

Study of Cardiac Manifestation in Patients with Seropositive Dengue Fever and to Find Correlation with Subclinical Cardiac Involvement

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ABSTRACT

Objective: The main objective of the present study was to observe the electrocardiogram (ECG) changes in dengue fever and to find correlation with subclinical cardiac involvement.

Methods: This was an observational, prospective, non-randomized study. High grade fever for one to five days diagnosed as dengue infection later confirmed by dengue tests (NS1, IgG and IgM ELISA) were included in this study. Prior to the commencement of the study informed consent was taken from all the participants. With 12 lead ECG taken during the febrile phase of dengue fever randomly selected serologically confirmed cases of dengue fever were evaluated at an interval of 24 hrs. for a total of five days. On the day of admission when the patient was afebrile, echocardiography was done. Plasma leakage was diagnosed by presence of any one of four: subcutaneous oedema (pedal oedema, facial puffiness) or pleural effusion or pericardial effusion or ascites.

Result: A total 80 patients who were admitted to hospital during study periods due to symptoms of dengue fever and IgM dengue positive status were included in this study. Among this total population of 80 patients (N=80) 48 were male and 32 were female. Out of these, majority were diagnosed as DF 52 (65%), 23 (29%) were diagnosed as DHF and rest only 5 (6%) were diagnosed as DSS. Total 54 patients were found to have normal ECG among which 35 were having dengue fever, 16 were having DHF and 3 were having DSS. Total 2 patients were diagnosed to have left ventricular hypertrophy among which one had dengue fever and rest two had DHF. ST

depression was observed in total 7 patients in which 5 were had dengue fever and 2 were had DHF. Relative bradycardia was found in 14, tall t waves in 2 and ventricular ectopics in 1 patient (table 2). Abnormal ECG findings were compared using Chi-square test and were found to be statistically significant ($P < 0.05$) in dengue fever and DHF. There was statistically significant correlation between ECG abnormalities and abdominal pain and mucosal bleed. The presence of plasma leakage was observed among 77 (96.3%) patients. Proportion of echocardiography abnormalities were higher among patients with plasma leak 6 (30%) as compared to without plasma leak 9 (15%), this difference was not found to be statistically significant

Conclusion: In all type of Dengue infections incidence of cardiac involvement was quite high. Due to the overlapping clinical manifestations such as capillary leak associated with DENV infection, tachycardia, pulmonary edema, and hypotension as well as due to the low index of clinical suspicion cardiac involvement in dengue fever is often underdiagnosed.

Keywords: Cardiac manifestation, dengue infection, echocardiography, electrocardiography.

INTRODUCTION

The dengue virus is an arbovirus from genus Flavivirus Family Flaviviridae. It is a single stranded RNA genome surrounded by an icosahedral nucleocapsid and covered by lipid envelope. Four serotypes: DEN-1,2,3,4 have been identified for the virus. Each serotype provides

specific lifetime immunity, but only a short-term cross-immunity. All serotypes can cause severe and fatal disease.

The vector for Dengue is the *Aedes aegypti* mosquito which is also known as the Tiger mosquito, due to the characteristic striped body appearance. It is a highly domesticated mosquito and lays eggs and produces larvae preferentially in artificial containers. Two peaks of biting activity are known for the mosquito - 2-3 hours after the daybreak and in the evening a couple of hours before sundown. The mosquito is a silent and fearless biter and does not buzz. It often feeds on several persons during a single blood meal in a short period of time. If infective, it can transmit the virus even while probing without taking blood meal [1].

