Original Research Article

Study of cardiac manifestations of dengue fever

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Abstract

Background: Cardiac manifestations in dengue virus infection can range from asymptomatic bradycardia to life threatening myocarditis. Patients with dengue do not have a formal cardiac assessment, so the frequency of subclinical dengue myocarditis and its relative contribution to the hemodynamic instability in severe dengue remains to be demonstrated. Aim: To evaluate the cardiac manifestations of dengue fever. Material and Methods: A total of 110 patients who presented with dengue fever were studied for cardiac manifestations with the help of clinical examinations, laboratory cardiac markers, electrocardiography and echocardiography findings. Results: Based on abnormal cardiac enzymes, echocardiography and ECG 60.09% of the patients were found to have cardiac manifestations. CK-MB at admission was > 25 in 43.64% of the patients. Troponin I at admission was positive in 11.8% of the patients. 36.4% patients had sinus bradycardia; 3.6% patients had sinus tachycardia and 10.9% patients had NSST-T changes. 0.9% patients had first degree AV block, 4.65% had QTc prolongation and RBBB was noted in 1.8%. Echocardiography showed pericardial effusion in 0.91% patients, systolic dysfunction in 1.82% patients; while 2.73% patients had diastolic dysfunction. Conclusion: ECG, cardiac enzymes and echocardiography are the main tools to diagnose the myocardial involvement in dengue fever. Echocardiography can prove a useful tool especially in patients with hemodynamic instability to plan for more efficient management.

Key Words: Dengue fever, Cardiac enzymes, electrocardiography, echocardiography

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INTRODUCTION

Dengue is the most common and important arthropodborne viral illness in humans and a major public health problem. The actual numbers of dengue cases are underreported and many cases are misclassified.¹ Several outbreaks of dengue have occurred over past decades in many countries, causing significant morbidity and mortality. Dengue virus infection is currently an area of great concern due to its wide geographic spread and also due to the vast majority of world population under its potential influence. Severe dengue involves various organs like cardiovascular, central nervous system, hepatic, respiratory, renal and muscular systems. Cardiac manifestations in dengue virus infection can range from asymptomatic bradvcardia life threatening to myocarditis.^{2,3} Patients with dengue do not have a formal cardiac assessment, so the frequency of subclinical dengue myocarditis and its relative contribution to the hemodynamic instability in severe dengue remains to be demonstrated. The literature review revealed that there are only few studies conducted in India evaluating the cardiac manifestations of dengue fever. Although there are studies reporting myocarditis complicating dengue fever, the thorough investigation of the cardiac involvement in dengue has been poorly understood. Hence, this study was conducted with the objective of evaluating the cardiac manifestations of dengue fever.

MATERIAL AND METHODS

This descriptive cross-sectional study was conducted in the Department of Medicine, in tertiary care hospital on patients admitted in hospital suffering with dengue over a period of two years.

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Sample size

Sample size was calculated by using the formula: n=4pq/L2. Where, n= Sample size; p=positive character=37%; q=1-p=1-37%=63%; L=allowable error in p (25%)=9.25. n=4pq/L2=4x37x63/(9.25)2 =108.90 \square 110. Thus, a total of 110 cases were studied.

Inclusion criteria

Patients admitted in ward/ICU hospital having

•Age group of \geq 13 years.

•Fulfilling the WHO criteria for dengue.

•Confirmed dengue serology (Dengue IgG/IgM/NS1 positive)

• Willing to give written and informed consent.

Exclusion criteria

•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 suffering from mixed infections (Malaria, leptospira).

•Patients not willing to give consent for the study.

Ethical clearance

Prior to initiating the study, ethical clearance for same was obtained from the Institutional Ethics Committee.

Method of collection of data

Patient details such as name and demographic details were noted. All Patients were subjected to detailed history taking interview so as to ascertain the details of the current illness, any past illnesses similar or otherwise, ongoing medications and to rule out any cardiac disease. All patients underwent general physical and systemic examination. All patients also underwent investigations as detailed further. During general physical examination patients pulse rates and ECG were recorded only after subsidence of fever. Daily monitoring of vital signs was done and lowest recorded pulse rates, blood pressures were noted for purpose of this study. Pulse rates of patients having disproportionate tachycardia were also noted. Laboratory investigations such as Complete blood count, Cardiac enzymes- CK MB, Troponin I, SGOT, Sr. LDH, Electrocardiography and 2D Echocardiography were done. Dengue patients positive for one of the following investigations with or without clinical features were considered as cardiac involvement. Features suggestive of rhythm disturbance, heart rate changes like sinus tachycardia or bradycardia, raised CKMB and/or troponin I and abnormal ECG and ECHO were considered for cardiac manifestations. ECG changes included sinus tachycardia, sinus bradycardia, nonspecific STT wave changes, inverted T waves, First degree heart block, right bundle branch block. Echocardiography changes were interpreted as;

Systolic dysfunction- refers to impaired ventricular contraction. Diastolic dysfunction – refers to an abnormality in the filling during diastole. Ejection fraction – The fraction of the blood pumped out of a ventricle with each heartbeat (Normal value – $67\pm12\%$) and Pericardial effusion- An abnormal accumulation of fluid in the pericardial cavity. Patients who were seropositive for Dengue were classified on the basis of WHO Criteria as follows: Dengue Fever (DF), Dengue Hemorrhagic Fever (DHF), Dengue Shock Syndrome (DSS).

