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Original Research Article

A Hospital Based Retrospective Study to Establish the Association between Cardiac Symptoms and the Severity of Dengue Illness

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Abstract

Aim: To establish a correlation between cardiac symptoms and the severity of dengue illness.

Material and Methods: The Department of Medicine, IGIMS, Patna, Bihar, India for one year, did this research on dengue fever hospitalized patients. This research covered 110 patients. Participants in this research were patients aged > 13 years, admitted to a hospital, with confirmed dengue serology (Dengue IgG/IgM/NS1 positive), meeting WHO criteria, and providing written informed permission. According to WHO standards, admitted patients were categorized as dengue fever, DHF, or shock syndrome.

Results: Out of 110 dengue patients, 69.1% had fever, 7.3% had shock syndrome, and 23.6% had hemorrhagic fever. 56.36% of patients had normal ECGs upon admission, whereas 43.64% had alterations. In the second ECG on day three, 87.27% were normal and 12.73% had changes. All dengue patients had normal ECGs upon discharge, suggesting transitory ECG alterations. In this research, 59.09% had normal sinus rhythm, 36.4% had sinus bradycardia, 3.6% had sinus tachycardia, and 10.9% showed NSST-T alterations. Six (75%) of eight DSS patients exhibited positive troponin I. Seven (26.9%) of 26 DHF patients reported positive troponin I. DF patients showed no troponin I positive. The proportion of dengue patients with positive troponin I corresponds with fever severity. The difference was substantial (P<0.001).

Conclusion: ECG, cardiac enzymes, and echocardiography are used to identify dengue fever myocardial involvement. DF patients demonstrated less cardiac involvement than DHF and DSS.

Key Words: Dengue, cardiac, electrocardiography, Echocardiography, markers, severity

Introduction

Dengue fever is a viral illness transmitted by mosquitoes that has emerged as a significant worldwide public health issue, particularly in tropical and subtropical areas. Dengue fever is caused by the dengue virus (DENV), which is spread mostly by Aedes aegypti and Aedes albopictus mosquitoes. The virus has four different serotypes, known as DENV-1 to DENV-4. Dengue fever presents with a variety of clinical symptoms, ranging from moderate fever to severe and possibly life-threatening illnesses including dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). Cardiac symptoms of dengue fever have gained significant interest owing to their influence on morbidity and death. [1,2] This introduction will examine the relationship between cardiac symptoms and the intensity of dengue fever, backed by recent research and discoveries. The pathophysiology of dengue fever is characterized by an intricate interaction between virus and host variables. After being infected, the virus invades dendritic cells and macrophages, which triggers the immune system's response and the production of pro-inflammatory cytokines. [3,4] Severe instances are often linked to an exaggerated immune response, leading to heightened permeability of blood vessels, leaking of plasma, and visible bleeding symptoms. The cardiac involvement in dengue fever is considered to be complex, including direct viral invasion of myocardial cells, immune-mediated injury, and metabolic abnormalities. The cardiac symptoms seen in cases of dengue fever might vary from ECG alterations without any noticeable symptoms to severe myocarditis and heart failure. Typical ECG abnormalities consist of sinus bradycardia, atrioventricular block, and nonspecific ST-T wave alterations. Myocarditis is a serious cardiac condition characterized by inflammation of the heart muscle. It may result in reduced cardiac output and heart failure. Pericardial effusion and cardiomyopathy have been documented in some instances as well. There is a correlation between the

severity of cardiac symptoms and the severity of dengue fever. Various mechanisms have been suggested to elucidate the cardiac implications of dengue illness. Myocarditis and myocyte necrosis may occur when virus particles directly invade the heart tissue. Moreover, the activation of the body's immune response, which involves the production of signaling molecules called cytokines including IL-6, TNF-α, and IFN-γ, may cause impairment of the heart's function and play a role in the progression of myocarditis. [5-7] Hypovolemia and shock, which are often seen in severe instances of dengue, may worsen cardiac dysfunction by decreasing blood flow to the heart and leading to ischemia.

