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Original Research Article

Acute kidney injury in hospitalized children with dengue infection: A tertiary care hospital study

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Abstract

Background: Dengue viral infection (DVI) is a prevalent arthropod-borne illness, particularly common in tropical regions, manifesting in various clinical presentations ranging from undifferentiated fever to severe hemorrhagic fever and shock. Despite its recognition, acute kidney injury (AKI) remains a lesser-known complication associated with DVI. This study aimed to investigate the incidence of AKI among pediatric patients diagnosed with DVI and analyze its clinical implications.

Materials and Methods: This cross-sectional observational study was conducted in the Department of Pediatrics at a Tertiary Care Hospital. A total of 202 pediatric patients aged 6 months to 18 years diagnosed with DVI were enrolled in the study. Demographic data, clinical characteristics, and AKI incidence were analyzed. AKI severity was classified according to the Kidney Disease: Improving Global Outcomes (KDIGO) criteria.

Results: Among the participants, 11.4% were diagnosed with AKI. Patients with multi-organ dysfunction syndrome (MODS) tended to have longer hospital stays, indicating the severity of their condition. Demographic analysis revealed vulnerabilities among children, particularly males and urban residents. The prevalence of AKI underscored the importance of vigilant monitoring of renal function in pediatric DVI cases.

Conclusion: The study highlighted the significant prevalence of AKI in pediatric patients with DVI, emphasizing the importance of early recognition and management to improve outcomes. Further research is warranted to explore preventive measures and optimize clinical management strategies for this vulnerable group.

Keywords: Dengue viral infection, Acute kidney injury, Pediatric patients, Tropical regions, Arthropod-borne illness, Clinical implications.

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1. Introduction

Dengue epidemic has become a significant public health concern since 2000 affecting new regions and intensifying in regions affected already. Bangladesh, India, Indonesia, Maldives, Myanmar, Sri Lanka, Thailand and Timor-Leste reported cases in 2003 wherein cyclical epidemics occurred more frequently in India, Bangladesh and the Maldives.[1] Currently, approximately 2.5 billion individuals, constituting 40% of the global population, reside in regions where there is a risk of dengue transmission.[2] Among these populations, children emerge as the most vulnerable demographic, experiencing a disproportionate burden of morbidity and mortality.[3,4] While dengue is commonly associated with fever, headache, rash, and muscle pain, its manifestations can range from mild flu-like symptoms to severe hemorrhagic fever and shock syndrome. One of the lesser-known complications of dengue infection, but one with potentially serious consequences, is AKI.[5] AKI denotes a sudden decline in kidney function, typically occurring within a timeframe of 48 hours. This is defined by either an absolute increase in serum creatinine (SCr) levels of ≥0.3 mg/dL or a percentage increase of ≥50% from baseline, or a reduction in urine output to less than 0.5 mL/kg/h for a duration of ≥6-12 hours.[4,5] In the context of dengue infection, AKI can occur due to various mechanisms, including direct viral invasion of renal tissues, immune-mediated injury, dehydration secondary to fever and vomiting, and systemic vascular leakage leading to hypovolemia.[5] Despite the growing recognition of AKI as a complication of dengue infection in adults, there remains a paucity of data on its prevalence, clinical characteristics, and outcomes in pediatric patients. Understanding the

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epidemiology and clinical features of AKI in children with dengue infection is essential for early recognition, prompt management, and improved outcomes. This study aims to provide an overview of the current understanding of AKI in hospitalized children with dengue infection. It will explore the pathophysiology of AKI in the context of dengue, discuss the clinical implications, highlight the challenges in diagnosis and management, and underscore the need for further research to elucidate optimal strategies for prevention and treatment.

2. Material and Methods

This cross-sectional observational study was conducted in the Department of Pediatrics at a tertiary care hospital. The study was issued ethical clearance from the Institutional Ethics Committee.

All patients diagnosed with dengue infection and admitted to hospital during a six-month period from July to December 2023 were eligible for enrollment in the study after obtaining proper consent from their parents or guardians.

2.1. Inclusion criteria

All patients aged 6 months to 18 years who meet the WHO criteria of dengue fever, i.e., clinical features plus either NS1 positive or dengue IgM positive or both Dengue IgM and IgG positive patients admitted to Tertiary Hospital.

