

Frequency and clinical factors associated with myocarditis among patients with dengue fever: A cross-sectional study from a tertiary care hospital in Karachi

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ABSTRACT

Objectives: The study aims to determine the frequency of myocarditis among patients presenting with dengue fever and identify the clinical factors associated with myocarditis at a tertiary care hospital in Karachi.

Material and Methods: This descriptive cross-sectional study was conducted at the Department of Internal Medicine, Memon Medical Institute, Karachi, over a period of six months from 22 September 2025 to 22 March 2026. A total of 387 patients aged 15–70 years with confirmed dengue fever were enrolled through non-probability consecutive sampling. Patients with pre-existing cardiac diseases, congenital heart defects, active viral infections other than dengue, pregnancy, and severe co-morbid illnesses were excluded. Demographic and clinical data were recorded on a structured proforma. All patients underwent electrocardiography and laboratory investigations including serum troponin I, serum bicarbonate, and serum creatinine. Echocardiography was performed when clinically indicated. Data were analyzed using SPSS version 26. Associations between myocarditis and study variables were assessed using the Chi-square test, with $p \leq 0.05$ considered statistically significant.

Results: The mean age of the participants was 36.8 ± 14.2 years, and 232 (59.9%) were males. Myocarditis was identified in 16 (4.1%) patients. Duration of fever ($p=0.049$), hospital stay duration ($p<0.001$), elevated troponin I ($p<0.001$), abnormal echocardiography ($p<0.001$), hypertension ($p=0.006$), diabetes mellitus ($p=0.009$), atrial fibrillation ($p<0.001$), low serum bicarbonate ($p<0.001$), and high serum creatinine ($p<0.001$) were significantly associated with myocarditis.

Conclusion: Myocarditis was an uncommon complication of dengue fever. Several clinical and laboratory factors were significantly associated with myocarditis and may aid in its early identification and timely management.

Keywords: Atrial fibrillation, Dengue fever, Echocardiography, Hypertension, Myocarditis, Troponin I.

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INTRODUCTION

Myocarditis is an inflammatory disease of the myocardium frequently resulting from viral infections or post-viral immune-mediated responses [1]. It is clinically diagnosed through a combination of symptoms, elevated cardiac biomarkers, electrocardiographic changes, and cardiac imaging findings according to standardized diagnostic criteria. The condition can reduce the heart's ability to pump blood. Myocarditis can cause chest pain, shortness of breath, and rapid or irregular heartbeats [2]. Myocarditis can present with a mildly raised cardiac enzyme to severe myocarditis leading to congestive heart failure, arrhythmias, cardiogenic shock, and death. It is a predictor of morbidity and mortality in

dengue-infected patients [3]. Dengue, an arthropod-borne viral

infection and one of its complications is myocarditis [4]. Dengue myocarditis is considered an uncommon complication of dengue, although its reported incidence is likely an underestimation [5].

The frequency of myocarditis in patients with dengue fever varies across studies [6]. A systematic review involving studies from multiple countries reported that the pooled prevalence of dengue-induced myocarditis was 21.0% [7]. compared to that from Latin America was 3.6% [8]. A study from China among hospitalized patients with dengue fever reported that 11.3% developed myocarditis [9]. Another study from Sri Lanka among patients with dengue fever reported myocarditis in 27% of cases [10].

It is crucial to acknowledge the significant burden of myocarditis among dengue patients in our population. Therefore, this study aims to explore not only the frequency of myocarditis but also to identify the key risk factors contributing to its development. Understanding these factors helped in improving clinical outcomes, guiding healthcare interventions, ensuring early recognition of the disease, and

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facilitating prompt management for patients with dengue fever. The objective of the study is to determine the frequency and associated factors of myocarditis in patients presenting with dengue fever at a tertiary care hospital in Karachi.

MATERIAL AND METHODS

A descriptive cross-sectional study was carried out in the Department of Internal Medicine of Memon Medical Institute, Karachi. The study was approved by the Ethical Review Committee of Memon Medical Institute (IRB/MMIH/2024/50 dated 07/11/2024 27th November 2024).

