4weeks.	
End stage	Persistent failure >3 months.	

Table 2: Creatinine criteria in relation to incidence of AKI.

	Creatinine clearance criteria		
STAGE	No AKI	AKI	Total
No AKI	326(100%)	0(0%)	326(67.9%)
Risk	0(0%)	93(60.38%)	93(19.3%)
Injury	0(0%)	46(29.8%)	46(9.5%)
Failure	0(0%)	15(9.74%)	15(3.2%)
Total	326(100%)	154(100%)	480(100%)

Chi Square test; P<0.001, significant

RESULTS

A total of 500 cases were admitted during the study period. Of these 20 cases were excluded and 480 cases were included in the study. Out of 480 included patients admitted to PICU during the study period, 154 had AKI making an incidence of 32.1%. Stage 'Risk' comprised maximum cases with 60.38% (93 cases), followed by 'Injury' comprised 29.8% (46 cases) and 'Failure' comprised 9.74% (15 cases).

Table 3: Association of age in years in relation to incidence of AKI.

Age (years)	No AKI (n=326)	AKI(n=154)
<1	78 =23.9%	47=30.5%
1-2	59=18.1%	26=16.9%
2-5	53=16.1%	35=22.7%
5-10	46=14.1%	25=16.2%
10-15	63=19.3%	15=9.7%
>15	27=8.4%	6=3.9%

Chi square test; P<0.001

Amongst the AKI cases creatinine criteria was used in all cases while urine output criteria were applied for 150 cases. Risk (R), Injury (I) and Failure (F) cases were 93 (60.38%), 46(29.8%) and 15(9.7%) respectively by eCrCL criteria. For urine output criteria, 45 cases had AKI. Among these cases, incidence of stage 'R' was 31.5%. 'I' was 46.6% and 'F' was 22.2% respectively.

Maximum AKI occurred in <1 year (30.5%) and incidence was highest among younger age group (p=0.003) (Table 3). Infections were the leading cause of AKI. Amongst infections sepsis (30.5%) was the most common etiology associated with AKI, followed by acute gastroenteritis (20.7%) and then pneumonia (16.9%) (Table 4). On univariate analysis, hypotension, nephrotoxic drugs, sepsis, need for mechanical ventilation were significant risk factors for AKI. Among the patients with AKI 56.9% were boys (p=0.818). There was no significant difference of AKI between males and females. Hypotension was found in 75.3% of patients with AKI (p<0.001). Nephrotoxic drugs were associated with 75.3% of AKI cases (p<0.001). Sepsis was present in 30.5% of AKI cases (p<0.001). Need for mechanical ventilation was there in 21.4% cases (p<0.001) (Table 5).

Table 4: Etiology of AKI.

AKI etiology	Number	Percentage
Sepsis	47	30.5%
Acute gastroenteritis	32	20.7%
Pneumonia	26	16.9%
Urinary tract infections	14	9.1%
Acute glomerulonephritis	11	7.1%
Neurological impairment	10	6.5%
Poisoning	9	5.8%
Cardiac failure	5	3.2%

A Backward Wald logistic regression was performed to ascertain the effects of hypotension, Sepsis, Ventilation and nephrotoxic drugs usage on the likelihood that participants have acute kidney injury. The logistic regression model was statistically significant P<0.001

drawing an inference that each of these risk factors were individually associated with occurrence of AKI.

Table 5: Correlation of clinical variables in relation to the incidence of AKI.

Variables	Rifle Stage		P value
	No AKI n=326	AKI n=154	
Gender			
Male	186(57.1%)	83(53.9%)	0.2
Female	140(42.9%)	71(46.1%)	
Sepsis			
Yes	39(11.9%)	47(30.5%)	<0.001
No	287(88.1%)	107(69.5%)	
Nephrotoxic drugs			
Yes	189(58%)	116(75.3%)	<0.001
No	137(42%)	38 (24.7%)	
Hypotension			
Yes	101(31%)	116(75.3%)	<0.001
No	225 (69%)	38 (24.7%)	
Ventilator			
Yes	26(8%)	33(21.4%)	<0.001
No	300(92%)	121(78.6)	

DISCUSSION

The present prospective study found the incidence of AKI to be 32.1% in critically ill children admitted to PICU. This was comparable to Krishnamurthy et al where incidence was 25.1%.[13] It was high compared to other studies conducted in developed countries such as Schneider et al where incidence was 10% which used only serum creatinine to define AKI and not change in eCrCL.[14] However it was lower than reported figure of 82% according to Akan-Arican et al, in which all patients had respiratory failure and were in receipt of mechanical ventilation.[15] This difference can be explained by heterogeneity of patient population, regional differences and sample size can explain this difference.

AKI stratum R, I, F was diagnosed in 60.38%, 29.8% and 9.74% OF AKI cases. The results are comparable to Mehta et al. Maximum number of AKI patients were in Stratum R. Altogether there was progression in grades in 76 cases, maximum progression was from 'No AKI' to stage R. Amongst the three pRIFLE stages maximum progression was seen in stage R to stage I.

This was similar to results of both Hoste et al and Hui et al which also showed maximum progression to stage I from stage R.[16,17]

Pediatric RIFLE criteria use both eCrCl and urine output criteria for classification of AKI stages. In this study urine output criterion was applied only to those patients who were catheterized for accurate measurement of urine output.

