

A Study on Acute Kidney Injury in Patients of Dengue Fever in Western Uttar Pradesh Population

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ABSTRACT

Introduction: Dengue fever is a systemic acute viral illness caused by Arbo virus from genus flavivirus highly prevalent in the tropics and subtropics, transmitted by *Aedes (aegypti and albopictus)* mosquito. Pathogenesis of AKI due to dengue include direct action by the virus, hemodynamic instability, rhabdomyolysis, hemolysis and acute glomerular injury. This study was planned to know the incidence and severity of AKI in patients of Dengue fever.

Material and methods: Our study was an observational retrospective study, done in Subharti Medical College, Deptt. Of Medicine, Meerut between July 2017-December 2018. Medical records of 320 Dengue IgM+ patients admitted during this period were studied. Patients were classified into dengue fever, dengue hemorrhagic fever, dengue shock syndrome.

Results: Out of total 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.

Conclusion: Our study concluded that AKI is a major and serious complication, and it is the major cause of Mortality and morbidity in dengue fever.

Keywords: Dengue, AKI

INTRODUCTION

Dengue fever is a systemic acute viral illness caused by Arbo virus from genus flavivirus highly prevalent in the tropics and subtropics.¹ Dengue is serious global health threat by the World Health Organization. It is transmitted by mosquitoes of the genus *Aedes (aegypti and albopictus)*, with *Aedes aegypti* as the main vector.¹ Dengue exhibits various patterns of clinical presentation with unpredictable clinical progression and outcomes, ranging from clinically inapparent forms to severe bleeding and shock, eventually resulting in death. Reinfection with a different serotype is associated with severe clinical manifestations, likely due to cross-reactive antibodies.

Dengue and AKI

AKI is a significant, and poorly studied complication of dengue. 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.² While none of the available evidence patently favors any such mechanisms at the expense of the others, often two or more mechanisms coexist simultaneously in the same

patient.

The data available are heterogeneous and mostly originate from retrospective case series and case reports. The reported frequency of this association shows wide variation in accordance to the different population assessed, severity of dengue, criteria which was used for the diagnosis of AKI and time of evaluation.

The present study was taken to evaluate the incidence and severity of acute kidney injury in dengue fever in Western Uttar Pradesh population.

MATERIAL AND METHODS

Our study was an observational retrospective study. The study was done in Subharti Medical College, Deptt. Of Medicine, Meerut between the period of July 2017-December 2018. Medical records of 320 Dengue IgM+ patients admitted during this period were studied and data regarding the severity of dengue fever, duration of stay, severity of kidney Injury was collected, tabulated and analysed.

Exclusion Criteria include known cases of Chronic Kidney Disease, patients of Chronic liver disease, patients positive for other Rickettsial illnesses like scrub typhus, patients of chronic viral illnesses like Hep C, Hep B and HIV. Dengue fever classification According to severity:³

Dengue Fever

- Acute Febrile illness with >2 of the following:
- Headache
- Retro-orbital Pain
- Myalgia
- Rash
- Hemorrhagic Manifestations
- Leukopenia

Dengue Hemorrhagic Fever

All of the following must be present:

- Fever Lasting 2-7 days, occasionally biphasic
- Hemorrhagic Manifestations with at least one of the

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following –

- A Positive Torniquet test
- B Petechiae ecchymoses or purpura
- C Bleeding from Mucosa, gastrointestinal tract, injection sites, or other locations.
- D Hematemesis or melena

- Thrombocytopenia (<1lac)
- Evidence of plasma leakage manifested by at least one of the following:
 - A - Increase in hematocrit level by 20% for age, sex and population.
 - B - Decrease in hematocrit after volume replacement by >20% of baseline.
 - C - Signs of plasma leakage such as pleural effusion, ascites and hypoproteinemia.

Dengue Shock Syndrome

Criteria for DHF associated with:

- Tachycardia
- Pulse pressure <20mmHg
- Hypotension for age
- Cold Skin
- Restlessness

Laboratory Confirmation

At least one of the following:

- Isolation of dengue virus from serum autopsy samples
- >4 fold change in IgG or IgM antibody specific to dengue virus.
- Detection of dengue virus in tissue, serum or cerebrospinal fluid by immunohistochemistry, immunofluorescence, or enzyme linked immunosorbent assay.

Staging of aki according to kidney disease improving global outcome(kdigo) 2012 criteria:[4]		
Staging	Sr. Creatinine	Urine Output
KDIGO I	Sr. Cr. > .3 mg/dl or increased by 1.5-1.9 folds baseline	<0.5ml/kg/hr for > 6-12 hrs
KDIGO II	Increase in Sr Cr. > 2-2.9 times of baseline	<0.5 ml/kg/hr (for >12 hrs)
KDIGO III	Sr Creat. Increased by >3 times baseline or Sr Cr. >4mg/dl or Hemodialysis	<0.3ml/kg/hr for 24 hrs or Anuria for >12 hours

RESULTS

Out of Total 320 patients positive for dengue IgM, 48 patients were found to develop AKI according to 2012 KDIGO Criteria for Acute Kidney Injury.