2.2. Exclusion criteria

Children with pre-existing renal disease and those with only a single-positive result for dengue IgG.

2.3. Methodology

Assessment involved a detailed history and physical examination of all patients within the age range of 6 months to 18 years diagnosed with dengue infection. Blood samples were collected to assess renal function using tests such as blood urea and creatinine, serum electrolytes, complete blood count, serum albumin, total serum protein, CPK, LDH, and serum cholesterol. Urine samples were also obtained for assessment of urinary sodium, urinary potassium, urinary creatinine, urinary urea, and urinary albumin levels. Additionally, ultrasound of the abdomen, kidneys, ureters, and bladder was performed. All the aforementioned investigations were readily available at the hospital. Patients were considered to have AKI as per the KDIGO guidelines.

The primary objective of this study was to investigate the incidence of AKI in children aged 6 months to 18 years diagnosed with dengue infection. Secondary objectives included studying the severity of AKI at the time of presentation according to KDIGO staging, assessing the incidence of prerenal and intrinsic AKI using Fractional Excretion of Sodium (FENa), examining the involvement of other organs in patients with dengue infection (MODS), and evaluating the outcome of management offered. Data collection for each patient included gender, demographic information, age, clinical manifestations, treatment received (intravenous fluids, inotropes/vasopressors, need for dialysis/RRT), medical history of any underlying diseases (co-morbidities, obesity, hypertension, diabetes mellitus, etc.), history of dengue infection, clinical course, and final outcome (improved, death, loss to follow-up).

3. Results

In this section, the results of the study will be described:

Table 1: Demographic characteristics of study children

		No.	%age
Age (Years)	< 5 Years	27	13.4
	5-10 Years	50	24.8
	10-15 Years	69	34.2
	≥ 15 Years	56	27.7
Gender	Male	134	66.3
	Female	68	33.7
Residence	Rural	59	29.2
	Urban	143	70.8
Mean±SD (Range)=10.9±4.69 (6 Months to 18 Years)			

Table 1 presents the demographic characteristics of the study children. The age distribution shows that 27 children (13.4%) were under 5 years old, 50 children (24.8%) were between 5 and 10 years old, 69 children (34.2%) were between 10 and 15 years old, and 56 children (27.7%) were 15 years or older. In terms of gender, there were 134 male participants (66.3%) and 68 female participants (33.7%). Regarding residence, 59 children (29.2%) were from rural areas, while 143 children (70.8%) were from urban areas. The mean age of the participants was 10.9 years, with a standard deviation of 4.69 years, ranging from 6 months to 18 years.

Table 2: Incidence of AKI in study children

AKI	No.	%age
Present	23	11.4
Absent	179	88.6
Total	202	100

Table 2 presents the incidence of AKI in the study children. Out of a total of 202 participants, 23 children, constituting 11.4% of the sample, were found to have AKI.

Table 3: Severity of AKI according to KDIGO staging

KDIGO Staging of AKI	No.	%age
Stage 1	19	9.4
Stage 2	4	2.0
Stage 3	0	0.0
Total	23	11.4

Table 3 presents the severity of AKI categorized according to the KDIGO staging criteria. Among the observed cases, 19 individuals, constituting 9.4% of the total,

were classified under Stage 1 AKI. Additionally, 4 cases, representing 2.0% of the total, fell into Stage 2 AKI. Notably, no cases were identified as Stage 3 AKI in the observed sample. Overall, the table summarizes a total of 23 cases, encompassing 11.4% of the analyzed population, across the various stages of AKI as per the KDIGO classification system.

The incidence of prerenal AKI and intrinsic AKI was evaluated using the FENa. Among the total of 23 AKI cases, 7 (30.4%) were identified as having prerenal AKI (FENa <1%) while 16 (69.6%) were characterized as intrinsic AKI (**Figure 1**). The analysis encompassed a total of 23 cases, representing the entirety of the sample. Among the total 202 children assessed, 9 children, constituting 4.5% of the sample, were diagnosed with MODS (**Figure 2**) 6 children with MODS also had AKI representing 66.6% of population (fig 3) Furthermore, 6 (26.6%) out of 23 who were diagnosed with AKI developed MODS, whereas 3(1.67%) out of 179 who didn't have AKI developed MODS with relative risk (RR) of developing MODS >1 which is clinically significant.

