

## ORIGINAL ARTICLE

### CARDIAC MANIFESTATIONS OF DENGUE FEVER IN CHILDREN

Siddappa FD\*, Koushik H\*\*, V H Ratageri\*, P K Wari\*

#### Abstract

**Background:** Dengue fever has varied manifestations in children of which cardiac manifestation are also known. This study was undertaken to study the cardiac manifestations of dengue in children.

**Methods:** This prospective study was done in Department of Pediatrics, Karnataka Institute of Medical Sciences (KIMS), Hubballi, India from December 2013 to November 2014. Inpatient children aged less than 12 years confirmed to have dengue either by a positive NS1 antigen or IgM MAC ELISA were included in the study. Those with congenital /acquired heart disease were excluded. All included children underwent cardiac assessment in form of clinical examination, serum Creatine Kinase- MB (CK-MB) level, Chest X-ray, electrocardiogram (ECG) and 2 D Echocardiography (2D Echo). Patients were classified as severe dengue, dengue with/without warning signs as per World Health Organization (WHO) criteria.

**Results:** Out of 39 patients with dengue, 22 (56%) children had cardiac abnormalities. Cardiac abnormalities were seen in 5 (71%) out of 7 patients with severe dengue, 7 (53%) out of 13 with dengue with warning signs and 10 (52%) out of 19 with dengue without warning signs. One child had clinically overt cardiac failure. Serum CK-MB was raised in 2 (5%) patients. Left ventricular type of cardiomegaly on Chest X-ray was present in 3 (8%) children. ECG changes were present in 13 (33%) cases of which sinus tachycardia disproportionate to fever was seen in 9 (23%) patients followed by T wave inversion in 7 (17%), low QRS complex and sinus bradycardia in 2 (5%) each, ventricular ectopic and supraventricular tachycardia in 1 (2%) patient each. Abnormal 2D Echo findings were present in 11 (28%) cases with ejection fraction < 55% in 10 (25%) patients followed by left ventricular wall motion abnormality in 2 (5%) and pericardial effusion in 1 (2%). 2D Echo changes normalized by the time of discharge in 10 children except one with pericardial effusion who took 3 weeks' time to regress.

**Conclusion:** Cardiac manifestations in children with Dengue are not uncommon. But, most of the cardiac involvement in children with Dengue are subclinical with sinus tachycardia and decreased ejection fraction being the commonest manifestations. There is increase in trend of cardiac manifestations among patients with severe dengue.

#### Keywords

Dengue, Child, Myocarditis, Tachycardia, Ventricular Function.

#### Introduction

Dengue ranks as the most important mosquito-borne viral disease in the world. (1) In the last 50 years, incidence of dengue has increased 30-fold with spread to new countries and from urban to rural settings. (2)

Dengue is known to affect several systems in the human body. Myocardial involvement may be the direct effect of the virus itself or due to cytokine production. (3) Myocarditis has varied presentations;

can be clinical or subclinical. (4-7) Though there is a paucity of data regarding cardiac manifestation of dengue, the incidence of cardiac manifestation in various studies ranged from 16.7% -71% including cardiac failure, electrocardiogram (ECG) changes (sinus bradycardia, sinus tachycardia, t wave inversion), and 2 D Echocardiography (2D Echo) changes (reduced ejection fraction), elevated cardiac enzymes (Troponin T, CK MB). (4-6) This wide variation could be because of different criteria used for defining cardiac manifestations. We undertook this study to determine the cardiac manifestations of dengue in Indian children.

#### Methods & Materials

This prospective observational study was conducted in Department of Pediatrics, Karnataka Institute of Medical Sciences (KIMS), Hubli, India from December 2013 to November 2014. Total 39 children less than 12 years of age who were clinically suspected to have dengue and had a positive Dengue NS1 antigen and/or positive IgM MAC ELISA were included in the study after obtaining written informed consent from guardians. Those with congenital or acquired heart disease were excluded from the study. Institutional ethical committee clearance was obtained. Cardiac assessment was conducted according to a semi structured proforma and all children were treated according to World Health Organization (WHO) protocol for treatment of dengue. (1) Chest X ray (CXR), ECG and 2D Echo were done once the children were stable to be shifted for investigations. Serum creatine kinase (CK)-MB levels was done on the day of admission. Abnormalities in heart rate, rhythm, features of cardiac failure were analyzed clinically and corroborated with the above investigations. Standardized norms for vital parameters (8), ECG (8), 2D Echo (9,10) and CK-MB (11-13) in children were considered. Those diagnosed to have abnormal echocardiographic findings underwent a repeat 2D Echo at the time of discharge from the hospital.