Material and Methods

This study was conducted in the Department of Medicine, IGIMS, Patna, Bihar, India for one year, on patients admitted in hospital suffering with dengue fever. 110 patients were included in this study. Patients with age group of ≥ 13 years, Patients admitted in Ward/ICU hospital with confirmed dengue serology (Dengue IgG/IgM/NS1 positive), fulfilling the WHO criteria for dengue and written and informed consent were included in this study.

Patients on medications affecting the heart rate / rhythm, Patients with history of preexisting heart disease, Patients with electrolyte abnormalities affecting the heart rate/rhythm, Patients not willing to give consent for the study and Patients suffering from mixed infections (Malaria, Leptospira) were excluded from this study. Admitted patients were classified into dengue fever, dengue hemorrhagic fever (DHF), and dengue shock syndrome based on the World Health Organization (WHO) criteria.

Case definitions: Case definitions of dengue fever, DHF, and dengue shock syndrome were as follows:

Dengue fever: Acute febrile illness with two or more of the following: headache, retro-orbital pain, myalgia, arthralgia/bone pain, rash, hemorrhagic manifestations, leukopenia (white blood cells ≤5000 cells/mm3), thrombocytopenia (platelet count <150,000 cells/mm3), and rising hematocrit (5%–10%). And at least one of the following: supportive serology test, occurrence at the same location, and time as confirmed cases of dengue fever.

Dengue hemorrhagic fever

Four cardinal features of DHF as defined by the WHO are as follows:

- Fever or history of fever lasting 2-7 days occasionally biphasic
- Thrombocytopenia (<100 × 103/mm3)
- Hemorrhagic manifestations shown by anyone of the following – A positive tourniquet test, petechiae, ecchymosis, or purpura, bleeding from the mucosa or injection site, hematemesis, melena, and hematuria
- Evidence of plasma leakage owing to increased vascular permeability shown by any one of the following: rising hematocrit/hemoconcentration
- ≥20% from baseline, signs of plasma leakage such as pleural effusion, ascites, or hypoproteinemia.

Dengue Shock Syndrome

DHF plus circulatory failure with signs of shock such as rapid and weak pulse, narrow pulse pressure (<20 mmHg) or hypotension (<90 mmHg), cold clammy skin, and mental status alteration.

Methodology

Upon admission, patients underwent physical and systemic exams, including complete blood count, platelet count, hematocrit, electrocardiography, two-dimensional echocardiography, and CK-MB (normal range: 0-20 IU). ECG was done on admission while the patient was afebrile. ECG characteristics included heart rate, PR interval, ST-T alterations, large QRS complexes, and QT interval. Observations on echocardiography revealed systolic dysfunction (impaired cardiac contraction) and pericardial effusion (abnormal fluid buildup).

Statistical analysis

Statistical Package for Social Sciences (SPSS 19.0) was used for analysis of data. A probability value (‘p’ value) of less than or equal to 0.05 at 95% CI was considered as statistically significant.

Results

62% of patients were male and 38% female in this research. Male-female ratio was 1.62:1. The study population had a mean age of 35.15±13.2, ranging from 16 to 68 years. The mean and median age of men were 33.9±13.5 years and 30 years (range 16-63). FEMALES: 37.05±12.5 years and 34 (range 16-68 years) years. Out of 110 dengue patients, 69.1% had fever, 7.3% had shock syndrome, and 23.6% had hemorrhagic fever. 56.36% of patients had normal ECGs upon admission, whereas 43.64% had alterations. In the second ECG on day three, 87.27% were normal and 12.73% had changes. All dengue patients had normal ECGs upon discharge, suggesting transitory ECG alterations. In this research, 59.09% had normal sinus rhythm, 36.4% had sinus bradycardia, 3.6% had sinus tachycardia, and 10.9% showed NSST-T alterations. Additionally, 0.9% had first-degree AV block and 4.65% had 1.8% had QTc prolongation and RBBB. NSST alterations and sinus bradycardia or normal sinus rhythm overlapped in some cases. A few individuals exhibited sinus bradycardia and QTc prolongation.