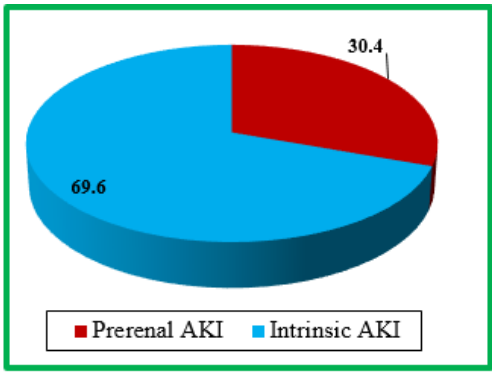

Figure 1: Incidence of prerenal AKI and intrinsic AKI using FENa

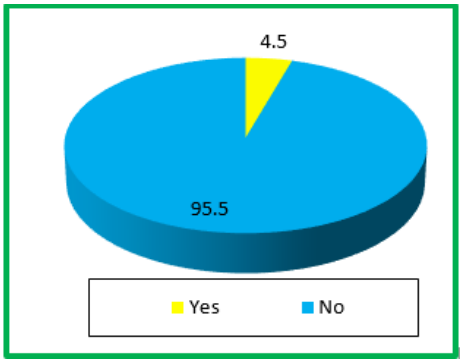

Figure 2: Incidence of multi organ dysfunction syndrome (MODS) in study children

Table 4 presents the hospital stay duration in days for the study children. Out of a total of 202 participants, 58 children (28.7%) had a hospital stay ranging from 1 to 5 days, within which AKI constituted 5 children (8.7%). The majority of participants, accounting for 93 children (46.0%), had a hospital stay between 6 to 10 days, wherein children with AKI constituted 6 (6.5%). Additionally, 45 children (22.3%) stayed in the hospital for 11 to 15 days, wherein AKI children constituted 9 (20%). Only 6 children (3.0%) had a hospital stay exceeding 15 days, where 3 children (50%) had AKI. The mean hospital stay duration was calculated to be 8.1 days with a standard deviation of 3.65 days, ranging from 1 to 19 days, whereas for children with AKI the mean duration was 8.5 days with a standard deviation of 4.35 days ranging from 1 to 17 days.

Table 5 presents the final outcomes of the study children, indicating the number and percentage of participants in each outcome category. Among the 202 children, 2 children (8.6%) out of 23 with AKI had mortality which was clinically significant with relative risk of death (RR) being >1. There was no death due to non-AKI conditions. The majority of participants, comprising 195 children (96.5%), showed improvement in their health status. Additionally, 5 children (2.5%) were classified as "LAMA" (Left Against Medical Advice).

Table 4: Hospital stay (Days) of study children

Hospital Stay (Days)	No.	%age	AKI	%age	Non-AKI	%age
1-5 Days	58	28.7	5	8.7	53	91.3
6-10 Days	93	46.0	6	6.5	87	93.5
11-15 Days	45	22.3	9	20	36	80
> 15 Days	6	3.0	3	50	3	50
Total	202	100	23	11.4	179	88.6
Mean±SD (Range)=8.1±3.65 (1-19 Days)						

