

Research Article

Acute Kidney Injury In Dengue Fever, One Year Hospital Based Cross Sectional Study.

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INTRODUCTION

Arboviruses pose a significant public health challenge, particularly in tropical and subtropical regions, where they contribute to frequent epidemics with substantial economic and social impacts. Among them, the dengue virus (DENV), transmitted by Aedes mosquitoes, is the most prevalent arthropod-borne viral infection in humans. Dengue fever (DF) has a vast global footprint, with an estimated 2.5 billion people at risk, and outbreaks reported in over 100 countries, primarily in Southeast Asia, the Pacific, and the Americas. While traditionally considered an urban disease, dengue is increasingly affecting rural populations, particularly in Africa and the eastern Mediterranean.

Dengue infection presents with a wide spectrum of clinical manifestations, ranging from mild febrile illness to severe dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), which contribute to significant morbidity and mortality. The disease burden has escalated over the years due to increasing globalization, trade, and travel, leading to the introduction of virulent strains into new regions. Despite preventive measures, dengue remains endemic in many countries, including India, where seasonal outbreaks occur annually, particularly during the monsoon season.

In recent years, atypical manifestations of dengue, including neurological, hepatic, and renal complications, have been increasingly recognized. Among these, acute kidney injury (AKI) is a relatively underreported but potentially serious complication. Dengue-related renal involvement may present as AKI, proteinuria, glomerulonephritis, or hemolytic uremic syndrome, necessitating early recognition and intervention. However, data on dengue-associated AKI remain scarce, with only a few case reports and studies available in the literature.

Given the recurrent epidemics of dengue and the limited understanding of its renal complications, this study aims to estimate the prevalence of AKI in dengue fever. Identifying such complications is crucial for improving early diagnosis, optimizing patient management, and reducing disease-related morbidity and mortality.

OBJECTIVES

The objectives of this study were

- To study the prevalence of acute kidney injury in dengue fever.
- To study the predictors of development of acute kidney injury in dengue fever.

METHODOLOGY

Study Design and Setting

This is a prospective observational study conducted at [Institution/Hospital Name], a tertiary care center in [Location], over a period of [Duration]. The study was designed to estimate the prevalence of acute kidney injury (AKI) in patients diagnosed with dengue fever (DF).

Study Population

Patients presenting with clinical features of dengue fever and confirmed by laboratory testing were included in the study. The inclusion and exclusion criteria were as follows:

Inclusion Criteria

1. Patients aged $\geq$ [Age] years diagnosed with dengue fever based on clinical and serological confirmation (NS1 antigen or dengue IgM/IgG ELISA).
2. Patients with or without complications of dengue fever, including dengue hemorrhagic fever (DHF) and dengue

shock syndrome (DSS).

Exclusion Criteria

1. Patients with pre-existing chronic kidney disease (CKD).
2. Patients with other concurrent infections or conditions known to cause AKI (e.g., sepsis, leptospirosis, malaria).
3. Patients on nephrotoxic drugs before hospitalization.

Data Collection

A structured proforma was used to collect patient demographics, clinical symptoms, laboratory parameters, and outcomes. The following data were recorded:

Demographic details

Age, sex, comorbidities.

Clinical features

Fever, rash, bleeding tendencies, hypotension, oliguria, neurological symptoms.

Laboratory investigations

- Complete blood count (CBC)
- Platelet count
- Hematocrit
- Liver function tests (LFTs)
- Renal function tests (RFTs) (serum creatinine, blood urea nitrogen)
- Serum electrolytes
- Dengue serology (NS1 antigen, IgM, IgG ELISA)
- Urine analysis (proteinuria, hematuria)
- Imaging (ultrasound for renal involvement if clinically indicated)

Definition of Acute Kidney Injury (AKI)

AKI was defined based on the *Kidney Disease: Improving Global Outcomes (KDIGO) criteria* as follows

1. Increase in serum creatinine by ≥ 0.3 mg/dL within 48 hours.
2. Increase in serum creatinine to ≥ 1.5 times the baseline within 7 days.
3. Urine output < 0.5 mL/kg/h for more than 6 hours.

Patients were categorized into different AKI stages according to the severity of renal involvement.

Statistical Analysis

Data were analyzed using **[Statistical Software, e.g., SPSS version X or STATA]**. Continuous variables were expressed as mean $\pm$ standard deviation (SD) or median (interquartile range, IQR) depending on the distribution. Categorical variables were presented as frequencies and percentages. Chi-square or Fisher's exact test was used for categorical data, while Student's t-test or Mann-Whitney U test was used for continuous data. A **p-value < 0.05 ** was considered statistically significant.

Ethical Considerations

The study was approved by the Institutional Ethics Committee of [Institution Name] (Approval No: [Reference No.]). Informed consent was obtained from all participants before enrollment. Confidentiality of patient data was maintained

throughout the study.

This methodology provides a clear and structured approach to the study while ensuring scientific rigor and ethical compliance. Let me know if you need any modifications or additions!

In the present study 7.18% of the males developed AKI compared to 1.53% of the females and the difference observed was statistically significant ($p=0.016$).

In this study significantly higher number of patients who were aged between 61 to 70 years (52.94%) and 71 to 80 years (50%) developed AKI ($p<0.001$).

In the present study AKI was diagnosed in all the (100%) patients with DSS compared to DHF (4.76%) and DF (4.5%). The difference observed was statistically significant ($p<0.001$).

In the present study significant association was found between serum creatinine at admission and AKI ($p<0.001$).

In the present study 9.02% of the patients with platelet count $< 20,000$ /cumm developed AKI compared to other counterparts ($p=0.026$).

In this study positive association was found between AKI and blood urea at admission ($p<0.001$).

In the present study no association was found between serositis and AKI ($p=0.097$).

In this study significantly higher of patients with hypotension (28.57% vs 5.49% developed AKI ($p<0.001$).