The sample size was calculated using the OpenEpi sample size calculator with a 95% confidence level and a 5% margin of error, considering an expected frequency of myocarditis among patients with dengue fever of 4.2% based on previously reported literature [3]. Non-probability consecutive sampling was used. Patients of either gender aged 15–70 years diagnosed with dengue fever according to the operational definition, with or without co-morbidities, including those co-infected with malaria, and willing to provide written informed consent were included in the study. Patients with negative NS1 antigen and Dengue IgM tests, those positive only for Dengue IgG antibody, patients with pre-existing cardiovascular diseases (including ischemic heart disease, chronic heart failure, or arrhythmias), congenital heart disease, active viral infections other than dengue, pregnant or breastfeeding women, and patients with severe co-morbid illnesses such as malignancy or end-stage renal disease were excluded.

All subjects signed a written informed consent form prior to enrolling. Detailed history and examination was done and demographic details such as age, gender, duration of fever and hospital stay were documented on a structured proforma. Acute dengue infection was defined as a positive NS1 antigen test and/or dengue IgM antibody test. Dengue IgG was not used as a diagnostic test for acute dengue infection and was only perceived as a marker of past infection. All patients had 12-lead ECG. The hospital laboratory facilities were used to measure serum troponin-I, NT-proBNP, serum bicarbonate and serum creatinine levels. Patients were referred for echocardiography when there was a clinical suspicion of cardiac involvement, such as shortness of breath, elevated cardiac biomarkers or electrocardiographic abnormalities. Patients without an echocardiogram did not get a diagnosis of normal echocardiographic findings. Echocardiographic abnormalities were considered to be low ejection

fraction (<50%), regional wall motion abnormalities, or pericardial effusion (>5 mm). On the study proforma, it was noted whether or not a patient experienced myocarditis and any other clinical or laboratory findings associated with it.

Dengue fever was diagnosed in patients presenting with fever ($\geq 38.5^{\circ}\text{C}$) and compatible clinical features, confirmed by positive dengue serology (NS1 antigen or dengue IgM/IgG antibodies) within 7 days of symptom onset. Myocarditis was diagnosed in patients with chest pain or shortness of breath, elevated troponin I (>0.1 ng/mL), and electrocardiographic abnormalities (ST-segment elevation) and/or echocardiographic evidence of myocardial dysfunction (ejection fraction <50%), confirmed by clinical assessment within 14 days of symptom onset. Elevated troponin I was labeled when the serum level was >0.1 ng/mL. Abnormal echocardiography was labeled when reduced ejection fraction (<50%), regional wall motion abnormalities, or pericardial effusion (>5 mm) were present. Hypertension was labeled in patients with a documented history of hypertension or blood pressure $\geq 140/90$ mmHg on two separate readings during admission. Diabetes mellitus was labeled in patients with a documented history of diabetes, current use of antidiabetic medications, or fasting blood glucose ≥ 126 mg/dL. Atrial fibrosis was regarded as a new onset arrhythmia occurring during the dengue illness diagnosed by electrocardiography showing an irregularly irregular rhythm with no P waves and variable ventricular reaction. The study excluded patients with a history of atrial fibrillation.

All the collected data were entered and analysed with SPSS version 26. For continuous variables (such as age, duration of fever, and hospital stay), data were given as mean $\pm$ standard deviation or median (interquartile range), depending on the data distribution. Frequencies and percentages were used to describe categorical variables such as gender, myocarditis, elevated troponin I, abnormal echocardiography, hypertension, diabetes mellitus, atrial fibrillation, low serum bicarbonate and high serum creatinine. The Shapiro–Wilk test was used to determine normality of continuous variables. The percentage of myocarditis was determined by the number of cases per 10,000 cases of acute coronary and myocardial ischemia per year. The Chi-square test or Fisher's exact test was used, as appropriate, for the evaluation of association between myocarditis (dependent variable) and categorical independent variables, such as gender, hypertension, diabetes

mellitus, atrial fibrillation, elevated troponin I, abnormal echocardiography results, decreased serum bicarbonate, and increased serum creatinine. The independent sample t-test and Mann–Whitney U test were used as appropriate to compare the continuous variables (age, duration of fever and hospital stay) among patients with and without myocarditis. Univariable analysis p-values <0.20 were used for variable selection in the multivariable logistic regression model to determine independent factors associated with myocarditis. The dependent variable was myocardialitis and the independent variables were clinical and laboratory features. Statistically significant p-values of ≤0.05 were used.

