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Original Article

Prevalence of Acute Renal Failure in Dengue at a Tertiary Care Hospital in J and K

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Abstract

Background: Dengue has emerged globally as the most frequent and medically relevant viral infection transmitted by a mosquito bite. Acute kidney injury is a known complication of dengue. Patients who suffer from dengue have various patterns of clinical presentation with unpredictable clinical course, ranging from clinically in apparent forms to severe bleeding and shock, eventually resulting in death that occurs in dengue shock syndrome or dengue hemorrhagic fever.

Aim: The aim of the study was to study the prevalence of acute renal failure in dengue disease at a tertiary hospital.

Materials and Methods: This study was a prospective observational and one point analysis. The study group comprised dengue patients admitted in GMC Kathua, J and K.

Results: A total of 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.

Key words: Acute renal failure, Dengue, Creatinine

INTRODUCTION

Dengue disease has emerged globally as the most frequent and medically relevant viral infection transmitted by a mosquito bite. Acute kidney injury (AKI) is a serious complication of dengue.[1] The clinical spectrum of dengue ranges from selflimiting illness to lifethreatening dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS)[2,3] Acute renal failure is a rare but well recognized complication of dengue infection.[4]

This disease is caused by four closely related serotypes (DENV-1, DENV-2, DENV-3, DENV-4) of dengue virus, an arbovirus belonging to "*Flaviviridiae*" family. This virus is transmitted among humans by the bite of infective female mosquitos.[5] The vector mosquito first appeared in Africa, then disseminated together with the slave trade from the fifteenth to nineteenth centuries. The disease is transmitted through mosquito bites from female *Aedes Aegypti* infected with the virus, which require blood meals to obtain the protein needed for oviposition. This mosquito is a domestic vector with diurnal anthropophilic and zoophilic habits. The virus multiplies inside the mosquito's digestive system then spreads to different tissues. After an extrinsic incubation period of 7–11 days, on average, the virus reaches the mosquito's salivary glands; the period of virus transmission then begins and lasts throughout its lifetime.[6]

Patients who suffer from dengue have various patterns of clinical presentation with unpredictable clinical progression and outcomes, ranging from clinically in apparent forms to severe bleeding and shock, eventually resulting in death that occurs in DSS/DHF.[1] Incidence of DHF/DSS varies from 0.3% to 3.3% in different populations. Reinfection with a different serotype of dengue virus is associated with severe clinical manifestations, likely due to cross-reactive antibodies.[7] The first manifestation of classic dengue is sudden onset of fever, accompanied by headache, prostration, myalgia, arthralgia, retro-orbital pain, and non-maculopapular but itchy exanthema. In

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Table 1 : Clinical presentation

Clinical parameters	Dengue fever (*n*=42)	DSS/DHF (*n*=18)	Total (*n*=60)	*P*-value
Renal Failure	1	9	10	*P*<0.007
Hematuria	1	3	4	*P*<0.004
Proteinuria	2	4	6	*P*<0.003

Table 2: Clinical & Lab parameters

Variables	Renal Failure	
	Absent (*n*=50)	Present (*n*=10)
Urea	28.41±8.4	56.74±8.40
Creatinine (Day 1)	0.86±0.26	1.62±0.31
Creatinine (Day 14)	0.67±0.12	0.90±0.14
Hematocrit (%)	44.56±7.2	47.64±6.4
Platelet (cells/CMM)	81306±64322.24	30946.71±24686.15
Bilirubin (mg/dl)	1.12±1.02	1.89±2.61
Sodium (mmol/l)	134.80±14.30	130.31±6.76
Systolic blood pressure (mm hg)	112.84±12.84	90.81±8.71
Diastolic blood pressure (mm hg)	73.044±7.32	64.32±9.60

addition, anorexia, nausea, vomiting and diarrhea might be present in some of the patients. The initial symptoms in DHS/DSS are similar to those of the classic dengue fever that is followed by bleeding and/or cavity effusion, hemodynamic instability, and/or shock. The hemorrhagic manifestations are associated with decrease in platelet levels.

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.[8,9] AKI is a significant, poorly studied, and complication that occurs due to dengue. The data available are heterogeneous and mostly originate from retrospective case series and case reports.

