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Predictors of Acute Kidney Injury in Hospitalized Dengue Patients: A Cross-sectional Study

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Abstract

Background: Dengue is an endemic RNA viral infection in Bangladesh. It can affect different organ systems, acute kidney injury (AKI) is one of them. The study aimed to detect the prevalence and predictors of dengue-associated acute kidney injury (DAKI) and in-hospital outcome.

Methods: This cross-sectional study was carried out from July to September 2023 at the peak of dengue outbreak in the Department of Medicine in Shaheed Monsur Ali Medical College Hospital, Dhaka, Bangladesh. A total of 203 confirmed cases of dengue aged > 12 years were finally included in the study.

Results: The prevalence of DAKI was 7.9%. The mean age of DAKI cases was higher than the non-AKI cases (p-value 0.008). AKI was significantly associated with DHF (43.8% vs 17.6%), higher HCT, higher neutrophil count and lower lymphocytes. In multivariate analyses age more than 60 years, dengue haemorrhagic fever (DHF) and multiple organ dysfunction (MODS) were the independent predictors of DAKI. AKI itself was the independent predictor of hospital stay for more than three days (OR 4.67; 95% CI 1.29-16.92). There was no mortality in the study participants. All were discharged home with resolved AKI.

Conclusion: Age more than 60 years, DHF and MODS are the independent risk factors of DAKI. Future studies are required to find out the risk factors for early diagnosis and prompt management.

Key words: Dengue, DAKI, DHF, risk factors

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Introduction:

Dengue is a mosquito-borne endemic arboviral infection in Bangladesh.[1] This RNA virus has affected about 3.7 million people and 200 dengue deaths have been reported globally in 2023 as of August 23.[2] In Bangladesh about 244698 people are affected with 1190 deaths in 2023 as of October 17.[3] Dengue fever can affect many organ systems of which Acute kidney injury (AKI) could be a serious one. The prevalence of AKI in dengue is widely variable ranging from 0.9% to as high as 69.4% in different literatures depending upon the classification systems. [4-8] The mortality rate in DAKI is 11.3-60%. [4-7,9-12] Several mechanisms have been postulated for the pathogenesis of dengue-associated AKI (DAKI), including direct action by the virus, haemodynamic instability, rhabdomyolysis, haemolysis, and acute glomerular injury. [13] The risk factors of DAKI are many, including male gender, older patient, diabetes mellitus (DM), hypertension (HTN), obesity, severe dengue, delayed hospitalization, rhabdomyolysis, multiple organ dysfunction, low haemoglobin, leukopenia, lymphopenia, thrombocytopenia, transaminitis and use of nephrotoxic drugs.[5,14,15] Early identification of DAKI in at-risk patients will help to reduce the disease severity and fatal consequences.

The prevalence of AKI in dengue patients and its associated risk factors are not well described yet in the Bangladeshi people. The primary outcome of the study was to identify the prevalence and predictors of DAKI in hospitalized patients. The secondary outcome was to assess the short-term in-hospital outcome.

Materials and methods:

This cross-sectional study was conducted in the Department of Medicine of Shaheed Monsur Ali Medical College Hospital, Dhaka, Bangladesh on 203 confirmed cases of hospitalized dengue patients during the peak of the outbreak from July to September 2023. Ethical clearance was sought from the Institutional Ethical Review Board (IERB) (ref: SMAMC/04/2023/790). Consecutive sampling was done to enroll the

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study participants. Confirmed case was defined as NS1 antigen or IgM positive. Dengue patients aged d" 12 years, with co-existing infection, pregnancy, known chronic kidney disease (CKD) and without complete data were excluded from the study. After obtaining informed written consent data was collected on a case record form including demographics, clinical characteristics and laboratory investigations. Data on the need for advanced renal support and short-term hospital outcomes including ICU care and mortality was also collected. Laboratory investigations included complete blood count, serum transaminase levels (SGPT), creatinine, electrolytes and urine routine microscopy. To detect other organ dysfunction S. lipase, amylase, Troponin-I, ECG, Chest X-ray and USG abdomen was done as appropriate. KDIGO criteria based on s. creatinine only was used to define and stage AKI. We did not incorporate urine output (UO) due to incomplete records. AKI was diagnosed if s. creatinine raised e" 0.3 mg/dl or 1.5 times the baseline. Stages of AKI were defined according to increase in s. creatinine from baseline as stage 1 if e" 0.3 mg/dl or to 1.5-1.9 times, stage 2 if 2–2.9 times or stage 3 if 3 times from baseline or initiation of renal replacement therapy (RRT).[5]