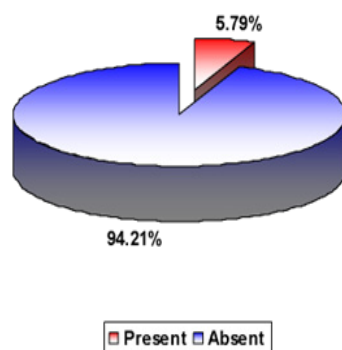
In this study significantly higher mortality was noted in patients with AKI (100% vs 0%; $p<0.001$).

RESULTS

Table 1. Distribution of patients according to the AKI

AKI	Distribution (n=535)	
	Number	Percentage
Present	31	5.79
Absent	504	94.21
Total	535	100.00

In the present study 7.18% of the males developed AKI compared to 1.53% of the females and the difference observed was statistically significant ($p=0.016$).

Figure 1. In this study 5.79% of the patients developed AKI.**Graph 12. Distribution of patients according to the AKI****Table 2.** Association of AKI with sex.

Sex	AKI					
	Absent		Present		Total	
	No.	%	No.	%	No.	%
Male	375	92.82	29	7.18	404	100.00
Femle	129	98.47	2	1.53	131	100.00
Total	504	94.21	31	5.79	535	100.00

p = 0.016

In the present study 7.18% of the males developed AKI compared to 1.53% of the females and the difference observed was statistically significant (p=0.016).

Table 3. Association of AKI with age.

Age group (Years)	AKI					
	Absent		Present		Present	
	No	%	No	%	No	%
18 to 30	309	97.48	8	2.52	317	100.00
31 to 40	112	94.92	6	5.08	118	100.00
41 to 50	44	88.00	6	12.00	50	100.00
51 to 60	29	96.67	1	3.33	30	100.00
61 to 70	8	47.06	9	52.94	17	100.00
71 to 80	1	50.00	1	50.00	2	100.00
81 to 90	1	100.00	0	0.00	1	100.00
Total	504	94.21	31	5.79	535	100.00

p < 0.001

In this study significantly higher number of patients who were aged between 61 to 70 years (52.94%) and 71 to 80 years (50%) developed AKI (p<0.001).

Table 4. Association of AKI with severity of dengue fever.

Severity of dengue fever	AKI					
	Absent		Present		Total	
	No.	%	No.	%	No.	%
Dengue fever	424	95.50	20	4.50	444	100.00
Dengue haemorrhagic fever	80	95.24	4	4.76	84	100.00
Dengue shock syndrome	0	0.00	7	100.00	7	100.00
Total	504	94.21	31	5.79	535	100.00

$p < 0.001$

In the present study AKI was diagnosed in all the (100%) patients with DSS compared to DHF (4.76%) and DF (4.5%). The difference observed was statistically significant ($p < 0.001$).

Table 5. Association of AKI with serum creatinine at admission.

Serum creatinine (mg/dL)	AKI					
	Absent		Present		Total	
	No.	%	No.	%	No.	%
< 0.7	95	97.94	2	2.06	97	100.00
0.7 to 1.20	56	70.89	23	29.11	79	100.00
> 1.20	353	98.33	6	1.67	359	100.00
Total	504	94.21	31	5.79	535	100.00

$p < 0.001$

In the present study significant association was found between serum creatinine at admission and AKI ($p < 0.001$).

Table 6. Association of AKI with platelet count at admission.

Platelet count (x 103 /cumm)	AKI					
	Absent		Present		Total	
	No.	%	No.	%	No.	%
<20	121	90.98	12	9.02	133	100.00
20 to 49	173	97.74	4	2.26	177	100.00
50 to 99	108	90.76	11	9.24	119	100.00
100 to 150	68	97.14	2	2.86	70	100.00
>150	34	94.44	2	5.56	36	100.00
Total	504	94.21	31	5.79	535	100.00

$p = 0.026$

In the present study 9.02% of the patients with platelet count < 20,000 /cumm developed AKI compared to other counterparts ($p = 0.026$).

Table 7. Association of AKI with blood urea at admission.

Blood urea (mg/dL)	AKI					
	Absent		Present		Total	
	No.	%	No.	%	No.	%
<17	163	99.39	1	0.61	164	100.00
17 to 49	15	45.45	18	54.55	33	100.00
> 49	326	96.45	12	3.55	338	100.00
Total	504	94.21	31	5.79	535	100.00

$p < 0.001$

In this study positive association was found between AKI and blood urea at admission ($p < 0.001$).

Table 8. Association of AKI with serositis.

Serositis	AKI					
	Absent		Present		Total	
	No.	%	No.	%	No.	%
Present	245	92.45	20	7.55	265	100.00
Absent	259	95.93	11	4.07	270	100.00
Total	504	94.21	31	5.79	535	100.00

$p = 0.097$

In the present study no association was found between serositis and AKI ($p = 0.097$).

Table 9. Association of AKI with hypotension.

Hypotension	AKI					
	Absent		Present		Total	
	No.	%	No.	%	No.	%
Present	5	71.43	2	28.57	7	100.00
Absent	499	94.51	29	5.49	528	100.00
Total	504	94.21	31	5.79	535	100.00

$p < 0.001$

In this study significantly higher of patients with hypotension (28.57% vs 5.49% developed AKI ($p < 0.001$).

Table 10. Association of AKI with mortality.

Mortality	AKI					
	Absent		Present		Total	
	No.	%	No.	%	No.	%
Survivor	504	95.09	26	4.91	530	100.00
Non survivor	0	0.00	5	100.00	5	100.00
Total	504	94.21	31	5.79	535	100.00

$p < 0.001$

In this study significantly higher mortality was noted in patients with AKI (100% vs 0%; $p < 0.001$).

DISCUSSION

Dengue infection presents with a wide clinical spectrum, ranging from asymptomatic cases and undifferentiated febrile illness to severe forms such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). While classical dengue fever is characterized by biphasic fever, myalgia, retro-orbital pain, rash, leukopenia, and thrombocytopenia, severe cases may lead to hemorrhagic manifestations, multi-organ dysfunction, and fatal outcomes. As dengue continues to emerge globally, atypical presentations and complications such as acute kidney injury (AKI) are increasingly recognized but may be underreported due to a lack of awareness.

