



A STUDY OF CARDIAC MANIFESTATIONS IN DENGUE FEVER

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ABSTRACT **Background Of Study:** Dengue Fever is an acute febrile infectious disease, caused by any of four serotypes. Severe dengue infections may give rise to many complications such as liver failure, disseminated intravascular coagulation, encephalopathy, myocarditis, and acute renal failure. ST segment and T wave changes in the electrocardiogram together with low ejection fraction and global hypokinesia on 2D echocardiography have been found. Hence, this study was intended to assess the cardiac manifestations in dengue fever patients. **Objective:** To determine the clinical profile of Dengue patients in the study and to Study the cardiac manifestations in patients with dengue fever. **Method:** The work was carried out in the outpatient Medicine department of Chalmeda Anand Rao institute of medical sciences. All the cases which satisfy the inclusion criteria were included in the study. Serological tests for the detection of IgM dengue antibodies and NS1 antigen were done. All the subjects were subjects for laboratory investigations. **Results:** CK-MB and Troponin I at admission were raised by 18% and 72% respectively. On ECG, 56% of the patients had normal rhythm, 15% had sinus Bradycardia, 9% had sinus tachycardia, 10% had T wave changes, 3% had ST Changes, 2% had Sinus Bradycardia with T Wave Changes, 2% had Sinus Tachycardia with T wave changes and 1% had LVH and 2% had Abnormal Rhythm. **Conclusion:** From this study, we can conclude that cardiac manifestations cause significant morbidity and no mortality. Hence cardiac manifestations are important in the management and assessing the prognosis of patients with dengue.

KEYWORDS :

INTRODUCTION

Dengue Fever is an acute febrile infectious disease, caused by any of four serotypes 1,2,3,4 of a virus from the genus flavivirus, called dengue virus. The highest incidence of dengue is seen in Southeast Asia, India and the American tropics. Dengue affects people of all ages. Severe dengue infections may give rise to many complications such as liver failure, disseminated intravascular coagulation, encephalopathy, myocarditis, and acute renal failure.

Although shock in DHF/DSS has been attributed largely to decreased intravascular volume due to capillary leakage of plasma into the interstitial space, a few recent studies have reported that it may be due to cardiac involvement. Acute reversible myocarditis has been reported in patients with dengue infections. ST segment and T wave changes in the electrocardiogram together with low ejection fraction and global hypokinesia on radionuclide ventriculography have been found. Thus Dengue fever is not only a serious illness it is emerging as a public health problem, so the need for a study.

In a study by Carlos Henrique Miranda et al (1) in Brazil, Eighty-one patients were evaluated and twelve patients (15%) presented with elevated biomarker levels. Compared to controls, they had higher leukocyte ($p < 0.001$) and platelet counts ($p = 0.005$); higher C reactive protein ($p = 0.02$) and a lower viral load ($p = 0.03$). There was no difference according to clinical dengue classification; DHF/DSS severity; duration of symptoms and prevalence of secondary infection between the two groups. Two patients died secondary to cardiogenic shock before imaging studies.

Necropsic findings were compatible with myocarditis in both, and immunohistochemistry for the dengue virus showed increased staining on mononuclear cells located in the myocardial tissue. Out of the ten patients who underwent ECHO, depressed left ventricular ejection fraction (LVEF) was identified in one; left ventricular segmental abnormalities with preserved LVEF in two, and an important pericardial effusion with tamponade in another. Cardiac involvement was confirmed by CMR in these four patients.

In a study conducted by Khongphatthanayathin A et al(2) in Thailand, left ventricular performance was evaluated using echocardiography in dengue haemorrhagic fever patients. 24 patients with serologically confirmed dengue fever were subjected to ECHO. ejection fraction was significantly lower in these patients. The study concluded that the mechanism of decreased cardiac output in DHF is complex.

Because of the increasing incidence of dengue fever as well as the

rising morbidity and mortality due to this, the study of both the sub-clinical and clinical cardiac manifestations in dengue via clinical examination, cardiac biomarkers, ECG and ECHO cardiography was undertaken.

Though, cases of dengue-like illness have been reported as early as 1912 (3), the first outbreak of dengue fever/DHF was reported from Kolkata in 1963 . DEN-2 was the main causative agent and children below 10 years were the main victims. Around 30% of the cases were of DHF.

Vector:

Dengue viruses are transmitted by the bite of female Aedes(Ae) mosquitos. Ae. aegypti is the most potential vector but other species such as Ae. Albopictus, Ae.polynesiensis and Ae.niveus have been incriminated as secondary vectors. In India Ae.aegypti is the main vector in most urban areas; however, Ae albopictus is also found as a vector in a few areas of southern India.

