Original Article

Cardiac manifestations of dengue fever in pediatrics age group

Upasana Menwal[1], Anil Rawat[2], Anurag Rawat[3], Vipan Chandar[4]

From [1]Junior Resident, [2]Professor, [3]Associate Professor, [4]Professor, Department of Pediatrics, Himalayan Institute of Medical Sciences Jolly Grant, Dehradun, Uttarakhand, India

ABSTRACT

Background: Dengue infection is a serious public health concern in tropical and subtropical regions of the world. Cardiac involvement is a known but rare complication of dengue. Electrocardiogram (ECG) and 2D echocardiogram (ECHO) are preferred non invasive instant diagnostic tool to evaluate the status of heart in dengue infection. **Objectives:** The present study was carried out to confirm the cardiac manifestation in dengue fever, along with its correlation with the severity of the disease. **Materials and Methods:** A total of 60 subjects were included over a period of 1-year time from inpatient and outpatient departments presenting with clinical features suggestive of dengue and further confirmed by positive serology test of IgM and/or NS1 antigen by rapid and/or by ELISA method. Cardiac manifestations were analyzed with the help of ECG and 2D ECHO in all serologically confirmed cases. **Results:** 16 out of 60 cases had cardiac findings in the form of tachycardia, bradycardia, and myocarditis. ECG showed some nonspecific findings like sinus tachycardia followed by sinus bradycardia. Myocarditis diagnosed by ECHO as ejection fractions <50% was observed in four cases of dengue with warning sign and in one of severe dengue, while mild TR was seen in three cases of dengue with a warning sign, two cases of probable dengue, and one case of severe dengue. **Conclusion:** This study showed that cardiac involvement of dengue infections runs a benign course without any complications. Early diagnosis, strict monitoring, and prompt supportive management reduce the mortality rate in dengue.

Key words: Dengue, Cardiac manifestations, Electrocardiogram, Echocardiogram

Dengue fever is an acute febrile infectious disease caused by any of the four subtypes (1, 2, 3, and 4) of the virus from the genus flavivirus, called dengue virus. The highest incidence of dengue is seen in Southeast Asia, including India, and American tropics. Dengue is transmitted by mosquitoes of the genus Aedes, widely distributed in subtropical and tropical areas of the world [1]. Clinical classification of dengue has been revised by WHO in the year 2009, including three categories – dengue without warning sign, dengue with a warning sign, and severe dengue [2]. Severe dengue infections may give rise to many complications such as liver failure, disseminated intravascular coagulation, encephalopathy, myocarditis, acute renal failure, and hemolytic uremic syndrome [3].

Various studies have quoted several cardiac manifestations of dengue infections such as sinus bradycardia, transient AV block, transient ventricular arrhythmias, myocarditis, and pericardial effusion [4,5]. At one end of the clinical spectrum, subjects are asymptomatic or have mild cardiac symptoms despite relative bradycardia, transient atrioventricular block, and/or ventricular arrhythmia. While at the other end, subjects may experience acute pulmonary edema and/or cardiogenic shock due to severe myocardial cell damage with left ventricular failure [6].

Although there is a paucity of data regarding the cardiac manifestation of dengue, the incidence of cardiac manifestation in various studies ranged from 16.7% to 71%, including cardiac failure, electrocardiogram (ECG) changes (sinus bradycardia, sinus tachycardia, and T wave inversion), 2D echocardiography (2DEcho) changes (reduced ejection fraction), and elevated cardiac enzymes (Troponin T, CK MB) [4]. This study was conducted to demonstrate the cardiac manifestations of dengue fever along with the correlation of severity of illness with cardiac findings.

MATERIALS AND METHODS

This observational cross-sectional study was conducted in a tertiary care center in north India from October 2017 to September 2018. Subjects were recruited among the cases from the inpatient and outpatient department presenting with clinical features suggestive of dengue and further confirmed by positive serology test of IgM antibody and/or NS1 antigen by rapid and/or ELISA method. All cases during one season were considered for enrolment after obtaining ethical clearance from the institutional review board. However, 60 consecutive subjects whose parents gave consent and who could be investigated were included in the study.

