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Original Research Article

Clinical Correlation of Cardiac Function and Troponin-I & CPK MB in Dengue Fever in Children

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Abstract

Background: Dengue virus infection in children is a major health problem in many parts of the world. Its manifestations range from mild fever to severe and life-threatening disease. Although cardiac involvement has been reported in DVI.

Objectives: We conducted this study to analyze association between Clinical Profile, Cardiac Functions and Troponin I and CPK-MB (cardiac biochemical markers) in children with Dengue Fever.

Methods: This was a prospective observational study in which 100 paediatric patients who were hospitalized and diagnosed to be having Dengue fever were included. All patients were stratified into either of the 3 groups- Dengue without warning signs, Dengue with warning signs and severe Dengue. A detailed history and thorough clinical examination were done for all patients. Cardiac function was assessed by ECG, 2D Echo, CPK-MB and Troponin-I.

Results: Dengue with and without warning signs was seen in 42.3% and 40% cases respectively whereas severe dengue was seen in 17% cases. Majority of patients were male. Mean duration of fever was 6 to 9 days. Among serological profile of dengue patients 36.9% were positive for IgM, 34.2% were positive for Ns1Ag and 28.9% positive for IgM+NS1. Among total dengue patients in this study, 21 (58.3%) had ECG changes, the majority of which belonged to the dengue with warning signs group. A significant correlation was noted between the cardiac markers, ECG and 2D ECHO findings with the severity of dengue ($P<0.05$).

Conclusion: Cardiac markers (CPK-MB and Troponin-I) have significant correlation between Dengue without warning signs, Dengue with warning signs and severe Dengue.

Keywords: Radiotherapy, Ulceromembranous Lesions, Inflammatory Etiology, Histopathological Examination.

Introduction

Dengue virus infection (DVI) is a major health problem in more than 100 countries in tropical and subtropical regions. Approximately 96 million people develop DVI annually [1]. DVI has a broad clinical spectrum, according to classification by the World Health Organization (WHO, 2009), which includes asymptomatic to dengue fever, dengue haemorrhagic fever (DHF), and dengue shock syndrome (DSS) [2]. Cardiac complications are amongst the important consequences of DVI. Dengue is the most rapidly spreading mosquito-borne viral disease in the World. 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 approximately 2.5 billion people live in dengue endemic countries [3]. The most significant vector Aedes aegypti is a daytime mosquito, capable of stinging many people in a short period of time and breeding in several types of human-made containers with water inside [4]. Dengue Fever, also known as the break bone fever, is the most common arboviral disease in the world. It is a mosquito-transmitted acute viral infection caused by dengue virus. Virus has 1 of 4 virus serotypes (DEN-1, DEN-2, DEN-3, and DEN-4) of the genus Flavivirus. Dengue Fever (DF) has been known for more than a century in the tropical areas of South East Asia and the Western Pacific regions. A significant increase in the incidence of this infectious disease has taken place in the last 20 years and Dengue has become a major international public health concern in recent years [5]. The

clinical manifestations in dengue range from asymptomatic infection to severe viral hemorrhagic fever as a prelude to plasma leakage and bleeding. However, during defervescence, plasma leakage is reversed and the extravasated fluid is reabsorbed, which is a prelude to fluid overload and reflected by the development of massive pleural effusion or pulmonary edema. Thus, the resulting respiratory manifestations have been the major cause of mortality in adults and children with severe dengue [6, 7]. Nevertheless, the cardinal mechanism of shock is due to hypovolemia, and the impaired cardiac function might also contribute to cardiac abnormalities. Several clinical studies have shown the existence of cardiac co-morbidity in dengue [8-10]. Clinically, cardiac involvement can differ broadly, from subclinical to severe myocarditis which can be fatal. Myocardial involvement may be attributed to direct viral invasion or cytokine-induced immune damage, or both. Nevertheless, research on cardiac manifestations of dengue is limited in the pediatric population. Reports from different studies have shown a 16.7%–71% incidence of cardiac involvement with features like cardiac failure, elevated cardiac enzymes (e.g. troponin T, creatine phosphokinase–myocardial band [CPK-MB]), abnormal electrocardiogram (sinus tachycardia, sinus bradycardia, T wave inversions, heart block), and echocardiogram changes (reduced ejection fraction) [11, 12].

Aims & Objectives: Objective of the study was to determine the incidence of cardiac involvement in pediatric patients with dengue and correlation between these cardiac findings with dengue severity.

Materials and Methods

This cross-sectional study was conducted in the department of pediatrics in a tertiary care center central India, A total of 100 patients with wide clinical presentation of dengue infection, together with subsequent positive dengue NS1 antigen and/ or IgM MAC ELISA tests during the study duration were enrolled.

Inclusion Criteria

- Age less than 18 years with both genders.
- Dengue confirmed by NS1Ag and/or IgM antibodies.
- Parents/Caretakers gave informed written consent for the study.