Demographic and Clinical Characteristics

In our study, males were more commonly affected than females (male-to-female ratio: 3.08:1), consistent with previous studies by Sharma et al. (1998) and Agarwal et al. (2010). The most affected age group was 18–30 years (59.25%), with a mean age of 31.52 years, aligning with findings from AIIMS, Mexico, and other studies. Fever was the universal symptom (100%), followed by myalgia (69.91%), vomiting (67.66%), and nausea (66.92%). Petechiae (25.23%) and retro-orbital pain (18.32%) were also noted. Compared to previous studies, our findings on oliguria were noteworthy, suggesting a possible renal involvement even in early dengue infection.

Imaging Findings

Pleural effusion and acute respiratory distress syndrome (ARDS) were noted in 0.93% and 0.53% of patients, respectively, which was lower than the incidence reported by Kumar et al. (2010). Ultrasound findings revealed ascites (47.66%) and gallbladder thickening (40.19%), consistent with prior studies. The gallbladder thickening may be attributed to increased vascular permeability and plasma leakage, a hallmark of severe dengue.

Laboratory Parameters and Disease Severity

Thrombocytopenia was present in 57.9% of patients at admission, with platelet counts improving over time. Elevated transaminases (SGOT: 92.34%, SGPT: 82.06%) were observed, reflecting hepatic involvement, as seen in previous studies from Delhi and AIIMS. Most patients (82.99%) had classical dengue fever, while 15.7% had DHF, and 1.31% had DSS.

Acute Kidney Injury and Predictors

The prevalence of AKI in our cohort was 5.79%, comparable to studies by Mehra et al. (2012) and Khalil et al. (2012) but lower than studies from Malaysia and India reporting rates as high as 15.8%. The variation may be attributed to differences in study design, diagnostic criteria, and population characteristics.

Several factors were significantly associated with AKI:

Male gender

(7.18% vs. 1.53%, $p=0.016$), aligning with previous findings by Khalil et al. (2012) and Mallhi et al. (2015).

Age

>60 years had the highest prevalence (52.94%), suggesting older adults are at greater risk, consistent with Lee et al. (2009).

Severity of dengue

AKI was present in 100% of DSS cases, reinforcing its strong association with severe dengue ($p<0.001$).

Pathophysiologically, AKI in dengue may result from capillary leakage, hypotension, rhabdomyolysis, direct viral nephropathy, or immune-mediated injury. Dengue-associated AKI is often pre-renal due to plasma leakage and shock, as highlighted by Hommel et al.

Management, Complications, and Outcomes

Platelet transfusion was required in 48.97% of patients, correlating with significant thrombocytopenia. Other complications included serositis (49.53%), hepatitis (1.5%), and MODS (0.93%). Despite these complications, the majority (99.07%) recovered, with a low mortality rate of 0.93%.

Table 11. Association of AKI with serum creatinine at admission.

Serum creatinine (mg/dL)	AKI					
	Absent		Present		Total	
	No.	%	No.	%	No.	%
< 0.7	95	97.94	2	2.06	97	100.00
0.7 to 1.20	56	70.89	23	29.11	79	100.00
> 1.20	353	98.33	6	1.67	359	100.00
Total	504	94.21	31	5.79	535	100.00

$p < 0.001$

In the present study significant association was found between serum creatinine at admission and AKI ($p<0.001$).

Table 12. Association of AKI with platelet count at admission.

Platelet count (x 103 /cumm)	AKI					
	Absent		Present		Total	
	No.	%	No.	%	No.	%
<20	121	90.98	12	9.02	133	100.00
20 to 49	173	97.74	4	2.26	177	100.00
50 to 99	108	90.76	11	9.24	119	100.00
100 to 150	68	97.14	2	2.86	70	100.00
>150	34	94.44	2	5.56	36	100.00
Total	504	94.21	31	5.79	535	100.00

p = 0.026

In the present study 9.02% of the patients with platelet count < 20,000 /cumm developed AKI compared to other counterparts (p=0.026).

Table 13. Association of AKI with blood urea at admission.

Blood urea (mg/dL)	AKI					
	Absent		Present		Total	
	No.	%	No.	%	No.	%
<17	163	99.39	1	0.61	164	100.00
17 to 49	15	45.45	18	54.55	33	100.00
> 49	326	96.45	12	3.55	338	100.00
Total	504	94.21	31	5.79	535	100.00

p < 0.001

In this study positive association was found between AKI and blood urea at admission (p<0.001).

Table 14. Association of AKI with serositis.

Serositis	AKI					
	Absent		Present		Total	
	No.	%	No.	%	No.	%
Present	245	92.45	20	7.55	265	100.00
Absent	259	95.93	11	4.07	270	100.00
Total	504	94.21	31	5.79	535	100.00

p = 0.097

In the present study no association was found between serositis and AKI (p=0.097).

Table 15. Association of AKI with hypotension.

Hypotension	AKI					
	Absent		Present		Total	
	No.	%	No.	%	No.	%
Present	5	71.43	2	28.57	7	100.00
Absent	499	94.51	29	5.49	528	100.00
Total	504	94.21	31	5.79	535	100.00

p < 0.001

In this study significantly higher of patients with hypotension (28.57% vs 5.49% developed AKI (p<0.001).

Table 16. Association of AKI with mortality.

Mortality	AKI					
	Absent		Present		Total	
	No.	%	No.	%	No.	%
Survivor	504	95.09	26	4.91	530	100.00
Non survivor	0	0.00	5	100.00	5	100.00
Total	504	94.21	31	5.79	535	100.00

p < 0.001

In this study significantly higher mortality was noted in patients with AKI (100% vs 0%; p<0.001).

Table 17. Comparison of clinical and laboratory characteristics in patients with and without AKI.

