Factors Associated with Dengue Mortality among Patients Admitted to a Tertiary Hospital in Chattogram, Bangladesh during 2023 Dengue Outbreak

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Abstract

Background: Chattogram City in Bangladesh is hyper-endemic for dengue and is one of the leading districts in reporting deaths due to dengue. As primary prevention of dengue has had limited success, the prevention of mortality through the identification of risk factors and efficient patient management is of utmost importance. The current study aimed to identify clinical predictors of mortality in adult patients with dengue in a public tertiary-level hospital in Chattogram, Bangladesh.

Materials and methods: A record-based retrospective case-control study was conducted at Chittagong Medical College Hospital (CMCH). 46 (Fourty six) death patients were included in the study as case and 46 age and sex matched survivors were enrolled as control who were admitted at CMCH during course of their illness. Demographic, clinical, and treatment-related factors were compared between the two groups. Most of the patients in the case group were admitted (47.6%) and expired (50%) during the evening shift (2.30-10.00 pm).

Results: In multivariate analysis for predicting mortality, patients from rural areas [Odds Ratio (OR): 7.40, 95% Confidence Interval (CI):1.53-15.23, p=0.012], Dengue Shock Syndrome (DSS) at admission (OR:8.72, 95% CI:1.89-21.21, p=0.006) presence of comorbidity (OR:6.76, 95% CI:1.53-21.11, p=0.012), and patients complicated with respiratory failure (OR: 8.84, 95% CI:3.16-31.21, p=0.001) were associated with mortality in patients with dengue.

Conclusion: The independent predictors of mortality were rural residence, DSS at admission, comorbidity and development of respiratory failure. Addressing these factors with more rigorously monitored treatment would likely reduce mortality.

Key words: Dengue; Mortality; Risk factors.

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Introduction

Ever since the first outbreak in Bangladesh in 2000, between January 01 and December 31, 2023, there were 321,179 dengue hospitalizations, including the highest number of 1,705 related deaths in Bangladesh's history of dengue fever reported by the Ministry of Health & Family Welfare (MOHFW).[1,2] In 2023, Bangladesh was the country most affected by dengue in Southeast Asia, with the highest number of deaths reported worldwide. Since 2019, Bangladesh has been one of the seven identified countries in this region that regularly reports Dengue Fever/Dengue Hemorrhagic Fever (DF/DHF) outbreaks. Bangladesh appears to be transforming into a significant hyper-endemic niche for dengue infection. Increasingly, previously unaffected areas are being struck by the dengue epidemic.[3,4] In 2023, The dengue virus affected all districts of Bangladesh, but Dhaka and Chattogram reported the most confirmed cases.[1]

In the year 2023, the Case Fatality Rate (CFR) due to dengue varies among countries, with the lowest being in Singapore (0.1%) and the highest in Bangladesh (0.5%).[5,6] The recent epidemiology of dengue in Bangladesh has imposed a substantial economic and disease burden on patients and the healthcare system with increased hospital stays, high morbidity and attendant mortality.[2,7,8] Despite the alarming increase in dengue-related deaths in Bangladesh, recent data describing factors associated with fatal cases are scarce. Efforts made by Afroz et al. lack statistical comparison between fatal and non-fatal cases and are limited to severe dengue cases.[9] These findings necessitate studies to differentiate characteristics among fatal and non-fatal dengue cases. Early identification of risk factors associated with mortality can help physicians in managing high-risk patients with dengue. These factors could also be used in formulating predictive scores to identify severely ill patients during future

outbreaks and to prioritize care that may translate into reduced morbidity and mortality. In this context, a retrospective case-control study was intended to investigate demographic, clinical and treatment-related characteristics associated with mortality among patients with dengue admitted to a tertiary care hospital in Chattogram, Bangladesh, during the 2023 outbreak.

Materials and methods

A case-control study was conducted using the hospital records of adult dengue patients admitted to Chittagong Medical College from January 2023 to December 2023. Chittagong Medical College Hospital, located in the southeastern part of Bangladesh, is the second-largest public hospital in Bangladesh. It provides comprehensive tertiary health care irrespective of economic or social status and disabilities.

A 'case' was defined as a patient who was admitted with a diagnosis of probable dengue confirmed by either NS1-antigen or IgM antibody detection and who died during the hospital stay. The 'controls were dengue-confirmed patients who recovered from the illness during their stay in the hospital and were subsequently discharged. There were 68 confirmed dengue deaths during the study period, and among them, 46 patients met the eligibility criteria and had completed medical records, these were selected as the cases. The patients who met the criteria for controls were enlisted, and 46 individuals were randomly selected from this list.

