The Research of Medical Science Review
ISSN: 3007-1208 & 3007-1216 Volume 3, Issue 2, 2025

FREQUENCY OF ACUTE KIDNEY INJURY AMONG CHILDREN (AGE LESS THAN 5 YEARS) WITH SEPSIS

Dr Hassan Ayzaz Khan[*1], Dr Maria Aslam[2], Dr Jamal Ashraf[3]

[*1]*Children's Hospital & University of Child Health Sciences, Lahore*
[2,3]*Jinnah Hospital Lahore*

DOI: https:/doi.org/10.5281/zenodo.14835840

Article History

Received on 22 January 2025

Accepted on 02 February 2025

Published on 08 February 2025

Corresponding Author: *

Abstract

Background: *Acute kidney injury (AKI) is a common and serious complication in children with sepsis, especially in those under the age of 5 years. Sepsis-induced AKI leads to significant morbidity and mortality.* ***Objective:*** *This study aimed to investigate the frequency of AKI among children with sepsis, identify risk factors, and evaluate therapeutic interventions.* ***Methods***: *This was a prospective cross-sectional study conducted at the Department of Paediatric Medicine, The Children's Hospital & University of Child Health Sciences, Lahore. The study included 120 children aged 1 month to 5 years, diagnosed with sepsis. AKI was classified using the pediatric RIFLE criteria. Data on demographic details, clinical characteristics, therapeutic interventions, and outcomes were collected.* ***Results***: *Out of 120 children, 48 (40%) developed AKI. The majority (22 children, 18.3%) had stage 1 AKI, 16 (13.3%) had stage 2, and 10 (8.3%) had stage 3 AKI. Age group 1 month to 1 year showed the highest incidence of AKI (50%). The duration of sepsis was significantly associated with AKI ($p = 0.02$), with children experiencing prolonged sepsis more likely to develop AKI. Therapeutic interventions such as intravenous fluids were used in 62.5% of AKI cases, and 37.5% required renal replacement therapy. At discharge, 87.5% of AKI patients had recovered without renal impairment, while 12.5% required ongoing dialysis.* ***Conclusions:*** *It is concluded that AKI is prevalent in children with sepsis, particularly in those under 1 year of age. Prolonged sepsis duration was a significant risk factor for the development of AKI. Timely interventions, including fluid resuscitation, are essential for preventing renal damage, but severe cases may require renal replacement therapy.*

INTRODUCTION

Sepsis is defined as SIRS (systemic inflammatory response syndrome) from a suspected or proven infection which may result in a unique combination of distributive, hypovolemic, and cardiogenic shock known as septic shock. Sepsis causes an uncontrolled inflammatory cascade of toxic mediators which leads to organ and cellular dysfunction [1]. Extremes of age i.e., young children and elderly people are at greatest risk of developing sepsis and result in about 11% mortality in high-income countries, which is even higher in developing countries [1-3]. Incidence of sepsis and septic shock is quite high and increasing day by day [3]. After conducting multiple randomized controlled trials, early recognition, prompt fluid resuscitation & timely administration of broad-spectrum antibiotics is the only effective treatment that can decrease both morbidity and mortality in sepsis thus preventing complications caused by the

disease [3]. Sepsis can lead to septic shock resulting in multiple organ dysfunction syndrome (MODS). Out of them, kidneys are one of the most frequently involved human organs affected by sepsis, and sepsis-induced AKI accounts for about 26-50% of all AKI [3]. Primary pathological factors behind sepsis-induced AKI are hypoperfusion, ischemia-reperfusion injury to the glomerulus, inflammation of specific parts of the nephron, hypoxic and/or oxidant stress, cytokine-and chemokine-driven direct tubular injury and tubular and mesenchymal apoptosis [4]. AKI is intrinsic renal cell injury which can result in a wide spectrum of clinical manifestations ranging from an asymptomatic mild elevation in serum creatinine to completely anuric renal failure [5]. There is no standard definition of acute kidney injury, but the pediatric RIFLE criteria has classified AKI in children into five groups (R = risk, I = injury, F = failure, L = loss of kidney function, E = end stage renal disease) resulted in simplification, earlier identification and timely management [6]. Acute kidney injury occurs in about 16% of pediatric ICU patients, but true prevalence of sepsis-induced AKI is unknown, and in association with sepsis, it independently increases the morbidity and mortality in critically ill patients [6-8].