Host Factor:

Dengue virus infects humans and several species of lower primates but in India man is the only natural reservoir of infection. All ages and both sexes are susceptible to dengue fever. Secondary dengue infection is a risk factor for DHF including passively acquired antibodies in infants. Travel to dengue endemic area is an important risk factor, if the patient develops a fever more than two weeks after travel, dengue is unlikely. Migration of patients during viremia to a non-endemic area may introduce it into the area.

Cardiac Manifestations In Dengue Fever:

The increase in capillary permeability that occurs in some patients, and can cause intravascular hypovolaemia and shock, is the best-known cardiovascular complication associated with dengue. Additionally, various specific cardiac manifestations have been described, ranging from rare fulminant myocarditis to more-common associations with functional myocardial impairment and arrhythmias. 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. In the past 2 decades, the critical role of myocardial impairment in the development of septic shock has become clear, distinct from cardiovascular compromise caused by reduced preload and systemic vascular resistance(4) Myocardial impairment is possibly mediated by circulating myocardial depressant factors. (5)By contrast, the contribution of cardiac dysfunction to haemodynamic compromise in DSS remains to be adequately defined.

Pathogenesis:

The pathogenic mechanisms underlying functional myocardial impairment remain to be elucidated, but as the majority of the patients do not have evidence of myocardial damage, direct viral invasion of cardiomyocytes is unlikely. Other postulated mechanisms include myocardial oedema from local capillary leakage, the presence of a circulating myocardial depressant factor (for example, one or more proinflammatory mediators), coronary hypoperfusion, altered calcium homeostasis or a combination of these factors.

Fulminant Myocarditis:

By contrast, in fulminant dengue myocarditis, evidence exists of widespread myocyte damage with substantial increases in levels of cardiac biomarkers, ST-segment changes on ECG mimicking acute myocardial infarction, cardiac-specific symptoms, and clear signs of functional impairment. (6)

Heart Failure And Cardiogenic Shock:

There are few reports of acute heart failure during dengue virus infection. In an evaluation of 17 dengue patients with radionuclide ventriculography, Wali et al. showed that seven patients had ejection fraction less than 40%, 12 had global hypokinesia, and, after three weeks of follow-up, all alterations had returned to normal (7). Acute pericarditis, characterized by chest pain, has been reported in dengue .

ECG Changes:

ECG alterations reported in dengue are often transient and nonspecific, including sinus bradycardia, atrioventricular block, T wave, and ST-segment abnormalities. (8) Classically, such rhythm disturbances were thought to occur primarily in the recovery phase. Primarily bradyarrhythmias such as first and second-degree heart block, as well as atrial and ventricular ectopic beats are noted. Tachyarrhythmias, including atrial fibrillation, have also been documented in patients with dengue, but are much less common than bradyarrhythmias.

Echocardiography Findings In Dengue Fever:

Approximately 20% of those who developed DHF have an LV ejection fraction of less than 50%, and are likely to return to normal within a few weeks (9)(Wali et al, 1998) A study in which echocardiography was used to evaluate 54 Indian children hospitalized with dengue demonstrated that nine patients (17%) had evidence of left ventricular (LV) systolic dysfunction (LV ejection fraction [LVEF] 50%. These changes were observed equally across the spectrum of dengue severity grades.

AIMS & OBJECTIVES:

To determine the clinical profile of Dengue patients in the study and to Study the cardiac manifestations in patients with dengue fever.

MATERIALS AND METHODS:

The work was carried out in the outpatient Medicine department of Chalmeda Anand Rao institute of medical sciences. It is an observational study.

Inclusion Criteria:

1. Dengue fever cases aged more than 18 years
2. Dengue fever cases confirmed by NS1Ag test or both NS1Ag and IgM, IgG positive cases.

Exclusion Criteria:

1. Patients with a previous history of any cardiac illness.
2. Admission ECG suggestive of old MI.
3. Medication affecting the heart rate.

RESULTS:

Table 1: In the study majority 36% were in the age group 20 to 29 years, followed by <20 years (22%) and others as shown below the table. The mean age of subjects was 30.32 ± 13.66 years.

Age	Count	%
<20 years	22	22.0%
20 to 29 years	36	36.0%
30 to 39 years	19	19.0%
40 to 49 years	12	12.0%
>50 years	11	11.0%
Total	100	100.0%

Table 2: Sex distribution of subjects

Sex	Count	%
Female	41	41.0%
Male	59	59.0%
Total	100	100.0%

In the study 59% were males and 41% were females.

