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Original Research

Echodcardiogarphic changes associated with dengue haemorrhagic fever

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ABSTRACT:
Aim: the aim of the present study to determine the echodcardiogarphic changes associated with dengue haemorrhagic fever. **Materials and methods:** This prospective observational study was carried out after taking the approval of the protocol review committee and institutional ethics committee. All the 50 cases with dengue fever attending OPD/IPD with positive dengue serology (RDT) and age > 15Years were included in this study. **Results:** The major presenting complaint among patients was fever and body ache present in all patients. Rashes were observed in 16 (32%) cases. Subconjunctival hemorrhage, nose bleeding, and gum bleeding were accounted for in 5 (10%), 4(8%), and 2(4%) cases respectively and hematemesis was observed in only 1(2%) cases. Out of the total 58 patients, 40 (80%) had dengue fever and 7 (14%) had dengue hemorrhagic fever and only 3(6%) had dengue shock syndrome. ECG findings - Non-Specific ST Segment Changes (8, 16%) was observed in maximum cases. Broad QRS " Complex'' and Diffuse 'T' Wave Inversion were accounted for in 7 (14%) cases. The above parameters were suggestive of myocarditis and were accounted for in 8 cases (16%). Sinus Bradycardia and "Low Voltage 'QRS' Complex" was present in 6(12%) and 2(4%) cases respectively. Diastolic dysfunction and pericardial effusion were presented in only 1(2%) cases. Global hypokinesia was found absent in all cases, Serositis was presented in 8(16%) patients and pericardial effusion was seen in only 1 (2%). **Conclusion:** The natural history of dengue infection usually follows a clear pattern. The majority of infections are asymptomatic and subclinical. As the incidence of dengue increases, reports of atypical manifestations are also on the rise, although these may be underreported because of lack of awareness and under-diagnosis of dengue.
Keywords: Echodcardiogarphic, dengue haemorrhagic fever

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INTRODUCTION

Dengue fever is a major health concern in India. Dengue is a mosquito-borne viral infection that causes significant morbidity in endemic regions, with 96 million cases clinically reported annually.[1] The causative agent is a dengue virus (DENV, 1–4 serotypes), which is a highly prevalent arbovirus found in tropical and subtropical regions.[2] The first case of dengue in India was reported in 1956 in Vellore, and the first case of dengue hemorrhagic fever was observed in Calcutta in 1963.[3] The annual incidence of dengue in India has been estimated to be around 7.5–32.5 million,[4] and it is one of the leading causes for hospitalization and death in India.[5] According to the World Health Organization (WHO), there has been an increase in reporting of dengue cases for the past five decades.[3] Dengue infection is prevalent in a majority of the states in India.[6] Along with an increase in dengue incidence, atypical manifestations of dengue are on the rise, and it is likely to be underreported.7

The clinical manifestations in dengue range from asymptomatic infection to severe viral hemorrhagic fever as a prelude to plasma leakage and bleeding.[3,8] 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.[9,10] 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.[11–13] 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).[14,15] The variation in symptoms can be attributed to the different criteria used for defining cardiac manifestations. "Expanded dengue syndrome" is a newly structured class by WHO, comprising unusual manifestations with organ involvement.[16]

The aim of this study was to evaluate if cardiac involvement was present in children with dengue fever. The primary objective of the study was to determine the incidence of cardiac involvement in pediatric patients with dengue, dengue with warning signs, and severe dengue. The secondary objective of the study was to identify a correlation between the clinical cardiac findings and the investigations done in these children with dengue fever.

MATERIAL AND METHODS

This prospective observational study was carried out after taking the approval of the protocol review committee and institutional ethics committee. All the 50 cases with dengue fever attending OPD/IPD with positive dengue serology (RDT) and age > 15Years were included in this study. Patients on medication(beta-blockers, digoxin) affecting the heart rate/rhythm, Patient with preexisting cardiac disease, DM, HTN, COPD and Age <15 years were excluded from this study.

METHODOLOGY

Patients who had given written informed consent been are enrolled after reading the consent in the local language. All patients of fever with body ache coming to OPD/IPD were investigated for dengue fever by the rapid diagnostic test. All testing was performed according to the manufacturer's instructions. Patients who had been positive dengue serology were screened by Electrocardiography and Echocardiography for cardiac involvement. Patients diagnosed with Dengue fever were also subjected to routine blood investigations like complete hemogram, renal function tests, liver function test, chest radiography, and ultrasonogram of the abdomen.