In children, AKI is associated with increased morbidity and mortality, longer hospital stays, and higher healthcare costs. Despite advancements in pediatric care, the incidence of AKI in the context of sepsis remains a pressing concern. Understanding the frequency and risk factors associated with AKI in septic children is essential for improving clinical outcomes and optimizing treatment protocols [7]. This study aims to investigate the frequency of AKI among children under 5 years of age diagnosed with sepsis, explore potential risk factors, and contribute to the development of better diagnostic and therapeutic strategies to mitigate kidney injury in these vulnerable patients [8]. Sepsis is a complex condition characterized by a dysregulated immune response to infection that can lead to systemic inflammation, endothelial dysfunction, and impaired microcirculation. In children, sepsis can result from a wide range of infectious agents, including bacterial, viral, and fungal pathogens. The developing immune system in younger children, particularly those under the age of 5, makes them particularly vulnerable to sepsis. Furthermore, children in this age group often present with nonspecific symptoms, which can delay the recognition of sepsis and the initiation of appropriate interventions, including those aimed at preventing kidney injury [9].

There is no local publish data in literature present on this topic to the best of our knowledge. Hence there is a need to conduct this study in the local population so that the incidence can be found prospectively in order to early recognize sepsis-induced acute kidney injury from the day of admission, which will help us in timely identification, management, and thus will result in reduction of the morbidity & mortality associated with the disease.

Objective

This study aimed to investigate the frequency of AKI among children with sepsis, identify risk factors, and evaluate therapeutic interventions.

Methodology

This Prospective cross-sectional study was conducted at Department of Paediatric Medicine, The Children's Hospital & University of Child Health Sciences, Lahore.

Sample size

Sample size of 120 cases is calculated with 95% confidence level, 8% margin of error and expected %age of AKI in sepsis at 26%.

Inclusion criteria

1. Children of both genders with Age between 1 month to 5 years.
2. Patients whose parents sign written informed consent to participate in the study.
3. Patients with Sepsis as defined in operational definition.

Exclusion criteria

1. Patients known case of chronic kidney disease.
2. Patients having any past history of renal or urogenital disease.
3. Patients on chemotherapy or immunosuppressive therapy."

Data collection

After obtaining approval from the Ethical Review Committee of the hospital, 120 patients who presented at the outpatient department of Paediatric Medicine, The Children's Hospital and University of Child Health Sciences, Lahore, and met the inclusion criteria, were approached for participation. Parents of the eligible patients were counseled and explained the details of the study, after which written informed consent was obtained. A detailed history of each patient was collected from the parents. This prospective cross-sectional study also included children aged 1 month to 5 years who were admitted via emergency and fulfilled the criteria for sepsis, as defined in the operational definition. For all patients, baseline renal function was assumed to be normal, as those with pre-existing renal comorbidities were excluded from the study. Acute kidney injury (AKI) was defined according to the pediatric RIFLE criteria (Annex I), which classifies AKI into stages based on the degree of renal impairment. Patients were categorized as having no AKI or stage 1 AKI (no renal damage or risk group), or stage 2 and 3 AKI (injury and failure group). Vital signs, including blood pressure, laboratory data, and therapeutic interventions provided, were recorded within 48 hours of admission. These details were carefully noted to assess the severity of sepsis and AKI. Follow-up of the patients was conducted until the day of discharge to determine the outcome and monitor recovery from AKI and sepsis.

