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Cardiac Manifestations in Patients with Dengue Fever: A Prospective Study at a Tertiary Care Centre in Western Uttar Pradesh

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Abstract

Background: Dengue fever, a mosquito-borne viral infection, can lead to significant cardiac complications. This study aimed to investigate the prevalence, characteristics, and clinical significance of cardiac manifestations in dengue patients at a tertiary care centre.

Methods: We conducted a prospective observational study on 385 confirmed dengue patients admitted to our institution. All patients underwent clinical evaluation, electrocardiography, and echocardiography. Cardiac biomarkers were measured in patients with suspected myocardial involvement.

Results: Cardiac manifestations were observed in 100 patients (26%, 95% CI: 21.7 - 30.3%). The most common findings were sinus bradycardia (12%), myocarditis (8%), and pericardial effusion (4%). Elevated cardiac biomarkers were found in 6% of patients. Severe dengue cases had a higher incidence of cardiac involvement compared to non-severe cases (42% vs. 20%, p <0.001). Patients with cardiac manifestations had longer hospital stays (median 7 days versus 5 days, p <0.001).

Conclusion: Cardiac manifestations are common in dengue fever, with approximately one-fourth of patients showing some form of cardiac involvement. Close cardiac monitoring is crucial, especially in severe dengue cases, to improve patient outcomes.

Key words: Dengue, sinus bradycardia, myocarditis, pericardial effusion.

Introduction

Dengue fever, caused by the dengue virus (DENV), is a major global health concern affecting millions of people annually[1,2]. The World Health Organisation (WHO) estimates that 390 million dengue infections occur each year, with about 96 million manifesting clinically[3]. While traditionally known for its haematological complications, growing evidence suggests significant cardiac involvement in dengue patients[4-6].

The dengue virus, a member of the Flaviviridae family, consists of four distinct serotypes (DENV-1 to DENV-4), with a potential fifth serotype (DENV-5) identified in 2013[7]. Infection with one serotype provides lifelong immunity against that particular serotype but only partial and temporary protection against other serotypes. Secondary infection with a different serotype often leads to more severe disease manifestations[1].

The spectrum of cardiac manifestations in dengue ranges from subtle electrocardiographic changes to severe myocarditis and even fulminant heart failure[8,9]. Recent studies have reported varying prevalence rates of cardiac involvement in dengue, ranging from 15% to 50%[10-13]. This wide range may be attributed to differences in study populations, severity of dengue cases, and diagnostic criteria used for cardiac involvement.

The pathogenesis of cardiac involvement in dengue is not fully understood but is thought to involve multiple mechanisms. These include direct viral invasion of cardiomyocytes, cytokine-mediated injury, immune-mediated mechanisms, and metabolic disturbances[1,14]. The expanded dengue syndrome, a term coined to describe atypical manifestations of dengue, includes various cardiac complications such as myocarditis, pericarditis, and arrhythmias[15].

Despite the growing recognition of cardiac involvement in dengue, the exact burden and characteristics of cardiac manifestations remain unclear, particularly in tertiary care settings where more severe cases are managed. Furthermore, the clinical significance of these cardiac manifestations, in terms of patient outcomes and long-term prognosis, is not well established.

This study aimed to investigate the prevalence, types, and clinical significance of cardiac manifestations in patients with dengue fever admitted to a tertiary care centre. By providing a comprehensive assessment of cardiac involvement in dengue, we hope to contribute to improved

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patient management and outcomes.

Material and Methods

Study Design and Setting: We conducted a prospective observational study at our hospital which is a tertiary care centre. The study included 385 patients aged ≥18 years with laboratory-confirmed dengue infection. Dengue was confirmed by either positive NS1 antigen or IgM antibody test. Patients with pre-existing cardiac conditions such as coronary artery disease, valvular heart disease, or cardiomyopathy were excluded to avoid confounding the assessment of dengue-related cardiac manifestation. The study protocol was approved by the Institutional Ethics Committee (IEC). Written informed consent was obtained from all participants or their legal representatives.

Clinical and Laboratory Evaluation: All patients underwent a detailed clinical examination upon admission and daily thereafter. Patients were classified according to the 2009 WHO dengue classification as non-severe dengue (with or without warning signs) or severe dengue[16].