**Statistical analysis:** Descriptive parameters were used for statistical analysis.

#### Results

A total of 124 children with suspected dengue were admitted during study period. Among them, Dengue NS1 and/or IgM MAC ELISA was positive in 39 cases. Mean age of presentation was 6.5+3.2 years with male: female ratio of 1: 0.9. They were classified according to WHO classification as Dengue with/without warning signs and severe dengue. Nineteen (48%) children had dengue without warning signs, 13 (33%) had dengue with warning signs and 7 (17%) had severe dengue. Cardiac abnormalities were seen in 5 (71%) out of 7 patients with severe dengue, 10 (52%) out of 19 with dengue without warning signs and 7 (53%) out of 13 with dengue with warning signs. Cardiac manifestations are depicted in Table 1. One child with overt congestive cardiac failure (CCF) had ejection fraction (EF) of <35%. 2D Echo changes normalized

**TABLE 1: Findings of Cardiac Evaluation**

	<b>Dengue without warning signs (n = 19) (%)</b>	<b>Dengue with warning signs (n = 13) (%)</b>	<b>Severe Dengue (n = 7) (%)</b>	<b>Total (n=39) (%)</b>
Congestive Cardiac Failure	0	0	1 (14)	1 (2)
Raised CK-MB	0	0	2 (28)	2 (5)
Cardiomegaly on Chest X ray	0	0	3 (42)	3 (7)
ECG Changes				
Disproportionate Sinus Tachycardia	5 (26)	3 (2)	1 (14)	9 (23)
Sinus Bradycardia	1 (5)	1 (7)	0	2 (5)
T-Wave inversion	4 (21)	3 (23)	0	7 (17)
Supraventricular tachycardia	0	0	1 (14)	1 (2)
Low voltage QRS	0	1 (7)	1 (14)	2 (5)
Ventricular Ectopic	0	0	1 (14)	1 (2)
Echocardiographic features				
Ejection Fraction <55%	6 (31)	2 (15)	2 (28)	10 (25)
Left Ventricular Wall Motion Abnormality	0	0	2 (28)	2 (5)
Pericardial Effusion	0	0	1 (14)	1 (2)

by the time of discharge in 10 children, except in one child with pericardial effusion who took 3 weeks' time to normalize.

**Discussion**

In our study, only one patient presented with overt cardiac symptoms suggestive of predominant subclinical cardiac involvement in Dengue as seen in other studies. (3,6) We did not find raised CK-MB levels in most patients and the 2 patients who had high CK-MB had severe dengue. However Gupta et al (6) reported that 78.5% of patients with severe dengue in their study had elevated CK-MB level. This may be due to the fact that majority of children in our study had dengue with/without warning signs in which CK-MB elevation is less likely to be elevated. Though incidence of sinus tachycardia in our study is comparable with others (5,6,14), both low voltage QRS complex and supraventricular tachycardia (SVT) are unique finding in our study which is not noticed by earlier studies. This low voltage QRS complex and SVT may be due to myocarditis. (15-17)

Transient decrease in ejection fraction, left ventricular wall motion abnormality which improves with time is known to occur in patients with dengue. (4,5). Similar findings were noted in our study. These cardiac changes were mild and self-limiting in majority of cases. However 1 child with overt congestive cardiac

failure and severe dengue had severe reduction of ejection fraction <35% which might have contributed to hemodynamic instability and disease severity. Inflammatory mediators like TNF-alpha, cytokines, interleukins, oxygen free radicals which are released during active viral infection can cause myocarditis. Direct effect of dengue virus and also dengue antigen associating with myocardial receptor site and triggering off an immunological response is also known to cause myocardial damage, which resolves with resolution of infection. (16-18) This can explain the transient ECG, 2D Echo changes as well as the 2D Echo findings.

The limitations of our study were that it was done in small number of patients, there was no control group and other cardiac markers like troponin could not be obtained.

**Conclusion**

Cardiac manifestations are present in over half of the patients with dengue though most have sub-clinical manifestations with sinus tachycardia and decreased ejection fraction being the commonest manifestations. Cardiac manifestations are more common in children with severe dengue.