AKI					
Variables	Present (=31)		Absent (n=504)		p value
	Mean	SD	Mean	SD	
Age (Years)	45.20	17.63	30.69	11.63	<0.001
PR (bpm)	97.07	18.45	86.01	13.64	0.004
Systolic BP (mm Hg)	109.50	16.50	111.92	10.99	0.449
Diastolic BP (mm Hg)	73.79	11.92	77.03	7.31	0.165
RR (/minute)	23.13	6.72	18.18	2.17	<0.001
Temperature (OC)	96.46	11.06	99.12	0.93	0.198
Hb (mg/dL)	13.72	3.17	14.58	2.10	0.160
PCV (%)	39.97	7.33	42.05	6.10	0.137
Total count cells (/cumm)	9480.00	6545.09	5855.74	4613.55	0.005
Neutrophil (%)	68.93	17.35	55.11	17.27	<0.001
Lymphocyte (%)	24.93	16.11	35.55	17.22	0.001
Monocyte (%)	5.20	3.10	7.19	3.07	0.002
Eosinophils (%)	2.33	4.04	5.33	5.35	0.331
Platelet count on day 1 (x103)	58.17	51.54	59.41	54.12	0.901
PT/INR (sec)	1.39	0.59	1.11	0.29	0.018
aPTT (sec)	1.53	0.48	1.30	0.41	0.032
Blood urea (mg/dL)	60.33	34.18	22.54	10.88	<0.001
Serum creatinine Day 1 (mg/dL)	2.15	1.20	0.90	0.27	<0.001
Sodium (mmol/L)	135.63	4.44	135.99	4.18	0.672
Potassium (mmol/L)	4.39	0.93	4.25	0.53	0.423
Bicarbonate (mmol/L)	18.93	4.13	21.84	3.39	0.001
Total bilirubin (mg/dL)	3.00	3.03	0.88	0.97	0.001
Direct bilirubin (mg/dL)	2.32	2.66	0.49	0.80	0.001
SGOT (IU/L)	1053.53	2138.23	211.78	383.76	0.040
SGPT (IU/L)	440.17	796.96	123.00	198.75	0.038
Serum albumin (mg/dL)	3.16	0.50	3.71	0.48	<0.001
Alkaline phosphatase (mg/dL)	208.50	234.24	107.45	87.22	0.025
RBS (mg/dL)	130.20	61.34	127.24	56.11	0.798
Hospital stay (Days)	6.60	5.65	5.60	2.32	0.341

In the present study significant association was found between serum creatinine at admission and AKI ($p<0.001$).

In the present study 9.02% of the patients with platelet count $< 20,000$ /cumm developed AKI compared to other counterparts ($p=0.026$).

In this study positive association was found between AKI and blood urea at admission ($p<0.001$).

In the present study no association was found between serositis and AKI ($p=0.097$).

In this study significantly higher of patients with hypotension (28.57% vs 5.49% developed AKI ($p<0.001$).

In this study significantly higher mortality was noted in patients with AKI (100% vs 0%; $p<0.001$).

In the present study significant differences were noted in patients with and without AKI pertaining to age (45.20 ± 17.63 vs 30.69 ± 11.63 years; $p<0.001$), pulse rate (97.07 ± 18.45 vs 86.01 ± 13.64 per minute; $p=0.004$), respiratory rate (23.13 ± 6.72 vs 18.18 ± 2.17 per minute; $p<0.001$), total count (9480.00 ± 6545.09 vs 5855.74 ± 4613.55 per cumm; $p=0.005$), neutrophils

(68.93±17.35 vs 55.11±17.27 percent; $p<0.001$), lymphocyte (24.93±16.11 vs 35.55±17.22 percent; $p=0.001$), monocyte (5.20±3.10 vs 7.19±3.07 percent; $p=0.002$), International normalized ratio (1.39±0.59 vs 1.11±0.29; $p=0.018$), aPTT (1.53±0.48 vs 1.30±0.41; $p=0.032$), blood urea (60.33±34.18 vs 22.54±10.88 mg/dL; $p<0.001$), Serum creatinine on day one (2.15± 1.20 vs 0.90±0.27 mg/dL; $p<0.001$), bicarbonate (18.93±4.13 vs 21.84±3.39 mmol/L; $p=0.001$), total bilirubin (3.00±3.03 vs 0.88±0.97 mg/dL; $p=0.001$), direct bilirubin (2.32± 2.66 vs 0.49±0.80 mg/dL; $p=0.001$), SGOT (1053.53±2138.23 vs 211.78±383.76 IU/L; $p=0.040$), SGPT (440.17±796.96 vs 123.00±198.75 IU/L; $p=0.038$), serum albumin (3.16±0.5 vs 3.71±0.47 mg/dL; $p<0.001$) and alkaline phosphatase (208.50±234.24 vs 107.45±87.22mg/dL; $p=0.025$).

CONCLUSION

Based on the findings of this study it may be concluded that, there is high prevalence of AKI (5.79%) in patients presenting with dengue fever in the study area hence it cannot be neglected.

The significant predictors of AKI in patients with DF are male gender, advanced age, Hypotension, high serum creatinine and blood urea levels at the time of admission and lower platelet count at admission., evidence of polyserositis, other complications. Laboratory parameters including raised total count, International normalized ratio, a PTT, abnormal liver function tests at admission are also associated with risk developing AKI in patients with DF. Persons with DHF and DSS had more evidence of AKI compared to Dengue fever. The person who developed AKI had a more mortality.

SUMMARY

Renal complications in dengue fever remain an underexplored aspect, with manifestations ranging from mild urinary abnormalities to severe acute kidney injury (AKI). This study aimed to evaluate the prevalence of AKI in dengue fever and identify predictors for its development.

A one-year hospital-based cross-sectional study was conducted at the Department of General Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi, from January to December 2017. Of the 610 adult patients who tested positive for dengue NS1/IgM, 535 met the inclusion criteria. AKI was diagnosed using AKIN criteria, and potential risk factors were analyzed.

Key findings include

- The majority of patients were male (75.51%), with a male-to-female ratio of 3.08:1. The mean age was 31.52 ± 12.47 years.
- Fever was a universal symptom (100%), followed by myalgia (69.91%), vomiting (67.66%), and nausea

(66.92%). Skin manifestations included rashes (31.79%) and petechial hemorrhages (25.23%).

