A Study on the Cardiac Manifestations of Dengue

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Abstract

Objectives: This study was done to study the prevalence of cardiac manifestations of dengue fever in patients presenting to our hospital and to find out the correlation of cardiac manifestations to warning signs of dengue and severe dengue.

Methods: The study was conducted at Sree Gokulam Medical College and Research Foundation, which is a tertiary care hospital, in the Department of Medicine in the month of July 2013. One hundred consecutive patients aged 13 years or more with positive dengue serology were interviewed and examined. ECG was done for all patients and selected patients underwent echo evaluation and troponin testing. The data was analyzed using statistical significance tests.

Results: Thirty-three patients had no warning signs, 58 patients had one warning sign or the other. Nine patients had severe dengue. The minimum pulse rate was 34/minute. The most common cardiac abnormalities noted were rhythm abnormalities of which the commonest was sinus bradycardia, found in 32 percent. There was statistically significant correlation between cardiac manifestations and all the warning signs except persistent vomiting. Among severe dengue, fluid accumulation causing respiratory distress was found to have a significant correlation with the cardiac manifestations.

Conclusions: The most common cardiac manifestations noted were transient rhythm abnormalities, of which sinus bradycardia was the commonest. There was no evidence of myocarditis in any of the patients. There was statistically significant correlation between cardiac manifestations and all the warning signs except persistent vomiting. Among severe dengue, fluid accumulation causing respiratory distress was found to have a significant correlation with the cardiac manifestations.

Introduction

Dengue fever is an acute febrile infectious disease, caused by any of the four serotypes (1, 2, 3 or 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.¹ Dengue is transmitted by mosquitoes of the genus Aedes. Cardiac manifestations in dengue virus infection can range from asymptomatic bradycardia to life threatening myocarditis.²³ Various studies have quoted several cardiac manifestations of dengue infection—sinus bradycardia, transient AV blocks, transient ventricular arrhythmias, myocarditis and pericardial effusion. There are only a few studies from Kerala focusing on the cardiac manifestations of dengue. We performed this study with the objective of studying the cardiac manifestations of dengue and to study the correlation of the cardiac manifestations to the severity of dengue.

Objectives of the Study

1. To study the prevalence of cardiac manifestations of dengue fever in patients presenting to our hospital.
2. To find out the correlation of cardiac manifestations to warning signs of dengue and severe dengue.

Patients and Methods

Study design
Cross-sectional study

Setting
The study was conducted at Sree Gokulam Medical College.
and Research Foundation, which is a tertiary care hospital, in the Department of Medicine in the month of July 2013.

**Inclusion Criteria**
- Age group of ≥ 13 years
- Fulfilling the WHO criteria for dengue
- Confirmed dengue serology

**Exclusion Criteria**
- Patients on medications affecting the heart rate / rhythm
- Patients with history of pre-existing heart disease
- Patients with electrolyte abnormalities affecting the heart rate/rhythm
- Patients not willing to give consent for the study

**Sample size**

The prevalence of cardiac manifestations of dengue according to various studies conducted previously was around 50%. The sample size in our study was fixed at 100, assuming the anticipated prevalence of cardiac manifestations in dengue to be around 50%, assuming an error 5% (Za = 1.96) and b error 20% (Zb = 0.842) and a power of 80%, with a precision of 5%, according to the following formula.

\[
\begin{align*}
  n & = \left( \frac{Z_a + Z_b}{p} \right)^2 \frac{p \cdot q}{d^2} \\
  & = \frac{(1.96 + 0.842)^2 \cdot 0.5 \cdot 0.5}{0.05^2}
\end{align*}
\]

**Method of sample collection**

Patients with fever, presenting to Medicine Department were interviewed and examined using a structured questionnaire. Dengue serology was done in all patients to confirm the diagnosis. One hundred consecutive patients were studied. Clinical profile was studied and patients were classified as - dengue fever, dengue with warning signs and severe dengue (as per the current WHO classification). ECG was taken in all the patients. Selected patients underwent troponin testing and echocardiographic evaluation.

**Statistical Tests**

Statistical method used was chi square test. It was used to study correlation between the cardiac manifestations of dengue with the warning signs and with severe dengue and to study whether the correlation is statistically significant. A value of \( p >0.05 \) is considered as not significant and \( p <0.05 \) as significant.

**Results**

The mean age of our study group was 45 years. The youngest patient was 13 years old and the oldest patient was 87 years old. There were 54 males and 46 females in our study.

Eighty-three patients presented to us within the first week of fever. Forty-seven were febrile at admission.

Of the 100 patients studied, 79 patients were dengue NS1 positive (ELISA), 21 were positive for IgM dengue (ELISA).

Of the 100 patients, 42 patients had persistent abdominal pain, 58 patients had persistent vomiting which was the commonest warning sign. Forty-six patients had mucosal bleeding, 12 had clinical evidence of fluid accumulation, five had restlessness, eight had hepatomegaly >2 cm (Table 1).

