A Study on Cardiac Manifestations of Dengue Fever

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Abstract

Aims: Incidence of cardiac involvement in dengue fever varies between 15 –50%. Cardiac manifestations of dengue fever include asymptomatic sinus bradycardia, transient AV blocks, transient ventricular arrhythmias, myocarditis and pericardial effusion. This study was done with the objective of finding actual incidence of different cardiac manifestations of dengue fever in our tertiary care hospital.

Methods: One hundred and twenty dengue patients were studied between January 2016 to December 2017. Routine biochemical parameters like complete haemogram, liver function tests, renal function tests, electrolytes were checked in all cases. ECG, echocardiography, Troponin T were evaluated in every patients and they were corroborated with clinical features like chest pain, dyspnoea, palpitation. Patients with electrolyte abnormalities, preexisting heart disease, drugs interfering with heart rhythm were excluded from study.

Results: Fifteen patients had cardiac involvement (12.5%). Eight patient had bradycardia (6.6%). Asymptomatic sinus bradycardia was commonest (3.3%). All had normal recovery within two weeks. Four patients had left ventricular systolic dysfunction (ejection fraction 35% - 45%) and there was spontaneous recovery within three months. Two patients had pericardial effusion which resolved within two weeks. Transient 2.1 AV block and atrial fibrillation were observed in two cases.

Conclusion: Cardiac manifestations of Dengue were present in 11.4 % of our patients. Brady arrhythmias (6.6%) were commonest manifestation which resolves spontaneously within seven to fourteen days. Left ventricular systolic dysfunction was present in 3.3% of patients which recovered within three months. Pericardial effusion was seen in 2.5% of patients. There were no significant tachyarrhythmias in our patients except one case of atrial fibrillation.

Introduction

Dengue is a self-limited systemic viral infection caused by Flavivirus and is being transmitted between people by the mosquitoes Aedes aegypti and Aedes albopictus. There are four serotypes of dengue viruses - DEN 1, DEN 2, DEN 3 and DEN 4.¹ Dengue fever (DF) may have wide spectrum of presentations ranging from uncomplicated self-limiting febrile illness to severe dengue including dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). According to The World Health Organization (WHO) data, 50 to 100 million infections occur yearly, including 500,000 dengue haemorrhagic fever (DHF) cases and 22,000 deaths, mostly among children.² Cardiac involvement in dengue has been poorly investigated and is uncommon. Cardiac manifestations of dengue fever include asymptomatic sinus bradycardia, transient AV blocks, transient ventricular arrhythmias, myocarditis and pericardial effusion. This study was done with the objective of finding actual incidence of different cardiac manifestations of dengue fever.

Materials and Methods

This prospective observational study was conducted at Department of Medicine and cardiology at EEDF hospital (Tertiary centre) in Calcutta. All consecutives dengue fever patients admitted between January 2016 to December 2017 were included in the study. Dengue cases were diagnosed according to the World Health Organization (WHO) 2009 criteria i.e. rapid test detection of nonstructural protein 1 (NS1) and/or immunoglobulin M (IgM) antibody on patients’ serum. One hundred and twenty patients were studied for two years. Minimum follow up period was six months and maximum two years. Informed consents were taken from all patients or their legal guardians and the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki with prior approval by institution’s human research committee. Routine biochemical parameters like complete haemogram, liver function tests, renal function tests, electrolytes were checked in all cases. Electrocardiogram was done in all cases for three consecutive days. If ECG is abnormal, daily monitoring was continued.

Echocardiogram and Troponin T were checked in all patients. Clinical features like chest pain, dyspnea, palpitation, abnormalities in heart rate and rhythm were analyzed clinically and corroborated with the above investigations. Quantitative variables are reported as mean and the categorical variables as frequency or percentage.

Objectives of the Study

To study the incidence of different cardiac manifestations of dengue fever in our hospital.