RESULTS

A total of 387 patients with dengue fever were included in the study. The mean age of the participants was 36.8 (SD 14.2) years. The mean duration of fever was 5.8 (SD 1.9) days, while the mean hospital stay duration was 4.9 (SD 2.3) days. Among the participants, 232 (59.9%) were males and 155 (40.1%) were females, as shown in Table-I. Among the 387 patients with dengue fever, myocarditis was identified in 16 (4.1%) patients, whereas 371 (95.9%) patients did not have myocarditis, as shown in Figure-I.

The frequency of associated clinical and laboratory factors among patients with dengue fever is presented in Table-II. Elevated troponin I was observed in 24 (6.2%) patients, abnormal echocardiography in 21 (5.4%), hypertension in 78 (20.2%), diabetes mellitus in 64 (16.5%), atrial fibrillation in 12 (3.1%), low serum bicarbonate in 59 (15.2%), and high serum creatinine in 42 (10.9%) patients. The association between demographic and clinical characteristics and myocarditis is presented in Table-III. Age and gender were not significantly associated with myocarditis (p=0.491 and p=0.853, respectively). However, duration of fever and hospital stay duration showed significant associations with myocarditis (p=0.049 and p<0.001, respectively). The association between clinical and laboratory factors and myocarditis is presented in Table-IV. Elevated troponin I, abnormal echocardiography, hypertension, diabetes mellitus, atrial fibrillation, low serum bicarbonate, and high serum creatinine were significantly associated with myocarditis (all p<0.05). Among patients with atrial fibrillation, myocarditis was present in 4 (33.3%) patients compared with 12 (3.2%) patients without atrial fibrillation (p<0.001).

Table-I: Baseline characteristics of the study population (n = 387).

Variables	n (%) / Mean (SD)
Age (years)	
Mean (SD)	36.8 (14.2)
15–40 years	227 (58.7)
41–70 years	160 (41.3)
Gender	
Male	232 (59.9)
Female	155 (40.1)
Duration of fever (days)	
Mean (SD)	5.8 (1.9)
≤5 days	208 (53.7)
>5 days	179 (46.3)
Hospital stay duration (days)	
Mean (SD)	4.9 (2.3)
≤5 days	238 (61.5)
>5 days	149 (38.5)

Table-II: Frequency of associated factors among patients with dengue fever (n = 387).

Variable	n (%)
Elevated Troponin I	24 (6.2)
Abnormal Echocardiography	21 (5.4)
Hypertension	78 (20.2)
Diabetes Mellitus	64 (16.5)
Atrial Fibrillation	12 (3.1)
Low Serum Bicarbonate	59 (15.2)
High Serum Creatinine	42 (10.9)

Table-III: Association of demographic and clinical characteristics with myocarditis (n = 387).

Variable	Category	Myocarditis Yes n (%)	Myocarditis No n (%)	Total n (%)	p-value
Age (years)	15–40	8 (3.5)	219 (96.5)	227 (58.7)	0.491
	41–70	8 (5.0)	152 (95.0)	160 (41.3)	

Gender	Male	10 (4.3)	222 (95.7)	232 (59.9)	0.853
	Female	6 (3.9)	149 (96.1)	155 (40.1)	
Duration of fever (days)	≤5	5 (2.4)	203 (97.6)	208 (53.7)	0.049
	>5	11 (6.1)	168 (93.9)	179 (46.3)	
Hospital stay duration (days)	≤5	4 (1.7)	234 (98.3)	238 (61.5)	<0.001
	>5	12 (8.1)	137 (91.9)	149 (38.5)	

Note: p-values were calculated using the Chi-square test or Fisher's exact test where appropriate.

Table-IV: Association of clinical factors with myocarditis (n = 387).

Variable	Category	Myocarditis Yes n (%)	Myocarditis No n (%)	Total n (%)	p-value
Elevated Troponin I	Yes	15 (62.5)	9 (37.5)	24 (6.2)	<0.001
	No	1 (0.3)	362 (99.7)	363 (93.8)	
Abnormal Echocardiography	Yes	14 (66.7)	7 (33.3)	21 (5.4)	<0.001
	No	2 (0.5)	364 (99.5)	366 (94.6)	
Hypertension	Yes	8 (10.3)	70 (89.7)	78 (20.2)	0.006
	No	8 (2.6)	301 (97.4)	309 (79.8)	
Diabetes Mellitus	Yes	7 (10.9)	57 (89.1)	64 (16.5)	0.009
	No	9 (2.8)	314 (97.2)	323 (83.5)	
Atrial Fibrillation	Yes	4 (33.3)	8 (66.7)	12 (3.1)	<0.001
	No	12 (3.2)	363 (96.8)	375 (96.9)	
Low Serum Bicarbonate	Yes	9 (15.3)	50 (84.7)	59 (15.2)	<0.001
	No	7 (2.1)	321 (97.9)	328 (84.8)	
High Serum Creatinine	Yes	8 (19.0)	34 (81.0)	42 (10.9)	<0.001
	No	8 (2.3)	337 (97.7)	345 (89.1)	

