Open Access

Original Article

Etiological Spectrum and Outcome of Acute Kidney Injury in Children: A Tertiary Care Experience

Muhammad Atif Anjum, Naureen Akhtar, Shahida Parveen, Adeela Chaudry, Noor ul Ain, Muhammad Sahir Saud

Department of Medicine, University of Child Health Sciences & Children's Hospital, Lahore Pakistan

ABSTRACT

Objective: To determine the aetiologies and outcomes which would help reduce preventable deaths from acute kidney injury.
Study Design: Prospective longitudinal study.
Place and Duration of Study: Paediatric Nephrology unit at University of Child Health Sciences, The Children's Hospital Lahore Pakistan, from Aug 2021 to Jul 2022.
Methodology: A total of 149 children who fulfilled the selection criteria were included in the study. Kidney Disease: Improving Global Outcomes guidelines were used for defining and staging acute kidney injury. The aetiology for each case of acute kidney injury was determined using standard workup/protocol and classified as pre-renal, renal and post-renal. Outcome parameters were recovery, improvement, death and progression to chronic kidney disease.
Results: The mean age of children was 61.79±52.26 months, predominantly boys (68.5%). The most common etiological group was renal (73,49%), followed by pre-renal (53,35.6%) and post-renal (23,15.4%). It was observed that the majority of children had stage-3 AKI (63.8%), with kidney replacement therapy (KRT) given in 92(61.7%) cases. Mortality was seen in 30.9%, while recovery, improvement and death occurred in 69(46.3%), 44(29.5%) and 36(24.2%), respectively, at the time of discharge. At three months of follow-up, recovery, progression to chronic kidney disease, and death occurred in 73(49.0%), 20(13.4%) and 10(6.7%) children, respectively.
Conclusion: Intrinsic renal disease was the most common etiological group occurring primarily in the form of AGN, and sepsis was found to be the most common underlying aetiology. Most patients presented in Stage 3 of acute kidney injury, and recovery was seen in many patients.

Keywords: Aetiology, Acute kidney injury, Children, Outcome.

How to Cite This Article: *Anjum MA, Akhtar N, Parveen S, Chaudry A, Ain NU, Saud MS. Etiological Spectrum and Outcome of Acute Kidney Injury in Children: A Tertiary Care Experience. Pak Armed Forces Med J 2023; 73(4) 1037-1040. DOI: https://doi.org/10.51253/pafmj.v73i4.9201*

INTRODUCTION

Acute kidney injury (AKI) is a common condition in children and a significant contributor to childhood morbidity and mortality.[1] AKI can be community-acquired, resulting from an injury or infection before admission to the hospital or can be hospital-acquired, arising as a complication.[2] Children who develop AKI risk progressing to chronic kidney disease several years after the initial insult.[3] Sepsis and diarrhoea are usual causes of AKI and intrinsic renal causes in low-income countries. Kidney Disease: Improving Global Outcomes (KDIGO) defined AKI as a sudden decrease in glomerular filtration rate (GFR) manifested by an increase in serum creatinine or oliguria within 48 hours to 7 days, with stage determined by the severity of derangement in serum creatinine or oliguria.[4,5] Novel biomarkers of kidney injury increase before creatinine and may be helpful in the detection of AKI but are not yet in routine clinical use.[6]

There needs to be more data on the epidemiology and causes of AKI in low-resource countries.[7,8] A multicentre study in China reported an incidence of 0.32%, while a single-centre study in India reported 25.1%. The yearly incidence of 0.8/100,000 population was stated by the United Kingdom, and figures from the USA were found to be 0.39%.[9] Bhojani *et al*. described an overall incidence of AKI as 10.8% in English children admitted to selected hospitals.[10]

Only a few centres in Pakistan are providing KRT to children owing to limited trained human resources and infrastructure. This leads to a need for more data on AKI in children at the national level. We aimed to determine the aetiology and outcome of AKI in our tertiary care centre.

METHODOLOGY

The prospective longitudinal study carried out from August 2021 to July 2022 at the Paediatric Nephrology unit of the University of Child Health Sciences, The Children's Hospital Lahore Pakistan, after approval (Ref Number 2021-422-CHICH) was taken from the Institutional Review Board (IRB). Written informed consent was taken from the parents/ guardians of the patients. The sample size was

Correspondence: Dr Muhammad Atif Anjum, Department of Medicine, Children Hospital, Lahore Pakistan
Received: 06 Sep 2022; revision received: 25 Nov 2022; accepted: 30 Nov 2022

calculated using the estimated frequency of AKI in hospitalized children as 10.8%,[10] using WHO calculator.