Inclusion Criteria

a. Age ≥ 12 years
b. Fulfilling the WHO criteria for dengue
c. Confirmed dengue serology

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Results

The mean age of our study group was 32 years. The youngest patient was 13 years old and the oldest patient was 74 years old (Table 1). There were 74 males (61%) and 46 (38%) females in our study. Fifteen patients had cardiac complications. Incidence was 12.5%. Bradycardias were the most common cardiac manifestations in our study. There were eight patients (6.6%) having different types of bradyarrhythmia (Figure 1). Four patients had sinus bradycardia with varying heart rate between 40 to 50 beats/minute. Heart rate of 50 or less was taken as inclusion criteria. All of them had recovery within seven days. Those who had heart rate of 45 or less were put on orciprenaline. Criteria for putting temporary pacemaker was heart rate of less than forty. Three patients had junctional bradycardia with heart rate ranging from forty to forty five beats per minute. All of them were on orciprenaline and their heart rate came back to normal within seven days. Only one patient had 2:1 AV nodal block and he had a heart rate of 35 to 38 beats/minute. He was only 16 years old and took almost two weeks to recover. He was on temporary pacemaker for two weeks. Occasional ventricular ectopics were seen in few patients but they were not clinically significant.

Patients who had experienced bradyarrhythmias were in the age group of sixteen to forty. Left ventricular systolic function was assessed in every patient by echocardiography. Four patients (3.3%) had left ventricular systolic dysfunction. Regional wall motion abnormalities were absent but there were global hypokinesia. All of them were having mid-range left ventricular systolic dysfunction (ejection fraction 35% to 45%) (Figure 2). Two them presented with left ventricular failure and they responded to medical therapy. Left ventricular systolic dysfunction recovered within three months. But troponin T was not elevated in none of the patients. Two patients were in age group of twenty to thirty and two were in thirty to forty years age group. Pericardial effusion was observed in two patients (1.6%). Both of them were having moderate pericardial effusion. None of the cases progressed to massive pericardial effusion or tamponade. Echocardiogram was done serially and pericardial effusion resolved within three weeks. There was no associated pleural effusion, left ventricular dysfunction or pneumonia. They were in twenty to thirty years age group. None of the patients had thrombocytopenia, deranged liver or renal function tests. Only one patient had atrial fibrillation and she was seventy years old. Pharmacological cardioversion was done by amiodarone infusion.

Discussion

Dengue like many viral infections can cause myocardial injury, either by direct invasion or by autoimmune reaction resulting in myocardial inflammation. Direct invasion incites different cytokines and can release inflammatory mediators like TNF-alpha, interleukins, oxygen free radicals. Dengue virus and antigen may associate with myocardial receptor site and can trigger cell mediated immune response causing myocardial injury, which recovers with resolution of infection. The cardiac abnormalities in dengue are transient and self-limited. It could be attributed to subclinical viral myocarditis. Cardiac manifestation in dengue fever ranges from asymptomatic bradycardia to severe myocarditis. Cardiac rhythm abnormalities such as sinus bradycardia, junctional bradycardia, first degree AV block, transient AV block, transient ventricular arrhythmias have been observed in different studies during acute or convalescence phase of dengue infection. Transient myocarditis, systolic and diastolic dysfunction and pericardial effusion have also been reported during acute phase of infection. In the study by Thein, Leo et al, minimum pulse rate was 34/minute and the maximum pulse rate was 140/minute. In the study by Latheef et al mean heart rates were significantly lower in the dengue group 87.6 beats/min (dengue) compared to the control group. In our study minimum pulse rate was thirty five per minute and patient was suffering from 2:1 AV nodal block. Best of the patients with rhythm abnormalities had heart rate of forty to forty five beats per minute. Those patients who had acute lung injury or dengue shock syndrome in our study had sinus tachycardia with heart rate in the range of 120-140/ min (Figure 3). Other patients did not have tachycardia. Asymptomatic sinus bradycardia was commonest rhythm.

