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Original Research Article

Evaluation of cardiac biomarkers in predicting severity of dengue fever

[1]Dr. Chetan Kerur, [2]Dr. Khizerulla Sharief, [3]Dr. Mohana [4]Dr. Pragalatha Kumar,

[1]Assistant Professor, Department of Paediatrics, Akash Institute of Medical Sciences and Research Centre, Bangalore, Karnataka, India
[2]Associate Professor, Department of Paediatrics, Akash Institute of Medical Sciences and Research Centre, Bangalore, Karnataka, India
[3]Professor and Head, Department of Paediatrics, Akash Institute of Medical Sciences and Research Centre, Bangalore, Karnataka, India
[4]Professor, Department of Paediatrics, Indira Gazdhi Institute of Child Health, Bangalore, Karnataka, India

Corresponding Author:
Dr. Chetan Kerur

Abstract

Dengue virus will affect several systems of the body. Myocardial involvement may be the direct effect of the virus itself or may be due to cytokine production. Myocarditis has a varied presentation, it may be clinical or subclinical. Myocarditis can present as cardiac failure, Electrocardiogram (ECG) changes (sinus bradycardia, sinus tachycardia, T wave inversion), 2 D Echocardiography changes (reduced ejection fraction) and elevated cardiac enzymes (Troponin T, CPK, CPK-MB, LDH, N terminal-BNP). The study was approved by the institutional ethical committee. Informed written consent was obtained from the parents of each patient before enrollment. History and examination findings were recorded in a pre-structured proforma. Children with clinically diagnosed dengue fever (WHO criteria) & serologically confirmed and admitted cases between the age group of 2months to 18 years formed the study group. In 110 biomarker positive cases, 32(17.3%) had a shock, 14 (7.6%) had bleeding manifestations, 78(42.2%) cases had elevated SGOT and SGPT and PT and aPTT elevated in 84(45.4%) and 44(23.8%) cases respectively.

Keywords: Cardiac biomarkers, prediction of severity, dengue fever

Introduction

Dengue is a mosquito-borne viral disease. Dengue virus is transmitted by a female mosquito called Aedes aegypti and a smaller extent by Aedes albopictus. This mosquito also involved in the transmission of chikungunya, yellow fever and Zika virus infection. Dengue is widespread throughout the tropics, with local variations in risk influenced by rainfall, temperature, and unplanned rapid urbanization. Severe dengue was first recognized in the 1950s during epidemics in Thailand and the Philippines. Today sever dengue affects most of the Asian and Latin America and has become a leading cause of hospitalization among children and adults in these regions [1].

In 2015, Delhi, India recorded its worst outbreak since 2006 with over 15000 cases. After a

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drop in the number of cases in 2017-18, a sharp increase in cases is being observed in 2019. An estimated 5,00,000 people with severe dengue require hospitalization every year and with 2.5% case fatality [2].

Dengue virus will affect several systems of the body. Myocardial involvement may be the direct effect of the virus itself or may be due to cytokine production. Myocarditis has a varied presentation, it may be clinical or subclinical. Myocarditis can present as cardiac failure, Electrocardiogram (ECG) changes (sinus bradycardia, sinus tachycardia, T wave inversion), 2 D Echocardiography changes (reduced ejection fraction) and elevated cardiac enzymes (Troponin T, CPK, CPK-MB, LDH, N terminal-BNP). Cardiac involvement in pediatric dengue has been poorly investigated and few inconclusive studies are available. Hence present study shall be undertaken to detect the severity of dengue fever by evaluating cardiac biomarkers in dengue fever and early intervention can be undertaken to prevent morbidity and mortality in dengue fever [3, 4].

Methodology

Source of data

Children with clinically and serologically diagnosed dengue fever admitted.

Type of study

Hospital-based prospective observational study.

Method of data collection

The study was approved by the institutional ethical committee. Informed written consent was obtained from the parents of each patient before enrollment. History and examination findings were recorded in a pre-structured proforma. Children with clinically diagnosed dengue fever (WHO criteria) & serologically confirmed and admitted cases between the age group of 2months to 18 years formed the study group. These children were subjected for following investigations. complete blood count, C-reactive protein, serum aspartate aminotransferase (AST), alanine aminotransferase (ALT) levels. They are also investigated for myocarditis with following cardiac biomarkers. CPK, CPK-MB, LDH, Troponin T and N terminal fragment of B-type natriuretic peptide (NT-proBNP). CPK >195U/L, CPK-MB > 25U/L, LDH >450U/L level considered elevated. Troponin T levels >0.1 ng/mL were considered abnormal. NT-proBNP levels were used to identify patients with suspected left ventricular dysfunction. NT-proBNP levels were considered >450pg/ml considered elevated.

Inclusion criteria

- All clinically and serologically diagnosed dengue fever cases, fulfilling WHO criteria, between the age group of 2 months to 18 years.

Exclusion criteria

1. Those who have not given consent.
2. Age less than 1month.
3. Those not confirmed dengue fever i.e NS1/Dengue IgM negative.

Results

Table 1: Elevation of cardiac biomarkers

Total score	Frequency	Percent
1	47	25.4
2	50	27.0
3	40	21.6
4	16	8.6
5	26	14.1

In 185 subjects, only one cardiac biomarker was elevated in 47 cases (25.4%) and all the five were elevated in 26 cases (14.1%).