Laboratory investigations included:

1. Complete blood count (daily)
2. Liver function tests (admission and as clinically indicated)
3. Renal function tests (admission and as clinically indicated)
4. Serum electrolytes (admission and as clinically indicated)
5. Coagulation profile (admission and as clinically indicated)

Cardiac Evaluation: All patients underwent comprehensive cardiac evaluation, which included:

1. 12-lead electrocardiography (ECG): Performed daily during hospitalisation.
2. Transthoracic echocardiograph: Performed on admission and repeated if clinically indicated.
3. Cardiac biomarkers: Troponin I and NT-pro BNP were measured in patients with suspected myocardial involvement based on clinical features, ECG changes, or echocardiographic abnormalities.

Cardiac manifestations were defined as the presence of one or more of the following:

- ECG abnormalities: Sinus bradycardia (heart rate <60 beats per minute), ST-segment or T-wave changes, conduction disturbances, or arrhythmias.
- Echocardiographic abnormalities: Left ventricular systolic dysfunction (ejection fraction <50%), diastolic dysfunction, pericardial effusion, or regional wall motion abnormalities.
- Elevated cardiac biomarkers: Troponin I >99th percentile of the upper reference limit or NT-pro BNP >125 pg/mL.
- Clinical features of heart failure or myocarditis.

Myocarditis was diagnosed based on the presence of at least two of the following criteria:

1. Cardiac symptoms (chest pain, dyspnoea, palpitations).
2. New-onset ECG changes (ST-segment elevation or depression, T-wave inversion, conduction disturbances).
3. Elevated cardiac biomarkers.
4. Echocardiographic evidence of new-onset systolic or diastolic dysfunction.

Data Collection: Demographic data, clinical features, laboratory results, and cardiac evaluation findings were recorded using a standardised case report form. All data were entered into a secure electronic database with double-entry verification to minimise errors.

Statistical Analysis: Assuming a prevalence of cardiac manifestations of 15 - 50% based on previous studies, with a precision of 5% and a confidence level of 95%, the required sample size was calculated to be 385. Data were analysed using SPSS version 25.0. Categorical variables were expressed as frequencies and percentages, while continuous variables were expressed as mean ± standard deviation or median with interquartile range (IQR) depending on the distribution of data. The chi-square test or Fisher's exact test was used to compare categorical variables between groups (patients with and without cardiac manifestations, severe and non-severe dengue). Student's t-test or Mann-Whitney U test was used for continuous variables, as appropriate. A p-value <0.05 was considered statistically significant. Multivariate logistic regression analysis was performed to identify independent predictors of cardiac manifestations in dengue patients. Variables with a p-value <0.1 in univariate analysis were included in the multivariate model.

Results

Demographics and Clinical Characteristics: Of the 385 patients enrolled, 210 (54.5%) were male, and the mean age was 36.7 ± 14.3 years. According to the WHO classification, 285 (74%) patients had non-severe dengue, and 100 (26%) had severe dengue. The median duration of fever at presentation was 4 days (IQR: 3-5 days) (Table I).

Table I: Demographics and clinical characteristics of the study participants.

Characteristic	Value
Total patients	385
Male	210 (54.5%)
Female	175 (45.5%)
Mean age (years)	36.7 ± 14.3
Non-severe dengue	285 (74%)
Severe dengue	100 (26%)
Median fever duration (days)	4 (IQR: 3-5)

The most common presenting symptoms were fever (100%), headache (82%), myalgia (78%), and arthralgia (65%). Warning signs were present in 180 (46.8%) patients, with abdominal pain (30%) and persistent vomiting (25%) being the most frequent.

Prevalence of cardiac manifestations: Cardiac manifestations were observed in 100 patients (26%, 95% CI: 21.7 - 30.3%). The prevalence was significantly higher in patients with severe dengue compared to non-severe dengue (42% *versus* 20%, p <0.001).