**Table 1: Distribution of age group, dengue cases and cardiac abnormalities**

<table>
<thead>
<tr>
<th>Age group in years</th>
<th>13-20</th>
<th>21-30</th>
<th>31-40</th>
<th>41-50</th>
<th>51-60</th>
<th>61-70</th>
<th>71-80</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of Dengue fever</td>
<td>36</td>
<td>24</td>
<td>22</td>
<td>16</td>
<td>10</td>
<td>8</td>
<td>4</td>
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<tr>
<td>Sinus bradycardia</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Junctional bradycardia</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>AV nodal block</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Left ventricular systolic dysfunction</td>
<td>0</td>
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<td>2</td>
<td>0</td>
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<td>Pericardial effusion</td>
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<td>2</td>
<td>0</td>
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</tr>
</tbody>
</table>

**Exclusion criteria**

a. Patients with medications which can affect heart rate.

b. Patients with preexisting heart disease.

c. Patients with electrolyte abnormalities.

**Fig. 1: Incidence of cardiac manifestations in Dengue fever**

**Fig. 2: Different cardiac manifestations of Dengue fever**
abnormalities in our study (3.3%). Junctional bradycardia was observed in three patients (2.5%). In the study by Gupta et al., sinus bradycardia was found in 14.28%, and sinus tachycardia 21.4%. AV dissociation with sinus node dysfunction was observed in one patient, which resolved in 24 hours. Kaushik et al have described atioventricular dissociation and sino atrial exit block in a child with dengue fever. In a study by Leo et al incidence of different rhythm abnormalities were: sinus bradycardia in 60%, first degree heart block in 11%, and ventricular ectopics in 15% of cases. Low voltage QRS complex and supraventricular tachycardia (SVT) were reported by Sheetal et al but it was not found in our study. This low voltage QRS complex and SVT was ascribed to subacute myocarditis. Chuah et al have described transient ventricular arrhythmias as a cardiac manifestation of dengue fever. We did not observe significant ventricular arrhythmias in our study. On the contrary one patient had developed atrial fibrillation. Obeyesekere et al have described direct cardiac involvement in dengue fever patients as evidenced by positive cardiac biomarkers. Wichmann et al showed that 25% of dengue patients presented with one or more elevated markers of myocardial injury, such as myocardial, CK-MB, troponin T, NT-proBNP, and/or heart-type fatty acid binding protein levels (h-FABP). In our study quantitative troponin was not elevated in any of our patients. In the study by Gupta et al, systolic dysfunction was absent in all patients and mild diastolic dysfunction was present in 14.28% of cases. However Gupta et al reported that 78.5% of patients with severe dengue in their study had elevated CK-MB level. Diastolic dysfunction was not included in our study but systolic dysfunction was present in four patients (3.3%). Recovery occurred within three months. Transient decrease in ejection fraction, left ventricular wall motion abnormality which improves with time is known to occur in patients with dengue. Similar findings were noted in our study. We could not find any association between severity of dengue fever and cardiac manifestations. Kabra et al in their study also couldn’t find any correlation between myocardial involvement and severity of dengue fever. 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 patients had an ejection fraction of 40% and 12 had global hypokinesia, and that, after 3 weeks of follow-up, all abnormalities had returned to normal. In our series four patients had left ventricular dysfunction but only two of them presented with heart failure. None of our patients had suffered from cardiogenic shock. Weerakoorn et al performed autopsies in five patients who died due to dengue complications and showed histopathological evidence of myocarditis. The main histological findings were interstitial edema with inflammatory cell infiltration and necrosis of myocardial fibers and, in one case, evidence of pericarditis. **Limitations**

It was a single centre study. We did not include different biomarkers like myoglobin, CPK MB, heart fatty acid binding protein. Cardiac MRI is the gold standard for diagnosis of myocarditis which was not included in our study.

**Conclusion**

Cardiac manifestations of Dengue were present in 11.4% of our patients. Incidence vary between 15 to 50% in different series. Bradyarrhythmias were commonest manifestation in our study (6.6%) which resolves spontaneously within seven to fourteen days. Left ventricular systolic dysfunction was present in 3.3% of patients which recovered within three months. Pericardial effusion was less common and it resolved within two weeks. We did not observe significant tachyarrhythmias in our patients except one case of atrial fibrillation.

**References**