**Table 1: Warning signs of dengue (N=100)**

<table>
<thead>
<tr>
<th>Warning signs</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>42</td>
</tr>
<tr>
<td>Persistent vomiting</td>
<td>58</td>
</tr>
<tr>
<td>Mucosal bleed</td>
<td>46</td>
</tr>
<tr>
<td>Fluid accumulation</td>
<td>12</td>
</tr>
<tr>
<td>Lethargy/restlessness</td>
<td>5</td>
</tr>
<tr>
<td>Hepatomegaly &gt;2 cm</td>
<td>8</td>
</tr>
<tr>
<td><strong>Total 58 pts.</strong></td>
<td></td>
</tr>
</tbody>
</table>

**Table 2 : Severe dengue (N=100)**

<table>
<thead>
<tr>
<th>Severe dengue</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shock</td>
<td>3</td>
</tr>
<tr>
<td>Fluid accumulation causing respiratory distress</td>
<td>9</td>
</tr>
<tr>
<td>Severe bleeding</td>
<td>9</td>
</tr>
<tr>
<td><strong>Total 9 pts.</strong></td>
<td></td>
</tr>
</tbody>
</table>

**Organ impairment**

| SGOT or SGPT >1,000         | 4            |
| Renal impairment            | 4            |
| Impaired consciousness      | 3            |
| ARDS                        | 4            |

Of the 100 patients studied, three were found to be in shock, as evidenced by a systolic BP <90 mm of Hg. Nine patients were observed to have fluid accumulation sufficient to cause respiratory distress. Six patients had severe bleeding per vaginum, one patient each had hematuria, massive hematemesis and massive hemoptyisis. Four patients developed ARDS (Figure 1). Four patients had severe hepatic derangement as evidenced by SGOT and SGPT values above 1000 IU. The highest SGOT and SGPT values were 1200 IU/L and 1567IU/L respectively. Four patients had renal impairment. The maximum serum creatinine value noticed was 2.1 mg/dl (Table 2).

The mean pulse rate of the study population was 70/minute. The minimum pulse rate was 34/minute and the maximum pulse rate was 140/minute.

Thirty-two patients had sinus bradycardia- it was the commonest rhythm abnormality noted.

Three patients had unexplained sinus tachycardia. Ventricular arrhythmias in the form of ventricular bigeminy, ventricular trigeminy (Figure 2) and ventricular
tachycardia were noted in one patient each. All these changes reverted back to sinus rhythm in 24 hours. AV dissociation with sinus node dysfunction (Figure 3) was observed in one patient, which resolved in 24 hours. ST-T changes were noted in 11 patients.

Troponin T testing was done in 18 patients and it was found to be negative in all. Echocardiographic evaluation was done in 18 patients. 3 patients were noticed to have mild pericardial effusion. Echocardiographic evidence of myocarditis was not seen in any patient. All the cardiac manifestations of dengue are summarised in Figure 4.

Ten patients had systemic hypertension, 12 had type 2 diabetes mellitus and one had hereditary spherocytosis. Of the 100 patients studied, two patients expired, they succumbed to ARDS.

There was statistically significant correlation (p value< 0.05, Chi square test) between cardiac manifestations and all the warning signs except persistent vomiting, which was the commonest warning sign noted (Table 3). Of the manifestations of severe dengue, only fluid accumulation causing respiratory distress was found to have a significant correlation (p value <0.05, Chi square test) with the cardiac manifestations of dengue (Table 4).

### 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 effects of cytokines / cellular mediators of immune response. The present study was done with the aim of studying the cardiac manifestations of dengue and its association with the warning signs.

### Table 3: Correlation of warning signs to cardiac manifestations

<table>
<thead>
<tr>
<th>Warning signs and correlation with cardiac manifestations</th>
<th>Cardiac manifestations</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>No 18, Yes 24</td>
<td>0.045</td>
</tr>
<tr>
<td>Persistent vomiting</td>
<td>No 30, Yes 28</td>
<td>0.37</td>
</tr>
<tr>
<td>Fluid accumulation</td>
<td>No 3, Yes 9</td>
<td>0.032</td>
</tr>
<tr>
<td>Mucosal bleed</td>
<td>No 20, Yes 26</td>
<td>0.005</td>
</tr>
<tr>
<td>Lethargy / Restlessness</td>
<td>No 0, Yes 5</td>
<td>0.018</td>
</tr>
<tr>
<td>Hepatomegaly &gt;2 cm</td>
<td>No 1, Yes 7</td>
<td>0.017</td>
</tr>
</tbody>
</table>

### Table 4: Correlation of severe dengue to cardiac manifestations

<table>
<thead>
<tr>
<th>Correlation of severe dengue to cardiac manifestations</th>
<th>Cardiac manifestations</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shock</td>
<td>No 1, Yes 2</td>
<td>0.44</td>
</tr>
<tr>
<td>Fluid accumulation causing respiratory distress</td>
<td>No 2, Yes 7</td>
<td>0.048</td>
</tr>
<tr>
<td>Severe bleeding</td>
<td>No 3, Yes 6</td>
<td>0.356</td>
</tr>
<tr>
<td>ARDS</td>
<td>No 1, Yes 3</td>
<td>0.257</td>
</tr>
</tbody>
</table>
manifestations of dengue and to study the correlation of the cardiac manifestations to the severity of dengue.