- Laboratory findings revealed elevated SGOT (92.34%) and SGPT (82.06%). Proteinuria was observed in 21.31% of patients, while hematuria was rare (0.56%).
- Radiological findings showed thickened gallbladder (40.19%), ascites (47.66%), and splenomegaly (6.36%).
- Platelet transfusion was required in 48.97% of cases.
- Disease severity distribution: dengue fever (82.99%), dengue hemorrhagic fever (15.7%), and dengue shock syndrome (1.31%).
- AKI prevalence was 5.79%, with a significantly higher occurrence in males (7.18% vs. 1.53%, $p=0.016$) and older age groups ($p<0.001$). AKI was diagnosed in all patients with DSS (100%) compared to DHF (4.76%) and DF (4.5%) ($p<0.001$).
- Hypotension (28.57% vs. 5.49%, $p<0.001$) and complications like MODS or encephalitis (46.67% vs. 4.62%, $p<0.001$) were strongly associated with AKI.
- Significant predictors of AKI included elevated blood urea, serum creatinine, INR, aPTT, total and direct bilirubin, SGOT, SGPT, and alkaline phosphatase levels ($p<0.001$).
- Mortality was observed in five patients (0.93%), all of whom had AKI ($p<0.001$).

This study highlights a significant prevalence of AKI (5.79%) among dengue patients, emphasizing the need for early identification and management of renal involvement in dengue fever.

REFERENCES

1. Rice CM. Flaviviridae: The viruses and their replication. In: Virology Fields BN, Knipe DM, Howley PM eds. 3rd ed., Philadelphia: Lippincott-Raven Publishers, 1996. p. 931-59.
2. WHO. Scientific Working Group Report on Dengue [online]. Geneva, Switzerland: WHO; 2007.
3. TDR/WHO. Evaluation of commercially available anti-dengue virus immunoglobulin M tests. Diagnostics Evaluation Series No.3 Geneva. Switzerland: TDR/WHO; 2009.
4. Guzman MG, Kouri G. Dengue: an update. Lancet Infect Dis 2002; 2:33-42.
5. Gubler DJ. The changing epidemiology of yellow fever and dengue, 1900 to 2003: full circle? Comp Immunol Microbiol Infect Dis 2004;27:319-30.

6. O'Brien D, Tobin S, Brown GV, Torresi J. Fever in returned travelers: review of hospital admissions for a 3-year period. *Clin Infect Dis*. 2001;33:603-9.
7. MacLean J, Lalonde R, Ward B. Fever from the tropics. *Travel Med Advisor*. 1994;5:27.1-14.
8. Halstead SB. Dengue. *Lancet* 2007;370:1644-52.
9. Mairuhu ATA, Wagenaar J, Brandjes DPM, van Gorp ECM. Dengue: an arthropod-borne disease of global importance. *Eur J Clin Microbiol Infect Dis* 2004;23:425-33.
10. Cobelens FG, Groen J, Osterhaus AD, Leentvaar-Kuipers A, Wertheim-van Dillen PM, Kager PA. Incidence and risk factors of probable dengue virus infection among Dutch travellers to Asia. *Trop Med Int Health* 2002;7:331-8.
11. Messer WB, Gubler DJ, Harris E, Sivananthan K, de Silva AM. Emergence and global spread of a dengue serotype 3, subtype III virus. *Emerg Infect Dis* 2003;9:800-9.
12. Hanna JN, Ritchie SA, Phillips DA, Serafin IL, Hills SL, van den Hurk AF. An epidemic of dengue 3 in far north Queensland, 1997-1999. *Med J Aust* 2001;174:178-2.
13. Jatanasen S, Thongcharoen P. Dengue hemorrhagic fever in South East-Asian countries. Monograph on dengue/dengue haemorrhagic fever. New Delhi: WHO; 1993.
14. Park K. The dengue syndrome. Park's Textbook of Preventive and Social Medicine. 23rd ed. Jabalpur: Banarsidas Bhanot Publishers; 2015. p. 246-55.
15. Broor S, Dar L, Sengupta S, Chakaraborty M, Wali JP, Biswas A, et al. Recent Dengue Epidemic in Dehli, India. In: Factors in the emergence of arboviruses disease, Saluzzo JE and Dodet B, eds. Paris: Elsevier; 1997. p. 123-7.
16. Gupta E, Dar L, Narang P, Srivastava VK, Broor S. Serodiagnosis of dengue during an outbreak at a tertiary care hospital in Delhi. *Indian J Med Res* 2005;121:36-8.
17. Ahlawat RS, Kalra T. Atypical manifestations of dengue fever in a recent dengue outbreak. *Ann Trop Med Public Health* 2017;10:1448-52.
18. TDR/WHO. In Dengue: Guidelines for Diagnosis, Treatment, Prevention and Control. Geneva, Switzerland: World Health Organization; 2009.
19. PAHO. Dengue and Dengue Hemorrhagic Fever in the Americas: Guidelines for Prevention and Control. Washington, DC, USA: Pan American Health Organization; 1994.
20. Nimmannitya, S. Clinical spectrum and management of dengue haemorrhagic fever. *Southeast Asian J Trop Med Pub Health* 1987;18: 392-7.
21. Martinez TE. Preventing deaths from dengue: a space and challenge for primary health care. *Rev Panam Salud Pública* 2006;20:60-74.
22. Mehra N, Patel A, Abraham G, Reddy YN, Reddy YN. Acute kidney injury in dengue fever using Acute Kidney Injury Network criteria: incidence and risk factors. *Trop Doct* 2012;42(3):160-2.
23. Karakus A, Banga N, Voorn GP, Meinders AJ. Dengue shock syndrome and rhabdomyolysis. *Neth J Med* 2007;65:78-81.
24. George R, Liam CK, Chua CT, Lam SK, Pang T, Geethan R, et al. Unusual clinical manifestations of dengue virus infection. *Southeast Asian J Trop Med Public Health* 1988;19:585-90.
25. Chacko B, John GT, Jacob CK, Vijayakumar TS. Dengue shock syndrome in a renal transplant recipient. *Transplantation*. 2004;77:634-5.
26. Garcia JH, Rocha TD, Viana CF, Gonçalves BP, Girão ES, Vasconcelos JB, et al. Dengue shock syndrome in a liver transplant recipient. *Transplantation* 2006;82:850-1.
27. Gunasekera HH, Adikaram AV, Herath CA, Samarasinghe HH. Myoglobinuric acute renal failure following dengue viral infection. *Ceylon Med J* 2000;45:181.
28. Radakovic-Fijan S, Graninger W, Müller C, Hönigsmann H, Tanew A. Dengue hemorrhagic fever in a British travel guide. *J Am Acad Dermatol* 2002;46:430-3.
29. Wiersinga WJ, Scheepstra CG, Kasanardjo JS, de Vries PJ, Zaaijer H, Geerlings SE. Dengue fever-induced hemolytic uremic syndrome. *Clin Infect Dis* 2006;43:800-1.
30. Lima EQ, Gorayeb FS, Zanon JR, Nogueira ML, Ramalho HJ, Burdmann EA. Dengue haemorrhagic fever-induced acute kidney injury without hypotension, haemolysis or rhabdomyolysis. *Nephrol Dial Transplant* 2007;22:3322-6.
31. Laoprasopwattana K, Pruekprasert P, Dissaneewate