Out of 234 patients diagnosed with dengue fever 26 Patients develop AKI which constitute 11%, while 16 patients (20%) developed AKI out of 80 patients diagnosed as dengue hemorrhagic fever. However, 100% of the patients developed AKI which were diagnosed as dengue shock syndrome. Out of total of 320 patients, 48 patients developed AKI which constitute 15% of the patients (table-1).

Out of the 48 patients with dengue IgM+, diagnosed with AKI, 34 patients (70.83%) fall under KDIGO I, while 10 patients(20.83%) constitute KDIGO II and remaining 4

Severity of Dengue IgM+ patients	Total Patients	Patients developing AKI	%
Dengue fever	234	26	11%
Dengue haemorrhagic fever	80	16	20%
Dengue shock syndrome	6	6	100%
Total	320	48	15%

Table-1: Classification of severity of dengue IgM+ patients developing AKI

KDIGO Staging	Dengue Patients Developing AKI	%
KDIGO I	34	70.83%
KDIGO II	10	20.83%
KDIGO III	4	8.33%

Table-2: Severity of AKI in dengue IgM+ patients (According to KDIGO Criteria 2012)

(8.33%) categorized under KDIGO III (table-2).

Total hospital Stay of dengue IgM+ patients landed up in AKI:

Number of Days:	Number of Patients:
5-7 days	12
8-14 Days	26
>15 Days	10

Out of 48 patients diagnosed with dengue IgM+ and developing AKI, 12 patients stayed for 5-7days, 26 patients stayed for 8-14 days and 10 patients had prolonged stay of more than 15days (table-3).

DISCUSSION

Tropical acute febrile illnesses are common causes of Acute Kidney Injury(AKI) in developing countries. Tropical infections like malaria, scrub typhus, enteric fever, leptospirosis and hantavirus have been reported to cause AKI⁵ along with dengue virus. AKI is a complication of dengue Viral Infection which has not been studied much. There are multiple proposed mechanisms for etiopathogenesis of renal impairment in dengue Viral Infection. Infection with dengue virus causes capillary leakage leading to loss of fluid from intravascular compartment into interstitial space^{6,7} which may lead to decreased kidney perfusion and acute tubular necrosis. Possible etiological factors for AKI in dengue Fever include hypotension with either hemolysis or rhabdomyolysis and shock as reported in various case reports.^{8,9} Cases of unexplained AKI has also been reported.¹⁰ Interestingly, dengue may cause glomerular injury in addition to the above-mentioned mechanisms as reported in one study Jessie K et al.¹¹ Viral antigen has also been isolated from tubular epithelial cells.¹²

Acute kidney Injury is a overlooked complication of dengue IgM+ patients. Lee et al¹³ reported an incidence of 3.3% among adults in Taiwan. Khalil et al.¹³ identified AKI in 13.3% of a series of patients with dengue confirmed by the presence of IgM antibodies. In our Study also out of 320 patients 48 patients (15%) Developed AKI according to Kidney Disease Global outcome (KDIGO, 2012) Criteria.

Mortality has been noted in vast majority of patients landing up in AKI, Laoprasopwattana et al.¹⁵ found that patients who had oliguric AKI had a higher mortality rate than those with non-oliguric AKI. Our study also concluded that 6 out of 48 patients landed up in oliguria/anuria requiring hemodialysis, out of which 2 patients (4.16%) died. Hence Patients landing up in severe dengue and anuria greater mortality has been noted.

Dengue is associated with significant morbidity and mortality as well as increase in economic burden.^{16,17} The average length of hospital stay in patients with dengue has been reported to be 3–4 days in various studies. Khan *et al.*¹⁸ from Saudi Arabia reported length of stay of 4 days. Similarly, Lye D¹⁹ et al conducted a study in Singapore reported the mean stay as 3 days. Parkash et al.²⁰ reported a mean hospital stay of 4 days in patients with associated hepatitis.

In our study also we found that longer hospital stay is associated with more severe infection leading to mortality and Hemodialysis. We did not come across any published literature looking at the impact of AKI on hospital stay in patients with Dengue Viral Infection.

This study has several limitations. The study is retrospective in nature and is of limited clinical use as the study focused on inpatients, therefore excluding patients who visited outpatient clinics and other hospitals. Also, the study was limited to a single center. Moreover, histopathology reports in clinically indicated cases were not available to elucidate etiopathogenesis of AKI. Patients were followed till discharge and there was no long term follow up. Prospective studies are needed with renal biopsy in clinically indicated cases along with a long-term follow-up to know more about the etiopathogenesis and outcome of AKI in Dengue Fever.

CONCLUSION

Our study concluded that AKI is a major and serious complication, and it is the major cause of Mortality and morbidity in Dengue fever.

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