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Original Research Article

A Prospective Observational Study on Patients with Dengue Fever Leading to Cardiac Complications

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Abstract:
Background: Dengue viruses, transmitted by Aedes aegypti mosquitoes, are the leading cause of arboviral disease globally. Cardiovascular involvement in dengue is more common in patients with severe disease compared to those with mild or asymptomatic infection. Despite the increasing recognition of cardiovascular involvement in dengue, there is no standardized approach for cardiac assessment in dengue patients. This study aims to address this research gap by thoroughly evaluating the cardiac manifestations associated with dengue fever.
Materials & Methods: This hospital-based prospective observational study was conducted on 150 patients the study included subjects aged 18 years or older who were Dengue NS1 positive and IgM antibody positive, as detected by ELISA test. All participants underwent a comprehensive clinical evaluation, including medical history, physical examination, and laboratory tests (tourniquet test, ECG, ECHO, cardiac enzymes) were performed, and the results were recorded. After appropriate data filtration, the data sheet was transferred and analysed using Statistical Package for Social Sciences (SPSS vs. 22.0).
Results: In a study of 150 patients, comprising 56% male and 44% female with a mean age of 43.34 years, fever was the most common symptom, present in all cases. The diagnoses included 97.4% Dengue Fever, 1.3% Dengue Haemorrhagic Fever Stage 3, and 1.3% Dengue Shock Syndrome. Patients with severe manifestations exhibited elevated Troponin I and CK-MB levels, a left ventricular ejection fraction (LVEF) < 55%, and ST elevation on ECGs. Laboratory results revealed significantly lower platelet and white blood cell counts in these patients compared to the non-cardiac group.
Conclusion: Our study highlights the considerable impact of dengue fever on cardiac health, particularly in patients presenting with severe manifestations such as Dengue Haemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS). Approximately 8% of the cohort demonstrated evidence of cardiac involvement, which was significantly correlated with thrombocytopenia and haemoconcentration.
Keywords: Dengue Shock Syndrome, Dengue Fever, Cardiac Manifestations, India.

Introduction

Dengue viruses, single-stranded positive-sense RNA viruses belonging to the Flaviviridae family, are the most common cause of arboviral disease globally. There are four distinct serotypes of dengue virus, known as dengue types 1-4, which are primarily transmitted by the Aedes aegypti mosquito, with Aedes albopictus also serving as a significant vector.

Currently, over two-fifths of the world's population, or approximately 2.5 billion people, live in areas at risk of dengue infection. [1] The burden of dengue virus infection (DVI) is most concentrated in Asia, accounting for 75% of global cases. [2] According to the World Health Organization (WHO), dengue fever accounts for an estimated 100 to 400 million new infections each year. The increasing severity of outbreaks has placed approximately 2.5 billion individuals at risk globally, with an annual mortality rate of approximately 20,000. [3] Dengue infection presents a broad spectrum of clinical manifestations. The disease is typically classified into three phases: febrile, critical, and recovery. During the febrile phase, common symptoms include high fever, severe headache, retro-orbital pain, muscle and joint pain, and a characteristic skin rash. [4]

As the disease progresses to the critical phase, patients may experience severe plasma leakage, leading to hypovolemia, shock, bleeding tendencies, and multi-organ dysfunction. The organs typically affected include the liver (hepatitis), central nervous system (neurological dysfunction), the coagulation system (coagulopathy), and the cardiovascular (CV) system. Cardiovascular involvement in dengue is more common in patients with severe disease compared to those with mild or asymptomatic infection. Cardiac manifestations in dengue may be seen in the form of asymptomatic bradycardia to life-threatening myocarditis. Sinus bradycardia, transient ventricular arrhythmias, prolongation of PR interval, nonspecific ST-segment and T-wave changes, and transient atrioventricular blocks are some of the findings that can be seen in cases of dengue. [5] Cardiac manifestations have been reported to range from elevated cardiac biomarker have been observed in 7.4% to 40% of dengue patients. [6,7] Additionally, echocardiograms and electrocardiograms have revealed cardiac dysfunction, including impaired heart function and abnormal electrical activity, in 22% to 64% of cases. [6-9] Myocarditis, though less commonly reported, has also been documented. The clinical presentation of cardiac involvement in dengue infection is highly variable, ranging from asymptomatic cases to severe manifestations. While some patients exhibit no overt symptoms, others may experience chest pain, palpitations, arrhythmias, hypotension, pulmonary edema, or even cardiogenic shock. [10] These cardiovascular complications are frequently implicated in the hemodynamic instability observed in severe dengue cases. The early recognition of these symptoms is crucial, as timely diagnosis and intervention are essential to mitigating adverse outcomes and preventing the progression to life-threatening cardiovascular failure.