The maximum number, 30.5% of AKI patients were below 1 year in this study which was comparable to Mehta et al. This shows that patients with AKI were younger than those without AKI. The etiology of AKI varies from developed and developing countries. While sepsis, glomerulonephritis, HUS and ATN predominate in developing countries, these are replaced by major surgery, haemato-oncological complications, nephrotoxic drugs and pulmonary failure as cause of AKI. In this study to infections contributed to the majority of AKI cases. Amongst infections sepsis was the most common etiology (30.5%) associated with AKI, followed by gastroenteritis (20.7%) and then pneumonia (16.9%). According to both Krishnamurthy et al and Mehta et al sepsis was the most common etiology associated with AKI. There is geographical variation in the etiology. There were no post renal etiologies detected in this study. This could be probably attributed to the post renal causes run a chronic course with progressive deterioration of renal function and also that their detection is more frequent in pediatrics wards than in PICU.

Pre-renal causes account for majority of the AKI (68%) as renal diseases were excluded from the study. In this study risk factors for AKI were hypotension, nephrotoxic drugs, sepsis and Need for Ventilation. Hypotension was found in 75.3% of patients with AKI ($p<0.001$). Nephrotoxic drugs were associated with 75.3% of AKI cases ($p<0.001$). Sepsis was present in 30.5% of AKI cases ($p<0.001$). Need for mechanical ventilation was there in 21.4% cases ($p<0.001$). This is comparable with Mehta et al and Mendonca et al.[18] The potential limitation of this study is the use of an assumed baseline eCrCl. Furthermore, urine output criteria could not be applied to all patients as only patients who were catheterized were included for urine output criteria.

CONCLUSION

It is emphasized that the incidence of AKI is high in children admitted to PICU especially younger ones. AKI is commonly associated with sepsis, gastroenteritis and pneumonia. It is amenable to the treatment provided early diagnosis and prompt intervention. Early identification requires uniform definition and staging system to guide intervention. This study supports use of the pRIFLE score as an easy and simple tool for identification and classifying AKI.

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REFERENCES

1. Mehta R, Cerda J. International Society of Nephrology's by 25 Initative for acute kidney injury: a human rights case for nephrology. The Lancet. 2015.

2. Susantitaphong P, Cruz DN, Cerda J, Abulfaraj M, Alqahtani F, Koulouridis I, Jaber BL. World incidence of AKI: a meta-analysis. Clinical Journal of the American Society of Nephrology. 2013 Sep 6;8(9):1482-93.
3. Andreoli SP. Acute kidney injury in children, Pediatr Nephrol. 2009;24:253-63.
4. Askenazi DJ, Feig DI, Graham NM, Hui-Stickle S, Goldstein SL. 3-5 years longitudinal follow-up of pediatric patients after acute renal failure. Kidney Int. 2006;69:184-9.
5. Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P. Acute renal failure: Definition, outcome measures, animal models, fluid therapy and information technology needs: The Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit Care. 2004;8:R204-12.
6. Lameire N, Biesen VW, Vanholder R. The changing epidemiology of acute renal failure. Nat Clin Pract Nephrol. 2006;2:364-77.
7. Cerdá J, Bagga A, Kher V, Chakravarthi RM. The contrasting characteristics of acute kidney injury in developed and developing countries. Nat Clin Pract Nephrol. 2008;4:138-53.
8. Cerda J, Lameire N, Pannu N, Uchino S, Wang H. Epidemiology of acute kidney inury. Clin J AM Soc Nephrol. 2008;3:881-6.
9. Mehta P, Sinha A, Sami A, Hari P, Kalaivani M, Gulati A, et al. Incidence of acute kidney injury in hospitalized children. Indian Pediatr. 2012;49(7):537-42.
10. Bowers LS, Wong ET. Kinetic serum creatinine assay II. A critical analysis and review. Clin Chem. 1980;26:555-61.
11. Goldstein B, Giroir B, Randolph A. International Pediatric Sepsis Consensus Conference: Definitions for sepsis and organ dysfunction in Pediatrics. Pediatr Crit Care Med. 2005;6:2-8.
12. Basu RK, Prasad DP, Wong H, Wheeler DS.An update and review of acute kidney injury in pediatrics. Pediatr Crit Care Med. 2011;12:339-47.
13. Krishnamurthy S, Mondal N, Narayanan P, Biswal N, Srinivasan S. Incidence and etiology of acute kidney injury in southern india. Indian J Pediatr. 2013;80:183-9.
14. Schneider J, Khemani R, Grushkin C. Serum creatinine as stratified in the RIFLE score for acute kidney injury is associated with mortality and length of stay for children in the pediatric intensive care unit. Crit Care Med. 2010;38:933-9.
15. Akcan-Arikan A, Zappitelli M, Loftis LL, Washburn KK, Jefferson LS. Modified RIFLE criteria in critically ill children with acute kidney injury. Kidney Int. 2007;71:1028-35.
16. Hoste EA, Clermont G, Kersten A, Venkataraman R, Angus DC, De Bacquer D, et al. RIFLE criteria for acute kidney injury are associated with hospital mortality in critically ill patients: A cohort analysis. Crit Care. 2006;10:R73-82.
17. WF Hui, Chan W, Miu TY. Acute kidney injury in the pediatric intensive care unit: identification by modified RIFLE criteria. Hong Kong Med J. 2013;19:13-9.
18. De Mendonça A, Vincent JL, Suter PM, Moreno R, Dearden NM, Antonelli M, et al. Acute renal failure in the ICU: risk factors and outcome evaluated by the SOFA score. Intensive Care Med. 2000;26(7):915-21.

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