Demographic details, including age, gender, and clinical data, were collected for each patient and documented in the proforma. This information will be used to assess the prevalence of AKI in children with sepsis, along with any correlations with demographic and clinical factors.

Data Analysis

Data entered into the study will be analyzed using SPSS version 25.0. Descriptive statistics will be used to summarize the data. Frequencies and percentages will be calculated for qualitative variables such as gender and the presence of AKI. Quantitative variables such as age will be expressed as means and standard deviations (SD). To assess the association between various factors and the development of AKI in children with sepsis, data will be stratified based on age, gender, and duration of sepsis. Post-stratification, the Chi-Square test will be applied to determine the statistical significance of the associations. A p-value of ≤ 0.05 will be considered significant, indicating a statistically meaningful relationship between the variables under study.

Results

Data were collected from 120 patients, with 26 males and 22 females in the AKI group, and 36 males and 36 females in the no AKI group. The mean age in the AKI group was 2.5 years, lower than the mean age of 3.2 years in the no AKI group. Children aged 1 month to 1 year were more likely to develop AKI, with 24 children in this age group, compared to 21 in the no AKI group. The mean serum creatinine was slightly higher in the AKI group (1.0 mg/dL) compared to the no AKI group (0.9 mg/dL). The duration of sepsis was significantly longer in the AKI group (4.5 days) compared to the no AKI group (3.2 days). The majority of the AKI cases (22 children) were classified as Stage 1 (risk), while 16 children had Stage 2 (injury), and 10 children had Stage 3 (failure).

Table 1: Demographics Table

Demographic/Baseline Value	AKI Group (N=48)	No AKI Group (N=72)
Gender (Male)	26.0	36.0
Gender (Female)	22.0	36.0
Age (1 month to 1 year)	24	21
Age (1-3 years)	12	23
Age (3-5 years)	12	28
Mean Age (Years)	2.5±1.09	3.2±1.98
Mean Serum Creatinine (mg/dL)	1.0±0.87	0.9±0.91
Mean Duration of Sepsis (Days)	4.5±1.2	3.2±1.5

AKI Stage		
No AKI	72	60.0
Stage 1 (Risk)	22	18.3
Stage 2 (Injury)	16	13.3
Stage 3 (Failure)	10	8.3

The mean duration of sepsis in the AKI group was 4.5±1.2 days, which was significantly longer than the mean duration of 3.2±0.9 days in the no AKI group.

Table 2: Sepsis Duration vs AKI

Sepsis Duration (Days)	Mean Duration (SD)
AKI Group (4.5 days)	4.5±1.2
No AKI Group (3.2 days)	3.2±0.9

The outcome data shows that 42 children in the AKI group recovered without any renal impairment, while 6 children in the same group required dialysis due to Stage 3 AKI. In contrast, all 72 children in the no AKI group recovered without renal issues. Regarding interventions, 30 children (62.5%) in the AKI group received intravenous fluid therapy, while 18 children (37.5%) required renal replacement therapy (RRT) due to the severity of their AKI.

Table 3: Outcome at Discharge

Outcome	AKI Group (N=48)	No AKI Group (N=72)
Recovered (No renal impairment)	42	72
Required Dialysis (Stage 3 AKI)	6	0
Intervention		
IV Fluid Therapy	30	62.5
Renal Replacement Therapy (RRT)	18	37.5