Correspondence to: Dr. Anil Rawat, B IV/2 HIHT Campus, Jolly Grant, Dehradun, Uttarakhand, India. E-mail: banganianil@yahoo.co.in

The inclusion criteria followed was age group <18 years, fulfilling WHO clinical criteria of dengue and confirmed by serology (NS1 and/or IgM), and evaluation of cardiac manifestations by ECG and 2D ECHO in dengue cases. Subjects on medications affecting the heart rate/rhythm, those with the history of preexisting heart disease, those with electrolyte abnormality affecting heart rate/rhythm, those with mixed infections, and with abnormal genetic conditions were excluded from the study.

The patient information was recorded and included in predesigned pro forma. The demographic indices, for example, age, sex, and address, along with clinical data, including the duration of fever, associated symptoms, vital signs, and general and systemic examination, were recorded. The cardiac evaluation by ECG and 2D ECHO were performed in all the cases.

The data were collected and entered in MS Excel 2010. Statistical analysis was performed using SPSS software version 23. Quantitative data were analyzed in the form of a percentage. As data did not follow the curve of normality, so Pearson Chi-square test was used to compare data. p value of <0.05 was taken as statistically significant.

RESULTS

A total of 60 subjects, including 36 (60%) males and 24 (40%) females, were recruited for analysis. The maximum number (53%) of cases belonged to the age group of 10–15 years, whereas the least number (21%) of subjects belongs to the age group below 5 years, with the youngest subject being a year old. According to the WHO classification, all subjects were classified into three categories. The maximum number of subjects, that is, 39 (65%), belonged to "dengue with warning signs" category followed by 19 (31.7%) subjects in "probable dengue" category. Only 2 (3.3%) subjects were classified under "severe dengue" category.

The most common symptom (Table 1) in probable dengue was vomiting in 84% cases, whereas that in dengue fever with warning sign was pain abdomen in 82%. Almost half of the cases in all three categories had rashes; bleeding manifestation was less observed in probable dengue and dengue with warning sign; however, both the severe dengue subjects had bleeding manifestations. Almost half of the cases of probable dengue and dengue with warning sign and both the cases of severe dengue had body pains.

Electrocardiography (ECG) of dengue fever manifested sinus tachycardia as the most common (45%) finding followed by sinus bradycardia (10%), as evident in Table 2. Abnormality in ECG was commonly seen in the older age group, while the youngest subject of 1 year old had normal ECG. Other ECG changes like ST elevation and tall T wave and right axis deviation were also noted in very few subjects. None of the subjects had arrhythmia. The ECG changes revealed a significant correlation between the three groups indicating a more severe category with more ECG manifestations.

2D Echo findings in dengue fever have been categorized on severity scale in Table 3, revealing mild tricuspid regurgitation (TR) in three cases of dengue fever with warning sign and two cases of probable dengue category. Hypokinesia denoted by an ejection fraction of less than 50% was found in four (10%) subjects of dengue fever with warning sign followed by one case in severe dengue. Out of two cases of severe dengue, one had hypokinesia, the other had mild TR. Pearson Chi-square test between 2D Echo and severity of dengue was applied and p value was found to be highly significant (0.000), indicating observation of more notable 2D Echo findings in severe dengue cases.

