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Original Article

Myocarditis in Admitted Patients with Dengue Fever in a Tertiary Care Hospital of Bangladesh

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Abstract

Background: *Severe dengue may be associated with fatal cardiac complications including myocarditis. The incidence of cardiac complications in patients with dengue illness varies greatly from one series to another and there is a paucity of available data on the prevalence of dengue- associated myocarditis in Bangladesh. This study aimed to investigate the occurrence and association of myocarditis in adult patients with dengue in a public tertiary-level hospital in Chattogram, Bangladesh.*

Materials and methods: *A prospective observational study was conducted among 268 admitted patients 18 years of age having confirmed dengue fever at Chittagong Medical College Hospital (CMCH) fromJanuary 2023 to December 2023. Electrocardiography (ECG) cardiac biomarkers, and echocardiography were done for all patients. Diagnosis of myocarditis was as per European Society of Cardiology (ESC) 2013 criteria. Outcome was assessed at in-hospital mortality or discharged.*

Results: *The mean age of 34.6±15.5 years and 66.8% were males. ECG abnormalities were observed in 44 (24%) patients, biomarkers were elevated in 27 (10.1%) patients and 24 (9%) patients had echocardiographic abnormalities. According to ESC 2013 criteria, dengue fever with myocarditis was diagnosed in 40 [14.9% (95% CI: 10.9-19.8%] patients. The patients with myocarditis were more likely to have comorbidity, chest pain and respiratory distress. In-hospital mortality rate was 2.5% and 3.9% in patients with and without myocarditis, respectively (p=0.656).*

Conclusion: *Myocarditis among admitted dengue patients is not uncommon. However, further study is needed to understand its effect on morbidity and mortality among hospitalized dengue patients.*

Key words: Dengue; Myocarditis; Outcome; Morbidity and mortality.

INTRODUCTION

Dengue fever is caused by any of the four serotypes of the dengue virus transmitted by the mosquito species Aedes aegypti and Aedes albopictus. The clinical course of dengue is divided into three distinct phases: a febrile phase, lasting 3–7 days, a critical phase, lasting 2–3 days around defervescence and a recovery phase.[1] The increase in capillary permeability that occurs in some patients in a critical phase and can cause intravascular hypovolemia and shock is the best-known cardiovascular complication associated with dengue. Additionally, various specific cardiac manifestations have been described, ranging from rare functional myocardial impairment to arrhythmias and myocarditis.[2-4] Myocarditis has now been included in the definition of severe dengue adopted in the 2009 WHO revised classification, but the true incidence of myocarditis remains unknown owing to the lack of screening in most countries where DENV is endemic.[5]

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The definitive diagnosis of myocarditis depends on an endomyocardial biopsy. However, the clinically suspected diagnosis is based on history, clinical examination, and biochemical and radiological profile. The European Society of Cardiology (ESC) 2013 consensus statement suggested the presence of at least one clinical and one diagnostic criterion for the diagnosis of clinicallysuspected myocarditis. Clinical criteria include acute new-onset or worsening dyspnea, palpitations, and unexplained shock. The diagnostic criteria include ECG or Holter changes, raised cardiac biomarkers, functional and structural abnormalities on cardiac imaging, and tissue characterization on Cardiac Magnetic Resonance (CMR) imaging.[4,6] Literature on dengue myocarditis prevalence and outcomes must be more consistent due to varied diagnostic criteria. The reported range of myocarditis varies from 2.4–78% of dengue patients with a pooled prevalence of dengue-induced myocarditis of 21.0%.[7]

In 2023, Bangladesh was the country most affected by dengue in Southeast Asia, with the highest number of deaths reported worldwide. 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.[8,9] In 2023, The dengue virus affected all districts of Bangladesh, but Dhaka and Chattogram reported the most confirmed cases.[10] 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%).[11,12] 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.[13-15] Despite the alarming increase in dengue-related deaths in Bangladesh, there is a scarcity of comprehensive studies that specifically investigate myocarditis in this context within Bangladesh.

This study was conducted to provide valuable insights into the incidence of myocarditis among dengue fever patients and assess the impact of myocarditis on outcomes among patients admitted to a tertiary care hospital in Chattogram, Bangladesh, during the 2023 outbreak. Understanding the occurrence and clinical manifestations of myocarditis in dengue-infected patients was crucial for health care professionals in managing and treating individuals with this disease, particularly in regions where dengue is endemic.