Inclusion Criteria: All children aged one month to 15 years presenting with AKI as per KDIGO criteria were included.

Exclusion Criteria: Known cases of chronic kidney disease, children admitted to the medical intensive care unit and post-operative patients were excluded.

Staging of AKI was done per KDIGO criteria: Stage-1: Serum creatinine increased by 1.5-1.9 times of baseline OR ≥0.3 mg/dl increase OR urine output decreased to <0.5 ml/kg/hour for 6–12 hours. Stage-2: Serum creatinine increased by 2.0-2.9 times baseline, OR urine output decreased to <0.5 ml/kg/hour for over 12 hours. Stage-3: Serum creatinine increased by >3.0 times of baseline OR ≥4.0 mg/dl OR initiation of renal replacement therapy OR urine output <0.3 ml/kg/hour for 24 hours OR anuria for 12 hours or more.[11,12]

Recovery was defined as the complete resolution of AKI determined by serum creatinine returning to the normal range. Improvement in clinical condition was described as a decrease in serum creatinine towards baseline without achieving normal value.[13] All children underwent standard workup of AKI to determine the aetiology. Specific treatment for the underlying aetiology was given to all patients along with kidney replacement therapy (KRT) where indicated - either in the form of haemodialysis or acute peritoneal dialysis, depending upon the weight and hemodynamic status of the child.

Serum creatinine levels were sent daily, and strict fluid intake and urine output records were maintained. Follow-up was scheduled for each case individually, with a mandatory follow-up three months after discharge.

Data were analysed using Statistical Package for the Social Sciences (SPSS) version 25:00. Quantitative data like age was presented as mean and standard deviation. Qualitative data such as gender, stage of AKI, etiological factors, renal replacement therapy, and outcome at discharge and three months were presented as frequencies and percentages.

RESULTS

A total of 149 children were enrolled in the study. The mean age of the subjects was 61.79±52.26 months. There were 102(68.5%) boys and 47(31.5%) girls. Age stratification revealed that 85(57.0%) patients were below five years of age. Intrinsic renal disease was seen in 73(49%) children, pre-renal AKI was present in 53(35.6%) and post-renal aetiology was found in 23(15.4%) patients. Among the pre-renal causes, sepsis was the most common cause present in 36(24.2%) children. For intrinsic renal aetiology, acute glomerulonephritis (AGN) was seen in 26(17.4%) subjects. In comparison, bilateral pelvic-ureteral junction (PUJ) obstruction was observed as a post-renal cause of AKI in 8(5.4%) patients (Table-I). At the time of discharge, recovery occurred in 69(46.3%) patients, improvement was seen in 44(29.5%) cases, and 36(24.2%) children died. Sepsis was the leading cause of death and was observed in 17(11.4%) cases, followed by HUS(3.3%). Recovery of AKI was excellent in cases with AGN and acute diarrhoea (Table-II). At three months, recovery was seen in 73(49.0%) patients, the disease progressed to chronic kidney disease (CKD) in 20(13.4%) subjects, 10(6.7 %) cases were lost to follow-up, and death occurred in 10(6.7%) patients resulting in an overall mortality of 46(30.9%). The outcome in terms of

Table-I: Aetiological Spectrum of Acute Kidney Injury (n=149)

Intrinsic-renal	n(%) 73(49 %)	Pre-renal	n(%) 53(35.6%)	Post-renal	n(%) 23(15.4%)
AGN	26(17.4%)	Acute diarrhoea	16(10.7%)	PUJO	8 (5.4%)
Anti- GBM disease	1(0.7%)	Contrast nephropathy	1(0.7%)	PUVs	6(4%)
Congenital nephrotic syndrome	3(2%)	Sepsis	36(24.2%)	MCDK	1(0.7%)
Drug induced	2(1.3%)	-	-	Stone disease	4(2.7%)
Envenomation (Bee)	1(0.7%)	-	-	Primary VUR	4(2.7%)
Primary FSGS	3(2%)	-	-	-	-
IgA- Vasculitis	2(1.3)	-	-	-	-
HUS	11(7.4%)	-	-	-	-
IgA-Nephropathy	1(0.7%)	-	-	-	-
Nephrotic syndrome	4(2.7%)	-	-	-	-
RPGN	10(6.7%)	-	-	-	-
Lupus Nephritis	2(1.3%)	-	-	-	-
Acute pyelonephritis	7(4.7%)	-	-	-	-