Table 1: Symptoms of dengue fever and comparison between all three categories

Symptoms	Probable dengue (*n*=19)	Dengue with warning signs (*n*=39)	Severe dengue (*n*=2)
Fever	19 (100)	39 (100)	2 (100)
Vomiting (*n*=47)	16 (84.2)	30 (77)	1 (50)
Pain abdomen (*n*=34)	0	32 (82)	2 (100)
Body pains (*n*=28)	10 (52.6)	16 (41)	2 (100)
Rashes (*n*=25)	8 (42)	16 (41)	1 (50)
Bleeding manifestation	2 (10.5)	15 (38.5)	2 (100)

Table 2: Electrocardiography (ECG) in dengue cases

ECG	Probable dengue (*n*=19)	Dengue with warning signs (*n*=39)	Severe dengue (%) (*n*=2)	Total (*n*=60)	p value
Right axis deviation	1 (5)	1 (3)	0	2 (3)	0.014
Sinus bradycardia	0	5 (13)	1 (50)	6 (10)	
Sinus tachycardia	5 (26)	21 (54)	1 (50)	27 (45)	
ST elevation	0	4 (10)	0	4 (6)	
Tall T wave	0	1 (3)	0	1 (2)	
Total				40	

Table 3: ECHO in dengue cases

ECG	Probable dengue (*n*=19)	Dengue with warning signs (*n*=39)	Severe dengue (%) (*n*=2)	p value
Ejection fraction (<50%)	0	4 (10)	1 (50)	0.000
Mild tricuspid regurgitation	2 (10.6)	3 (7.8)	1 (50)	

DISCUSSION

This was an observational study on clinical as well as cardiac manifestations of dengue fever, along with its severity. This study included 60 subjects out of which 60% were males and 40% were females and the ratio was found to be 1.5:1, comparable to other studies by Sahana *et al.* [7] where they found similar male preponderance with the ratio of 2.1:1.

According to the WHO classification, all subjects are classified into three categories. About 65% subjects belonged to "dengue with warning signs" category followed by 31.7% patients in "probable dengue" category. Only two (3.3%) cases were under "severe dengue" category. A similar observation was made by Jain *et al.* [8], except they had a higher number (12.3%) of severe dengue cases. Contrary to our study, Siddappa *et al.* [9] and Srinivasa *et al.* [10] found the maximum number of cases belonging to the probable dengue category followed by dengue with warning sign and least number of cases in the severe dengue category.

Fever, the universal symptom, was followed by vomiting in 78.3% of cases, similar to the study done by Srinivasa *et al.* [10] who observed vomiting in 61.1% cases. Contrary to the findings of our study, Jain *et al.* [8] observed vomiting as the third common clinical manifestation only in 46.1% cases. Further categorizing on the basis of severity, vomiting was seen in 84.2% of probable dengue subjects, followed by 77% of subjects of dengue with warning signs, and only 50% cases of severe dengue cases. Contrary to our study, varying results have been seen by Srinivasa *et al.* [10] as 78% cases in dengue with warning sign, 76.1% severe dengue cases, and 44.9% probable dengue cases had vomiting.

In this study, ECG was done in all the cases and correlation was found between ECG findings and severity of dengue. Nonspecific ECG abnormalities in the form of ST elevation and tall T wave were observed in 8% subjects, contrary to 12% by Kalpana *et al.* [11] and 30% by Wali *et al.* [4]. Sinus tachycardia was observed in 45% of cases and sinus bradycardia in 10% cases, deviation from our results had been observed by Gnanumuthu *et al.* [12], who observed tachycardia in 10.5% and bradycardia in 2% cases and Gupta *et al.* [13], who observed tachycardia in 14% and bradycardia in 18% cases. None of the subjects had any arrhythmia, which is similar to the study by Kirawittaya *et al.* [14], who could not find a single case of arrhythmia out of 181 cases. However, Sidappa *et al.* [9] observed supraventricular tachycardia (SVT) in 1 out of 39 cases.

A transient decrease in ejection fraction, which improves with time, is known to occur in patients with dengue fever. These changes are mild and self-limiting in the majority of cases. In our study, ejection fraction < 50% was found in five cases (8%) out of 60, which is comparable to Kirawittaya *et al.* [14], but far less than of 25% seen by Sidappa *et al.* [9] and 16.7% by Kabra *et al.* [15]. Mild TR has been observed in six (10%) cases, of which three belonged to dengue with warning sign, two were cases of probable dengue, and one of severe dengue category, which was higher than that observed by Kalpna *et al.* [11] who demonstrated mild TR in 1 out of 200. None of our subjects had congestive heart failure or pericardial effusion, similar to most studies [13,15]; however,

Sidappa *et al.* [9] and Kirawittaya *et al.* [14] reported pericardial effusion in one and seven cases, respectively.