Echocardiography revealed pericardial effusion in 0.91%, systolic dysfunction in 1.82%, and diastolic dysfunction in 2.73%.
Based on abnormal cardiac enzymes, echocardiography, and ECG, 60.09% of patients had cardiac symptoms. In eight dengue shock patients, one (0.9%) had pericardial effusion and two (1.8%) experienced systolic and
diastolic dysfunction. One (0.9%) of 26 DHF patients exhibited diastolic dysfunction. All echocardiography data showed a substantial difference in dengue severity (P<0.05).
Six (75%) of eight DSS patients exhibited positive troponin I. Seven (26.9%) of 26 DHF patients reported positive troponin I. DF patients showed no troponin I positive. The proportion of dengue patients with positive troponin I corresponds with fever severity. The difference was substantial (P<0.001).

Compared to 42.3% and 39.5% in dengue hemorrhagic fever and dengue fever, 87.5% of eight dengue shock syndrome patients had elevated CKMB values. This shows that dengue fever severity corresponds with aberrant CKMB percentage. The difference met statistical significance (P<0.05). All dengue patients in this research recovered and no deaths occurred.

Table 1: Comparison of Echocardiography findings with dengue severity

			Dengue severity			Total	p- value
			DF	**DHF**	**DSS**		
Pericardial effusion	Absent	No.	76	26	7	109	0.002
		%	69.1%	23.6%	6.4%	99.1%	
	Present	No.	0	0	1	1	
		%	0%	0%	0.9%	0.9%	
Total		No.	76	26	8	110	
		%	69.1%	23.6%	7.3%	100%	
Systolic Dysfunction	Absent	No.	76	26	6	108	0.000
		%	69.1%	23.6%	5.5%	98.2%	
	Present	No.	0	0	2	2	
		%	0%	0%	1.8%	1.8%	
Total		No.	76	26	8	110	
		%	69.1%	23.6%	7.3%	100%	
Diastolic Dysfunction	Absent	No.	76	25	6	107	0.000
		%	69.1%	22.7%	5.5%	97.3%	
	Present	No.	0	1	2	3	
		%	0%	0.9%	1.8%	2.7%	
Total		No.	76	26	8	110	
		%	69.1%	23.6%	7.3%	100%	

Table 2: Comparison of Troponin I with dengue severity

Dengue Severity		Troponin I		Total	p- value
		Negative	Positive		
Dengue Fever	No.	76	0	76	0.000
	%	69.1%	0%	69.1%	
Dengue haemorrhagic fever	No.	19	7	26	
	%	17.3%	6.4%	23.6%	
Dengue shock syndrome	No.	2	6	8	
	%	1.8%	5.5%	7.3%	
Total	No.	97	13	110	
	%	88.2%	11.8%	100%	

Table 3: Comparison of CKMB with dengue severity

Dengue Severity	**CKMB**			**Total**	**P Value**
		25 or less	**>25**		
Dengue Fever	No.	46	30	76	0.03
	%	41.8%	27.3%	69.1%	
Dengue hemorrhagic fever	No.	15	11	26	
	%	13.6%	10%	23.6%	
Dengue shock syndrome	No.	1	7	8	
	%	0.9%	6.4%	7.3%	
Total	No.	No.	48	110	
	%	%	43.6%	100%	