MATERIALS AND METHODS

A prospective observational study was conducted among adult dengue patients admitted to CMCH 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. The ethics board of Chittagong Medical College granted research approval (Memo No: CMC/ 59.27.0000.013.19.PG.2023.009/ Dated: 5/12/2023) and informed consent was obtained from the patients or their caregivers.

Consecutive patients aged ≥18 years diagnosed with probable dengue confirmed by either NS1- antigen or IgM antibody detection were included. Patients on medications affecting heart rhythm/rate, patients with preexisting heart disease (Myocarditis, myocardial ischemia, myocardial infarction, heart failure, coronary artery disease, rheumatic heart disease, valvular heart disease and congenital heart disease) or patients with electrolyte abnormalities potentially affecting heart rate/rhythm were excluded from the study.

The patients were evaluated daily by meticulous history and ECG during their hospital stay. Clinical features of myocarditis considered in this study were acute chest pain, new-onset (Days up to 3 months) or worsening of dyspnoea at rest or exercise and/or fatigue, with or without left and/or right heart failure signs, palpitation and/or unexplained arrhythmia symptoms and/or syncope, and/or aborted sudden cardiac death, unexplained cardiogenic shock. ECG features of myocarditis included any of the following:atrioventricular block, or bundle branch block, ST/T wave change (ST elevation or non-ST elevation, T wave inversion), sinus arrest, ventricular tachycardiaor fibrillation and asystole, atrial fibrillation, reduced Rwave height, intraventricular conduction delay (widened QRS complex), abnormal Q waves, low voltage, frequent premature beats, supra-ventricular tachycardia. If symptoms and ECG changes were suggestive of myocarditis, the patient was further evaluated by Troponin-I and echocardiography. The biomarkers were measured using an enzyme-linked fluorescent assay (VIDAS Troponin-I Ultra). Trop I was considered to be raised when serum levels were more than 19 ng/L, The ESC diagnostic criteria for clinically suspected myocarditis (2013) was used to diagnose dengue myocarditis. Ituses clinical features along with i) Characteristic changes on ECG ii) Myocardiocytolysis markers iii) functional and structural abnormalities on cardiac imaging [Echo/angio/Cardiovascular Magnetic Resonance (CMR)] and iv) Tissue characterization by CMR. The diagnosis of myocarditis requires clinical features and ≥ one diagnostic criterion from different categories, in asymptomatic patients, ≥2 diagnostic criteria need to be fulfilled.[6] All patients were followed up till their discharge/ death (Which was earlier).

Data entry and analysis were completed in SPSS version 25.0. The qualitative variables were compared with the Chi-square or Fisher's exact test. Quantitative variables with a normal distribution were compared using Student'st-test for two-group analysis. Ap-value of less than

0.05 was considered significant and the confidence interval was set at 95%.

RESULTS

A total of 306 admitted patients were screened for eligibility and 268 patients with confirmed dengue satisfying the inclusion and exclusion criteria were included in this study. According to ESC 2013 criteria, dengue fever with myocarditis was diagnosed in 40 [14.9% (95% CI: 10.9- 19.8%] patients. The mean age of the patients was 34.6±15.5 years, and the mean age of the patients with myocarditis was significantly higher than those without myocarditis (Table I).

Table I Demographic characteristics of the patients (n=268)

Variables	Total (n=268)		Dengue with myocarditis (n=40)		Dengue without myocarditis (n=228)		p value
	n	%	n	%	n	%	
Age, years (Mean±SD)	34.6±15.5		46.3±18.7		32.5±13.9		<0.001†
Sex							
Male	179	66.8	23	57.5	156	68.4	0.176*
Female	89	33.2	17	42.5	72	31.6	
Residence							
Rural	179	66.8	28	70.0	151	66.2	0.640*
Urban	89	33.2	12	30.0	77	33.8	

*Chi-square test, †Independent sample test.

The patients with myocarditis were more likely to have comorbidity, chest pain, palpitation, respiratory distress, syncope and bradycardia than the patients without myocarditis (Table II).