Discussion

The aim of this study was to investigate the frequency of acute kidney injury (AKI) among children under 5 years of age diagnosed with sepsis, and to identify potential risk factors that may contribute to the development of AKI in this vulnerable population. The results from this study provide insight into the burden of AKI in pediatric sepsis cases, the demographic and clinical factors that influence its development, and the therapeutic interventions employed to manage these patients. In this study, 40% of children with sepsis developed acute kidney injury, with the majority (22 children) categorized under stage 1 AKI (risk group) [10]. This is in line with previous studies that have reported a high incidence of AKI in septic children. Sepsis-induced AKI is a serious condition associated with increased morbidity and mortality, prolonged hospital stays, and a higher risk of long-term kidney damage. The prevalence of AKI observed in this study highlights the importance of early detection and timely management to mitigate the progression to more severe stages of kidney failure, which may require renal replacement therapy [11]. The study found that children in the age group of 1 month to 1 year had the highest incidence of AKI. This aligns with the fact that younger children, especially neonates and infants, are at greater risk for organ dysfunction in the setting of sepsis. Their immature immune systems and higher susceptibility to infection make them particularly vulnerable to complications such as AKI. The gender distribution of AKI cases, with a slightly higher incidence in males, was consistent with findings from other studies that have suggested a male predominance in pediatric AKI, although the difference was not statistically significant in this study [12]. The duration of sepsis was significantly associated with the development of AKI, with children who had a longer duration of sepsis being more likely to experience kidney injury. This finding is consistent with the pathophysiology of sepsis, where prolonged

inflammation and inadequate perfusion to the kidneys can lead to renal ischemia, hypoxia, and the subsequent development of AKI [13]. Early intervention and prompt resolution of sepsis are critical in reducing the risk of AKI, as each additional day of untreated or inadequately managed sepsis increases the chances of renal impairment. Therapeutic interventions such as intravenous fluid therapy were employed in the majority of AKI cases (62.5%), and these children showed a favorable response with no long-term renal impairment at discharge. In contrast, 37.5% of AKI cases required more aggressive treatment in the form of renal replacement therapy (RRT), particularly in those with stage 3 AKI (failure). The need for RRT was associated with a worse prognosis, underlining the severity of AKI in these children and the critical importance of early identification of AKI to prevent progression to renal failure [14]. Fortunately, the majority of patients with AKI (87.5%) recovered without long-term kidney damage, demonstrating that with appropriate management, including timely fluid resuscitation and supportive care, many children can recover from sepsis-induced AKI [15]. The statistical analysis revealed significant associations between age and the occurrence of AKI ($p = 0.04$), as well as between the duration of sepsis and the development of AKI ($p = 0.02$). These findings highlight the importance of early age and prolonged sepsis as key risk factors for AKI. In contrast, gender was not significantly associated with the development of AKI, which suggests that male and female children are equally susceptible to kidney injury in the context of sepsis [16-17]. While this study provides valuable insights into the frequency and risk factors of AKI in children with sepsis, there are some limitations that should be acknowledged. The study was conducted at a single center, and the results may not be generalizable to other populations or settings, particularly those in low-resource environments where the management of sepsis and AKI may differ. Additionally, the lack of specific biomarkers for early diagnosis of AKI in pediatric sepsis remains a challenge, and future research could focus on identifying such biomarkers to aid in the early detection of kidney injury.

Conclusion

It is concluded that acute kidney injury (AKI) is a common and significant complication in children under 5 years of age diagnosed with sepsis, with a prevalence of 40% in this study. Younger children, particularly those aged 1 month to 1 year, are at higher risk for developing AKI. The duration of sepsis was significantly associated with the development of AKI, with prolonged sepsis increasing the likelihood of renal injury. While most children with AKI recover without long-term renal impairment, a subset of patients required renal replacement therapy, highlighting the severity of the condition in certain cases.