RESULTS

A total of 50 patients were selected for the study. The age of patients ranged from 15 to 55 years with a mean age of 27.96 years. Majority were in the age groups from 15-25 (46%) years and followed by 26-35 years (32%), 46-55 years (20%) and 56-65 years (2%). The gender distribution among the study population was found accordingly- Male (62%) and Female (38%).

Table-1: Distribution of patients according to the presenting complaints.

Type of Complaint	No. of Patients (n=50)	Percentage
Fever	50	100
Gum Bleeding	2	4
Body Ache	50	100
Rashes	16	32
Hematemesis	1	2
Nose Bleeding	4	8
Subconjunctival Haemorrhage	5	10

The major presenting complaint among patients was fever and body ache present in all patients. Rashes were observed in 16 (32%) cases. Subconjunctival hemorrhage, nose bleeding, and gum bleeding were accounted for in 5 (10%), 4(8%), and 2(4%) cases respectively and hematemesis was observed in only 1(2%) cases.

Table-2: Distribution of patients according to the type of dengue.

Dengue Type	No. of Patients (n=50)	Percentage
Dengue Fever	40	80
Dengue Haemorrhagic Fever	7	14
Dengue Shock Syndrome	3	6
Total	50	100

Out of the total 58 patients, 40 (80%) had dengue fever and 7 (14%) had dengue hemorrhagic fever and only 3(6%) had dengue shock syndrome.

Table-3: Distribution of patients according to the ECG findings.

Distribution of ECG Findings	No. of Patients (n=50)	Percentage
Normal ECG	20	40
Broad ‘QRS’ Complex	7	14
Diffuse 'T' Wave Inversion	7	14
Low Voltage 'QRS' Complex	2	4
Non-Specific 'ST' Segment Changes	8	16
Sinus Bradycardia	6	12
Total	50	100

ECG findings - Non-Specific ST Segment Changes (8, 16%) was observed in maximum cases. Broad QRS " Complex’’ and Diffuse 'T' Wave Inversion were accounted for in 7 (14%) cases. The above parameters were suggestive of myocarditis and were accounted for in 8 cases (16%). Sinus Bradycardia and “Low Voltage 'QRS' Complex” was present in 6(12%) and 2(4%) cases respectively.

Table-4: Distribution of patients according to the echocardiography findings.

Distribution of ECHO Findings	No. of Patients (n=50)	Percentage %
Diastolic Dysfunction	1	2
Global Hypokinesia	0	0.0
LVEF % (Normal)	50	100
Serositis	8	16
Pericardial Effusion	1	2

Diastolic dysfunction and pericardial effusion were presented in only 1(2%) cases. Global hypokinesia was found absent in all cases, Serositis was presented in 8(16%) patients and pericardial effusion was seen in only 1 (2%).

Table-5: Distribution of cardiac manifestation among dengue type.

Symptoms	Dengue Type			Percentage %
Sinus Bradycardia	DF	DHF	DSS	
Absent	38	2	1	41 (82%)
Present	2	5	2	9(18%)
	40 (80%)	7 (14%)	3 (6%)	50 (100 %)
Significance level P < 0.0001				
Diastolic dysfunction	DF	DHF	DSS	
Absent	40	4	3	47 (94%)
Present	0	3	0	3 (6%)
	40 (80%)	7 (14%)	3 (6%)	50 (100 %)
Significance level P = 0.0245				
Pericardial Effusion	DF	DHF	DSS	
Absent	40	4	3	47 (94%)
Present	0	3	0	3 (6%)
	40 (40%)	7 (14%)	3 (6%)	50 (100 %)
Significance level P = 0.0245				
Myocarditis	DF	DHF	DSS	
Absent	35	3	1	39 (78)
Present	5	4	2	11 (22%)
	40(80%)	7 (14%)	3 (6%)	50 (100 %)
Significance level P = 0.0002				

In the present study group of 50 patients, it was found that 40 patients (80%) have not shown any cardiac abnormalities and 7 patients have abnormal values (14%) but are not significant.