Serum creatinine was done on admission and/or during the critical phase, on discharge and if there is any significantly reduced urine output complained by the patient. The highest value was used for staging of AKI. The lowest creatinine value was considered as the baseline. Patients with a single s. creatinine Modification of Diet in Renal Disease equation (MDRD) was used to calculate baseline creatinine assuming a glomerular filtration rate of 75 mL/minute/ 1.73 m^2, for patients with only a single s. creatinine result.[16] Dengue haemorrhagic fever (DHF) was defined as thrombocytopenia (<100000/cmm), the rise of haematocrit (HCT) e"20% from the baseline, any bleeding and clinical evidence of plasma leakage (ascites or pleural effusion). Dengue shock syndrome (DSS) was defined as blood pressure <90/60 or narrow pulse pressure in patients of DHF.[17] Severe hepatitis was defined as SGPT >300 IU/L[18]. Multiple organ dysfunction syndrome (MODS) was defined as severe dysfunction of at least two organs (severe hepatitis, pancreatitis and myocarditis) including AKI. Hospital admission after three days of illness was considered late hospitalization.[14] Categorical variables were expressed as frequency (%). Continuous variables were expressed as mean ± standard deviation (SD) or median± interquartile range (IQR) as appropriate. The association of demographic, clinical and laboratory parameters with DAKI as well as the short-term in-hospital outcome was assessed by appropriate statistical test using SPSS 22.0. A p-value <0.05 was considered statistically significant.

Results

A total of 203 cases of laboratory-confirmed dengue cases were included in the study. The mean age of the study participants was 32.65±12.23 years. Males (56.7%) were more than females (43.3%). NS1 antigen was positive in 195 (96.1%) cases and the rest were IgM positive. Of the dengue classes dengue fever (DF) was the most prevalent one (62.1%), followed by DHF class I and II (19.7%), DSS (14.3%) and DF with bleeding (3.9%).

The prevalence of AKI was 7.9%. Of the AKI cases stage 1 and 2 were 87.5% and 12.5% respectively. The mean age of DAKI patients (40.44±15.4) was higher than that of non-DAKI cases 31.98±11.73 (p-value 0.008).

DHF was higher in the AKI group (43.8% vs 17.6%). Higher HCT, higher neutrophil count and lower lymphocytes were associated with AKI. There were no significant differences in terms of gender, vomiting, diarrhoea, DSS, pre-existing hypertension, DM, late hospitalization, any bleeding (10% vs 5.7%) or requirement of blood products (18.8% vs 12.8%), lowest WBC and platelet count and SGPT levels. Cases of MODS were higher among the AKI group (6.3% vs 0.5%). (Table 1).

Univariate analysis of the risk factors was done and variables with a p-value of <0.25 were analyzed in multivariate model by Forward stepwise Wald method. After adjusting the covariates, age more than 60 years, DHF and MODS were the independent predictors of DAKI. (Table 2)

Table-I

Comparison of patients between AKI and non-AKI groups with dengue (n=203)

Parameters	Overall patients (n=203)	AKI group (n=16)	Non-AKI group (n=187)	p-value
Age (Mean ±SD)	32.65±12.23	40.44±15.4	31.98±11.73	0.008*
Male, n (%)	115 (56.7%)	13 (81.3%)	102 (54.5%)	0.063
Dengue class				
DHF, n (%)	40 (19.7%)	7 (43.8%)	33 (17.6%)	0.012*
DSS, n (%)	29 (14.3%)	1 (6.3%)	28 (15%)	0.478
MODS, n (%)	2 (1%)	1 (6.3%)	1 (0.5%)	0.152
Co-morbidities				
HTN, n (%)	8 (3.9%)	2 (12.5%)	6 (3.2%)	0.123
DM, n (%)	17 (8.4%)	3 (18.8%)	14 (7.5%)	0.138
Late hospital admission >3 days, n (%)	103 (50.7%)	10 (62.5%)	143(76.5%)	
0.231				
Vomiting	188 (92.6)	16 (100%)	172 (92%)	0.614
Diarrhoea	36 (17.7%)	5 (31.3%)	31 (16.6%)	0.14
Hb (gm/dl)	12.36 ±1.94	12.74±1.0	12.33±1.99	0.411
HCT (%)	41.25±5.52	44.2±3.9	41±5.57	0.026*
Lowest WBC count (per cmm)	3790.87±1479.28	4268.75±1557.66	3749.98±1469.52	0.179
Neutrophil, n (%)	56.84±13.78	64.31±13.94	56.2±13.61	0.023*
Lymphocyte, n (%)	36.04±13.46	28.31±11.8	36.7±13.41	0.016*
Lowest platelet count (per cmm)	68000 (32000-109000)	47500 (22500-86500)	69000 (33000-109000)	0.084**
SGPT (U/L)	66 (39-96)	70.5 (49.75-148.75)	65 (35-91)	0.234**y