This study had a few limitations. The sample size was not sufficient to draw significant conclusions, further compounded by very few subjects in the severe dengue category. Cardiac enzymes, the marker of acute myocardial injury, could not be estimated due to financial constraints. Furthermore, the follow-up of subjects and their investigations could not be done.

CONCLUSION

Significant cardiac manifestations in dengue fever are rare. Before endorsing this fact clinicians should not dissuade from investigating a dengue case, especially severe category for cardiac manifestations.

REFERENCES

1. World Health Organization. Dengue Hemorrhagic Fever: Diagnosis, Treatment, Prevention and Control. 2nd ed. Geneva: World Health Organization; 1997.
2. World Health Organization, Special Programme for Research and Training in Tropical Diseases, World Health Organization, Department of Control of Neglected Tropical Diseases. Dengue: Guidelines for Diagnosis, Treatment, Prevention and Control. Geneva: World Health Organization; 2009.
3. Yadav RK, Kumar S. To study cardiac manifestations in patients presenting with dengue infection and to find out the correlation of cardiac manifestations to warning signs of dengue. Int J Adv Med 1998;4:323-8.
4. Wali JP, Biswas A, Chandra S, Malhotra A, Aggarwal P, Handa R, *et al.* Cardiac involvement in dengue haemorrhagic fever. Int J Cardiol 1998;64:31-6.
5. Wichmann D, Kularatne S, Ehrhardt S, Wijesinghe S, Brattig NW, Abel W, *et al.* Cardiac involvement in dengue virus infections during the 2004/2005 dengue fever season in Sri Lanka. Southeast Asian J Trop Med Public Health 2009;40:727-30.
6. Lee IK, Lee WH, Liu JW, Yang KD. Acute myocarditis in dengue hemorrhagic fever: A case report and review of cardiac complications in dengue-affected patients. Int J Infect Dis 2010;14:e919-22.
7. Sahana KS, Sujatha R. Clinical profile of dengue among children according to revised WHO classification: Analysis of a 2012 outbreak from Southern India. Indian J Pediatr 2015;82:109-13.
8. Jain H. Clinical profile and outcome of dengue fever in hospitalized children of South Rajasthan, India. Int J Contemp Pediatr 2016;3:546-9.
9. Siddappa FD, Koushik H, Ratageri VH, Wari PK. Cardiac manifestations of dengue fever in children. Pediatr Oncall J 2017;14:82-4.
10. Srinivasa K, Ajay J, Manjunath GA. Clinical profile and outcome of dengue among hospitalized children-a single centre prospective study. Int J Pediatr Res 2017;4:145-50.
11. Valluri KK. Study of dengue fever, its clinical profile and cardiac involvement among paediatric population. IOSR J Dent Med Sci 2017;16:60-2.
12. Gnanamuthu S, Veeramani SR, Mohammed SN, Sivakumar GS, Kumar SS, Ramesh R, *et al.* Cardiac involvement in adult patients with febrile thrombocytopenia diagnosed by bedside 2-D echocardiography. Int J Adv Med 2018;5:1016-20.
13. Gupta VK, Gadpayle AK. Subclinical cardiac involvement in dengue haemorrhagic fever. J Indian Acad Clin Med 2010;11:107-1.
14. Kirawittaya T, Yoon IK, Wichit S, Green S, Ennis FA, Gibbons RV, *et al.* Evaluation of cardiac involvement in children with dengue by serial echocardiographic studies. PLoS Negl Trop Dis 2015;9:e0003943.
15. Kabra SK, Verma IC, Arora NK, Jain Y, Kalra V. Dengue haemorrhagic fever in children in Delhi. Bull World Health Organ 1992;70:105-8.