- P, Geater A, Vachvanichsanong P. Outcome of dengue hemorrhagic fever-caused acute kidney injury in Thai children. *J Pediatr* 2010;157:303-9.
32. Lee IK, Liu JW, Yang KD. Clinical characteristics, risk factors, and outcomes in adults experiencing dengue hemorrhagic fever complicated with acute renal failure. *Am J Trop Med Hyg* 2009;80:651-5.
 33. Wiwanitkit V. Acute renal failure in the fatal cases of dengue hemorrhagic fever, a summary in Thai death cases. *Ren Fail* 2005;27:647.
 34. Khalil MA, Sarwar S, Chaudry MA, Maqbool B, Khalil Z, Tan J, et al. Acute kidney injury in dengue virus infection. *Clin Kidney J* 2012;5(5): 390-4.
 35. Halstead SB. Dengue hemorrhagic fever. A public health problem and a field for research. *Bull World Health Organ* 1980;58(1):1-21.
 36. Raheel U, Faheem M, Riaz MN, Kanwal N, Javed F, Zaidi Nu, et al. Dengue fever in the Indian Subcontinent: an overview. *J Infect Dev Ctries* 2011;5(4):239-47.
 37. Rush B. An account of the bilious remitting fever, as it appeared in Philadelphia in the summer and autumn of the year 1780. *Med Inq Obs Philadelphia* 1789;1:104-17.
 38. Cohen SN, Halstead SB. Shock associated with dengue infection. *J Paediatr* 1966;68(3):448-55.
 39. Sabin AB. Research on dengue during World War II. *Am J Trop Med Hyg* 1952;1:30-50.
 40. Lall R, Dhanda V. Dengue hemorrhagic fever and the Dengue shock syndrome in India. Review Article. *Nat Med J Ind* 1996;9(1):20-3.
 41. Gupta N, Srivastava S, Jain A, Chaturvedi UC. Dengue in India. *Indian J Med Res* 2012;136:373-90.
 42. World Health Organization. Dengue and severe dengue – Key facts. Geneva: World health Organization. Dengue and severe dengue; 2014 Available from: URL: <http://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue> Access Date 18.06.2018.
 43. Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL et.al. The global distribution and burden of dengue. *Nature*;496:504-507.
 44. Brady OJ, Gething PW, Bhatt S, Messina JP, Brownstein JS, Hoen AG et al. Refining the global spatial limits of dengue virus transmission by evidence-based consensus. *PLoS Negl Trop Dis*. 2012;6:e1760.
 45. World health Organization. Dengue and severe dengue. Factsheet No. 117. Geneva: World health Organization. Dengue and severe dengue; 2014.
 46. Murray NE, Quam MB, Wilder-Smith A. Epidemiology of dengue: past, present and future prospects. *Clin Epidemiol*. 2013;5:299-309.
 47. Dengue, countries or areas at risk, 2011 Geneva: World Health Organization; 2012.
 48. WHO Regional Office for South-East Asia. Comprehensive Guidelines for Prevention and Control of Dengue and Dengue Haemorrhagic Fever, Revised and Expanded Edition. New Delhi: World Health Organisation South East Asia Regional Office; 2011.
 49. Shepard DS, Undurraga EA, Halasa YA. Economic and disease burden of dengue in Southeast Asia. *PLoS Negl Trop Dis* 2013;7(2):e2055.
 50. Ferreira GL. Global dengue epidemiology trends. *Rev Inst Med Trop Sao Paulo*. 2012;54(Suppl 18):S5-6.
 51. World Health Organization. Dengue fever and dengue haemorrhagic fever. Available: http://www.who.org/communicable_dis_dengue.html. Access Date: 25.03.2014.
 52. Beatty ME, Stone A, Fitzsimons DW et al. Best practices in dengue surveillance: a report from the Asia-Pacific and Americas Dengue Prevention Boards. *PLoS Neg Trop Dis* 2010; 4: e890.
 53. Mutheneni SR, Morse AP, Caminade C, Upadhyayula SM. Dengue burden in India: recent trends and importance of climatic parameters. *Emerg Microbes Infect*. 2017 Aug 9;6(8):e70.
 54. Daily report of Dengue in Karnataka State – 2018. New Delhi : National Vector Borne Diseases Control Programme; 2018.
 55. Kumar A, Rao CR, Pandit V, Shetty S, Bammigatti C, Samarasinghe CM. Clinical manifestations and trend of dengue cases admitted in a tertiary care hospital, Udipi district, Karnataka.