**Funding:** None

**Conflict of Interest :** None

## References :

1. World Health Organization (WHO). Global strategy for dengue prevention and control 2012-2020. Available from [http://apps.who.int/iris/bitstream/10665/75303/1/9789241504034\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/75303/1/9789241504034_eng.pdf). Accessed on 2nd October 2017
2. Ratgeri VH, Shepur TA, Wari PK, Chavan SC, Mujahid IB, Yergolkar PN. Clinical Profile and Outcome of Dengue Fever Cases. *Indian J Pediatr.* 2005; 72 (8): 705-706.
3. Satarasinghe RL, Arulnithy K, Amarasena NL, Bulugahapitiya U, Sahayan DV. Asymptomatic myocardial involvement in Acute Dengue virus infection in a cohort of Adult Sri Lankans admitted to a tertiary hospital. *Br J Cardiol.* 2007;14:171-73.
4. Kabra SK, Juneja R, Madhulika, Jain Y, Singhal T, Dhar L et al. Myocardial dysfunction in children with dengue hemorrhagic fever. *Natl Med J India* 1998; 11: 59-61.
5. Yadav DK, Choudhary S, Gupta PK, Beniwal MK, Agarwal S, Shukla U, et al. The TEI index and asymptomatic myocarditis in children with severe dengue. *Pediatr Cardiol.* 2013;34:1307-13.
6. Gupta VK, Gadpayle AK. Subclinical Cardiac Involvement in Dengue Haemorrhagic Fever. *JIACM.* 2010; 11: 107-11
7. Khongphatthanayothin A, Lertsapcharoen P, Supachokchaiwattana P, La-orkhun V, Khumtonvong A, Boonlarptaveechoke C et al. Myocardial depression in dengue hemorrhagic fever: Prevalence and clinical description. *Pediatr Crit Care Med.* 2007; 8:524-29.
8. Engorn B, Flerlage J. *The Harriet Lane handbook.* 20th Edn. Philadelphia. Saunders. 2015. p 2.
9. Park MK. *Park's Pediatric Cardiology for Practitioners.* 6th Edition. Philadelphia. Saunder. 2014.
10. Lai WW, Mertens LL, Cohen MS, Geva T. *Echocardiography in Pediatric and Congenital Heart Disease: From fetus to Adult.* Oxford. Blackwell Publishing Ltd. 2009.
11. Bremmer FW. Cardiac Disease and hypertension. In: Kaplan LA and Pesce AJ (eds). *Clinical Chemistry theory, analysis and correlation.* CV Mosby. St. Louis, USA. 1987:233-294
12. Chapman JF, Woodard LL, Silverman LM. Creatinine Kinase isoenzymes. In: Kaplan LA and Pesce AJ (eds). *Clinical Chemistry theory, analysis and correlation.* CV Mosby. St. Louis, USA. 1987:500-501
13. Strømme JH, Rustad P, Steensland H, Theodorsen L, Urdal P. Reference intervals for eight enzymes in blood of adult females and males measured in accordance with the International Federation of Clinical Chemistry reference system at 37 degrees C: part of the Nordic Reference Interval Project. *Scand J Clin Lab Invest.* 2004;64(4):371-84
14. 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.
15. Dhan R, Khanna M, Chaturvedi UC, Mathur A. Effect of dengue virus-induced cytotoxin on capillary permeability. *J Exp Pathol.* 1990;71:83-8.
16. Matsumoria A, Sasayama S. Immunomodulating agents for the management of heart failure with myocarditis and cardiomyopathy—lesson from animal experiments. *Eur Heart J.* 1995;16:140-3.
17. Hober D, Poli L, Roblin B, Gestas P, Chungue E, Granic G, Imbert. Serum levels of tumor necrosis factor-alpha (TNF-alpha), interleukin-6 (IL-6), interleukin 1 beta (IL-beta) in Dengue-infected patients. *Am J Trop Med Hyg virus infections.*1993;48:324-31.

---

**From:** \*Department of Pediatrics, Karnataka Institute of Medical Sciences, Hubballi. India \*\*Department of Pediatrics, Kasturba Medical College, Manipal, India.

**Address for Correspondence:** Dr Koushik H, Address: #16/5, B Type Quarters, KMC Campus, Manipal 576104, India.



**Email :** koushikural@gmail.com

**DOI :** 10.7199/ped.oncall.2017.55

---