Anti-GBM disease (anti glomerular basement membrane disease), FSGS (Focal segmental glomerulonephritis), MCDK (Multicystic dysplastic kidney), PUJO (Pelvic-ureteral junction obstruction), PUVs (posterior urethral valves), VUR (Vesicoureteral reflux), RPGN (rapidly progressive glomerulonephritis).

different etiological factors revealed that death occurred in 4(2.7%) cases each of rapidly progressive glomerulonephritis (RPGN) and sepsis and 2(1.3%) cases of posterior urethral valves (PUVs). Excellent recovery was seen in AGN, acute diarrhoea and survivors of AKI due to sepsis at three months. Most cases of AKI are due to post-renal causes, and RPGN progresses to CKD (Table-III).

Table-II: Outcome of Acute Kidney Injury according to Underlying Aetiologies (n=149)

Aetiology	Outcome at discharge			Outcome at three months			
	Recovery	Improvement	Death	Recovery	Lost to follow	Death	CKD
Bilateral-PUJO	3(2%)	4(2.7%)	1(0.7%)	2(1.3%)	1(0.7%)	0	4(2.7%)
PUVs	3(2%)	2(1.3%)	1(0.7%)	2(1.3%)	0	2(1.3%)	1(0.7%)
MCDK	0	01(0.7%)	0	0	0	0	1(0.7%)
Stone disease	1(0.7%)	2(1.3%)	1(0.7%)	1(0.7%)	1(0.7%)	0	1(0.7%)
Primary VUR	2(1.3%)	2(1.3%)	0	2(1.3%)	0	0	2(1.3%)
Acute diarrhoea	11(7.4%)	2(1.3%)	3(2%)	11(7.4%)	2(1.3%)	0	0
Contrast nephropathy	1(0.7%)	0	0	1(0.7%)	0	0	0
Sepsis	11(7.4%)	8(5.3%)	17(11.4)	14(9.4%)	0	4(2.7%)	1(0.7%)
AGN	23(15.4%)	3(2%)		25(16.8%)	1(0.7%)		0
Anti- GBM Disease	0	1(0.7%)	0	0	0	0	1(0.7%)
Congenital Nephrotic Syndrome	0	0	3(2%)	0	0	0	0
Drug induced	2(1.3%)	0	0	0	0	0	2(1.3%)
Envenomation (Bee)	1(0.7%)	0	0	0	1(0.7%)	0	0
Primary FSGS	0	3(2%)	0	1(0.7%)	0	0	2(1.3%)
IgA- Vasculitis	2(1.3%)	0	0	2(1.3%)	0	0	0
HUS	2(1.3%)	4(2.7%)	5(3.3%)	2(1.3%)	1(0.7%)	0	3(2%)
IgA-Nephropathy	1(0.7%)	0	0	0	1(0.7%)	0	0
Nephroticsyndrome	0	2(1.3%)	2(1.3%)	2(1.3%)	0	0	0
RPGN	0	8	2(1.3%)	0	2(1.3%)	4(2.7%)	2(1.3%)
Lupus Nephritis	2(1.3%)	0		2(1.3%)	0	0	0
Acute pyelonephritis	4(2.7%)	2(1.3%)	1(0.7%)	6(4%)	0	0	0
TOTAL	69(46.3%)	44(29.5%)	36(24.2)	73(49.0%)	10(6.7%)	10(6.7%)	20(13)

Table-III: Outcome OF AKI according to KDIGO Stage (n=149)

Stage	Outcome at discharge			Outcome at 3 months			
	Death	Improvement	Recovery	CKD	Death	Lost to follow up	Recovery
Stage I 19(12.8%)	0(0%)	0(0%)	19(12.8%)	0(0%)	0(0%)	0(0%)	19(12.8%)
Stage II 35(23.5%)	5(3.4%)	10(6.7%)	20(13.4%)	2(1.3%)	2(1.3%)	0(0%)	26(17.4%)
Stage III 95(63.8%)	31(%)	34(22.1%)	30 (19.5%)	18(12.0%)	8(5.4%)	10(6.7%)	28(18.8%)
TOTAL	36(24.2%)	44(29.5%)	69(46.3%)	20(13.4%)	10(6.7%)	10(6.7%)	73(49.0%)

Kidney replacement therapy (KRT) was given to 92(61.7%) children. Acute peritoneal dialysis (PD) was carried out in 83(55.7%) and haemodialysis (HD) in 22(14.8%) cases. Sepsis was the most common cause requiring KRT, with 32(21.4%) cases, followed by acute diarrhoea and haemolytic uremic syndrome (HUS), each with 11(7.4%) cases. The mortality rate in children receiving KRT was 34.7% (32/92).