Types of cardiac manifestations: Various cardiac manifestations seen have been mentioned in Table II. Some patients had multiple cardiac manifestations. Sinus bradycardia was the most common ECG abnormality, consistent with previous studies[17,18]. The median heart rate in patients with sinus bradycardia was 54 beats per minute (IQR: 50 - 58).

Table II: Types of cardiac manifestations in Dengue fever.

Manifestation	Frequency
ECG Abnormalities	
Sinus bradycardia	46 (12%)
ST-T changes	19 (5%)
Conduction disturbances	8 (2%)
Arrhythmias	4 (1%)
Echocardiographic Abnormalities	
Left ventricular systolic dysfunction	23 (6%)
Diastolic dysfunction	15 (4%)
Pericardial effusion	15 (4%)
Regional wall motion abnormalities	8 (2%)
Elevated cardiac biomarkers	
Troponin I elevation	19 (5%)
NT-pro BNP elevation	23 (6%)
Clinical myocarditis	31 (8%)

Myocarditis, diagnosed based on clinical features, biomarker elevation, and echocardiographic findings, was observed in 8% of patients. This rate is similar to those reported in other studies[19,20]. Among patients with myocarditis, the mean left ventricular ejection fraction was 42 ± 6%.

Temporal pattern of cardiac manifestations: ECG abnormalities were often observed early in the course of illness, with sinus bradycardia typically occurring between days 3 and 7 of fever. Myocarditis and elevated cardiac biomarkers were more commonly seen during the critical phase (days 4 - 6) or early recovery phase of dengue (Fig.1).

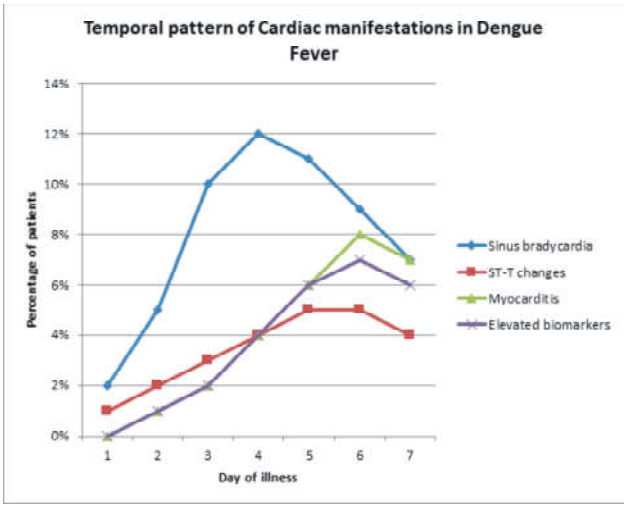

Fig.1: *Temporal pattern of cardiac manifestations in Dengue fever.*

Factors associated with cardiac manifestations: In multivariate analysis, several factors were independently associated with the presence of cardiac manifestations as shown in Table III.

Table III: Factors associated with cardiac manifestations.

Factor	Odds Ratio	95% CI	p-value
Severe Dengue	2.8	1.7 - 4.6	**<0.001**
Age >40 years	1.9	1.2 - 3.0	**0.006**
Presence of warning signs	1.7	1.1 - 2.7	**0.02**
Platelet count <50,000/μL	1.6	1.0 - 2.5	**0.04**

CI: Confidence Interval

Clinical Outcomes: Patients with cardiac manifestations had a longer hospital stay compared to those without (median 7 days *versus* 5 days, p <0.001). Three patients (0.8%) died during the study period, all of whom had severe myocarditis with cardiogenic shock.

Among patients with myocarditis, 26 (84%) showed improvement in left ventricular function at the time of discharge. Five patients (16%) had persistent left ventricular

dysfunction and were scheduled for follow-up echocardiography.

Discussion

Our study found that approximately one-fourth of dengue patients admitted to a tertiary care center experienced cardiac manifestations. This prevalence is consistent with previous studies, which have reported rates ranging from 15% to 50%[10-13]. The wide range in reported prevalence may be due to differences in study populations, severity of dengue cases, and diagnostic criteria used.