The mean age of our study population was 45 years. Eighty-three percent of the study population presented to us within the first week of fever. Of the 100 patients studied, 79 patients were Dengue NS1 positive (ELISA), 21 were positive for IgM dengue (ELISA). In the study by Wichman et al, IgM and IgG dengue testing was done to make a diagnosis of primary dengue infection and secondary dengue infection, respectively.

The most common warning sign observed was persistent vomiting, seen in 58 percent of the patients; whereas restlessness/lethargy was the least common warning sign noted, seen in 5% of the patients. Fifty-eight percent of the patients had one warning sign or the other. In the study by Thein, et al on 108 patients with confirmed dengue fever, persistent vomiting was noted in 39% and it was the most common warning sign. Hepatomegaly was the least common warning sign, seen in 2%, in their study. In their study also, 58% of the patients had one warning sign or the other.

Three patients had shock, nine had fluid accumulation causing respiratory distress and nine had severe bleeding. Severe hepatic impairment was seen in four patients, renal impairment in four, ARDS in four and impaired consciousness in three patients. In the study by Thein, Leo et al on 108 patients with confirmed dengue fever, persistent vomiting was noted in 39% and it was the most common warning sign. Hepatomegaly was the least common warning sign, seen in 2%, in their study. In their study also, 58% of the patients had one warning sign or the other.

In the study by Gupta et al, in 30 patients who underwent echocardiographic study, three had mild pericardial effusion. Troponin T was done in 18 patients and was negative in all.

Three patients had shock, nine had fluid accumulation causing respiratory distress and nine had severe bleeding. Severe hepatic impairment was seen in four patients, renal impairment in four, ARDS in four and impaired consciousness in three patients. In the study by Thein, Leo et al, 30 patients had severe dengue. Four patients had severe hepatic derangement as evidenced by SGOT and SGPT values above 1000 IU. The highest SGOT and SGPT values were 1200 IU/L and 1567 IU/L respectively. Four patients had renal impairment. The maximum serum creatinine value noticed was 2.1 mg/dl. Four patients had ARDS.

The mean pulse rate of the study population was 70/minute. The 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 (±12.5) beats/min (dengue) compared to the control group. The commonest rhythm abnormality noted was sinus bradycardia, found in 32%. Three patients had unexplained sinus tachycardia. In the study by Gupta et al, sinus bradycardia was found in 14.28%, and sinus tachycardia 21.4 percent. AV dissociation with sinus node dysfunction was observed in one patient, which resolved in 24 hours. Kaushik et al have described atrioventricular dissociation and sino atrial exit block in a child with dengue fever. Ventricular arrhythmias in the form of ventricular bigeminy, ventricular trigeminy and ventricular tachycardia was noted in one patient each. AV dissociation with sinus node dysfunction was observed in one patient. All these changes reverted back to sinus rhythm in 24 hours. Chuah et al and Veloso et al have described transient ventricular arrhythmias as a cardiac manifestation of dengue fever.

Troponin T testing was done in 18 patients and it was found to be negative in all. Obeyesekere et al have described direct cardiac involvement in dengue fever patients as evidenced by positive cardiac biomarkers. 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 percent. Wiwanitkit et al have described cases of dengue myocarditis.

There was statistically significant correlation between the cardiac manifestations and all the warning signs except persistent vomiting, which was the commonest warning sign noted. Kabra et al in their study couldn’t find any correlation between myocardial involvement and clinical severity of dengue. Among severe dengue, fluid accumulation causing respiratory distress was found to have a significant correlation with the cardiac manifestations.

Conclusions

Of the 100 patients studied, 33 patients had no warning signs, 58 patients had one warning sign or the other. Nine patients had severe dengue. The most common cardiac abnormalities noted were rhythm abnormalities of which the commonest was sinus bradycardia, found in 32 percent. Ventricular arrhythmias in the form of ventricular bigeminy, ventricular trigeminy and ventricular tachycardia was noted in one patient each. AV dissociation with sinus node dysfunction was observed in one patient. All these changes reverted back to sinus rhythm in 24 hours (Figure 4). Of the 18 patients who underwent echocardiographic study, three had mild pericardial effusion. Troponin T was done in 18 patients and was negative in all.

There was statistically significant correlation between cardiac manifestations and all the warning signs except persistent vomiting. Among severe dengue, fluid accumulation causing respiratory distress was found to have a significant correlation with the cardiac manifestations.

References

5. Wichmann, Kularatne et al. Cardiac

6. Thein, Leo et al. Risk Factors for Fatality among Confirmed Adult Dengue Inpatients in Singapore: A Matched Case-Control Study;DOI: 10.1371/journal.pone.0081060


