European Journal of Molecular & Clinical Medicine (EJMCM)
ISSN: 2515-8260 Volume 08, Issue 04, 2021

Original research article

Study of Cardiac Manifestation of Dengue Fever in Children Less Than 12 Years Age

Dr. Shanu Prabhakar[1], Dr. Chandra Bhushan Kumar[2]

[1]Senior Resident, Department of Paediatrics, N.M.C.H. Jamuhar Sasaram, Rohtas, Bihar, India

[2]Professor, Department of Paediatrics, N.M.C.H. Jamuhar Sasaram, Rohtas, Bihar, India

Corresponding Author: Dr. Shanu Prabhakar

Abstract

Background: Dengue fever will present with varied manifestations in children. Cardiac manifestation in Dengue fever are rare but not unknown. Hence this study was undertaken to evaluate Cardiac Manifestations in children with dengue fever.

Materials And Methods: This is a prospective study done at Department of Paediatrics, at N.M.C.H. Jamuhar Sasaram, Rohtas. Inclusion Criteria Children <12 years, admitted to Department of Paediatrics , who are confirmed (positive Non Structural 1 Antigen or IgM ELISA) cases of dengue fever. Exclusion Criteria: Children with congenital /acquired heart disease.

Conclusion: Cardiac manifestations in children with Dengue are not uncommon regardless of clinical type of Dengue, though most of the cardiac involvement in children with Dengue are subclinical. ECG changes noticed in 13(33%) of cases. Sinus tachycardia, bradycardia, ST- T changes, reduction ofejection fraction were common in Dengue With or Without Warning Signs.

Keywords: Dengue; Tachycardia, Sinus;Ventricular Function, Left.

Introduction

Dengue fever will present with varied manifestations in children. Cardiac manifestation in Dengue fever are rare but not unknown. Dengue ranks as the most important mosquito-borne viral disease in the world.Outbreaks exert a huge burden on populations, health systems and economies in most tropical countries of the world. The emergence and spread of all four dengue viruses serotypes from Asia to the Americas, Africa and the Eastern Mediterranean regions represent a global pandemic threat. Although the full global burden of the disease is still uncertain, the patterns are alarming for both human health and the economy.[1] In the last 50 years, incidence has increased 30-fold with increasing geographic expansion to new countries and in the present decade, from urban to rural settings. An estimated 50 million dengue infections occur annually and approximately 2.5 billion people live in dengue endemic countries[2]. Dengue constitutes a major cause of paediatric morbidity and mortality in South East Asian countries. Dengue virus (DEN) is a small single-stranded RNA virus comprising four distinct serotypes (DEN-1 to 4). Dengue virus belongs to the genus Flavivirus, family Flaviviridae. The various serotypes of the dengue virus are transmitted to humans through the bites of infected Aedes mosquitoes, principally Ae. Aegypty. Dengue fever (DF) is known to affect several systems in the human body. Myocardial involvement may be because of direct

effect of virus itself or may be because of cytokine production. Dengue antigen binding to the receptor site in myocardium and causing myocarditis is another possibility. Presentation of myocarditis has wide variation; can be symptomatic or asymptomatic. There can be atrioventricular regurgitation, mono or biventricular dilatation, reduced ejection fraction and rarely global hypokinesia. Relative bradycardia is a well-known presentation. ST and T segment changes, T wave inversion, conduction blocks are ECG changes in children with Dengue fever. There is large input of cases diagnosed with dengue with varied manifestations in our department.

Objectives

To study the cardiac manifestations in children less than 12 years with dengue fever**.**