Table 5: Final outcome of study children

Outcome	No.	%age
Death	2	1.0
Improved	195	96.5
LAMA	5	2.5
Total	202	100

4. Discussion

Dengue viral infection (DVI) has emerged as a prominent arthropod-borne illness, particularly prevalent in tropical regions. Manifesting across a spectrum of clinical presentations, DVI encompasses symptoms ranging from undifferentiated fever to severe hemorrhagic fever and shock, often accompanied by multi-organ dysfunction. Despite its recognition, AKI remains a lesser-known complication associated with DVI. While existing studies have reported varying incidences of AKI in DVI cases among pediatric populations, precise incidence rates remain elusive primarily due to the retrospective nature of most investigations conducted thus far. The present study was objectively conducted to examine the incidence of AKI among children aged 6 months to 18 years diagnosed with dengue infection. The age distribution of patients with dengue infection demonstrated a notable proportion of pediatric cases, with a substantial number of children under 15 years old. Specifically, 13.4% of patients were under 5 years old, 24.8% were between 5 and 10 years old, and 34.2% were between 10 and 15 years old. This observation aligns with existing literature highlighting children as a vulnerable population for dengue infection due to factors such as immature immune systems, increased exposure to mosquito vectors, and behaviors placing them at higher risk of mosquito bites.[6,7] The mean age of participants in our study was recorded as 10.9 years, with a standard deviation of 4.69 years, indicating a predominantly young population afflicted by dengue infection. This demographic observation resonates with the findings of Agarwal et al., (2010) whose study reported a mean age of 10.25 ± 10.9 years among their patient cohort.[8] Similarly, in the study by Senthil et al., (2018) it was noted that the most common age of presentation was above 10 years, with a mean age of admission recorded as 8.9 years, aligning closely with the demographics observed in our investigation.[9] These parallel findings underscore the significance of targeted preventive strategies such as vaccination campaigns, rigorous vector control initiatives, and community-based interventions. By focusing efforts on reducing mosquito breeding sites and fostering heightened awareness among both children and caregivers, we can effectively mitigate the burden of dengue infection within susceptible populations.[10,11] Moreover, the gender distribution among dengue patients in our study revealed a notable predominance of males, comprising 66.3% of participants compared to 33.7% females. This observation aligns with findings from studies conducted by Rathod et al. (2018) and Khan et al. (2021), both of which also reported a male predominance among pediatric patients with Dengue Viral Infection (DVI).[12,13] The underlying reasons for this gender disparity in dengue cases may stem from variances in outdoor activities, occupational exposures, and behavioral factors influencing mosquito exposure. Regarding residence, a majority (70.8%) of dengue patients were from urban areas compared to 29.2% from rural areas, which is consistent with Gupta et al and Nayak et al.[14,15] Urban environments often provide favorable breeding grounds for Aedes mosquitoes, the primary vectors for dengue transmission, due to factors such as population density, inadequate waste management, and water storage practices, contributing to higher disease burden in urban settings.

AKI in children is a significant health concern that requires prompt recognition and management to prevent adverse outcomes. In our study, we observed that out of a total of 202 participants, 23 children, representing 11.4% of the sample, were diagnosed with AKI. This finding underscores the importance of vigilance in monitoring renal function in pediatric populations, particularly in settings where risk factors for AKI may be prevalent. The prevalence of AKI in our study aligns with existing literature, which reports varying rates of AKI among pediatric populations depending on the underlying etiology, patient demographics, and geographical location. For instance, a study by Sultana et al. (2020) found that the incidence of AKI in hospitalized children was 9.8%, with higher rates observed in critically ill patients.[16] A systematic review by Sutherland et al. (2019) reported a pooled prevalence of AKI in children of approximately 19.6%, further highlighting the burden of this condition in pediatric healthcare.[17] In our study, the majority of participants (88.6%) did not present with AKI. While this is reassuring, it is essential to recognize the secondary causes including sepsis, nephrotoxic medications, and hypovolemia, among others. Therefore, ongoing monitoring of renal function and prompt intervention in at-risk pediatric populations remain critical aspects of clinical care.

According to the KDIGO classification system, our study identified 19 individuals (9.4%) classified under Stage 1 AKI, with 4 cases (2.0%) falling into Stage 2 AKI. Remarkably, no instances of Stage 3 AKI were identified in our observed sample. It is noteworthy that the distribution of AKI severity according to KDIGO criteria varies across studies, as evidenced by the findings of Griffin BR et al., Diptyanusa A et al., and Wang C et al. Griffin BR et al. reported that out of a total of 297 patients in their study, 18.3% developed Stage 1 AKI, while 52 patients (3.2%) developed Stage 2-3 AKI.[18] Similarly, Diptyanusa A et al. observed that 83.1% of their patients were classified as Stage 1 AKI, with 4.2% as Stage 2 AKI, and 12.7% as Stage 3 AKI.[19] Additionally, Wang C et al. documented that among their patient cohort, 35.1% developed AKI, with 43.5%, 18.8%, and 37.7% classified as Stages 1, 2, and 3 AKI, respectively.[20] The variability in the distribution of AKI severity across these studies may be attributed to differences in patient demographics, comorbidities, study designs, and healthcare settings. Such variations underscore the importance of contextualizing study findings within the broader landscape of AKI research and clinical practice, facilitating a comprehensive understanding of AKI epidemiology and its implications for patient care. As observed in numerous tropical infections, dengue infection is

