

Study of acute kidney injury in dengue positive patients at a tertiary hospital

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Abstract

Background: Dengue is a mosquito-borne viral infection that causes significant morbidity in endemic regions. Various patterns of renal involvement have been observed in patients with dengue that include increase in serum creatinine level, AKI, acute tubular necrosis, hemolytic uremic syndrome, proteinuria, glomerulopathy, and nephrotic syndrome. Present study was aimed to study renal complications in dengue positive patients at a tertiary hospital. **Material and Methods:** Present study was prospective, comparative study, conducted in patients of age > 18 years, either gender, diagnosed with dengue viral fever, having confirmed diagnosis of Dengue Fever with positive IgM and/or NS1 Ag, had acute kidney injury on admission or during treatment. Results: Incidence of AKI in present study was 16.01 %. According to severity of dengue disease among total dengue cases, 69.79 %, 26.89 % & 3.32 % patients with dengue fever, dengue hemorrhagic fever & dengue shock syndrome. In patients with AKI incidence of dengue fever, dengue hemorrhagic fever & dengue shock syndrome was 9.09%, 25.84 %, 81.82 %. Among AKI cases, majority were from > 60 years age (47.17 %), were male (60.38 %). Male to female ratio with AKI in present study was 1.52:1. Overall, 50.94 %, 28.3 % & 20.75 % incidence noted in AKI stage I,II & III respectively. Stage I AKI was common in dengue fever (76.19 %) & in dengue hemorrhagic fever (47.83 %), while stage 3 AKI was common in dengue shock syndrome (66.67 %). Majority patients had complete recovery (69.81 %), while 5 patients (9.43 %) had partial recovery. 17 patients (32.08 %) required Renal replacement therapy. Mortality was noted in 11 patients (20.75 %). Conclusion: Acute kidney injury in patients of dengue was noted in male gender, advanced age (> 60 years) & dengue shock syndrome.

Keywords: acute kidney injury, dengue fever, dengue shock syndrome. Renal replacement therapy

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Introduction

Dengue is a mosquito-borne viral infection that causes significant morbidity in endemic regions. Globalization, increased air travel, lack of effective mosquito control measures and unplanned urbanization have led to an increase in its incidence with expansion of its geographic and demographic distribution.¹ Infection with a dengue virus serotype can produce a spectrum of clinical illness, ranging from asymptomatic or may cause

undifferentiated febrile illness (viral syndrome), DF, or dengue hemorrhagic fever (DHF) including dengue shock syndrome (DSS).²

Similar to other tropical infections, dengue infection is associated with multiple organ dysfunction involving liver, muscles, heart, brain, and kidneys.³ In majority of patients, dengue is manifested as a mild self-limiting disease, however, some of the patients may also require critical clinical management in intensive care unit (ICU) and the progression to severe clinical manifestations is usually unpredictable.⁴

Various patterns of renal involvement have been observed in patients with dengue that include increase in serum creatinine level, AKI, acute tubular necrosis, hemolytic uremic syndrome, proteinuria, glomerulopathy, and nephrotic syndrome.⁵ Several mechanisms have been proposed to account for the etiopathogenesis of dengue fever-induced AKI, including direct action by the virus, hemodynamic instability, rhabdomyolysis, hemolysis and acute glomerular injury.⁶ Present study was aimed to study renal complications (in terms of acute kidney injury) in dengue positive patients at a tertiary hospital.

Material And Methods

Present study was prospective, comparative study, conducted in department of general medicine, at VMMC & Safdarjung Hospital, New Delhi, India. Study duration was of 2 years (January 2021 to December 2022). Study approval was obtained from institutional ethical committee.

Inclusion criteria

- Patients of age > 18 years, either gender, diagnosed with dengue viral fever, having confirmed diagnosis of Dengue Fever with positive IgM and/or NS1 Ag, had acute kidney injury on admission or during treatment, willing to participate in present study

Exclusion criteria

- Patients with pre-existing substantial chronic liver, kidney or heart disease ,
- Patients with history of hematological disorders
- Known cases of diabetic nephropathy and hypertensive nephropathy.
- Infectious diseases like malaria and enteric fever.
- History of treatment with NSAIDs.

Study was explained to patients in local language & written consent was taken for participation & study. A detailed history (demographic, symptoms) was taken and careful clinical examination was performed. Routine investigations such as hemoglobin, total leucocyte count (TLC) and differential leucocyte count (DLC), platelet count, peripheral blood smear for malarial parasite, hematocrit (HCT), liver function tests (LFT), blood urea, and serum creatinine were done. Other investigations like malarial antigen, IgM antibodies and Widal test for typhoid, and X-ray chest and ultrasonography (USG) of abdomen were also done according to the clinical conditions of the patients.