Hb= haemoglobin, *independent sample *t*-test, **Mann-Whitney *U* test

Table-II

Risk factors of DAKI

Parameters	Univariate analysis			Multivariate analysis		
	p-value	cOR	95% CI for OR	p-value	aOR	95% CI for OR
Age > 60 years	0.097[a]	5.2	0.92-29.26	0.014	9.87	1.58-61.61
Male gender	0.063[a]	0.28	0.08-1.0			
DHF	0.02[b]	3.63	1.26-10.44	0.005	5.23	1.65-16.59
MODS	0.152[a]	12.4	0.74-208.3	0.03	24.67	1.37-443.61
Diarrhoea	0.14[b]	2.29	.74-7.05			
Hypertension	0.063[a]	0.28	0.08-1			
DM	0.138[a]	2.85	0.73-11.21			

[a]= Fisher's exact test, [b] = Chi-square test, aOR= adjusted odds ratio, cOR= crude odd's ratio

AKI itself was the independent predictor of hospital stay for more than three days (OR: 4.67, 95% CI: 1.29-16.92, p-value 0.017)

There was no mortality in the study participants. All were discharged home with resolved AKI.

Discussion

This present study was done in a tertiary healthcare facility in Dhaka. In this study the prevalence of was DAKI 7.9%. Great variation is observed among different studies due to the different classification criteria. A study from Vietnam reported a 2.7% prevalence of AKI.[5] Other studies from Thailand and India, using KDIGO criteria for diagnosing AKI, reported a prevalence of 4.8% and 69% respectively.[6,19] In our study a higher prevalence than that of Vietnam and Thailand. These could be due smaller sample size and associated DHF.[19,20] Most of our cases were in stage 1 and 2, no stage 3 cases. Some studies reported stage 3 AKI in DF requiring haemodialysis.[19] The possible reason is the aggressive and timely fluid management and avoiding nephrotoxic medication following the national guideline. In our study we found increased mean age, DHF (43.8% vs 17.6%), higher HCT, higher neutrophil count and lower lymphocytes to be associated with DAKI. DHF causes plasma leakage resulting in hypoperfusion of the kidneys, ultimately resulting in AKI. Dengue causes the release of reactive oxygen species from neutrophils that cause renal tubular cell damage and different cytokines from lymphocytes that cause the progression of inflammation in AKI.[19] The rise of neutrophil to lymphocyte ratio is reported to be associated with AKI in sepsis.[20] Male gender, DM, HTN and rhabdomyolysis as predictors of AKI in dengue patients.[5,14,21] However, we did not find gender, severe thrombocytopenia (50000/cmm), DM, HTN or DSS to be significantly associated with it. Our study is similar in terms of high HCT, raised neutrophil and lower lymphocyte mean values and DHF.[5,11,14,21] Though DSS is an important predictor of AKI, our study did not find the same.[7,9] In the present study we had only one case of AKI who had DSS. In the present study, only serum creatinine was used to report AKI, which may have missed DAKI in DSS cases. Moreover, AKI may occur in EDS even without DHF/DSS.[17] Studies reported severe thrombocytopenia as a complication of AKI, but our study did not find the same.[22] In the multivariate model, age more than 60 years, DHF and MODS were the independent predictors of DAKI. These findings are similar to different studies.[6,11,14,22]

AKI was an independent predictor of longer hospital stays of more than three days. Studies by Khalil et al, Mallhi et al and Patel et al support the same.[10,14,19]

The limitations of the study were small sample size and single-centre study. We only enrolled hospitalized dengue cases. So, the results cannot be generalized to the general population. We relied only on s. creatinine for detecting AKI. No data on UO was collected. However, some studies showed AKI cases defined by s. creatinine were severely ill in comparison to UO criteria of AKI.[22] We did not find out the exact cause of AKI in dengue by histopathological study. However, the findings of our study can be used in the future as a pilot for extensive study.

Conclusion:

This study will alert clinicians about the possibility of developing AKI in dengue patients having risk factors. Early identification of DAKI will reduce morbidity, mortality and overall burden on the healthcare system.

Conflict of interest: None

Recommendation

Studies with larger samples and from different centers need to be carried out to find out the predictors of DAKI.

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