Note: p-values were calculated using the Chi-square test or Fisher's exact test where appropriate.

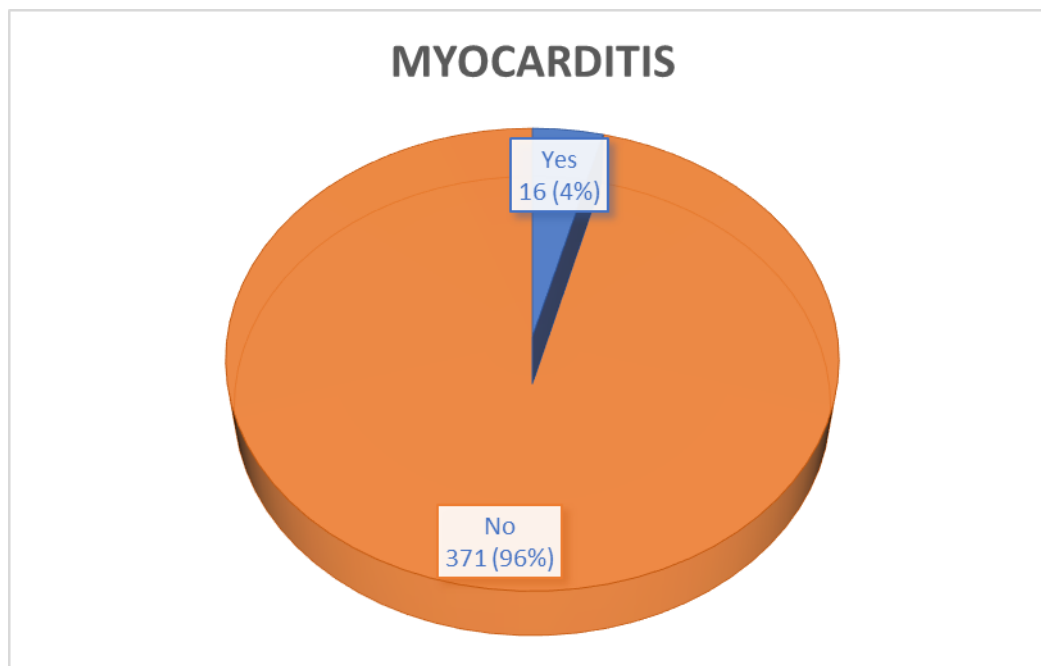


Figure-I: Frequency of myocarditis among patients with dengue fever (n = 387).

DISCUSSION

Dengue fever is a major mosquito-borne viral illness and an important public health concern in tropical and subtropical countries, including Pakistan [13]. Although most patients recover without complications, dengue can involve multiple organ systems, including the cardiovascular system. Myocarditis is an uncommon but potentially life-threatening complication that may present with arrhythmias, heart failure, or cardiogenic shock if not recognized early. Owing to its nonspecific clinical

presentation, myocarditis is often underdiagnosed in patients with dengue fever. Determining its frequency and identifying associated factors may facilitate early diagnosis and appropriate management [14, 15]. Therefore, this study was conducted to determine the frequency and associated factors of myocarditis among patients presenting with dengue fever at a tertiary care hospital in Karachi.

Hussain *et al.* (2017) from Pakistan evaluated 24 patients with dengue myocarditis presenting with cardiogenic shock. The mean age was 32 years, and

83.3% of the patients were males, which is comparable to our findings of a mean age of 36.8 ± 14.2 years and 59.9% male predominance. They reported elevated cardiac biomarkers and echocardiographic abnormalities in all patients (100%), while atrial fibrillation was present in 8.3% of cases. In our study, elevated troponin I and abnormal echocardiography were also significantly associated with myocarditis (both $p < 0.001$), and atrial fibrillation showed a significant association (33.3% vs. 3.2%, $p < 0.001$). Hussain *et al.* also reported a very high mortality rate (83.3%), reflecting the inclusion of critically ill patients with cardiogenic shock, whereas the present study included all hospitalized dengue patients irrespective of disease severity.