Exclusion criteria

- Age more than 18 years.
- Presence of congenital or acquired heart disease.
- Patients with any pre-existing severe systemic illness.
- Patients on drugs or electrolyte imbalances affecting the heart rate or rhythm.
- Parents/Caregivers Refused consent.

A detailed history, Anthropometric data and clinical examination was done in all cases. Pulse rate, respiratory rate and blood pressure were recorded in all the cases. Complete blood count and liver function test, ECG, 2D-ECHO, CPK-MB and TROPONIN-I were also done in all the cases. CPK-MB and TROPONIN-I were determined with kits using ELISA method.

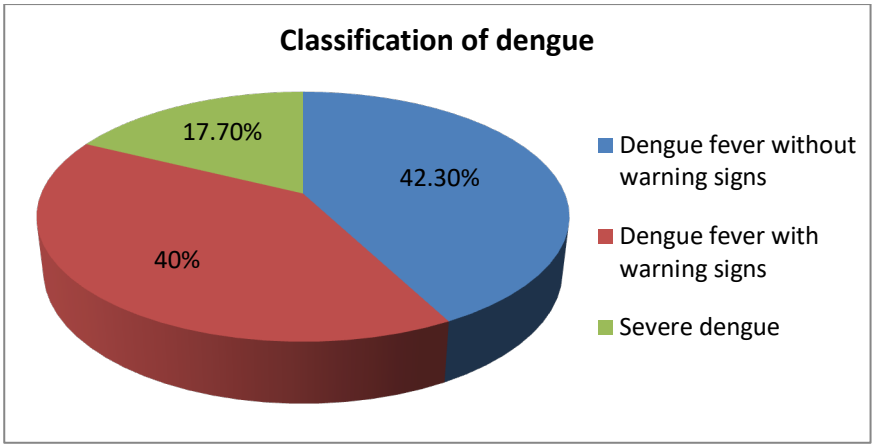
Dengue Fever with Warning Signs defined as following: Abdominal pain or tenderness, Persistent vomiting, Clinical fluid accumulation (ascites, pleural effusion), Mucosal bleeding, Lethargy, restlessness, Liver enlargement >2 cm, increased hematocrit concurrent with rapid decrease in platelet count. Severe Dengue: Dengue fever with at least one of the following criteria: Severe plasma leakage leading to shock, Fluid accumulation with respiratory distress, Severe bleeding as evaluated by clinician, severe organ involvement, Liver Enzymes: AST or ALT ≥1000 U/L, impaired consciousness, Failure of heart and other organs.

Based on reports, cardiac involvement was considered present if dengue positive (NS1/IgM) patients exhibited any two or more of the following factors: elevated CPK-MB, abnormal ECG findings, and/or abnormal echocardiography findings. Those patients with features suggestive of cardiac involvement were placed on follow-up with the pediatric cardiologist.

Statistical analysis: SSPS 22.0 version software was used for statistical analysis and p value less than 0.05 was taken as statistically significant.

Results

A total of 90 cases of dengue based on clinical and laboratory profile were subjected to cardiac evaluation were analysed in this study. Among total dengue patients, most of them (42.3%) were dengue fever without warning signs, 40% of dengue with warning signs, and 17% with severe dengue [Figure 1].



The mean age of the participants in dengue without warning signs, dengue with warning signs and severe dengue were 8.43 years, 7.45 years and 6.26 years respectively. Majority of patients were male. Mean duration of fever was 6 to 9 days. Among serological profile of dengue patients 36.9% were positive for IgM, 34.2% were positive for Ns1Ag and 28.9% positive for IgM+NS1. The analysis of the nutritional status of these patients showed that majority of the cases (81.6%) had a normal nutritional status, whereas Moderate Acute Malnutrition (MAM) and Severe Acute Malnutrition (SAM) were present in 13.2% and 5.2% patients respectively. Pallor and rash were significantly higher among severe dengue cases as compared to dengue without warning signs cases [table: 1].

Table 1: Comparison of gender, duration of fever, nutritional status, serology, pallor and skin manifestation among the study groups

Distribution of cases		Dengue without warning signs (n=38)	Dengue with warning signs (n=36)	Severe dengue (n=26)	P value
Mean age of patients		8.43 years	7.45 years	6.26 years	>0.05
Gender	Male	71.1 %	76.3%	53.8%	>0.05
	Female	28.9%	23.7%	46.3%	
Mean duration of fever (days)		6.14 days	7.32 days	8.71 days	>0.05
Serological profile	IgM Positive	36.9%	41.6%	38.5%	>0.05
	NS1 Positive	34.2%	27.8%	26.9%	
	IgM+NS1 Positive	28.9%	33.4%	34.6%	
Pallor	Present	28.9%	47.3%	96.2%	<0.05
	Absent	71.1%	52.7%	3.8%	
Rash	Present	10.5%	58.4%	88.5%	<0.05
	Absent	89.5%	41.6%	11.5%	
Nutritional status	MAM	13.2%	13.8%	19.2%	>0.05
	Normal	81.6%	77.9%	69.3%	
	SAM	5.2%	8.3%	11.5%	

Among total cases 54.5% had cardiac involvement, Cardiac involvement was higher in severe dengue (73.1%) cases as compared to dengue with warning signs (52.8%) and dengue without warning signs (28.9%) [Table: 2].