Statistical analysis

SPSS 18.0 (Statistical Package for Social Sciences) was used for analysis of data. The categorical data was expressed as rates, ratios and proportions. The continuous data was expressed as mean \pm standard deviation (SD).

RESULTS

In the present study, 62% of the patients were males and 38% were females. The male to female ratio was 1.62:1. The mean age of the study population was 35.15 ± 13.2 . with range of 16 to 68 years. The mean and median age among males was 33.9±13.5 years and 30 (Range 16 to 63) years. In females the same was 37.05 ± 12.5 years and 34 (range 16 to 68 years) years respectively. Bradycardia was the most common sign observed in 36.36% of the patients followed by positive tourniquet test and petechiae seen in 23.64% and 17.27% patients respectively. None of the patients had pedal oedema or raised jugular venous pressure. Systemic examination findings revealed cardiovascular findings in 42.73%, respiratory system findings in 7.27% and per-abdominal findings in 12.73% of the patients. CVS findings included those of bradycardia and signs of vascular involvement like cold peripheries; no CVS finding was noted apart from these. Respiratory system findings included those of crepitations and decreased air entry. Per abdomen examination findings included those of hepatomegaly and splenomegaly. No central nervous system findings were noted. In the present study, IgM and IgG were positive in 34.55% and 19.09% of the patients respectively; while NS1 was positive in 75.45% patients. CK-MB at admission was raised (>25) in 43.64% of the patients. Out of the 48 patients with abnormal CK-MB levels at admission, 41 (85.42%) patients were found to have normal CK-MB levels at the time of discharge. Troponin I at admission was positive in 11.8% of the patients. SGOT was > 46 U/L in 64.55% and Serum LDH was >400 U/L in 41.82% of the patients at admission. Out of 110 dengue patients, 69.1% had dengue fever, 7.3% had dengue shock syndrome and 23.6% had dengue hemorrhagic fever.

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ECG Findings	Total number of subjects (n=110)		
	Number	Percentage (%)	
Normal Sinus Rhythm	65	59.09	
Sinus Tachycardia	4	3.6	
Sinus Bradycardia	40	36.4	
NSST-T Changes	12	10.9	
1st degree AV block	1	0.9	
QTc Prolongation	5	4.6	
RBBB	2	1.8	

Table 1: Distribution of dengue patients according to ECG findings at admission

In this study, 59.09% patients had normal sinus rhythm, 36.4% patients had sinus bradycardia; 3.6% patients had sinus tachycardia and 10.9% patients had NSST-T changes. Also 0.9% patients had first degree AV block, 4.65% had QTc prolongation and RBBB was noted in 1.8%. Some patients had overlapping changes like NSST changes with sinus bradycardia or normal sinus rhythm. Some patients had sinus bradycardia with QTc prolongation.

Table 2: Serial ECG findings in dengue patients							
ECG Findings		Total number of subjects (n=110)					
		Number	Percentage (%)				
At Admission	Normal ECG	62	56.36				
	ECG changes present	48	43.64				
	Total	110	100				
Second	Normal ECG	96	87.27				
ECG changes present		14	12.73				
	Total	110	100				
At Discharge	Normal ECG	110	100				
	ECG changes present	0	0				
	Total	110	100				

ECG at admission revealed normal ECG in 56.36% of the patients while ECG changes were noted among 43.64%. The second ECG done on day three showed normal ECG in 87.27% and ECG changes were noted in 12.73% patients. At the time of discharge normal ECG was seen in all the patients (100%) indicating transient ECG changes in patients with dengue.

Table 3: Echocardiography findings in patients					
Echocardiography findings	No.	of patients	Percentage		
Systolic dysfunction		2	1.82%		
Diastolic dysfunction		3	2.73%		
Pericardial effusion		1	0.91%		

In this study, echocardiography showed pericardial effusion in 0.91% patients, systolic dysfunction in 1.82% patients; while 2.73% patients had diastolic dysfunction. Based on abnormal cardiac enzymes, echocardiography and ECG 60.09% of the patients were found to have cardiac manifestations.