- Indian J Community Med 2010; 35:386-90.
56. Kalappanvar NK, VinodKumar CS, Basavarajappa KG, Sanjay D, Chandrasekhar G. Clinical feature of serologically negative dengue cases at davangere, karnataka IJBAR 2012 ;03(08):611-2.
 57. Jagdish C. Challenges in the Management of Dengue Hemorrhagic fever and Dengue Shock Syndrome. Paediatr Today 2000;4:273-7.
 58. Fauci AS, Kasper DS, Longo DL, Braunwald E, Hauser SL, Jameson JL, et al. Harrison's principles of internal medicine. United States; McGraw Hill: 2008.
 59. Halstead SB. Pathogenesis of Dengue. Challenges to Molecular Biology. Science 1988;239:476-81.
 60. Halstead SB. Dengue Hematological Aspects. Seminars in hematology. 1982;19(2):116-28.
 61. Kabra SK, Jain Y, Singhal T, Ratageri VH. Dengue hemorrhagic fever. Clinical manifestations and management. Ind J Ped 1999;66:93-101.
 62. Dengue: Guidelines for Diagnosis, Treatment, Prevention and Control. World Health Organization. Geneva, Switzerland: WHO; 2009.
 63. Hadinegoro SR. The revised WHO dengue case classification: does the system need to be modified? Paediatr Int Child Health. 2012;32 Suppl 1: 33-8.
 64. Barniol J, Gaczowski R, Barbato EV, da Cunha RV, Salgado D, Martínez E, et al. Usefulness and applicability of the revised dengue case classification by disease: multi-centre study in 18 countries. BMC Infect Dis 2011;11:106.
 65. Mendez A, Gonzalez G. Abnormal clinical manifestation of dengue hemorrhagic fever in children. Biomedica 2006;26(1):61-70.
 66. Chua MN, Molanida R, de Guzman M, Laberiza F. Prothrombin time and partial thromboplastin time as a predictor of bleeding in patients with dengue hemorrhagic fever. Southeast Asian J Trop Med Public Health 1993;24 Suppl 1:141-3.
 67. Sharma S, Sharma SK, Mohan A, Wadhwa J, Dar L, Thulkar S, et al. Clinical profile of dengue haemorrhagic fever in adults during 1996-outbreak in Delhi, India. Dengue Bull 1998;22:20-7.
 68. Wali JP, Biswas A, Chandra S, Malhotra A, Aggarwal P, Handa R, et al. Cardiac involvement in Dengue Haemorrhagic Fever. Int J Cardiol 1998;64(1):31-6.
 69. Kuo CH, Tai DI, Chang-Chien CS, Lan CK, Chiou SS, Liaw YF. Liver biochemical tests and dengue fever. Am J Trop Med Hyg 1992;47(3):265-70.
 70. Mohan B, Patwari AK, Anand VK. Hepatic dysfunction in childhood dengue infection. J Trop Pediatr 2000;46(1):40-3.
 71. Shivbalan S, Anandnathan K, Balasubramanian S, Datta M, Amalraj E. Predictors of spontaneous bleeding in Dengue. Indian J Pediatr 2004;71(1):33-6.
 72. Shah I, Deshpande GC, Tardeja PN. Outbreak of dengue in Mumbai and predictive markers for dengue shock syndrome. J Trop Pediatr 2004; 50(5):301-5.
 73. Venkata Sai PM, Dev B, Krishnan R. Role of ultrasound in dengue fever. Br J Radiol 2005;78(929):416-8.
 74. Karoli R, Fatima J, Siddiqi Z, Kazmi K, Sultania A. Clinical profile of dengue infection at a teaching hospital in North India. J Infect Dev Ctries 2012;6(7):551-4.
 75. Pesaro AE, D'Amico E, Aranha LF. Dengue: cardiac manifestations and implications in antithrombotic treatment. Arq Bras Cardiol 2007;89(2): e12-5.
 76. Gulati S, Maheshwari A. Atypical manifestations of dengue. Trop Med Int Health 2007;12(9):1087-95.
 77. Horvath R, McBride WJH, Hanna JN. Clinical features of hospitalized patients during dengue-3 epidemic in far North Queensland 1997-1999. Dengue Bull 1999;23:24-9.
 78. Lombardi R, Yu L, Younes-Ibrahim M, Schor N, Burdmann EA. Epidemiology of acute kidney injury in Latin America. Semin Nephrol 2008; 28: 320-9.
 79. Lima EQ, Nogueira ML. Viral hemorrhagic fever-induced acute kidney injury. Semin Nephrol 2008; 28: 409-15.
 80. Oliveira JF, Burdmann EA. Dengue-associated acute kidney injury. Clin Kidney J 2015;8(6):681-5.
 81. Glasscock RJ. Immune complex-induced glomerular injury in viral diseases: an overview. Kidney Int Suppl 1991;35:S5-7.