Table 3: Dengue serology among subjects

Dengue Test	Count	%
Ns1 Positive	50	50.0%
IgM positive	20	20.0%
IgG Positive	12	12.0%
IgM and IgG positive	8	8.0%
IgM and NS1 Positive	7	7.0%
NS1 and IgG Positive	2	2.0%
IgG, IgM and NS1 Positive	1	1.0%
Total	100	100.0%

In the study 50% were NS1 positive, 20% were IgM positive, 12% were IgG Positive, 8% were IgM and IgG positive, 7% were IgM and NS1 Positive, 2% were NS1 and IgG Positive and 1% were IgG, IgM and NS1 Positive.

Table 4: Troponin Levels Distribution among subjects

Troponin	Count	%
Positive (>0.017)	18	18.0%
Negative (<0.017)	82	82.0%
Total	100	100.0%

In the study 18% were positive for Troponin I and 82% were negative for Troponin I.

Table 5: CK-MB Distribution among subjects

CK-MB	Count	%
<25	12	28.0%
>25	88	72.0%

In the study, 28% had CK-MB <25 and 72% had CK-MB >25. Mean CK-MB was 85.99 ± 75.73.

Table 6: ECG findings among subjects

ECG	Count	%
Normal	56	56.0%
Sinus Bradycardia	15	15.0%
Sinus Tachycardia	9	9.0%
T wave changes	10	10.0%
ST Changes	3	3.0%
Sinus Bradycardia with T-Wave Changes	2	2.0%
Sinus Tachycardia with T wave changes	2	2.0%
LVH	1	1.0%
Abnormal Rhythm	2	2%

In the study 56% had normal ECG, 15% had Sinus Bradycardia, 9% had Sinus Tachycardia, 10% had T wave changes, 3% had ST Changes, 2% had Sinus Bradycardia with T Wave Changes, 2% had Sinus Tachycardia with T wave changes and 1% had LVH and 2% had Abnormal Rhythm.

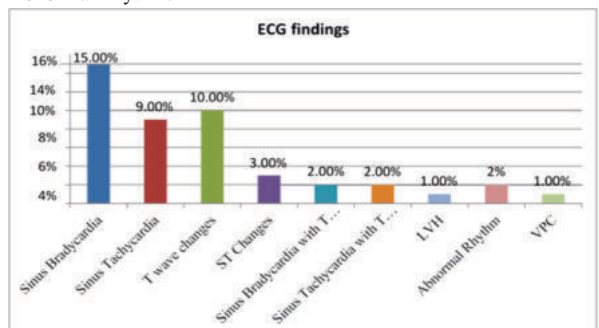


Table 7: ECHO Findings among subjects

ECHO Findings	Count	%
Normal	85	85.0%
Bradycardia	5	5.0%
Anterior Wall Hypokinesia	4	4.0%
Mild PAH and Mild TR	1	1.0%

Bradycardia + Mild MR	1	1.0%
Mild PAH, Mild TR, Hypokinesia Ant. wall	1	1.0%
LVH	1	1.0%
DCM Secondary to Dengue Myocarditis	1	1.0%
Bradycardia, Mild AML Prolapse	1	1.0%

In the study 85% had normal ECHO, 5% had Bradycardia, 4% had Anterior Wall Hypokinesia, 1% had Mild PAH and Mild TR, Bradycardia + Mild MR, Mild PAH, Mild TR, Hypokinesia Ant. wall, LVH, DCM SECONDARY. TO DENGUE MYOCARDITIS and BRADYCARDIA, MILD AML PROLAPSE respectively

Table 8: Association between Troponin and Dengue serology

		Troponin				P Value
		Positive(>0.017)		Negative (<0.017)		
		Count	%	Count	%	
Dengue Test	IgG Positive	11	14.7%	1	4.0%	$\chi^2 = 7.351$, df = 6, p = 0.290
	IgG, IgM and NS1 Positive	1	1.3%	0	0.0%	
	IgM and IgG positive	5	6.7%	3	12.0%	
	IgM and NS1 Positive	7	9.3%	0	0.0%	
	IgM positive	16	21.3%	4	16.0%	
	NS1 and IgG Positive	1	1.3%	1	4.0%	
	NS1 Positive	34	45.3%	16	64.0%	
	Total	75	100.0%	25	100.0%	

In the study, there was no significant association between Dengue serology and Troponin I.

DISCUSSION:

Cardiac manifestations in dengue virus infection can range from asymptomatic Bradycardia to life-threatening myocarditis. Various studies have quoted several cardiac manifestations of dengue infection viz. sinus Bradycardia, transient AV blocks, transient ventricular arrhythmias, myocarditis, systolic and diastolic dysfunction and pericardial effusion. Myocardial involvement may be the direct result of dengue virus infection in susceptible individuals or may be due to the effects of cytokines / cellular mediators of the immune response(10). The present study was done to determine the clinical profile of Dengue patients and to Study the cardiac manifestations in patients with dengue fever.