A semi-structured questionnaire was used to collect the study variables. The study variables included demographic characteristics, such as age, sex, residential location, and clinical severity at admission. The presence of comorbidities, complications developed during the treatment, therapeutic modalities used, e.g maximum oxygen requirement, amount of IV fluid infused, antibiotic, steroid and ICU requirement, the time of hospital admission, and the time of death were recorded.

Data entry and analysis were completed in SPSS version 25.0. All the variables were categorized. Chi-square and Fisher's exact tests were used for the bivariate analysis. Univariate and multivariable binary logistic regression analyses were used to determine the independent predictors of in-hospital mortality in dengue patients. Results were expressed as OR and 95% CI for OR. The ethics board of Chittagong Medical College granted research approval (Memo No: CMC/59.27.0000.013.19 PG.2024/320, Dated 26/06/2024). The need for informed consent was waived.

Results

A total of 92 patients were included in this study. Age ranged between 14-75 years, with a mean age of 39.2±16.3 years. The mean age of the patients who expired was 43.3±14.4 and 33.9±13.3 years. In the case group, 37% and 17.4% of the patients were in the 41-60 and >60 age group, compared to 26.1% and 4.3% of the controls. The male-to-female ratio in both groups was similar (p=0.832). Regarding residential status, the mortality rate was significantly higher among patients from rural areas than those from urban (59% vs. 32.3%, p=0.015).

Table I Demographic characteristics of the patients

Variables		Case (n=46)		Control (n=46)		p value*
		n	%	n	%	
Age						
	≤ 40 years	21	45.6	32	69.6	
	41-60 years	17	37.0	12	26.1	0.034
	>60 years	8	17.4	2	4.3	
Sex						
	Male	18	39.1	19	41.3	0.832
	Female	28	60.9	27	58.7	
Residence						
	Rural	36	78.3	25	54.3	0.015
	Urban	10	21.7	21	45.7	

Case: Dengue admitted patients died during the hospital stay, Control: Dengue admitted patients who recovered and discharged, *Chi-square test.

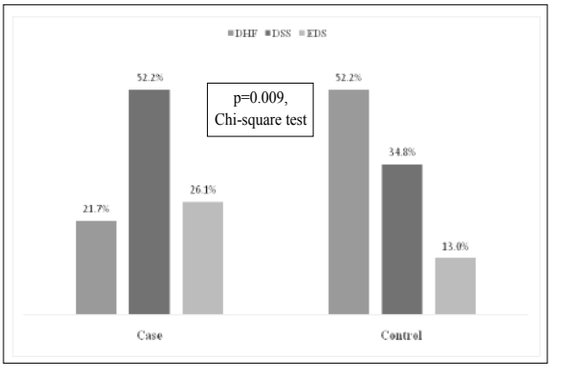

Figure 1 Association between admission dengue severity and the outcome (DHF: Dengue Hemorrhagic Fever, DSS: Dengue Shock Syndrome, EDS: Expanded Dengue Syndrome)

In the case group 52.2% and 26.1% of the patients had DSS and EDS at admission, respectively. On the other hand, 34.8% and 13% of the patients had DSS and EDS at admission, respectively, in the control group (Figure 1). Laboratory diagnosis of dengue fever was confirmed by NS 1 antigen only, IgM only and both in 41.3%, 34.8% and 23.9% of the cases, respectively. In the control group the corresponding figures were 78.3%, 8.7%, and 13%, respectively.

Overall, significantly higher proportion of the patients in the case group had associated comorbid conditions than control group (p=0.001) (Table II). Regarding individual comorbidity, diabetes mellitus was more frequent among case group than control group (28.3% vs. 10.9%, p=0.036).

Table II Comorbidity profile of the patients

Comorbidity	Case (n=46)		Control (n=46)		p value
	n	%	n	%	
No comorbidity	31	67.4	15	32.6	0.001*
Diabetes mellitus	13	28.3	5	10.9	0.036*
Hypertension	8	14.4	9	16.9	0.788*
Ischemic heart disease	4	8.7	6	13.0	0.503†
Pregnancy	2	4.3	4	8.7	0.674†
Bleeding disorder	5	10.9	0	0	0.056*
Others	7	15.2	4	8.7	0.335*

*Chi-square test, †Fisher's exact test.