Despite the increasing recognition of cardiovascular involvement in dengue, there is no standardized approach for cardiac assessment in dengue patients, particularly those with severe forms of the disease. As a result, the frequency of subclinical dengue myocarditis and its contribution to the hemodynamic instability observed in these patients remain poorly understood. In the Indian context, there are only a limited number of studies that have evaluated the cardiovascular manifestations of dengue fever and also the full spectrum of cardiac involvement has not been thoroughly investigated. This lack of comprehensive cardiac assessment in dengue patients highlights a significant gap in the existing literature. Given the increasing incidence of dengue fever and the severity of its complications, it is imperative to gain a deeper understanding of its cardiovascular impact. This study aims to address this research gap by thoroughly evaluating the cardiac manifestations associated with dengue fever.

Materials and Methods

This hospital-based prospective observational study was conducted in the Emergency Medicine Department of Apollo Hospital, Bengaluru, involving 150 patients from December 2017 to April 2019. The study included subjects aged 18 years or older who were Dengue NS1 positive and IgM antibody positive, as detected by ELISA test. Patients with co-morbidities such as hypertension, diabetes mellitus, and chronic kidney disease, who had provided written informed consent, were also included. Patients with history of pre-existing ischemic heart disease and/or on medications affecting the heart rate / rhythm were excluded. Patients were categorized based on relevant factors such as age, gender, medical history, symptoms and signs at presentation, etc. All participants underwent a comprehensive clinical evaluation, including a detailed medical history, physical examination, and assessment for signs of bleeding, shock, and other relevant clinical manifestations. Laboratory tests such as the tourniquet test, ECG, ECHO, and case-specific cardiac enzymes were performed, and the results were recorded. Patients were continuously monitored throughout their hospital stay to observe outcomes. There are four grades of DHF classified as below, and same is used in our analysis:

Grade 1: Fever and non-specific symptoms are present and the only hemorrhagic manifestation is provoked, which is a positive tourniquet test.

Grade 2: Along with Grade 1 manifestations, there is spontaneous bleeding.

Grade 3: Incipient shock with signs of circulatory failure.

Grade 4: The patient has profound shock, with undetectable blood pressure and pulse.

After appropriate data filtration, the data sheet was transferred and analyzed using Statistical Package for Social Sciences (SPSS vs. 22.0). Baseline characteristics of the patients were summarized as frequencies for categorical variables and as means with standard deviations for continuous variables.

Ethical approval:

The study was approved by Institutional Ethics Committee Ref No: 0030/2017; dated 22 Dec, 2017. Also, a written informed consent was obtained from the patient for the study participation.

Results

Out of total 150 patients, 56% were male and 44% female, with a mean age of 43.34 ± 16.02 years (Table 1). Fever was the most common symptom, present in 100% of the patients, followed by rash in 28.7% of cases (Table 2). Most patients (97.4%) were diagnosed with Dengue Fever (DF), while

1.3% had Dengue Hemorrhagic Fever (DHF) Stage 3, and another 1.3% had Dengue Shock Syndrome (DSS) (Table 3). Of the 150 patients, cardiac enzyme tests were performed on 87 (58%), among 87 patients, 83 (95.4%) had normal Troponin I and CK-MB levels, while 4 (4.6%) showed abnormal values. (Table 4). Most patients (75.3%) had normal ECGs. Non-specific ST-T changes were observed in 14% of patients, sinus bradycardia in 8%, and diffuse ST elevation in 2.6% (Table 5). Left Ventricular Ejection Fraction (LVEF) was ≥ 55% in 82% of the patients, while 18% had LVEF < 55%.