Review of Literature

Dengue is the most rapidly spreading mosquito borne viral disease in the world, with 30 fold increase in the incidence over last 5 decades. According to WHO, 50-100 million new infections occur annually in greater than 100 endemic countries[2.] Every year hundreds of thousands of severe dengue cases arise of which 20,000 leads to death. Loss to economy is 264Disability Adjusted Life Year (DALY)/ Million population/year[1,11]. Approximately 1.8 billion (>70%) of population at risk of dengue worldwide live in member states of South East Asian Region(SEAR) & Western Pacific Region which bear nearly 70% of current global disease burden due to dengue.[1] Dengue often presents in the form of large outbreaks. There is, however, also aseasonality of dengue, with outbreaks occurring in different periods of the year. After an incubation period of 4--10 days, infection by any of the four virus serotypes can produce a wide spectrum of illness, although most infections are asymptomatic or subclinical. Primary infection is thought to induce lifelong protectiveimmunity to the infecting serotype. Young children in particular may be less able than adults to compensate for capillary leakage and are consequently at greater risk of dengue shock.[2] Seroepidemiological studies have shown that secondary heterotypic infection as a risk factor for severe dengue, although there are a few reports of severe cases associated with primary infection. Severe dengue is also regularly observed during primary infection of infants born to dengue-immune mothers. Plasma leakage, hemoconcentration and abnormalities in homeostasis characterize severe dengue. The mechanisms leading to severe illness are not well defined but the immune response, the genetic background of the individual and the virus characteristics may all contribute to severe dengue. Recent data suggest that endothelial cell activation could mediate plasma leakage, is thought to be associated with functional rather than destructive effects on endothelial While most patients recover following a self-limiting non-severe clinical course, a small proportion progress to severe disease, mostly characterized by plasma leakage with or without haemorrhage even ending in death.

Changes in the epidemiology of dengue have led to problems with the use of the earlier WHO classification. Symptomatic dengue virus infections were grouped into three categories: undifferentiated fever, dengue fever (DF) and dengue haemorrhagic fever (DHF). DHF was further classified into four severity grades, with grades III and IV being defined as dengue shock syndrome (DSS) [12]. There have been many reports of difficulties in the use of this classification. Difficulties in applying the criteria for DHF in the clinical situation, together with the increase in clinically severe denguecases which did not fulfil the strict criteria of DHF, led to the request for the classification to be reconsidered. cells. Laboratory diagnostic methods for confirming dengue virus infection mayinvolve detection of the virus, viral nucleic acid, antigens or antibodies, or a combination of these techniques. After the onset of illness, the virus can be detected in serum, plasma, circulating blood cells and other tissues for 4–5 days.

During the early stages of the disease, virus isolation, nucleic acid or antigen detection can be used to diagnose the infection. At the end of the acute phase of infection, serology is the method of choice for diagnosis. IgM antibodies are the first immunoglobulin isotype to appear. Dengue is known to affect multiple organ systems, including cardiovascular system. Traditionally shock in severe dengue fever is thought to be secondary to plasma volume loss into interstitial space due to increased capillary permeability and bleeding. However profound shock of sudden onset cannot be accounted by these pathogenic mechanisms. Dengue virus infects both CD4+ and CD8+ T cells.[41] Following primary infection, both serotype specific and serotype cross reactive memory T cells formed and the latter on secondary exposure to the virus augment infection producing various cytokines A cohort study was conducted in Sri lanka, to detect cases of asymptomatic myocardial involvement in dengue fever. Two hundred and seventeen patients with dengue fever were taken up for the study. Out of these 24% had echocardiographic myocarditis; all had relative bradycardia. The 2-D echocardiographic abnormalities showed chamber dilatation, an irregular jerky movement of the ventricular wall, and aminor degree of atrioventricular valvular regurgitation. The treatment of CHF consists of (1) elimination of the underlying causes, (2) treatment of the precipitating or contributing causes (e.g., infection, anemia, arrhythmias, fever) (3) control of heart failure state. General measures include rest, Oxygen, adequate calories and fluid, salt restriction in older children, respiratory support if needed. Three major classes of drugs are commonly used in the treatmentof CHF in children: inotropic agents, diuretics, and afterload-reducing agents. Diuretics remain the principal therapeutic agent to control pulmonary and systemic venous congestion. Diuretics only reduce preload and improves congestive symptoms, but do not improve cardiac output or myocardial contractility. Satar singhe RL et.al[6] none had overt clinical manifestation of myocarditis but 24% of the patients had 2D Echocardiographic evidence of myocarditis. Follow-up showed that 96% and 100% of the myocarditis group had normal 2-D echocardiographic findings within three weeks and three months, respectively.

Materials And Methods

This is a prospective study done at Department of Paediatrics, at Narayan Medical College and Hospital, Jamuhar Sasaram, Rohtas Bihar. Inclusion Criteria :Children <12 years, admitted to Department of Paediatrics , who are confirmed (positive Non Structural 1 Antigen or IgM ELISA) cases of dengue fever. Exclusion Criteria: Children with congenital /acquired heart disease.