DISCUSSION

This study describes the diseases causing AKI in children and their outcomes in our hospital. We found a male predominance (68.5%) similar to studies conducted in other developing countries.[13-15] Our study showed that the most frequent cause of AKI was intrinsic renal disease (49%), followed by pre-renal aetiology (35.6%). Among the renal factors, the commonest cause of AKI was AGN (17.4%), followed by HUS (7.4%) and RPGN (6.7%). The most common pre-renal aetiologies were sepsis (24.2%) and diarrhoea (10.7%). Among post-renal causes, bilateral PUJ obstruction (5.4%) and PUVs (4%) were the two common causes of AKI. Studies carried out in Karachi by Bai *et al*.[16] and in India by Mahesh *et al*.[11] revealed pre-renal failure as the common cause of AKI, followed by renal and post-renal factors. These findings suggest that pre-renal factors contributed significantly to the development of AKI compared to our study, which concluded renal factors as the common cause. Literature reveals a wide variation in the aetiology of AKI between developed and developing nations. In developed countries, AKI mainly occurs in hospitalized children, whereas community-acquired conditions frequently cause AKI in developing nations.[17,18] Similarly, Bresolin *et al*. discovered that shock and sepsis were the primary causes of AKI.[19] On the other hand, low-income countries exhibit a different range of

aetiologies.[20] Our study demonstrated that the common cause was sepsis, followed by AGN and diarrhoea.

The outcome of AKI in our study at the time of discharge showed that 46.3% recovered, 29.5% improved, and 24.2% expired. At three months, most children recovered (49.0%), 13.4% progressed to CKD, 6.7% died, and 6.7% were lost to follow-up. International data show variable recovery rates ranging from 40-90%.[20,21] Recovery was more in patients with AGN, diarrhoea and sepsis. Progression to CKD was considerably higher in patients with bilateral PUJ obstruction, HUS and RPGN. The overall mortality rate in our study was 30.9%, in contrast to a mul-ticentre study by Cao *et al*.[1] and Tresa *et al*.[9] which revealed low mortality rates of 3.4% and 5.2%, respectively.

LIMITATIONS OF STUDY

Post-operative and ICU cases were not enrolled, significantly contributing to the development of AKI in the paediatric population. Our study offers pertinent data on the paediatric AKI spectrum seen at a government tertiary care referral facility in a developing nation.

CONCLUSION

We observed diverse aetiologies of AKI. Intrinsic renal disease was the common cause of AKI, followed by sepsis and acute diarrhoea. We found that most patients reach late in KDIGO Stage 3, requiring KRT. Fortunately, the majority recovered; however, some developed CKD. The outcome can be improved by increasing awareness and integrating international society for nephrology (ISN) programs and goals related to AKI into local circumstances.

Conflict of Interest: None.

Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

MAA & NA: Conception, data analysis, data interpretation, approval of the final version to be published.

SP & AC: Study design, drafting the manuscript, critical review, approval of the final version to be published.