Table II Clinical profile of patients (n=268)

Variables	Total (n=268)		Dengue with myocarditis (n=40)		Dengue without myocarditis (n=228)		p value*
	n	%	n	%	n	%	
Comorbidity							
Absent	217	81.0	26	65.0	191	83.8	0.005
Present	51	19.0	14	35.0	37	16.2	
Chest pain							
Absent	238	88.8	24	60.9	214	93.9	<0.001
Present	30	11.2	16	40.0	14	6.1	
Palpitation							
Absent	240	90.2	29	72.5	211	93.4	<0.001
Present	26	9.8	11	27.5	15	6.6	
Respiratory distress							
Absent	232	86.6	21	52.5	211	92.5	<0.001
Present	36	13.4	19	47.5	17	7.5	
Syncope							
Absent	253	94.4	34	85.0	219	96.1	0.005
Present	15	5.6	6	15.0	9	3.9	
Tachycardia							
Absent	203	75.7	29	72.5	174	76.3	0.604
Present	65	24.3	11	27.5	54	23.7	
Bradycardia							
Absent	255	95.1	31	77.5	224	98.2	<0.001
Present	23	4.9	9	22.5	4	1.8	

*Chi-square test.

Out of a total of 268 patients with dengue, 48 (18%) patients demonstrated non-specific ST segment changes. Sinus tachycardia or bradycardia was observed in 14 (5.2%) patients and AVB/BBB was seen in 13 (4.9%). Cardiac TnI enzyme was elevated in 12 (4.5%) patients and NT-pro BNP was elevated in 19 (7.1%) patients. Among these 61 patients who underwent echocardiography, 24 (39.3%) patients had echocardiographic evidence of myocarditis.

Table III Laboratory profile of patients (n=268)

Variables	Total (n=268)		Dengue with myocarditis (n=40)		Dengue without myocarditis (n=228)		p value*
	n	%	n	%	n	%	
Any ECG abnormality							
Absent	209	78.0	11	27.5	198	86.8	<0.001
Present	59	22.0	29	72.5	30	13.2	
ST change							
Absent	219	82.0	15	37.5	204	89.9	<0.001
Present	48	18.0	25	62.5	23	10.1	
Arrythmia							
Absent	254	94.8	32	80.0	222	97.4	<0.001
Present	14	5.2	8	20.0	6	2.6	
AVB/BBB							
Absent	255	95.1	34	85.0	221	96.9	0.001
Present	13	4.9	6	15.0	7	3.1	
Cardiac TroponinI							
Not done	156	57.8	0	0	155	68.0	
Raised	12	4.5	12	30.0	0	0	<0.001
No change	101	37.7	28	70.0	73	32.0	
NT-proBNP							
Not done	246	91.8	20	50.0	226	99.1	
Raised	19	7.1	18	45.0	1	0.4	<0.001
No change	3	1.1	2	5.0	1	0.4	
Echo change							
Not done	207	77.2	8	20.0	199	87.3	
Present	24	9.0	24	60.0	0	0.0	<0.001
Absent	37	13.8	8	20.0	29	12.7	
Pericardial effusion							
Notdone	211	78.7	9	22.5	202	88.6	
Present	10	3.7	10	25.0	0	0.0	<0.001
Absent	47	17.5	21	52.5	26	11.4	

AVB: Atrio Ventricular Block, RBB: Right Ventricular Block, NT-pro BNP: N-terminal pro-B-type natriuretic peptide, *Chi-square test.

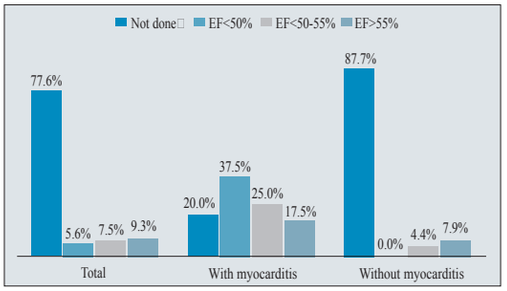

Figure 1 Left ventricular ejection fraction of the dengue patients

Overall, left ventricular systolic ejection fraction could be detected in 50 out of 268 dengue admitted patients only 5.6% had low EF (<50%). Out of 40 patients with myocarditis 15(37.5%), 10(25%) and7(17.5%) patients had EF<50%, 50-55% and >55%.

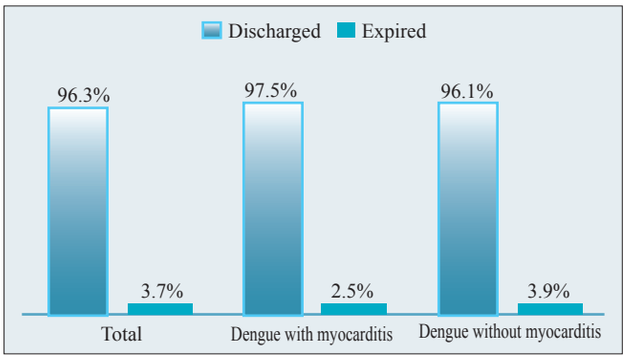

Figure 2 Outcome of the dengue patients

There was a total of 10 (3.7%) deaths in the study population. Among them one (2.5%) and 9 (3.9%) patients was in the group with myocarditis and without myocarditis, respectively (p=0.656, Chi-square test).