Inclusion criteria

Children less than 12 years, admitted in Department of paediatrics, NMCH, Sasaram, Rohtas. with Dengue NS1 ELISA and/or IgM MAC ELISA positive.

Exclusion criteria

Children with congenital or acquired heart disease.

After obtaining informed written consent, patients were clinically evaluated and cardiac assessment was conducted in a predefined proforma. Children were treated according to recent WHO protocol.[1] Children were investigated with Chest Xray, ECG and 2 D Echocardiography once stable to be shifted for investigations. Serum CKMB levels were done on the day of admission. Features of cardiac manifestations like abnormalities in heart rate, rhythm, features of cardiac failureand other parameters will be analyzed clinically and evidence for the same shall be looked for in the above investigations. Ejection Fraction was considered as a marker of Left ventricular function. Ejection Fraction <55% was considered as abnormal. 2D Echo was done using BLUE STAR Mobile Digital Color Doppler ultrasound system, Ejection Fraction was measured using 2D Mode, Modified Simpson’s method. Ejection fraction is the

percentage change in LV volume from end-diastole toend-systole. Its calculation requires determination of left ventricular volumes.

Results

Total of 124 children with suspected dengue were admitted. Among them Dengue NS1 and/or IgM MAC ELISA was positive in 39 cases. Only those 39 confirmed[1] cases were taken into study.

Table 1: Proportion of Serology Proven Cases with suspected cases of DengueFever

Serology	Number	Percentage (%)
Positive	39	31
Negative	85	69
Total	124	100

Table 2:Distribution of children according to age (n=39)

Age	No. of children	Percentage
<1 year	1	2
>1year	38	98
Total	39	100

most common symptom in our study in the order of frequency was fever (100%), abdominal pain 15(38%), nausea/vomiting 13(33%), myalgia8 (20%), rashes7 (17%), bleeding6 (15%), swelling/facial puffiness 5(12%), lethargy3 (7%), convulsion2 (5%), altered sensorium2 (5%). One child who hadhurried breathing also on examination had features of congestive cardiac failure. Noneof them had palpitation, dyspnea, ororthopnea.

Table 3: Cardiac Manifestation (n=39)

Cardiac Manifestation	Number	Percentage
Congestive Cardiac	1	2%
Raised CKMB	2	4%
Cardiomegaly in CXR	3	7%
ECG changes	13	33%
2D Echo Changes	11	28%

Our study 22 (56%) children had one or the other cardiac manifestation(clinical/ CKMB/ CXR/ECG/2D Echo). One (2%) had congestive cardiac failure, 2(4%) had Raised CKMB >25U/L, 3 (7%) hadcardiomegaly in CXR which was left ventricular type, 13(33%) had ECG changes, 11(28%) had 2D Echo changes. Sinus Tachycardia Disproportionate to fever which was present in 5(26%) cases was commonest in Dengue without warningSigns, whereas in Dengue with Warning Signs Sinus Tachycardia Disproportionate to fever and T wave inversion 3each (23%) was common. Among Severe Dengue cases 1 each had Tachycardia Disproportionate to fever, Ventricular ectopic, Supraventricular Tachycardia, low voltage QRS. Dengue Without Warning Signs 5(26%)children, Dengue with Warning signs 2(15%) children, Severe Dengue 2(28%)children had Ejection Fraction <55%. 2 children with Severe Dengue had LV wall Motion abnormality, 1 had pericardial Effusion(14%).

Table 4: ECHO Changes (n=39)

2 D ECHO Finding	Number	Percentage (%)
Ejection Fraction <55%	10	26%
Left Ventricular Wall Motion Abnormality	2	5%
Pericardial Effusion	1	3%

10(26%) cases had Ejection Fraction <55%, Left Ventricular Wall Motion Abnormality was present in 2(5%), pericardial effusion in 1(3%) cases.