The mean LVEF was 58 ± 6.3%. (Table 6). A clear correlation was observed between specific ECG changes and cardiac enzyme levels, as well as echocardiographic findings. (Table 7) In the group without cardiac manifestations, the mean platelet count was notably higher at 77,496 µL (range 12,000 – 136,000 µL) compared to 48,583 µL (range 10,000 – 93,000 µL) in the suspected cardiac manifestation group.

Additionally, the white blood cell (WBC) count was significantly elevated in the non-cardiac group, with a mean of 4,106 µL (range 1,200 – 7,000 µL) versus 2,883 µL (range 1,200 – 5,000 µL) in the suspected cardiac group (Table 8).

Table 1: Demographic details of subjects involved in the study

Parameter	Frequency	Percentage (%)	Mean Age ± SD (Years)
Gender			
Male	84	56	47.21 ± 16.02
Female	66	44	38.40 ± 15.66
Total	150	100	43.34 ±16.02
Age			
18 to 39 Years	80	53.3	30.26 ±7.24
40 to 59 Years	40	26.7	51.45 ±5.90
≥ 60 Years	30	20	67.4 ±5.68

Table 2: Spectrum of clinical manifestations reported by subjects.

Symptoms	Frequency	Percentage (%)
Fever	150	100
Headache	19	12.7
Nausea	34	22.7
Vomiting	41	27.3
Joint Pain	40	26.7
Rash	43	28.7
Body-ache	29	19.3
Altered Sensorium	2	1.3
Bleeding manifestation	4	2.6

Table 3: Distribution of dengue diagnosis in subjects.

Diagnosis	Patient		Mortality
	Frequency	Percentage (%)	
DF	146	97.4	0
DHF Stage 3	2	1.3	1
DSS	2	1.3	1
Total	150	100	2

Table 4: Distribution of troponin level in dengue diagnosed subjects

Diagnosis	Troponin I & CK-MB (N=87)	
	Positive	Negative
DF	0	83
DHF Stage 3	2	0
DSS	2	0
Total	4 (4.6%)	83 (95.4%)

Table 5: Distribution of dengue diagnosed subjects on the basis of their ECG changes

Diagnosis	ECG changes			
	Normal sinus rhythm	Non- specific ST -T changes	Sinus Bradycardia	Diffuse ST elevation
DF	113	21	12	0
DHF Stage 3	0	0	0	2
DSS	0	0	0	2
Total	113 (75.3%)	21 (14%)	12 (8%)	4 (2.7%)

Table 6: Distribution of dengue diagnosed subjects on the basis of ECHO findings

Diagnosis	Ejection Fraction		RWMA, Global Hypokinesia	
	EF ≥ 55%	EF < 55%	Present	Absent
DF	123	23	3	84
DHF Stage 3	0	2	2	0
DSS	0	2	2	0
Total	123 (82%)	27 (18%)	7 (4.7%)	143 (95.3%)

Table 7: Distribution of specific ECG changes Vs. Cardiac Enzyme & ECHO findings

ECG changes*	Cardiac Enzyme (Troponin I & CK-MB)		Ejection Fraction		RWMA, Global Hypokinesia	
	Positive	Negative	EF ≥ 55%	EF < 55%	Present	Absent
Nonspecific ST -T changes (N=21)	0	21	15	6	0	21
Sinus Bradycardia (N=12)	0	12	10	2	0	12
Diffuse ST elevation (N=4)	4	0	0	4	4	0
Total = 37	4	33	25	12	4	33

Table 8: Comparison of lab values.