Table 2: Elevation of cardiac biomarkers

Cardiac biomarkers	Frequency	Percent
Nil	75	40.5
1*	61	33.0
2*	23	12.4
3*	26	14.1
Total	185	100.0

1. Troponin-T/LDH/BNP.
2. Any two of the above.
3. All the three (Troponin-T, LDH, BNP).

To assess the severity of dengue infection by evaluating cardiac markers we divided the study group into two groups based on cardiac marker elevated or not. The cases having any of these three elevated i.e. Troponin T or LDH or NT pro-BNP formed one group i.e. Biomarker positive and no elevation of any one of these biomarkers formed another group i.e. biomarker negative.

Table 3: Showing two groups

Cardiac biomarkers*	Frequency	Percentage
Not elevated	75	40.5
Elevated	110	59.5
Total	185	100.0

*Anyone of the three (Troponin-T, LDH and Nt pro-BNP) cardiac marker elevation

Cases with biomarker positive are 110 cases (59.5%) and biomarker negative is 75 cases (40.5%).

Table 4: Showing Troponin-T variation in biomarker positive cases

Troponin-T	Cases	Percentage
Elevated	84	45.4%
Not elevated	26	14.1%
Total	110	59.5%

In 110 cases with cardiac biomarker positive cases, showed 84 cases (45.4%) had elevated Troponin-T.

Table 5: Showing LDH variation with biomarker positive cases

LDH	Cases	Percentage
Elevated	16	8.6%
Not elevated	94	50.8%
Total	110	59.5%

In 110 cardiac biomarker positive cases, 16 cases (8.6%) had elevated LDH.

Table 6: Showing NT pro-BNP variation in biomarker positive cases

NT pro-BNP	Cases	Percentage
Elevated	45	24.3%
Not elevated	65	35.2%
Total	110	59.5%

In 110 cardiac biomarker positive cases, 45 cases (24.3%) had elevated NT pro-BNP

Table 7: Comparison of the severity of illness between elevated and normal cardiac biomarkers

Parameters	Biomarkers positive (n-110)	Percentage	p-value	Biomarkers negative (n-75)	Percentage
Shock	32	17.3	0.672	24	13
Bleeding manifestation	14	7.6	0.096	4	2.2
SGOT	78	42.2	0.24	47	25.4
SGPT	78	42.2	0.672	51	27.6
PT	84	45.4	0.04	47	25.4
aPTT	44	23.8	0.281	36	19.5

In 110 biomarker positive cases, 32(17.3%) had a shock,14 (7.6%) had bleeding manifestations, 78(42.2%) cases had elevated SGOT and SGPT and PT and aPTT elevated in 84(45.4%) and 44(23.8%) cases respectively.

Table 8: Comparison Between Patients with and Those Without Cardiac Biomarkers Elevation

Characteristics	With biomarker elevation (mean) (n-110)	Without biomarker elevation (n-75)	P-value
Age group (years)	7.72	6.82	0.18
Hemoglobin	10.68	10.80	0.14
TLC	8,198.62	8,853.33	0.56
PCV	34.32	34.67	0.35
PT	19.86	18.31	0.48
aPTT	52.56	52.27	0.00
Troponin T	0.07	0.02	0.00
LDH	1,071.42	98.07	0.00
NT pro-BNP	2,722.61	159.36	0.00

Discussion

Much of the literature on cardiac manifestation in dengue fever consists of case reports and small case series. The present study systematically evaluates cardiac involvement in dengue infection by assessing cardiac biomarkers. In the present study, cardiac biomarkers were elevated in 110 cases (59.5%) with clinical features ranging from an elevation of cardiac biomarkers, myocarditis, and death. Dengue is one of the most important emerging viral diseases worldwide. The disease is benign in the course, but some patient develops several

clinical manifestations which include bleeding, shock, myocarditis, Multi Organ Dysfunction Syndrome (MODS). In dengue endothelial dysfunction leads to increased capillary permeability, a cardiovascular collapse which in turn leads to myocardial dysfunction. Dengue myocarditis is a lethal complication of dengue infection [5, 6].
Cardiac dysfunction associated with dengue infection has been under-diagnosed in clinical practice, although dengue myocarditis is less common and is more commonly associated with DHF/DSS.

Table 9: Comparison of different studies

Study	Tawatchhai K *et al.* [7]	Banwari Lal Yadav [8]	Present Study
Place	USA	Jaipur, India	Bangalore
Sample size	119	104	110
Troponin-T	4.72	-	0.07
CPK-MB	11.4	93.64	213.28

There are fewer studies were conducted for the evaluation of cardiac biomarkers in dengue infection.

Table 10: Comparison of different studies

Study	Siddappa FD [9]	Gupta e*t al.* [10]	Present Study
Place	Hubballi Karnataka	Delhi	Bangalore
Sample size	39	28	110
CPK-MB	2	22(78.55%)	84
Troponin-T	-	12(42.8%)	

Gupta *et al*. conducted a study on 28 patients in new Delhi, which showed CPK-MB elevation in 22 patients and Troponin-T was elevated in 12 patients. Siddappa FD conducted a study of over 39 patients, in which 2 cases were positive for CPK-MB.

Conclusion

In 110 biomarker positive cases, 32(17.3%) had a shock,14 (7.6%) had bleeding manifestations, 78(42.2%) cases had elevated SGOT and SGPT and PT and aPTT elevated in 84(45.4%) and 44(23.8%) cases respectively.

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