Discussion

Our study was conducted to know cardiac manifestation of Dengue fever in < 12 year children. In the study period 124 suspected cases of dengue were admitted. Out of it 39 were Dengue NS1 ELISA and/or Dengue MAC ELISA IgM positive. Only those 39 confirmed cases were considered for final analysis. In a similar study conducted in Dr RML hospital Delhi by Yadav DK et al,67 children who satisfied WHO criteria for Dengue fever and who tested positive for IgM Dengue were enrolled to study Tei index and asymptomatic myocarditis in children with Severe Dengue. In a study conducted at King Chulalongkorn Memorial Hospital, Bangkok, Thailand by Khongaypatthin et al to know myocardial depression in dengue haemorrhagic fever, 91 children with serologically / PCR proven Dengue fever cases were enrolled. Dengue fever (DF) is known to affect several systems in the human body. Cardiac involvement in Dengue fever is rare, but not unknown. Presentation of myocarditis has a wide variation; can be symptomatic or asymptomatic. But regular follow up has showed that myocarditis in dengue runs a benign course, without long term complication.[6] Dengue infection can be severe with high mortality in infants[1]. Ourstudy showed 1(2%) case was in <1year, remaining 38(98%) cases in >1 year age, group. In a study conducted by Khongphatthanayothinet al age ranged was 10.5+/- 2.9 years. In a similar study by Yadav DK et al mean age was 10.4 years, most of them were 10-14 year age group. Mean age of patients was 6.3 years in a study conducted in AIIMS Delhi, by Kabra S K et al. Clinical manifestations in dengue fever is unpredictable and can range from undifferentiated mild febrile illness to severe disease with haemorrhage, massivebleeding and various organ involvement even ending in death. Most common symptom in our study in the order of frequency was fever (100%), abdominal pain in 15 (38%), nausea/vomiting in 13(33%), myalgia in 8 (20%), rashes in 7 (17%), bleeding in 6 (15%), swelling/facial puffiness in 5(12%), lethargy in 3 (7%), convulsion in 2 (5%), altered sensorium in 2 (5%) cases. Fever, abdominal pain, vomiting, myalgia being most common symptoms in our study is similar to other studies. Bleeding manifestations were reported among 15% of cases, which is quite less compared to other studies like Chandrakanth et al (38.8%), Batra p et al (40%). Four children had petechiae 2 had malena. Only one child had hurried breathing, same child had features of heart failure. None of the other patients were overtly symptomatic of myocarditis or heart failure. Fever is known to cause raise in heart rate (10 beats/min/1 Celsius). Heart rate disproportionate to fever was present in 9(23%) patients, which may be due to cardiac involvement. In a study by Gupta VK et al, reported incidence of tachycardia was 21.4%. 49% (19/39) of cases were dengue without warning signs, 33% (13/39) were dengue with warning signs, 18% (7/39) were severe dengue. The currentWHO case classification in to Dengue Without Warning Signs, Dengue with warning signs(DWS) and Severe Dengue(SD)[1] was suggested by an expert group (Geneva, Switzerland, 2008). In our study 22 (56%) cases had one or the other cardiac manifestation (congestive cardiac failure/ raised CKMB/ Cardiomegaly in CXR/ECG abnormality/2D Echo abnormality). Only one case presented with clinical features suggestive of overt CCF. Raised CKMB Level was present in 3 (7%) of patients. CXR showed cardiomegaly (C: T> 0.5) in 3(7%) patients. ECG Changes were present in 13(33%) patients which included disproportionate tachycardia, T wave inversion, ectopic beats, supraventricular tachycardia, low voltage QRS. 2D Echo changes

were present in 11(28%) patients which included decreased ejection fraction, LV wall motion abnormality, pericardial effusion. Increase in trend of cardiac manifestation among severe dengue cases were observed in our study, compared to dengue without and with warning signs. T wave inversion in Lead V1 and V2 can be normal in children up to adolescence. ST segment depression >1mm in relation to isoelectric line indicates ST segment depression. Low voltage QRS complexes are defined as presence of tallest R wave <5mm in limb leads, <10mm in precordial leads. Ejection Fraction was considered as marker of left ventricular function. Our study showed 10(25%) children with dengue had abnormally low ejection fraction (<55%). Left ventricular wall motion abnormality which indicates regional chamber malfunction, was present in 2(5%) children, one had pericardial effusion. In a study by Yadav DK et al, among 67 children with dengue 28(42%) had borderline to low ejection fraction (47± 4.65) at admission but significantly improved from admission to discharge. In a similar study by Kabra SK et al 9 children out of 54(16.7%) had reduced ejection fraction (<50%), 2 of these had significant reduction (<35%). Transient decrease in ejection fraction, which improves with time, is consistent with other similar studies, which again indicates mild, self-limiting cardiac involvement in majority of cases, whereas 2 cases of severe dengue had severe reduction of ejection fraction <35% which might have contributed to hemodynamic instability and disease severity.