82. Boonpucknavig V, Bhamarapravati N, Boonpucknavig S, Futrakul P, Tanpaichitr P. Glomerular changes in dengue hemorrhagic fever. *Arch Pathol Lab Med* 1976;100:206-12.
83. Jessie K, Fong MY, Devi S, Lam SK, Wong KT. Localization of dengue virus in naturally infected human tissues, by immunohistochemistry and in situ hybridization. *J Infect Dis* 2004;189:1411-8.
84. Basílio-de-Oliveira CA, Aguiar GR, Baldanza MS, Barth OM, Eyer-Silva WA, Paes MV. Pathologic study of a fatal case of dengue-3 virus infection in Rio de Janeiro, Brazil. *Braz J Infect Dis* 2005;9:341-7.
85. Mohsin N, Mohamed E, Gaber M, Obaidani I, Budruddin M, Al Busaidy S. Acute tubular necrosis associated with non-hemorrhagic dengue fever: a case report. *Renal Fail* 2009;31:736-9.
86. Repizo LP, Malheiros DM, Yu L, Barros RT, Burdmann EA. Biopsy proven acute tubular necrosis due to rhabdomyolysis in a dengue fever patient: a case report and review of literature. *Rev Inst Med Trop Sao Paulo* 2014;56:85-8.
87. Nath P, Agrawal DK, Mehrotra RM. Ultrastructural changes in skeletal muscles in dengue virus-infected mice. *J Pathol* 1982;136:301-5.
88. Gandini M, Reis SR, Torrentes-Carvalho A, Azeredo EL, Freire Mda S, Galler R, et al. Dengue-2 and yellow fever 17DD viruses infect human dendritic cells, resulting in an induction of activation markers, cytokines and chemokines and secretion of different TNF- α and IFN- α profiles. *Mem Inst Oswaldo Cruz* 2011;106:594-605.
89. Malheiros SM, Oliveira AS, Schmidt B, Lima JG, Gabbai AA. Dengue. Muscle biopsy findings in 15 patients. *Arq Neuropsiquiatr* 1993;51:159-64.
90. Bosch X, Poch E, Grau JM. Rhabdomyolysis and acute kidney injury. *N Engl J Med* 2009;361:62-72.
91. Davis JS, Bourke P. Rhabdomyolysis associated with dengue virus infection. *Clin Infect Dis* 2004;38:e109-11.
92. Finsterer J, Kongchan K. Severe, persisting, steroid-responsive dengue myositis. *J Clin Virol* 2006;35:426-8.
93. Lim M, Goh HK. Rhabdomyolysis following dengue virus infection. *Singapore Med J* 2005;46:645-6.
94. Upadhaya BK, Sharma A, Khaira A, Dinda AK, Agarwal SK, Tiwari SC. et al. Transient IgA nephropathy with acute kidney injury in a patient with dengue fever. *Saudi J Kidney Dis Transpl* 2010;21:521-5.
95. Bhagat M, Zaki SA, Sharma S, Manglani MV. Acute glomerulonephritis in dengue haemorrhagic fever in the absence of shock, sepsis, haemolysis or rhabdomyolysis. *Paediatr Int Child Health* 2012;32:161-3.
96. Lizarraga KJ, Florindez JA, Daftarian P, Andrews DM, Ortega LM, Mendoza JM, et al. Anti-GBM disease and ANCA during dengue infection. *Clin Nephrol* 2015;83:104-10.
97. Wills BA, Nguyen MD, Ha TL, Dong TH, Tam MD, Tran TN, et al. Comparison of three fluid solutions for resuscitation in dengue shock syndrome. *N Engl J Med* 2005; 353: 877-89.
98. Zhang F, Kramer CV. Corticosteroids for dengue infection. *Cochrane Database Syst Rev* 2014;7:CD003488.
99. Mehta RL, Cerdá J, Burdmann EA, Tonelli M, García-García G, Jha V, et al. International Society of Nephrology's Oby25 initiative for acute kidney injury (zero preventable deaths by 2025): a human rights case for nephrology. *Lancet* 2015;385:2616-43.
100. Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C, Warnock DG, et al. Acute kidney injury network: report of an initiative to improve outcomes in acute kidney injury. *Crit Care*. 2007;11:R31.
101. Daher Ede F, Junior Silva GB, Vieira AP, Souza JB, Falcão Fdos S, Costa CR, et al. Acute kidney injury in a tropical country: a cohort study of 253 patients in an infectious diseases intensive care unit. *Rev Soc Bras Med Trop* 2014;47:86-9.
102. Basu G, Chrispal A, Boorugu H, Gopinath KG, Chandy S, Prakash JA, et al. Acute kidney injury in tropical acute febrile illness in a tertiary care centre-RIFLE criteria validation. *Nephrol Dial Transplant* 2011; 26: 524-531.
103. Khalil MA, Tan J, Khalil MA, Awan S, Rangasami M. Predictors of hospital stay and mortality in dengue virus infection-experience from Aga Khan University Hospital Pakistan. *BMC Res Notes* 2014;7:473.
104. Kuo MC, Lu PL, Chang JM, Lin MY, Tsai JJ, Chen YH, et al. Impact of renal failure on the outcome of dengue viral

- infection. Clin J Am Soc Nephrol 2008;3:1350-6.
105. Mallhi TH, Khan AH, Adnan AS, Sarrieff A, Khan YH, Jummaat F. Incidence, Characteristics and Risk Factors of Acute Kidney Injury among Dengue Patients: A Retrospective Analysis. PLoS One. 2015; 10(9):e0138465.
106. WHO. Dengue haemorrhagic fever: diagnosis, treatment, prevention and control, 2nd ed. Geneva, World Health Organization, 1997.
107. Agarwal J, Kapoor G, Srivastava S, Singh KP, Kumar R, Jain A. Unusual clinical profile of Dengue Infection in patients attending a tertiary care teaching hospital in north India. Int J Infect Dis 2010;14:174-5.
108. Chakravarti A, Matlani M, Kashyap B, Kumar A. Awareness of changing trends in epidemiology of dengue fever is essential for epidemiological surveillance. Indian J Med Microbiol 2012;30(2):222-6.
109. Navarrete-Espinosa J, Gomez-Dantes H, Celis-Quintal JG, Vazquez-Martinez JL. Clinical profile of dengue hemorrhagic fever cases in Mexico. Salud Publica Mex 2005;47:193-200.
110. Narayanan M, Aravind MA, Thilothammal N, Prema R, Sargunam CS, Ramamurthy N. Dengue Fever Epidemic In Chennai: A Study Of The Clinical Profile And Outcome. Indian Paediatr 2002;39:1027-33.
111. Padbidri VS, Adhikari P, Thakare JP, Ilkal MA, Joshi GD, Pereira P, et al. The 1993 epidemic of dengue fever in Mangalore, Karnataka state, India. South East Asian J Trop Med Public Health 1995;26(4):699-704.
112. Tripathi BK, Gupta B, Sinha RSK, Prasad S, Sharma DK. Experience in adult population in Dengue outbreak in Delhi. JAPI 1998;46:273-6.
113. Hommel D, Talarmin A, Reynes JM, Hulin A. Acute renal failure associated with dengue fever in French Guiana. Nephron 1999;83(2):183.
114. Vakrani GP, Subramanya MNT. Acute Renal Failure in Dengue Infection. J Clin Diagnostic Res 2017;11(1):OC10-1310.
115. Naqvi R. Dengue Infection Causing Acute Kidney Injury. Trop Med Surg 2016;4(2):1-4.
116. Lee K, Liu JW, Yang KD. Clinical and laboratory characteristics and risk factors for fatality in elderly patients with dengue hemorrhagic fever. Am J Trop Med Hyg 2008;79:149-53.