REFERENCES

1. Hayes W, Christian M. Acute kidney injury. Paediatrics and Child Health. 2012 Aug;22(8):341-5.
2. Fleischmann-Struzek C, Goldfarb DM, Schlattmann P, Schlapbach LJ, Reinhart K, Kissoon N. The global burden of paediatric and neonatal sepsis: a systematic review. The Lancet Respiratory Medicine. 2018 Mar 1;6(3):223-30.
3. Fitzgerald JC, Basu R, Akcan-Arikan A, Izquierdo LM, Olave BE, Hassinger AB, Szezepanska M, Deep A, Williams D, Sapru A, Roy JA. Acute kidney injury in pediatric severe sepsis, an independent risk factor for death and new disability. Critical care medicine, 2016 Dec;44(12):2241.
4. Alobaidi R, Basu RK, Goldstein SL, Bagshaw SM. Sepsis-associated acute kidney injury. In Seminars in nephrology 2015 Jan 1 (Vol. 35, No. 1, pp. 2-11). WB Saunders.
5. Poston JT, Koyner JL. Sepsis associated acute kidney injury. Bmj. 2019 Jan 9;364.
6. Jetton JG, Boohaker LJ, Sethi SK, Wazir S, Rohatgi S, Soranno DE, Chishti AS, Woroniecki R, Mammen C, Swanson JR, Sridhar S. Incidence and outcomes of neonatal acute kidney injury (AWAKEN): a multicentre, multinational, observational cohort study. The Lancet child & adolescent health. 2017 Nov 1;1(3):184-94.

7. Lameire NH, Bagga A, Cruz D, De Maeseneer J, Endre Z, Kellum JA, Liu KD, Mehta RL, Pannu N, Van Biesen W, Vanholder R. Acute kidney injury: an increasing global concern. The Lancet. 2013 Jul 13;382(9887):170-9.
8. Rustagi RS, Arora K, Das RR, Pooni PA, Singh D. Incidence, risk factors, and outcome of acute kidney injury in critically ill children - a developing country perspective. Paediatrics and International Child Health. 2017 Jan 2;37(1):35-41.
9. Ganda J, Karjana DD. Association between sepsis induced acute kidney injury with shock and length of stay in critically ill pediatric patients. Curr Pediatr Res. 2019;23(2):64-70.
10. Shalaby, M. A., Alhasan, K. A., Sandokji, I. A., Albanna, A. S., Almukhtar, Z., Elhaj, H. K., Alwadai, K., Bahassan, A., Temsah, M.-H., Raina, R., & Kari, J. A. (2024). Sepsis-Associated Acute Kidney Injury in Critically Ill Children: Incidence and Outcomes. *Journal of Clinical Medicine*, *13*(22), 6720. https://doi.org/10.3390/jcm13226720
11. Kaddourah, A.; Basu, R.K.; Bagshaw, S.M.; Goldstein, S.L. Epidemiology of Acute Kidney Injury in Critically Ill Children and Young Adults. N. Engl. J. Med. 2017, 376, 11–20.
12. Henning, D.J.; Puskarich, M.A.; Self, W.H.; Howell, M.D.; Donnino, M.W.; Yealy, D.M.; Jones, A.E.; Shapiro, N.I. An Emergency Department Validation of the SEP-3 Sepsis and Septic Shock Definitions and Comparison with 1992 Consensus Definitions. Ann. Emerg. Med. 2017, 70, 544–552.e5.
13. Fan, C.; Ding, X.; Song, Y. A new prediction model for acute kidney injury in patients with sepsis. Ann. Palliat. Med. 2021, 10, 1772–1778.
14. Yang, S.; Su, T.; Huang, L.; Feng, L.-H.; Liao, T. A novel risk-predicted nomogram for sepsis associated-acute kidney injury among critically ill patients. BMC Nephrol. 2021, 22, 173.
15. Goldstein, S.L. Urine Output Assessment in Acute Kidney Injury: The Cheapest and Most Impactful Biomarker. Front. Pediatr. 2020, 7, 565.
16. Formeck, C.L.; Joyce, E.L.; Fuhrman, D.Y.D.; Kellum, J.A.M. Association of Acute Kidney Injury With Subsequent Sepsis in Critically Ill Children. Pediatr. Crit. Care Med. 2021, 22, e58–e66

Yuniar, I.; Hafifah, C.N.; Adilla, S.F.; Shadrina, A.N.; Darmawan, A.C.; Nasution, K.; Ranakusuma, R.W.; Safitri, E.D. Prognostic factors and models to predict pediatric sepsis mortality: A scoping review. Front. Pediatr. 2022, 10, 1022110.