Discussion

The cardiac abnormalities seen in dengue are consistently harmless, temporary, and self-restricted, and are caused by subclinical viral myocarditis. The cardiac symptoms seen in dengue fever vary from mild bradycardia without any symptoms to severe myocarditis. [6] The average age of the study population in our research is 35.15±13.2. The average and middle age among men was 33.9±13.5 years and 30, respectively. The average age for females was 37.05±12.5 years and 34 years, respectively. The youngest patient was 16 years old and the oldest patient was 68 years old. The male to female ratio of 1.62:1 indicates a greater number of males, implying a male predominance. The results of this investigation were similar to those of a study conducted by Miranda et al, [7] where the average age was 32 and the male-to-female ratio was 0.92:1. In separate research conducted by Malavige et al, the average age was 26.6 years and the male to female ratio was 1.4 to 1. Guilarde et al. [9] conducted another research, in which the participants had a mean age of 32+/-12 years and a male to female ratio of 1.7:1. Among the 110 dengue patients included in this research, 69.1% were diagnosed with dengue fever (DF), 7.3% with dengue shock syndrome (DSS), and 23.6% with dengue hemorrhagic fever (DHF). According to a research done by Guilarde et al. [9], 23.2% of the participants were categorized as having Dengue Hemorrhagic Fever (DHF) and 50.3% were categorized as having Dengue Fever (DF), which is consistent with the findings of our own study. In a separate investigation conducted by Arora et al [10], it was shown that 16.7% of patients had DF, 70.8% had DHF, and 12.5% had DSS. These findings differ somewhat from our research and from another study conducted before. Cardiac abnormalities, as detected by electrocardiography (ECG) and echocardiography, are often seen in individuals with dengue infection. These symptoms are often without noticeable symptoms and are temporary in individuals with dengue fever and DHF. These conduction anomalies are believed to be signs of the cardiac conduction system being affected by dengue illness. In this research, the electrocardiogram (ECG) performed upon admission showed a normal ECG in 56.36% of the patients, whereas ECG abnormalities were seen in 43.64% of the patients. On the third day, the second electrocardiogram (ECG) revealed a normal ECG in 87.27% of patients, whereas ECG alterations were seen in 12.73% of patients. All patients (100%) had normal ECG readings at discharge, suggesting temporary ECG alterations in individuals with dengue. Research conducted by Prasanth et al. [11] found that 30% of patients had electrocardiogram (ECG) alterations. In research conducted by Yadav et al. [12], it was found that 13% of the patients exhibited normal sinus rhythm. Other observed results included sinus bradycardia in 60% of the cases, first degree heart block in 11% of the cases, and ventricular ectopic in 15% of the instances. Gupta et al. [13] performed research which found that 4 patients (14.28%) had sinus bradycardia (heart rate < 60), whereas 6 patients (21.4%) had sinus tachycardia. No patients showed any QRS or ST alterations. The research conducted by Sheetal et al. [14] focused on the cardiac symptoms of dengue fever. The most often seen aberrant heart rhythm was sinus bradycardia, which occurred in 32% of patients. This was followed by inexplicable tachycardia in 3% of patients, as well as ventricular bigeminy and ventricular tachycardia, each occurring in 1% of patients. According to research conducted by Arora et al [10], 84.21% of the participants had a normal heart rate, 8.77% had sinus bradycardia, and 3.51% of the patients each had sinus tachycardia and NSST-T alterations. Out of the 6 patients who had an irregular heart rhythm at admission, 4 of them (66.67%) had first degree atrioventricular (AV) block, while the other 2 had right bundle branch block (RBBB) (33.33%). Nevertheless, the second and third electrocardiograms (ECGs) conducted on day three and day seven (or upon release, if sooner) showed a regular heart rhythm. Therefore, Sinus Bradycardia was the most often seen ECG finding after normal Sinus rhythm. The current investigation revealed that 60.09% of the patients had cardiac symptoms, as determined by abnormal cardiac enzymes, echocardiography, and ECG. According to a study conducted by Arora et al, the occurrence of heart-related symptoms was more frequent in patients with dengue shock syndrome. Out of 15 patients with this syndrome, eight (53.33%) had elevated levels of cardiac enzymes. In comparison, 30 (35.29%) out of 55 patients with dengue hemorrhagic fever and six (30%) out of 20 patients with dengue fever showed similar cardiac enzyme elevation. Despite the lack of statistical significance, with a p-value of 0.325. Our research found a statistically significant link ($p<0.05$) between echocardiography, cardiac enzymes, and dengue severity. This indicates that when the severity of dengue rises, such as in cases of DHF and DSS, there is a larger likelihood of heart involvement. Instances of DSS had the most significant cardiac participation, as shown by elevated levels of cardiac enzymes, abnormalities in electrocardiography (ECG), and findings from echocardiography.

Conclusion

The primary diagnostic methods for identifying myocardial involvement in dengue fever are ECG, cardiac enzymes, and echocardiography. The degree of cardiac involvement was greater in DHF and DSS patients compared to DF cases.

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