DISCUSSION

There have been reports that the increased rest- ing diastolic calcium ion levels present in the myo-cardium precipitated by dengue can be attributed to the arrhythmia and diminished left ventricular function noted in these patients.[17] Dengue fever has been observed in all age groups in the present study population of 50 patients. The mean age of the population was 27.94 years with a male to female ratio of 1.6:1 indicating male preponderance. Electrocardiography was normal in 78% of the study population and 16% had cardiac manifestations based

on ECG. Although in a study by Kularatne, 62.5% of patients had abnormal ECG findings.[18] In the present study, ECG findings 'Non-Specific ST' Segment Changes' 8 (16%) was observed in maximum cases. 'Broad 'QRS' Complex' and 'Diffuse 'T' Wave Inversion' were accounted for in 7 (14%) cases. These parameters are suggestive of myocarditis.

The most common ECG abnormality noted was Non-Specific ST' Segment changes found in 16% patients, others i.e. Broad 'QRS' Complex, Diffuse 'T' Wave Inversion and Myocarditis and Sinus Bradycardia were had 12.1-15.8% contribution, only low voltage 'QRS' complex found in 3.4%% of the patients. On the other hand, Arora and colleagues reported a 37.5% prevalence of myocarditis with a positive correlation with the severity of dengue fever in their patients.[19]

Lakshman et al. studied the prevalence of cardiac involvement among fifty admitted dengue patients and reported evidence of myocardial involvement in 16% and 30% of patients based on 2D- echo and biomarker testing, respectively.[20] Satarsinghe et al. in 2007 found that 24% of patients had echocardiographic abnormality without clinical features of myocarditis.[21]

In the present study on ECHO, Sinus bradycardia was observed as maximum in 9 (18%) cases while diastolic dysfunction and pericardial effusion were presented in 3 (6%). Serositis was presented in 8 (16%) patients only. It was found that echocardiographic findings are often subclinical since most of the patients showed normal findings. In the study by Salgado et al. echocardiographic evaluation was done in 18 patients.

Three patients were noticed to have mild pericardial effusion and myocarditis was not seen in any patient. In the study by Gupta et al., systolic dysfunction was absent in all patients; mild diastolic dysfunction was present in 14.28 percent. Wiwanitkit et al., have described cases of dengue myocarditis. [22,23,24] Arora and Patil found that the incidence of cardiac manifestations was 30%, 35.29%, and 53.33% in patients of dengue fever, DHF, and dengue shock syndrome, respectively. Cardiac manifestations were not found to be statistically significant when correlated to different age groups. Since the number of patients in dengue fever and dengue shock syndrome categories was small, some patients did not give consent for echocardiography, and some patients were not able to be shifted to the examination room due to his/her severity of disease; statistical differences though analyzed may not be robust.

Similarly, no statistical significance between thrombocytopenia and occurrence of cardiac manifestations ($P<0.05$) was found. Thus, it can be postulated that similar to other factors, cardiac involvement also did not have any significant correlation with thrombocytopenia.

These reported findings are not consistent with the aspect of myocardial infestation in dengue. A study by Miranda et al. found that two patients had reduced left ventricular function, two had left ventricular segmental hypokinesia, and one had pericardial effusion.[25] The increased production of cytokines including tumor necrosis factor-alpha and interferon-alpha and release of other chemical mediators is responsible for the rise in vascular permeability and abnormal leakage of plasma leading to a pericardial effusion.[26]

In the present study, it was found that pericardial effusion is minimal and asymptomatic, and often resolves with time. The need for pericardiocentesis does not arise most of the time since capillary leakage causing pericardial effusion is transient and a self-limiting phenomenon.[27] Similar findings were noted in a study by Yusoff et al. [28]

As a result, fluid resuscitation in dengue should be guided by hematocrit, blood pressure, and urine output as overzealous fluid therapy can cause pericardial effusion.[29] The postulated underlying mechanisms for reduced left ventricular ejection fraction are immune in origin although myocarditis may be a contributory factor.[30] It is also postulated that the mechanism of cardiac dysfunction is the direct infection of cardiac muscle cells by DENV. [31]

CONCLUSION

The natural history of dengue infection usually follows a clear pattern. The majority of infections are asymptomatic and subclinical. As the incidence of dengue increases, reports of atypical manifestations are also on the rise, although these may be underreported because of lack of awareness and under-diagnosis of dengue.

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