Table III depicts that all the patients in the case group encountered either one or more in-hospital complications compared to 91.3% in the control group. Among different complications, respiratory failure and DIC were significantly more frequent in case than control group.

Table III Complication developed during treatment

Complication	Case (n=46)		Control (n=46)		p value
	n	%	n	%	
No complication	0	0	4	8.7	0.117†
Respiratory failure	22	47.8	3	6.5	<0.001*
Shock	14	30.4	13	28.3	0.819
Encephalitis	11	23.9	5	10.9	0.099*
Myocarditis	6	13.0	10	21.7	0.271*
Hepatic failure	7	15.2	3	6.5	0.180*
Renal failure	9	19.6	6	13.0	0.397*
Sepsis	9	19.6	4	8.7	0.185*
Heart failure	5	10.9	1	2.2	0.203†
DIC	6	13.0	0	0	0.026†
Others	4	8.7	10	21.7	0.082*

DIC: Disseminated Intravascular Coagulation, *Chi-square test, †Fisher's exact test.

Table IV shows that ICU was indicated in significantly higher proportion of the patients in the case group than in the control group (97.8% vs 8.7%, p<0.001) and only 15.2% patients in the case group and none in the control group received ICU support. Intravenous steroid and antibiotic were used more frequently in the case group than control group. Oxygen requirement was more in patients in the case group than the control group (Table IV).

Table IV Treatment modalities used for the patients (n=92)

Variables	Case (n=46)		Control (n=46)		p value
	n	%	n	%	
Time of admission					
8.00 am -2.30 pm	12	26.1	16	34.0	0.130*
2.30pm-10.00 pm	22	47.8	13	27.7	
10.00pm -8.00 am	12	26.1	18	38.3	
ICU indicated	45	97.8	4	8.7	<0.001*
Treated in ICU	7	15.2	0	0	0.012†
Steroid					
Injectable	29	63.0	21	45.7	0.094*
None	17	37.0	25	54.3	
Antibiotic					
Injectable	39	84.8	24	52.2	<0.001*
None	7	15.2	22	47.8	
Maximum oxygen received					
5 L/min	23	50.0	15	32.6	<0.001*
5-10 L/min	13	28.3	1	2.2	
>10 L/min	2	4.3	0	0	
None	8	17.4	30	65.2	

ICU: Intensive Care Unit, *Chi-square test, †Fisher's exact test.

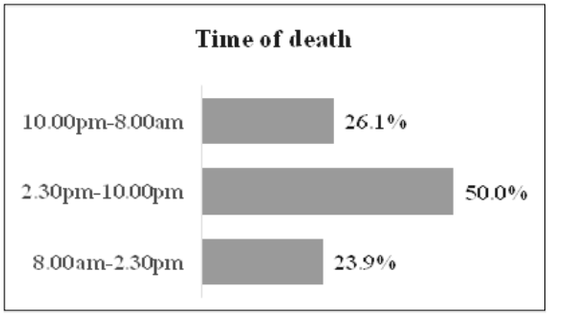

Figure 2 Time of death of the patients in the case group (n=46)

Figure 2 shows that, half of the patients in the case group expired during evening hours (2.30-10.00pm), followed by 26.1% in the night shift (10.00pm -8.00am) and 23.9% in the morning shift (8.00am-2.30pm).

Multivariate analysis showed that hailing from rural area (OR: 7.40, 95% CI:1.53-15.23, p=0.012), DSS at admission (OR:8.72, 95% CI:1.89-21.21, p=0.006) presence of comorbidity (OR:6.76, 95% CI:1.53-21.11, p=0.012) and in-hospital development of respiratory failure (OR: 8.84, 95% CI:3.16-31.21, p=0.001) were statistical significant predictor of mortality (Table V).

Table V Univariate and multivariable binary logistic regression analysis for predictors of death