Cardiac Manifestations:

In the present study, 56% had normal ECG and 44% had abnormal ECG findings, of them 15% had Sinus Bradycardia, 9% had Sinus Tachycardia, 10% had T wave changes, 3% had ST Changes, 2% had Sinus Bradycardia with T Wave Changes, 2% had Sinus Tachycardia with T wave changes and 1% had LVH and 2% had Abnormal Rhythm.

In the present study on ECHO, 5 had Bradycardia, 4% had Anterior Wall Hypokinesia, 1% had Mild PAH and Mild TR, Bradycardia + Mild MR, Mild PAH, Mild TR, Hypokinesia Anterior wall, LVH, DCM Secondary to Dengue Myocarditis And Bradycardia, Mild AML Prolapse Respectively In the study by Sheetal et al Echocardiographic evaluation was done in 18 patients.

Three patients were noticed to have Mild pericardial effusion. Echocardiographic evidence of myocarditis was not seen in any patient. In the study by Gupta et al, systolic dysfunction was absent in all patients; mild diastolic dysfunction was present in 14.28 per cent. Wiwanitkit et al have described cases of dengue myocarditis.

In the study by Carlos Henrique Miranda 2 patients had reduced LV function, two had LV segmental hypokinesia and one had pericardial effusion.

Laboratory Profile:

In the present study, 50% were NS1 positive, 20% were IgM positive, 12% were IgG Positive, 8% were IgM and IgG positive, 7% were IgM and NS1 Positive, 2% were NS1 and IgG Positive and 1% were IgG, IgM and NS1 Positive. In the study, 31% had Hb <12 gm% and 69% had Hb >12 gm%. Mean Hb was 12.68 ± 2.12 gm%. In the present study, 34% had a Total count of <4000 and 5% had a Total count of >11000. In the study, 26% had platelet count <20000, 32% had 20000 to 50000, 18% had 51000 to 100000 and 24% had platelet count

>100000. 18% were positive for Troponin I and 28% had CK-MB <25 and 72% had CK-MB >25. 29% had abnormal Liver function tests.

CONCLUSION:

The incidence of cardiac manifestations was present in 44% of the patients. A wide range of cardiac manifestations was observed in this study. CK-MB and Troponin I at admission were raised by 18% and 72% respectively. On ECG, 56% of the patients had normal rhythm, 15% had sinus Bradycardia, 9% had sinus tachycardia, 10% had T wave changes, 3% had ST Changes, 2% had Sinus Bradycardia with T Wave Changes, 2% had Sinus Tachycardia with T wave changes and 1% had LVH and 2% had Abnormal Rhythm. Hence Transient cardiac abnormality can be an important presentation among patients with Dengue fever and this should guide the treating physician to look for cardiac involvement.

Conflict Of Interest: None

REFERENCES

- Miranda C.H, Borges Mde.C, Matsuno A.K et al, Clinical Infectious diseases journal,2013; 57(6):812-9
- Khongphatthanayathin A , Suesaowalk M , Muangmingsook S , Bhattarakosol P , Pancharoen C. Hemodynamic profiles of patients with dengue hemorrhagic fever during toxic stage: an echocardiographic study. Intensive Care Medicine.2003;29:570-4.
- Kennedy RS. Some notes on an epidemic of Dengue-form fever amongst Indian troops, Calcutta. Indian Med Gaz 1912
- Pulido, J. N. et al. Clinical spectrum, frequency, and significance of myocardial dysfunction in severe sepsis and septic shock. *Mayo Clin. Proc.* 87, 620–628 (2012).
- Merx, M. W. & Weber, C. Sepsis and the heart. *Circulation* 116, 793–802 (2007).
- Daniel, R. A., Silva, A. R., Neppelenbroek, V. B., Feres, O. & Bestetti, R. B. Fulminant myocarditis and viral infection. *J. Clin. Virol.* 58, 1–3 (2013).
- Marques, N., Gan, V. C. & Leo, Y. S. Dengue myocarditis in Singapore: two case reports. *Infection* 41, 709–714 (2013).
- Khongphatthallayothin, A. et al. Morbidity type I second degree AV block during recovery from dengue hemorrhagic fever. *Southeast Asian J. Trop. Med. Public Health* 31, 642–645 (2000).
- Statler J, Mammen M, Lyons A, Sun W. Sonographic findings of healthy volunteers infected with dengue virus. *J Clin Ultrasound* 2008;36:413-417
- J M Pelupessy E R Allo,S Jota; Pericardial effusion in dengue haemorrhagic fever. *Paediatrica Indonesiana* 1989; 29:72-5