commonly linked with the occurrence of multiple organ dysfunction, encompassing the liver, muscles, heart, brain, and kidneys.

Renal injury encompasses pre-renal failure, intrinsic renal disease involving vascular insults, and obstructive uropathies. Pre-renal AKI typically arises from conditions where the kidney remains structurally intact, and renal function swiftly normalizes upon restoration of adequate renal perfusion. Conversely, acute tubular necrosis (ATN) involves intrinsic injury to the kidney, necessitating repair and recovery before renal function restores to baseline. In our study, we utilized the FENa method to assess the incidence of prerenal AKI and intrinsic AKI. Among the AKI cases scrutinized, 30.4% were categorized as prerenal AKI, while 69.6% were deemed intrinsic AKI.[21] These findings are consistent with a comprehensive study of adult patients, wherein pre-renal AKI accounted for 21% of cases and ATN emerged as the predominant cause, affecting 45% of patients, thus echoing the trends observed in our investigation. Additionally, literature underscores the significance of hypoxia/ischemia and nephrotoxin-induced AKI as pivotal contributors to AKI in neonates, children, and adolescents.[22,23] In our study involving 202 assessed children, 4.5% were diagnosed with Multiple Organ Dysfunction Syndrome (MODS), and MODS was more in AKI group underscoring its clinical significance in pediatric populations. This minority prevalence suggests the severity and complexity of MODS cases within our cohort. Regarding hospital stays, our findings revealed varying durations, with a substantial proportion of participants staying between 6 to 10 days (46.0%). This distribution, along with mean hospital stay duration of 8.1 days and a standard deviation of 3.65 days, highlights the variability in the length of hospitalization experienced by pediatric patients. Notably, patients diagnosed with MODS and AKI tended to have longer hospital stays, reflecting the challenges associated with managing this severe condition and the increased need for intensive medical care.[16,24,25] Tragically, mortality was observed in 1.0% of the total participants, with all death cases associated with multi-organ failure, severe dengue, and AKI stage 2. This aligns with previous research indicating a higher risk of adverse outcomes, including mortality, among patients with MODS and AKI.[16,26] AKI has been associated with increased morbidity and mortality rates in pediatric patients, as well as a higher risk of progression to chronic kidney disease (CKD) in the future (Basu et al., 2020).[27] Therefore, early detection and management of AKI are essential to mitigate these adverse effects and improve patient outcomes. Our findings are also consistent with Malhi et al.'s study, which reported an overall fatality rate of 1.1% and highlighted multiple-organ dysfunctions as independently associated with prolonged hospitalization.[28] This convergence of results underscores the robustness of our findings and emphasizes the critical importance of early recognition and appropriate management of MODS and its associated complications in pediatric care settings.

5. Conclusion

The study highlighted a significant prevalence of AKI among pediatric patients with dengue viral infection (DVI), underscoring the importance of early recognition and management to improve outcomes. Patients diagnosed with multi-organ dysfunction syndrome (MODS) experienced prolonged hospital stays, indicating the severity of their condition and the need for intensive medical care. Demographic analysis revealed vulnerabilities among children, particularly males and urban residents, emphasizing the importance of targeted preventive strategies. Despite variability in AKI incidence rates and severity classifications, the findings stress the necessity of vigilant monitoring of renal function in pediatric DVI cases. Overall, the study contributes to our understanding of DVI epidemiology and clinical implications, guiding efforts to mitigate disease burden and improve patient care in pediatric populations. Further research is needed to explore preventive measures and optimize clinical management strategies for this vulnerable group.

6. Source of Funding

None.

7. Conflict of Interests

All authors declare that they have no conflict of interests.

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