According to the criteria from the World Health Organization (WHO),² patients who have DF and hemorrhagic manifestations, low platelet count, and objective evidence of leaky capillaries (20% elevation in hematocrit, lower serum albumin, and pleural or other effusions) were classified as having DHF (WHO classification, DHF grades I/II).

Based on the Acute Kidney Injury Network (AKIN) criteria, the patients were evaluated for the diagnosis of AKI based on an increase in serum creatinine or urine output.

Table 1: Staging of AKI according to kidney disease improving global outcome (KDIGO) 2012 criteria ⁷

Stage	Serum creatinine criteria	Urinary Output Change
1	≥ 1.5-fold increase of serum creatinine or increase of ≥ 0.3 mg/dL	< 0.5 mL/kg/hr for 6–12 hr
2	≥ 2.0-fold increase of serum creatinine	< 0.5 mL/kg/hr for ≥ 12 hr
3	≥ 3.0-fold increase of serum creatinine or serum creatinine ≥ 4.0 mg/dL with acute increase of ≥ 0.5 mg/dL or Renal Replacement Therapy	< 0.3 mL/kg/hr for ≥ 24 hr or anuria for ≥ 12 hr

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Statistical analysis was done using descriptive statistics.

Results

During study period, among 331 patients having confirmed diagnosis of Dengue Fever took treatment at our hospital, acute kidney injury was noted in 53 cases, incidence of AKI in present study was 16.01 %. According to severity of dengue disease among total dengue cases, 69.79 %, 26.89 % & 3.32 % patients with dengue fever, dengue hemorrhagic fever & dengue shock syndrome. In patients with AKI incidence of dengue fever, dengue hemorrhagic fever & dengue shock syndrome was 9.09%, 25.84 %, 81.82 %.

Table 2: Classification of severity of dengue patients developing AKI

Severity of Dengue patients	Total Patients (n=231)	Patients developing AKI (n=53)	Percentage (AKI cases/dengue severity)
Dengue fever	231 (69.79 %)	21 (39.62 %)	9.09
Dengue haemorrhagic fever	89 (26.89 %)	23 (43.4 %)	25.84
Dengue shock syndrome	11 (3.32 %)	9 (16.98 %)	81.82
Total	331	53	16.01

Among AKI cases, majority were from > 60 years age (47.17 %), were male (60.38 %). Male to female ratio with AKI in present study was 1.52:1.

Table 3: General characteristics

Characteristics	No. of patients	Percentage
Age groups (in years)		
19-40 years	12	22.64
41-60 years	16	30.19
>60 years	25	47.17
Mean age (mean ± SD)	57.83 ± 12.03	
Gender		
Male	32	60.38
Female	21	39.62

Overall, 50.94 %, 28.3 % & 20.75 % incidence noted in AKI stage I,II & III respectively. Stage I AKI was common in dengue fever (76.19 %) & in dengue hemorrhagic fever (47.83 %), while stage 3 AKI was common in dengue shock syndrome (66.67 %). Severity of dengue infection can be correlated with higher grades of AKI.

Table 4: Frequency and severity of AKI in dengue viral infection

Stage of AKI	AKI at presentation/developed during treatment			Total (n=53)
	Dengue fever (n=21)	Dengue hemorrhagic fever (n=23)	Dengue shock syndrome (n=9)	
I	16 (76.19 %)	11 (47.83 %)	0	27 (50.94 %)
II	3 (14.29 %)	9 (39.13 %)	3 (33.33 %)	15 (28.3 %)
III	2 (9.52 %)	3 (13.04 %)	6 (66.67 %)	11 (20.75 %)
Total	21	23	9	53

In present study, majority patients had complete recovery (69.81 %), while 5 patients (9.43 %) had partial recovery. 17 patients (32.08 %) required Renal replacement therapy. Mortality was noted in 11 patients (20.75 %).

Table 5: Patients' Renal outcome at discharge

Outcome	No. of patients (n=53)	Percentage
Complete recovery	37	69.81
Partial recovery	5	9.43
Mortality	11	20.75
Renal replacement therapy required	17	32.08

Discussion

Rapid and accurate diagnosis of dengue in the acute phase of illness is important for initiation of therapy as well as for early enhancement of epidemic control measures especially in low endemic areas. Diagnosis is done by detection of specific IgM antibody by ELISA which rise after 4-5 days of fever. Tests to detect NS1 antigen can also be performed but are less reliable.^{8,9}

Supportive treatment was the mainstay mode of management. Raised hematocrit, thrombocytopenia, leucopenia and atypical lymphocytes in the peripheral smear will aid in early diagnosis of Dengue infection.¹⁰ Where some known features are still manifesting, few atypical features are noted from several parts of the world. So a continuous sero-epidemiological surveillance and timely interventions are needed to identify the cases, so that its complications, outbreak and mortality can be minimized.