The infected monocytes release vasoactive mediators, resulting in increased vascular permeability and hemorrhagic manifestations that characterise dengue hemorrhagic fever (DHF) and Dengue shock syndrome (DSS) [2]. Early bone marrow suppression causing leukopenia, thrombocytopenia, decreased neutrophil and monocytes are seen in DHF. Decreased levels of fibrinogen, prothrombin, factor II, VII, VIII, IX, X, XII, ATIII, protein C and S have been reported. The classical markers of disseminated intravascular coagulation may be absent. PT, aPTT, TT may be normal or increased. The levels of C3 and C5 are depressed and C3a and C5a are elevated [3]. The cause of thrombocytopenia observed in dengue fever is controversial. It has been proposed that there is impaired megakaryocytic production and increased platelet destruction. The causes of platelet injury have been attributed to the virus itself, circulating anti platelet antibodies, immune complexes and DIC. In addition, platelet function abnormalities contribute to bleeding [3]. Severe dengue infections may give rise to many complications such as hemolytic uremic syndrome, acute renal failure, myocarditis, disseminated intravascular coagulation, encephalopathy and liver failure.

The correlation of heart abnormalities and dengue is still postulated as rare events. Isolated cases of myocarditis, supra ventricular arrhythmias, atrioventricular block, junctional rhythm and other atrioventricular conduction disorder were reported in various medical literature [4,5]. Though acute phase of dengue hemorrhagic fever and ventricular dysfunction has been documented by various researchers but still in clinical practice it was under diagnosed [6].

The main objective of the present study was to observe the electrocardiogram (ECG) changes in dengue fever and to find correlation with subclinical cardiac involvement.

METHOD

This observational, prospective, non-randomized study was conducted at medicine department and conducted for the period of 12 months from March 2020 to February 2021. Prior to the commencement of the study informed consent was taken from all the participants. With 12 lead ECG taken during the febrile phase of dengue fever randomly selected serologically confirmed cases of dengue fever were evaluated at an interval of 24 hrs. for a total of five days. ECG changes included sinus bradycardia, sinus tachycardia, inverted T waves, nonspecific ST-T wave changes and first degree heart block. On the day of admission when the patient was afebrile, echocardiography was done. Parameters which were observed by the echocardiography Left ventricular ejection fraction (LVEF), Measurements of LV walls, Transmitral pulsed-wave Doppler velocities (peak E-and A-wave velocities), Peak tissue medial and lateral S-wave (S) and E-wave (e') velocities. Plasma leakage was diagnosed by presence of any one of four: subcutaneous oedema (pedal oedema, facial puffiness) or pleural effusion or pericardial effusion or ascites.

Inclusion criteria:

- High grade fever for one to five days diagnosed as dengue infection later confirmed by dengue tests (NS1, IgG and IgM ELISA).

Exclusion criteria:

- Patients with thyroid disease, mixed infection, pulmonary disease and any cardiac abnormality like conduction disorder, dilated cardiomyopathy, rheumatic heart disease,
- Patients on medication affecting heart rate such as B2 antagonist, B2 Agonist, Theophylline and its derivative.
- Electrolyte imbalance- Hyperkalemia, Hypokalemia, Hypercalcemia, Hypocalcemia etc.

Classification of patients:

The patients were classified according to WHO classification of dengue [7], dengue fever (DF), dengue haemorrhage fever (DHF) and dengue shock syndrome (DSS).

Dengue fever: This is an acute biphasic fever with headache, myalgias, arthralgia, rashes and leucopenia. Although DF is usually a benign lines, however it may present with severe debilitating arthralgia and myalgia with occasional haemorrhage.

Dengue hemorrhagic fever: DHF is most common in children less than 15 years and characterised by acute onset of fever associated with non-specific constitutional signs and symptoms. This is a hemorrhagic diathesis and tendency to develop fetal shock. Abnormal homeostasis and plasma leakage are the main patho-physiological changes with thrombocytopenia and hemoconcentration presenting as constant findings. DHF has sometime been documented in primary infections also. A hemorrhagic tendency shown by at least one of the following: petechiae, a positive tourniquet test, bleeding from infection site or other location, gastro-intestinal tract, mucosa, purport or ecchymoses, or hematemesis or melena.