Lab Values	Dengue diagnosed without any cardiac manifestation		Dengue diagnosed suspected with cardiac manifestation	
	Mean	Min-Max.	Mean	Min-Max.
Platelets (µL)	77,496	12,000 – 1,36,000	48,583	10,000 - 93,000
WBC (µL)	4,106	1,200 – 7,000	2,883	1,200 – 5,000
Hb (g/dL)	12.9	8.8 – 16.2	12.4	9.4 – 15.0
HCT (%)	39.5	28 - 49	38.9	33 - 46

Discussion

Dengue is a rapidly emerging viral disease globally, with its incidence increasing in India. While most symptomatic infections follow a benign course, some patients develop severe clinical manifestations, including bleeding, organ impairment, and cardiovascular complications. In our study population of 150 patients, dengue fever was observed across all age groups, with a mean age of 43.34 ± 16.02 years. The male-to-female ratio was 1.3:1, indicating a male preponderance. Additionally, 40% of the patients had one or more comorbidities, such as diabetes mellitus, chronic kidney disease, or hypertension.

In our study, the majority of patients (75.3%) had normal ECG findings. However, among those with abnormalities, the most common ECG abnormality was non-specific ST-T changes, observed in 14% of patients. This was followed by sinus bradycardia in 8% of patients, while diffuse ST elevation was noted in 2.7% of cases. Arora M et al. [11] found that sinus bradycardia was the most common ECG abnormality observed in 8.77% of the patients, followed by sinus tachycardia in 3.51% of the patients. Echocardiographic findings in our study were often subclinical, with most patients showing normal results. Elevated levels of Troponin I and CK-MB were observed in all patients with DHF Stage 3 and DSS, indicating cardiac involvement. Similar trends were recorded in a study by Papalkar et al. [5] where 52 patients (86.67%) had normal CK-MB levels and 8 patients had abnormal values (13.33%). Yadav et al. [12] found abnormal CK-MB values in 39 (37.5%) of 104 patients. The most common echocardiographic abnormality was global hypokinesia, reported in 2.7% of subjects. Satarsinghe et al. [13] found that 24% out of 217 patients had echocardiographic abnormality while none had clinical features of overt myocarditis.

Our findings indicate that cardiac manifestations were significantly more prevalent in patients with Dengue Hemorrhagic Fever (DHF) Stage 3 and Dengue Shock Syndrome (DSS). In-depth analysis of ECG results (excluding normal sinus rhythm) in relation to abnormal Left Ventricular Ejection Fraction (LVEF) revealed 12 patients suspected of having cardiac manifestations.

A marked distinction in LVEF was noted between dengue patients without suspected cardiac involvement (mean LVEF: $59 \pm 4.4\%$; $p < 0.05$, 95% CI 58.26 to 59.74) and those with suspected cardiac involvement (mean LVEF: $45.5 \pm 10\%$; $p < 0.05$, 95% CI 39.15 to 51.85), indicating statistically significant cardiac dysfunction in the latter group. Additionally, a similar relationship was observed when comparing hemoglobin (Hb) and hematocrit (HCT) levels between the two groups. A statistically significant correlation was also observed between thrombocytopenia and the occurrence of cardiac manifestations ($p < 0.05$). This reinforces the notion that cardiac involvement in dengue is closely linked to severe thrombocytopenia and hemoconcentration. Overall, the incidence of cardiac manifestations in our study population was 8%. Mortality in the study was 1.3%, with all deaths occurring in patients with DHF Stage 3 and DSS. Comparatively, Aggarwal A et al. [14] reported an overall mortality rate of 6%, while Ahmed et al. [15] noted a rate of 3%.

These differences could be due to delays in the recognition of disease severity or in seeking medical attention, underscoring the importance of prompt diagnosis and management in mitigating adverse outcomes.

Conclusion

Our study underscores the significant impact of dengue fever on cardiac health, especially in patients with severe disease manifestations such as DHF and DSS.

Approximately 8% of patients exhibited cardiac involvement, which was significantly correlated with thrombocytopenia and haemoconcentration.

The subclinical nature of many cardiac abnormalities, detected primarily through echocardiographic evaluation, emphasizes the need for vigilant monitoring and early intervention in dengue patients, particularly those with comorbidities.

Data availability statement: The data for the present study is available with the corresponding author of this article and will be shared on a specific request**.**

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