Viral infection-induced renal injury are due to various mechanisms like an immune-mediated mechanism triggered by viral antigens that are bound to glomerular structures, direct cytopathic effect of the viral protein on the glomerulus and tubules, tissue injury caused by immune complexes composed of viral antigens and antiviral antibodies and damage caused by inflammatory mediators released in response to the glomerular or tubular cytopathic effects of the viral antigens.[10]

Rhabdomyolysis is considered a rare complication of dengue. Histological abnormalities in kidney biopsy samples, muscle weakness, myalgia, and elevated serum creatine-kinase levels have been obtained in different populations of dengue patients.[11] The pathogenesis of dengue-associated rhabdomyolysis has not been well studied.

The aim of this study was to study about different clinical presentations, frequency, and severity of acute renal failure in dengue.

MATERIALS AND METHODS

This study was performed from August 2020 to January 2022 at Govt. Medical College Kathua, J and K. A total of 70 patients were enrolled for this study after qualifying inclusion/exclusion criteria. The diagnostic criteria of dengue illness were febrile illness associated with one of the following laboratory confirmation tests: (1) Detection of dengue specific IGM antibody or (2) Detection of NS1 Antigen. Exclusion criteria were patients having IgG antibody positive against the dengue virus and patients of chronic kidney disease.

DHF/DSS was labeled in the patients who were having dengue fever and hemorrhagic manifestation, low platelet count, elevation in hematocrit, pleural effusion or ascitis or shock. Patients were diagnosed as having acute renal failure if serum creatinine was more than 1.2 mg/dl.

Study Design

It is an observational prospective study of demographic data of age, gender with severity of dengue infection of each patient recorded. All baseline blood investigations were done at first hospital visit. Proteinuria was defined as *Urinary Protein* more than **1+** by Dipstick Test and more than 5 RBC/HPF was defined as *Microscopic hematuria*.

RESULTS

A total of 60 patients were taken in which 45 (75%) were males and 15 (25%) were females. Among the total of 60 patients, 42 (70%) had dengue fever and 18 (30%) had DHF/DSS. The patients with DHF/DSS were more susceptible to develop renal failure as compared to dengue fever group. Mean urea level was 28.41 ± 8.4 in the patients without renal failure as compared to 56.74 ± 8.40 in the patients with renal failure ($P < 0.001$). 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 ($P < 0.001$).

Mean creatinine at day 14 was 44.56 ± 7.2 versus 47.64 ± 6.4 in the patients without/with renal failure, respectively.

In our study, patients with renal failure had higher values of serum bilrubin, lower platelet levels, and higher hemoconcentration. There were no mortality and none of the patient underwent dialysis during hospitalization.

DISCUSSION

Dengue fever along with other tropical infections such as *malaria* and *leptospirosis* has been reported to cause AKI. Classic Dengue fever often presents as self-limiting illness whereas DHF/DSS have been associated with high mortality and morbidity. Renal failure in dengue illness is due to various proposed mechanisms. Dengue causes leakage from capillaries and loss of fluid leading to third space loss which leads to decreased blood flow to kidney and acute tubular necrosis. It also causes rhabdomyolysis, hemolysis and severe DIC which leads to ischemia and multi organ dysfunction. Although rhabdomyolysis is a rare complication of dengue, histological abnormalities in kidney biopsy, myalgia, and muscle weakness have been described in dengue patients. The muscle damage might be cause by direct viral invasion or cytokines. Analysis of renal biopsy samples from patients with severe dengue have shown IgG, IgM, and C3 deposit in Glomeruli, basement membrane thickening and deposition of immune complexes.

In our study, there were statistically significant frequencies of renal failure in DHF/DSS group than dengue fever group. Our findings were consistent with Kuo *et al*.[12] who have showed that patients with DHF/DSS in AKI group had higher mortality and morbidity than those without AKI.

Proteinuria has been associated with the severity of disease and is alleviated in severe dengue. Proteinuria was seen in 10% of patients in our study. Out study was consistent with the study by Eswarappa *et al*.[13] in which proteinuria was seen in 9% patients. There is a wide variability in overall incidence of proteinuria as it was seen as high as 74% in study by Horvath *et al*.[9] meanwhile Garcia *et al*.[14] retrospectively studied 74 patients with dengue fever or DHF who had a platelet count of <125,000/mm^3; the prevalence of proteinuria in this cohort was 30% Meanwhile, hematuria was seen in 6.6% patients.

Limitations

1. Study was a single centered study.
2. Histopathological reports of patients with dialysis were not available.
3. Limited case numbers.
4. There was a lack of long-term follow-up.

CONCLUSION

DHF remains to be viewed as a global issue. Understanding the pathogenesis and validating efficient prevention and control strategy are warranted against dengue invasions to humans. Prediction of the DHF development in the DF patient needs to be closely observed and more clinical manifestations and clinical laboratory tests be considered.

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