Table 2: Cardiac Involvement in Dengue Patients

Dengue Category	With Cardiac Involvement, N (%)	Without Cardiac Involvement, N (%)
Dengue without warning signs (n=38)	11 (28.9%)	25 (71.1%)
Dengue with warning signs (n=36)	19 (52.8%)	17 (47.2%)
Severe Dengue (n=26)	19 (73.1%)	7 (26.9%)
Total (n=90)	49 (54.4%)	41 (45.6%)

Among total dengue patients in this study, 21 (58.3%) had ECG changes, the majority of which belonged to the dengue with warning signs group. A significant correlation was noted between the cardiac markers, ECG and 2D ECHO findings with the severity of dengue (P<0.05).

Table 3: Correlation between Cardiac Findings and Dengue Severity

Cardiac Findings	Dengue without Warning Signs (n=38)	Dengue with Warning Signs (n=36)	Severe Dengue (n=26)	P value
CPK-MB				
Elevated	**25**	**29**	**20**	**<0.001**
Normal	**13**	**7**	**6**	
Troponin I				
Elevated	**28**	**30**	**19**	**<0.001**
Normal	**10**	**6**	**7**	
ECG findings				
ECG changes	**15**	**21**	**16**	>0.05
Normal ECG	**23**	**15**	**10**	
Echocardiogram				
Abnormal 2d ECHO	**14**	**20**	**17**	>0.05
Normal 2d ECHO	**24**	**16**	**11**	

Table 4: Comparison of cardiac vital & laboratory parameters and 2D ECHO findings in studied cases

Parameters	Dengue without Warning Signs (n=38)	Dengue with Warning Signs (n=36)	Severe Dengue (n=26)
Mean heart rate	78.27	79.74	81.15
Mean respiratory rate	25.43	26.25	24.70
Mean hemoglobin level	10.72	9.13	8.43
Mean hematocrit	31.74	29.33	28.17
Mean platelet count	2.05	1.12	0.76
Mean ejection fraction	64.45	62.65	60.90
Mean end systolic volume	29.14	28.23	28.24
Mean end diastolic volume	61.42	60.46	60.05

Discussion

Cardiac manifestations in patients with dengue fever include cardiac failure, ECG changes, 2D ECHO changes, and elevated cardiac enzymes. There is an increasing trend of cardiac involvement in dengue patients being reported. The clinical severity of dengue varies with age. Younger children with dengue hemorrhagic fever elicit more severe clinical outcomes and a higher fatality rate compared to adults [13]. In the present study, Dengue fever was more common in males as compared to females which correlate with the study of Vincet et al [14] and Mia MW et al [15]. This observation was in consonance with the fact that the incidence of myocardial infarction is more in male than in the female. In this study, a higher proportion of children affected with dengue were in the 5–9 years age group, similar to the observations of Iskandar B, et al [16] and Salgado DM.et al [17]. In our study, non-severe dengue without warning signs was seen in 42.3% patients, dengue with warning signs in 40% and severe dengue in 17.7% cases, our results similar with the J Abhinayaa, et al [18] and Chaudhary DG, et al [19], whereas Jain A, et al [20], reported that 76%) were non severe Dengue, 20% were Dengue with warning signs, and 3% were Severe Dengue. In the current study there was no significant association between malnutrition status and severity of dengue in children, this correlates with this study done by Nguyen TH, et al [21]. In this study among the clinical signs petechiae, rashes and hepato-splenomegaly were significantly associated with the severity of the dengue fever, in agreement with the Prathyusha et al [22]. In the present study the mean platelet value and hemoglobin was significantly lower in patients with severe Dengue than in patients with Dengue without warning signs, dengue with warning signs. This correlates with a study conducted by Alfredo J. et al [23], which showed that incidence of thrombocytopenia and anemia was more in patients with severe Dengue. In our study, the overall cardiac involvement among dengue patients in the pediatric population was 54.4%, predominantly in the severe dengue group, similar to the study conducted by Siddappa et al [24]. Severity of dengue was also directly proportional to the length of hospitalization in the current study, Concordance finding reported by Mishra et al [25]. In our study there was no significant difference in the ECG and 2D ECHO patterns among subjects with Dengue without warning signs, dengue with warning signs and severe dengue, constant results reported by Kularatne SA et al [26]. Present study reported that

cardiac enzymes like CPK-MB and troponin I was statistically significant elevated and associated with the dengue severity, our finding comparable with the Iskandar B, et al [27] and Khongphatthanayothin A, et al [28].

Conclusion

We have conclude that ECG and 2D ECHO findings are abnormal during Dengue illness, but do not have significant correlation between Dengue without warning signs, dengue with warning signs and severe dengue. Cardiac enzymes (CPKMB and Troponin-I) have statistically significantly associated with the Dengue without warning signs, dengue with warning signs and severe dengue.

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