DISCUSSION

Myocarditis in dengue infection was rarely reported from Bangladesh. Conducting a study on myocarditis in dengue fever patients in CMCH was essential to bridge existing knowledge gaps, enhance clinical care, and ultimately improve patient outcomes in the face of this recurring and widespread dengue. In the present study, 14.9% (95% CI: 10.9-19.8%) of admitted patients with dengue fever had evidence of myocarditis according to the ESC 2013 criteria. Few studies have evaluated the prevalence of myocarditis in patients with dengue. In a recent study from India, the prevalence of myocarditis in hospitalized dengue patients was found to be 7.1%.[16] In contrast, another study from India reported much higher prevalence of myocarditis in dengue patients (37.5%).[17]Another study from China the prevalence of myocarditis was 11.3%.[18] The wide variation of prevalence of myocarditis reported is due to different diagnostic criteria being used across studies.

In the present study, 22% patients had abnormalities on electrocardiography, 72.5% patients with myocarditis had characteristic ECG abnormalities. Cardiac TnI was elevated in 10.6% (12/113) and all of these patients were diagnosed to have myocarditis. In the study of Bhatt et al, cardiac enzymes were elevated in 14.8% patients, of which 40.7% patients had echocardiographic abnormalities and diagnosed as having myocarditis.[16]

A few studies have evaluated left ventricular function in patients with Dengue. Datta et al. in their study on120 dengue patients reported left ventricular systolic dysfunction (Ejection fraction 35–45%) through echocardiography in 3.3% of the patients.[19]In the present study overall, left ventricular systolic ejection fraction could be detected in 50 out of 268 dengue admitted patients only 5.6% had low EF (<50%). Out of 40 patients with myocarditis15(37.5%) patients had EF <50%.

In the present study the age of the admitted dengue patients ranged between 14-86 years with a mean age of 34.6±15.5 years. There was male predominance with a male to female ratio of 2:1. The age and sex distribution of the dengue patients agreed with the similar recent studies from Bangladesh.[20,21] This type of sex differences may be due to social background of the Asian countries. Males in this region are more likely to work outdoor rendering more exposed to the mosquito bites during day time either at their work places or while travelling. Moreover male patients have greater chance to go for health care facilities in Bangladesh. While dengue has traditionally been considered an urban disease, recent studies indicate that dengue transmission and mortality are also significant in rural areas.[22] In the present study, about two-third of the patients were from rural areas.

Literature from Bangladesh on myocarditis in dengue was scarce. Reza et al. recently described two cases of expanded dengue syndrome complicated with fulminant myocarditis which improved due to timely diagnosis and prompt management.[23] In the current study, the overall CFR was 3.7% and it was 2.5% in the patients with myocarditis. In the study of Bhatt et al there was a total of 5 (2.7%) deaths and all the patients who died, had severe dengue with myocarditis.[16] However, due to small number of patients with poor outcome it was not possible to comment on the association between myocarditis and in-hospital outcome in the present study,

The present study results add to the growing body of evidence regarding the cardiac manifestation of dengue infections and would help facilitate early diagnosis and intervention strategies. However, there are a number of significant limitations to the present study. Cardiovascular Magnetic Resonance (CMR) is an expensive investigation and is not widely available, so CMR could not be used in our study to diagnose myocarditis. The patients with myocarditis were not followed up as apart of this study to look for any persisting cardiac dysfunction. Further more, being a tertiary care referral centre, an over-reporting due to referral bias cannot be ruled out. Hence, our study's sample size may not truly represent the population. Finally, consecutive patients could not be screened as many patients were admitted briefly (< 24 h) and children (< 14 years) were excluded.

CONCLUSIONS

Myocarditis among admitted dengue patients is not uncommon. As existing evidence suggest that dengue fever complicated by myocarditis has prognostic implications, there is a need to have an algorithm for suspicion and diagnosis of myocarditis among patients with dengue fever. With an increasing incidence of dengue fever, newer treatment strategies are needed for the management of fulminant myocarditis and improvement of the outcome.

DISCLOSURE

All the authors declared no competing interest.

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