Conclusion

Our study noticed 22(56%) children with dengue had one or the other cardiac manifestation. So, cardiac manifestations in children with dengue are not uncommon regardless of clinical type of dengue, though overt manifestation as myocarditis / cardiac failure is less likely. Most of the cardiac involvement in children with dengue are subclinical. ECHO abnormalities were noticed in 11(28%) children, of which 10 hadnormal Echo by the time of discharge except one with pericardial effusion who took 3weeks for Echo to normalize.

References

1. WHO (2012) Global strategy for dengue prevention and control 20122020.WHO/HTM/NTD/VEM/2012.5.
2. WHO (2009) A Joint Publication Of The World Health Organization (WHO) And The Special Programme For Research And Training in Tropical Diseases (TDR). Dengue Guidelines for Diagnosis, Treatment, Prevention and Control.
3. Alam AS, Sadat SA, Swapann Z, Ahmed AU, Karim MN, Paul HK et al. Clinical Profile of Dengue Fever in Children. Bangladesh J Child Health. 2009. Vol; 33(2): 55-58.
4. Gurugama P, Garg P, Perera J, Wijewickrama A, Seneviratne SL. Dengue viral infections. Indian J Dermatol. 2010;55(1):68-78
5. Potts JA, Rothman AL. Clinical and laboratory features that distinguish dengue from other febrile illnesses in endemic populations. Trop Med Int Health. 2008 Nov; 13(11):1328-40.
6. Satarasinghe RL, Arultnithy 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.
7. Rigau Perez JG. The early use of break-bone fever (Quebrantahuesos, 1771) anddengue (1801) in Spanish. Am J Trop Med Hyg 1998; 59(2): 272-4
8. Sabin AB. Research on dengue during World War II. Am J Trop Med Hyg 1973;22:82-91.
9. Hammon WM, Rudnick A, Sather GE. Viruses associated with epidemic hemorrhagic fevers of the Philippines and Thailand. Science 1960;1102-3.
10. World Health Organization, Dengue hemorrhagic fever: Diagnosis, Treatment andControl, 2nd Edition.Geneva ; WHO 1986.

11. Suaya JA, Shepard DS, Siqueira JB, Martelli Ct, Lum LCS, Tan LH et al. Cost of Dengue cases in eight countries in America and Asia: A prospective study. American Journal of Tropical Medicine and Hygeine.2009; 80:846-855.
12. WHO Dengue haemorrhagic fever: diagnosis, treatment, prevention and control, 2nd ed. Geneva, World Health Organization, 1997.
13. Eva Harris, Bridget Wills, Angel Balmaseda, Samantha Nadia Hammond, Crisanta Rocha, Nguyen Minh Dung et al. The WHO dengue classification and case definitions: time for a reassessment. Lancet, 2006; 368:170--173.
14. Rigau PJ. Severe dengue: the need for new case definitions. Lancet Infectious Diseases, 2006; 6:297–302.
15. Gupta VK, Gadpayle AK. Subclinical Cardiac Involvement in Dengue Haemorrhagic Fever. JIACM 2010; 11(2):107-11.
16. Lai WW, Mertens LL, Cohen MS, GevaT.Echocardiography in Pediatric and Congenital Heart Disease: From fetus to Adult.Oxford:Blackwell Publishing Ltd;2009.
17. Paul VK, Bagga A, Sinha A. GhaiEssentialPediatrics. Eighth Edition. New Delhi: CBS Publishers and Distributors; 2013.
18. Barniol J, Gaczkowski R, Barbato EV, da Cunha RV, Salgado D, Martinez E, et al. Usefulness and applicability of the revised dengue case classification by disease: multi-centre study in 18 countries. BMC Infect Dis. 2011;11:106.

Received : 19-10-2021 Revised:17-11-2021 Accepted: 25-11-2021