Variables	Unadjusted OR (95% CI)	p value	Adjusted OR (95% CI)	p value
Age group				
≤40 years	References		References	
41-60 years	2.16 (0.86-5.24)	0.102	2.05 (0.53-7.89)	0.295
>60 years	6.10 (1.18-5.56)	0.031	4.34 (0.53-9.51)	0.172
Residence				
Urban	References		References	
Rural	3.02 (1.22-7.51)	0.017	7.40 (1.53-15.23)	0.012
Lab diagnosis of DF				
Only NS1 antigen	References		References	
Only IgM	7.58 (2.22-9.89)	0.001	2.68 (0.52-13.3)	0.242
Both NS1& IgM	3.47 (1.11-5.22)	0.032	2.32 (0.46-11.58)	0.308
Dengue severity				
DHF	References		References	
DSS	3.60 (1.36-6.66)	0.010	8.72 (1.89-21.21)	0.006
EDS	4.8 (1.41-8.45)	0.012	5.81 (0.92-19.21)	0.062
Any comorbidity				
Absent	References		References	
Present	4.27 (1.79-8.21)	0.001	6.76 (1.53-21.11)	0.012
Diabetes mellitus				
Absent	References		References	
Present	3.23 (1.05-9.89)	0.042	0.87 (0.15-5.03)	0.884
Develop RF				
No	References		References	
Yes	13.14 (3.56-15.21)	<0.001	8.84 (3.16-31.21)	0.001

RF: Respiratory Failure, OR: Odds Ratio, CI: Confidence interval.

Discussion

The dengue case fatality rate was relatively high compared to previous years in Bangladesh in the year 2023. The leading causes of death were disease severity, shock, bleeding and multiple organ failure.[4,5] This study investigated the factors influencing the mortality in admitted dengue patients at Chittagong Medical College Hospital during the 2023 outbreak. Existing findings suggest that age is a critical factor in dengue severity and mortality, with young and older individuals being more vulnerable.[10,11] Age was identified as an important determinant of mortality in adult and pediatric dengue patients in previous studies.[7,12] In the present study, the mean age of the expired patients was significantly higher than those who survived and were discharged. However, the association between age and mortality was not retained in multivariate analysis. This could be due to our study's small number of patients, which reduced the power to detect differences between populations with and without dengue complications. The male-to-female ratio was similar in both groups in the present study, indicating no association between gender and dengue mortality, which agreed with the previous studies.[12,13] While dengue has traditionally been considered an urban disease, recent studies suggest that dengue transmission and mortality are also significant in rural areas.[14] In the present study, rural residence had an independent association with dengue mortality. Factors such as limited access to healthcare, lower socioeconomic status, and differences in healthcare-seeking behavior in rural areas can contribute to higher dengue mortality rates.[14,15]

One of the most important predictors of mortality in this study was DSS at presentation, which agreed with other studies.[13] DSS is a severe life-threatening complication of dengue and occurs most often in older patients, during infection with certain DENVsero types and a second heterotypic DENVinfection. [16]

We found a higher proportion of patients in the case group had associated comorbid conditions than the control group and any comorbidity was an independent predictor of dengue mortality in the present study. A higher number of comorbidities was associated with an unfavorable prognosis for dengue.[17] This could be attributed to the fact that the presence of comorbidities complicates the clinical management of patients with dengue, especially in the case of cardiovascular, chronic renal and pulmonary diseases.[18]

In the present study, the most significant predictor of dengue mortality was respiratory failure; patients with respiratory failure had about nine times higher chance of mortality (OR:8.84, 95% CI:3.16-31.21) than those who did not have this

complication. Respiratory failure is a critical complication in severe dengue cases, particularly in patients with DSS. Studies have shown that acute respiratory failure is a significant cause of death in dengue patients.[19,20]

The study findings would assess the circumstances during the management of dengue patients that influence the outcome in Chittagong Medical College Hospital. However, the small sample size was a significant limitation of the study and is the reason for the wide CIs of the ORs. As the case fatality rates of dengue are low, especially in tertiary-level hospitals with good management, we could obtain only a small number of cases. Another drawback of the study was that the study was retrospective and used only information recorded in the case sheets. Therefore, specific crucial determinants of mortality, such as serotype and biochemical parameters, could not be studied.

Limitation

Some records and documents could not collected properly.

Conclusion

Patients with dengue fever who came from rural areas had DSS during admission, had comorbidities and developed respiratory failure in the hospital have a higher risk of mortality. Dengue patients with these clinical features should be given extra care and monitored rigorously to decrease mortality.

Recommendation

More study should be conducted to find out the actual picture about this issue.

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Contribution of authors

MAR-Acquisition of data, data analysis, drafting and final approval.
NM-Data analysis, interpretation of data, drafting and final approval.
MI-Interpretation of data, critical revision and final approval.
MMRC-Conception, critical revision and final approval.
MSA-Design, critical revision and final approval.
RAMEU-Data analysis, interpretation of data, drafting and final approval.
MKU-Acquisition of data, data analysis, drafting and final approval.

Disclosure

All the authors declared no conflict of interest.

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