Kirawittaya *et al.* (2015) from Thailand demonstrated that cardiac dysfunction was more pronounced among dengue patients with plasma leakage. Patients with plasma leakage had a significantly lower cardiac index (2695 ± 127 vs. 3188 ± 75 L/min/m²; $p = 0.003$), higher myocardial performance index (0.413 ± 0.021 vs. 0.328 ± 0.026 ; $p = 0.021$), and increased systemic vascular resistance (2478 ± 184 vs. 1820 ± 133 dynes·s/cm⁵; $p = 0.005$). Reduced left ventricular wall motion was also more common in patients with plasma leakage. Similarly, abnormal echocardiography was significantly associated with myocarditis in our study (66.7% vs. 0.5%, $p < 0.001$), supporting the importance of echocardiographic assessment in detecting myocardial involvement in dengue infection [16]. Mansanguan *et al.* (2021) from Thailand evaluated 81 adult patients with dengue infection and reported elevated cardiac biomarkers in 6 (7.41%) patients, left ventricular systolic dysfunction in 3 (3.70%), transient diastolic dysfunction in 3 (3.70%), small pericardial effusion in 6 (7.41%), and overall cardiac involvement in 22.2% of patients. However, myocarditis was suspected in only two patients, indicating that clinically significant myocarditis was uncommon. Likewise, our study found myocarditis in 16 (4.1%) of 387 patients, supporting the concept that although cardiac abnormalities may occur in dengue, definite myocarditis remains an uncommon complication [17]. Marisa *et al.* (2025) from Bangladesh studied 34 patients with dengue myocarditis and reported a mean age of 48.5 ± 20.1 years, with 61.7% being males. They found that patients with myocarditis had significantly higher inflammatory markers and liver enzymes, while multivariable logistic regression demonstrated that the presence of comorbidities (OR=10.5, 95% CI: 2.78–39.5) and raised neutrophil-

to-lymphocyte ratio (OR=11.9, 95% CI: 2.82–50.7) were independently associated with myocarditis. In our study, hypertension (10.3% vs. 2.6%, $p = 0.006$) and diabetes mellitus (10.9% vs. 2.8%, $p = 0.009$) were also significantly associated with myocarditis, indicating that underlying comorbid conditions may predispose dengue patients to cardiac involvement [18]. Sud *et al.* (2023) from India described a series of patients with dengue myocarditis who presented with cardiac manifestations including chest pain, dyspnea, palpitations, hypotension, and electrocardiographic abnormalities. All cases had elevated cardiac biomarkers, while echocardiography demonstrated reduced left ventricular ejection fraction or global hypokinesia, confirming myocardial involvement [19].

LIMITATIONS

This was a single-center study, which may limit the generalizability of the findings. The cross-sectional design did not allow assessment of temporal or causal relationships between associated factors and myocarditis. Advanced diagnostic modalities such as cardiac magnetic resonance imaging or endomyocardial biopsy were not performed for confirmation of myocarditis.

CONCLUSION

Myocarditis was an uncommon complication among patients with dengue fever in the present study. Prolonged fever, longer hospital stay, elevated troponin I, abnormal echocardiography, hypertension, diabetes mellitus, atrial fibrillation, low serum bicarbonate, and high serum creatinine were significantly associated with myocarditis. Early recognition of these factors may facilitate timely diagnosis and improve the management of affected patients.

CONFLICT OF INTEREST

None

GRANT SUPPORT & FINANCIAL DISCLOSURE

Declared none

AUTHORS CONTRIBUTION

Ariba Afzal: Substantial contribution to study design, data acquisition and interpretation, manuscript drafting / review, final approval, responsible for every aspect of the research

Abdul Rabb: Substantial contribution to concept, study design and methodology; supervision and

critical manuscript review, final approval, responsible for every aspect of the research

Sidra Noor: Substantial contribution to methodology, clinical guidance and data interpretation, critical manuscript review, final approval, responsible for every aspect of the research

Tooba Irfan: Substantial contribution to data acquisition, literature review and data organization, manuscript preparation/review, final approval, responsible for every aspect of the research

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