In dengue, complications such as plasma leakage, hemorrhage, and organ impairment are prevented by early case detection which can be done by clinical suspicion with laboratory evidence and early treatment. With early recognition and prompt treatment, dengue-related morbidity and mortality can be reduced.¹¹

Using the AKIN criteria in a retrospective analysis, Khalil et al.,¹² identified AKI in 13.3% of a series of patients with dengue confirmed by the presence of IgM antibodies, independent of the severity of disease; 64.8% of the patients were in Stage 1, 18.3% Stage 2 and 16.9% Stage 3 of the disease. In another study, the RIFLE classification was used to investigate the occurrence of AKI in patients with tropical acute febrile disease. The results showed that the incidence of AKI among patients with dengue upon admission to the hospital was 35.7%.¹³

In study by Sharma A et al.,¹⁴ 60 patients were taken in which 45 (75%) were males and 15 (25%) were females. Mean creatinine on day 1 was 0.86 ± 0.26 in the patients without renal failure as compared to 1.62 ± 0.31 in the patients with renal failure. Mean creatinine at day 14 was 44.56 ± 7.2 compared to 47.64 ± 6.4 in the patients without and with renal failure, respectively.

Amit K et al.,¹⁵ studied 320 patients positive for dengue IgM, 48 patients (15%) were found to develop AKI. Out of the total 48 patients developing AKI, 26 patients presented with Dengue fever, 16 were with Dengue Hemorrhagic Fever and 6 presented with dengue shock syndrome. Out of the 48 patients diagnosed with AKI, 34 patients fall under KDIGO criteria I, 10 patients fall under KDIGO II, 4 patients fall under KDIGO III.

Batra N et al.,¹⁶ noted that majority of the patients were males 57.5% and the male to female ratio was 1.35:1. Most of the patients were aged between 31 and 50 years (40.8%) and the mean age was 42.23 ± 16.28 years. The majority of the patients (72.5%) had DF, 13.3% of the patients had dengue fever with warning signs and 14.2% of the patients had severe dengue. The prevalence of AKI was 27.5% in patients with dengue fever. Other than AKI, Acute respiratory distress syndrome (ARDS) (11.7%), Multiple Organ Dysfunction Syndrome (MODS) (3.3%), and sepsis (0.8%) were the complications noted. The majority of the patients (83.3%) improved and were discharged and mortality was noted in 16.7% of the patients.

Diptyanusa A, et al.,¹⁷ studied 1,484 patients, 71 categorized into the AKI group. The prevalence of AKI was 4.8%. In the AKI group, the predominant age range was 18–40 years (71.8%), with a female to male ratio of 1:2.7. These patients showed significantly ($P < 0.05$) higher proportions of altered consciousness, dyspnea, low mean arterial blood pressure, high-grade fever, major bleeding, severe thrombocytopenia, hypoalbuminemia, severe transaminitis, coagulopathy, metabolic acidosis, rhabdomyolysis, proteinuria, hematuria, and pyuria. Older age, male sex, diabetes mellitus, obesity, severe dengue, and coexisting bacterial infection were significant associated factors for AKI in dengue by multivariate analysis.

The provision of adequate care to patients with suspected dengue in primary care settings requires effective clinical evaluation, laboratory testing, and qualified professionals who know how to recognize warning signs and give appropriate guidance to prevent expanded dengue.¹⁸

Timely access to proper treatment for dengue patients by primary healthcare professionals not only reduces the number of unnecessary hospital admissions but also lowers fatality rates below 1%.¹⁹ No specific preventive strategies are available for AKI apart from adequate fluid resuscitation, management of dengue-associated coagulopathies, and avoidance of nephrotoxic agents. Inotropic support is of benefit. Dialysis is certainly beneficial, although the exact role of dialysis remains controversial.¹²

Conclusion

Acute kidney injury (AKI) in patients of dengue was noted in male gender, advanced age (> 60 years) & dengue shock syndrome. AKI in dengue is likely to increase health-care burden that underscores the need for clinician's alertness to this highly morbid and potentially fatal complication for optimal prevention and management.

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