DISCUSSION

Various viral infections cause myocardial damage, either by invasion or an autoimmune reaction resulting in myocardial inflammation. The cardiac abnormalities in dengue are invariably benign, transient, and self-limited and are attributed to subclinical viral myocarditis. Cardiac manifestation in dengue fever ranges from asymptomatic bradycardia to severe myocarditis.⁴ Cardiac abnormalities including various ECG abnormality (sinus bradycardia, and prolongation of PR interval, transient AV block, transient ventricular arrhythmias), myocarditis, systolic and diastolic dysfunction and pericardial effusion have been observed during acute phase of viral dengue infection.^{3,5} Rhythm disturbance such as sinus bradycardia and ventricular ectopics have also been reported during convalescence period of dengue fever.⁶ Even though numerous studies are available detailing the various manifestations of dengue fever only a few highlight the cardiac manifestations in it. In the present study, while checking for dengue serology testing, IgM and IgG were positive in 34.55% and 19.09% of the patients respectively; while NS1 was positive in 75.45% patients. In a study conducted by MU Rabbani *et al*,⁷ 92.2% patients had NS1Ag positive, IgM antibody was raised in 19.3% patients and 15.8% patients had raised IgG antibody level. In a study done by S Sheetal *et al*,⁶ 79% patients were Dengue NS1 positive and 21% patients were Dengue IgM positive. The serology shows close to comparable results in these studies. In this study, out of 110 dengue patients; 69.1% had DF, 7.3% had DSS

and 23.6% had DHF. In a study conducted by Guilarde AO et al,⁸ 23.2% were classified as DHF and 50.3% were classified as DF showing almost similar finding compared to our study. Another study by M Arora et al,4 showed 16.7% patients with DF, 70.8% patients with DHF and 12.5% patients with DSS thus having some variations compared to our study and with the other study as compared to previously. In present study, CK-MB at admission was >25 in 43.64% of the patients. Troponin I at admission was positive in 11.8% of the patients. In a study done by Prasanth B et al,9 26% had elevation of at least one cardiac enzyme. In a study conducted by VK Gupta et al,¹⁰ CK-MB was elevated in 78.55% of patients and Trop I was weakly positive in 42.8% of patients. In a study done by M Arora et al,4 33.3% patients had elevated CK-MB and 26.7% patients had elevated Troponin I which was almost comparable to our study. In this study, 59.09% patients had normal sinus rhythm, 36.4% patients had sinus bradycardia; 3.6% patients had sinus tachycardia and 10.9% patients had NSST-T changes. Also 0.9% patients had first degree AV block, 4.65% had QTc prolongation and RBBB was noted in 1.8%. In the present study, ECG at admission revealed normal ECG in 56.36% of the patients while ECG changes were noted among 43.64%. The second ECG done on day three showed normal ECG in 87.27% and ECG changes were noted in 12.73% patients. At the time of discharge normal ECG was seen in all the patients (100%) indicating transient ECG changes in patients with dengue. In a study done by Prasanth B et al,9 ECG changes were seen in 30% of patients. In a study by RK Yadav et al,11 13% cases showed normal sinus rhythm, other findings seen were sinus bradycardia in 60%, first degree heart block in 11%, and ventricular ectopics in 15% cases. In a study conducted by VK Gupta et al,¹⁰ sinus bradycardia (HR <60) was present in 4 patients (14.28%), and sinus tachycardia in 6 patients (21.4%) and QRS and ST changes were not seen in any patient. In a study based on cardiac manifestations of dengue fever by S Sheetal *et al*,⁶ the commonest rhythm abnormality was sinus bradycardia in 32% patients followed by 3% unexplained tachycardia and ventricular bigeminy, ventricular tachycardia in 1% each. In a study by M Arora et al,⁴ 84.21% of them having normal heart rate, 8.77% having sinus bradycardia and 3.51% patients each having sinus tachycardia and NSST-T changes. Among 6 patients with abnormal rhythm at admission, 4 (66.67%) had first degree AV block and 2 had RBBB (33.33%). However, the second and third ECG done on day three and day seven (or at the time of discharge, whichever was earlier) showed normal rhythm. Hence, overall sinus bradycardia was the commonest ECG finding after normal Sinus rhythm. In this study, echocardiography

showed pericardial effusion in 0.91% patients, systolic dysfunction in 1.82% patients; while 2.73% patients had diastolic dysfunction. Echocardiography repeated for these patients on discharge showed normal findings. In a study done by Prasanth B *et al*,⁹ 16% patients had myocardial involvement based on echocardiography. In a study conducted by VK Gupta *et al*,¹⁰ mild diastolic dysfunction was seen in 14.2 % patients and no other abnormal echocardiography findings were observed.

Limitations of the study

We used the cardiac biomarker elevation for judging cardiac involvement in dengue. This could underestimate the real prevalence of dengue myocarditis (one of the commonest cardiac manifestation of dengue), as a large percentage of patients can have myocarditis without biomarker elevation; for example, troponin I has high specificity (89%) but limited sensitivity (34%) in the diagnosis of myocarditis. Testing for Troponin I was not done on quantitative basis, which could have provided better comparison with the severity of dengue fever. Cardiac biopsy which is the gold standard to diagnose myocarditis was not performed. Central venous pressure was not measured; correlation of the same to cardiac involvement was not done.

CONCLUSION

ECG, cardiac enzymes and echocardiography are the main tools to diagnose the myocardial involvement in dengue fever. DHF and DSS cases had higher degree of myocardial involvement as compared to DF cases. Cardiac involvement in dengue can contribute to hemodynamic instability in Dengue patients. Echocardiography can prove a useful tool especially in patients with hemodynamic instability to plan for more efficient management. Further studies are needed on a multicentre level to understand in detail the cardiac involvement of dengue fever which would help tackle management in critical and high risk cases.

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