NUA & MSS: Critical review, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Cao Y, Yi ZW, Zhang H, Dang XQ, Wu XC, Huang AW, et al. Etiology and outcomes of acute kidney injury in Chinese children: a prospective multicentre investigation. BMC Urol 2013; 13:41. https://doi.org/10.1186/1471-2490-13-41
2. Anigilaje EA, Adebayo AI, Ocheni SA. Acute kidney injury in children: A study of etiology, clinical profile, and short-term outcomes at the University of Abuja Teaching Hospital, Gwagwalada, Abuja, Nigeria. Saudi J Kidney Dis Transpl 2019; 30(2): 421-439. https://doi.org/10.4103/1319-2442.256849
3. Olowu WA, Niang A, Osafo C, Ashuntantang G, Arogundade FA, Porter J, et al. Outcomes of acute kidney injury in children and adults in sub-Saharan Africa: a systematic review. Lancet Glob Health 2016; 4(4): e242-250. https://doi.org/10.1016/s2214-109x(15)00322-8
4. Makris K, Spanou L. Acute Kidney Injury: definition, pathophysiology and clinical phenotypes. Clin Biochem Rev 2016; 37(2): 85-98
5. Levey AS, Eckardt KU, Dorman NM, Christiansen SL, Cheung M, Jadoul M, et al. Nomenclature for kidney function and disease-executive summary and glossary from a Kidney Disease: Improving Global Outcomes (KDIGO) consensus conference. Eur Heart J 2020; 41(48): 4592-4598. https://doi.org/10.1093/eurheartj/ehaa650
6. Sethi SK, Bunchman T, Chakraborty R, Raina R. Pediatric acute kidney injury: new advances in the last decade. Kidney Res Clin Pract 2021; 40(1): 40-51. https://doi.org/10.23876/j.krcp.20.074
7. Ponce D, Balbi A. Acute kidney injury: risk factors and management challenges in developing countries. Int J Nephrol Renovasc Dis 2016; 9: 193-200. https://doi.org/10.2147%2FIJNRD.S104209
8. Rahman H. Etiology and Outcomes of Acute Kidney Injury: A comprehensive study in four tertiary centers of dhaka. J Ped Nephrol 2017; 5(1). https://doi.org/10.22037/jpn.v5i1.13742
9. Tresa V, Yaseen A, Lanewala AA, Hashmi S. Etiology, clinical profile and short-term outcome of acute kidney injury in children at a tertiary care pediatric nephrology center in Pakistan. Ren Fail 2017; 39(1): 26-31. https://doi.org/10.1080/0886022x.2016.1244074
10. Bhojani S, Stojanovic J, Melhem N, Maxwell H, Houtman P, Hall A, et al. The incidence of paediatric acute kidney injury identified using an AKI e-alert algorithm in six english hospitals. Front Pediatr 2020; 8: 29. https://doi.org/10.3389/fped.2020.00029
11. Mahesh K, Vishwanath B, Kalpana S. Etiological spectrum and short term outcome of acute kidney injury in children: a prospective study. Int J Contemp Pediatr 2019; 6(5): 2121-24 https://doi.org/10.18203/2349-3291.ijcp20193737
1. 12.Gullipalli P, Anjani A. Spectrum of paediatric acute kidney injury - a referral hospital experience in a developing nation. IOSR J Dent Med Sci 2015; 14(2): 80-87.
12. Mehar F, Rabia S, Safdar RS, Khan AA, Naz M. Outcome of acute kidney injury in children at Nishtar Hospital, Multan, Pakistan. Rawal Med J 2020; 45(3): 598-601.
13. Esezobor CI, Ladapo TA, Osinaike B, Lesi FE. Paediatric acute kidney injury in a tertiary hospital in Nigeria: prevalence, causes and mortality rate. PLoS One 2012; 7(12): e51229. https://doi.org/10.1371/journal.pone.0051229
14. Halle MP, Lapsap CT, Barla E, Fouda H, Djantio H, Moudze BK, et al. Epidemiology and outcomes of children with renal failure in the pediatric ward of a tertiary hospital in Cameroon. BMC Pediatr 2017; 17(1): 202. https://doi.org/10.1186/s12887-017-0955-0
15. Bai S, Moorani KN, Naeem B, Ashfaq M, Rehman EU. Etiology, clinical profile, and short-term outcome of children with Acute Kidney Injury. Cureus 2022; 14(2). https://doi: 10.7759/cureus.22563
16. Bernardo EO, Cruz AT, Buffone GJ, Devaraj S, Loftis LL, Arikan AA, et al. Community-acquired Acute Kidney Injury among children seen in the pediatric emergency department. Acad Emerg Med 2018; 25(7): 758-768. https://doi.org/10.1111/acem.13421
17. Sutherland SM, Ji J, Sheikhi FH, Widen E, Tian L, Alexander SR, et al. AKI in hospitalized children: epidemiology and clinical associations in a national cohort. Clin J Am Soc Nephrol 2013 ; 8(10): 1661-1669. https://doi.org/10.2215/cjn.00270113
18. Bresolin N, Silva C, Halllal A, Toporovski J, Fernandes V, Góes J, et al. Prognosis for children with acute kidney injury in the intensive care unit. Pediatr Nephrol 2009; 24(3): 537-544. https://doi.org/10.1007/s00467-008-1054-0
19. Macedo E, Cerda J, Hingorani S, Hou J, Bagga A, Burdmann EA, et al. Recognition and management of acute kidney injury in children: The ISN 0by25 Global Snapshot study. PLoS One 2018; 13(5): e0196586. https://doi.org/10.1371/journal.pone.0196586
20. Olowu WA. Acute kidney injury in children in Nigeria. Clin Nephrol 2015; 83(7 Suppl 1): 70-74. https://doi.org/10.5414/cnp83s070