Sinus bradycardia was the most common ECG abnormality observed, which aligns with findings from other studies[17,21]. This relative bradycardia in dengue has been attributed to viral-induced autonomic dysfunction[22]. The exact mechanism remains unclear but may involve increased vagal tone or direct effects of inflammatory mediators on the sinoatrial node[21]. ST-T changes were also frequently observed, which could indicate myocardial involvement or electrolyte disturbances common in dengue[21]. These ECG changes were often transient and resolved with clinical improvement. However, their presence should prompt further cardiac evaluation to rule-out more significant myocardial involvement.

Myocarditis was diagnosed in 8% of our patients, which is within the range reported in previous studies[19,20]. The pathogenesis of myocarditis in dengue is not fully understood but may involve direct viral invasion of cardiomyocytes, cytokine-mediated injury, or immune-mediated mechanisms[1,14]. A study by Weerakoon *et al* demonstrated histopathological evidence of myocarditis in fatal dengue cases, supporting the concept of direct viral invasion[22].

The higher prevalence of cardiac manifestations in severe dengue cases (42% *versus* 20% in non-severe cases) underscores the importance of cardiac monitoring in these patients. This finding is consistent with other studies that have reported more frequent and severe cardiac involvement in dengue haemorrhagic fever and dengue shock syndrome[23,24]. The increased cardiac involvement in severe dengue may be related to the more pronounced inflammatory response and endothelial dysfunction seen in these cases[1].

Pericardial effusion was observed in 4% of patients, similar to rates reported in other studies[25,26]. While usually small and self-limiting, pericardial effusions can occasionally be large enough to cause haemodynamic compromise[6]. The development of pericardial effusion in dengue is thought to be related to increased vascular permeability and plasma leakage characteristic of severe dengue[14].

Our study identified several factors associated with an increased risk of cardiac manifestations, including severe dengue, age >40 years, presence of warning signs, and thrombocytopenia. These factors can help clinicians identify patients who may benefit from more intensive cardiac monitoring and earlier intervention.

The temporal pattern of cardiac manifestations observed in our study provides valuable insights into the natural history of cardiac involvement in dengue. The early occurrence of sinus bradycardia suggests that it may be a result of autonomic dysfunction rather than direct myocardial injury. In contrast, myocarditis and elevated cardiac biomarkers were more commonly seen during the critical phase or early recovery phase, possibly reflecting the peak of the inflammatory response and immune-mediated injury.

The majority of patients with myocarditis in our study showed improvement in left ventricular function by the time of discharge. This finding is consistent with other studies that have reported a generally favourable prognosis for dengue-associated myocarditis[19,20]. However, the persistence of left ventricular dysfunction in a small proportion of patients highlights the need for follow-up evaluation to assess for long-term cardiac sequelae.

The mortality rate in our study was low (0.8%), but all deaths occurred in patients with severe myocarditis, underscoring the potential lethality of this complication. This finding is consistent with other studies that have identified myocarditis as a significant risk factor for mortality in dengue[27,28].

Limitations of the study

Our study has several strengths, including its prospective design, large sample size, and comprehensive cardiac evaluation of all patients. However, there are also some limitations to consider. First, our study was conducted at a single tertiary care center, which may limit its generalisability to other settings, particularly primary care or community-based practices. Second, we did not perform cardiac magnetic resonance imaging (CMR), which could have provided more detailed information on myocardial involvement and tissue characterisation. CMR has been shown to be more sensitive than echocardiography in detecting subtle myocardial changes in viral myocarditis[29]. Additionally, we did not conduct long-term follow-up of patients with cardiac manifestations, which would have provided valuable information on the persistence or resolution of cardiac abnormalities. Future studies should consider incorporating CMR and long-term follow-up to address these limitations.

Conclusion

While the prevalence of cardiac manifestations in our cohort of dengue patients was lower than expected, it remains a significant clinical concern affecting approximately one-fourth of patients. The discrepancy between our findings and previous studies highlights the need for further research to understand regional variations and temporal trends in dengue-related cardiac complications. Clinicians should maintain a high index of suspicion for cardiac involvement, particularly in severe dengue cases, and consider routine cardiac evaluation in these patients. Future multi-center studies with standardised definitions and advanced cardiac imaging techniques are needed to better characterise the true burden of cardiac complications in dengue fever.

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