Dengue Shock Syndrome: DHF plus circulatory failure and can be associated with bronchial asthma and long-standing chronic host illness and presented with signs of shock such as narrow pulse pressure (<20 mmHg), weak and rapid pulse, hypotension (>90 mmHg), cold clammy skin and mental status alteration.

Statistical Analysis

Statistical Package for Social Sciences (SPSS) version 21.0 were used to conduct statistical calculation and analysis. Mean±SD were used to present continuous data whereas percentage data were used to present frequency data. By using descriptive test statistical analysis was done and inferential statistics using was done by using one-way ANOVA, Student's unpaired *t*-test and Chi-square test. A 'p' value < 0.05 was considered to indicate a significant association and as the level of significance.

RESULT

A total 80 patients who were admitted to hospital during study periods due to symptoms of dengue fever and IgM dengue positive status were included in this study. Among this total population of 80 patients (N=80) 48 were male and 32 were female.

Table 1: Baseline clinical characteristics of dengue patients

Character	Number of patient
Age (Years)	43.6 ± 11.6
<i>Gender</i>	
Male	48 (60%)
Female	32 (40%)
<i>Age range (years)</i>	
15-30	16 (20%)
31-45	33 (41.25%)
46-60	17 (21.25%)
>60	14 (17.5%)

Out of these, majority were diagnosed as DF 52 (65%), 23 (29%) were diagnosed as DHF and rest only 5 (6%) were diagnosed as DSS (Figure 1).

Table 2 demonstrated the comparison of Electrocardiography Findings of Patients with Different Clinical Types of Dengue. Total 54 patients were found to have normal ECG among which 35 were having dengue fever, 16 were having

DHF and 3 were having DSS. Total 2 patients were diagnosed to have left ventricular hypertrophy among which one had dengue fever and rest two had DHF. ST depression was observed in total 7 patients in which 5 were had dengue fever and 2 were had DHF. Relative bradycardia was found in 14, tall t waves in 2 and ventricular ectopics in 1 patient (table 2). Abnormal ECG findings were compared using Chi-square test and were found to be statistically significant ($P < 0.05$) in dengue fever and DHF.

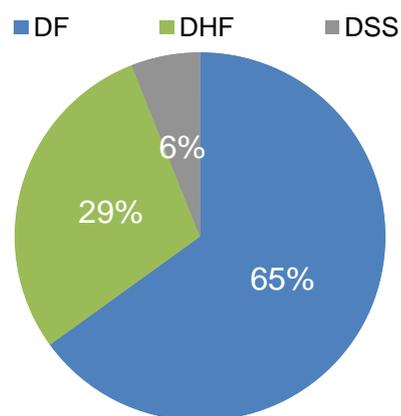


Figure 1. Percentage Distribution of Different Clinical Types of Dengue

Table 2: Comparison of Electrocardiography Findings of Patients with Different Clinical Types of Dengue

Electrocardiography Finding	Total (N=80)	Dengue Fever (n=65)	Dengue Haemorrhagic Fever (n=29)	Dengue Shock Syndrome (n=6)
Left Ventricular Hypertrophy	2 (2.5%)	1 (1.54%)	2 (6.89%)	0
Normal	54 (67.5%)	35 (43.75%)	16 (55.17%)	3 (50%)
ST Depression	7 (8.75%)	5 (6.25%)	2 (6.89%)	0
Relative Bradycardia	14 (17.5%)	6 (7.5%)	8 (27.58%)	0
Tall T Waves	2 (2.5%)	0	1 (3.44%)	1 (16.6%)
Ventricular Ectopics	1 (1.25%)	0		1 (16.6%)
P value	0.05	0.028	0.045	0.1

Table 3: Correlation of warning signs to ECG abnormality

Warning signs	ECG abnormality	
	Yes	No
Persistent vomiting	18	14
Mucosal bleed	8	2
Abdominal pain	31	9
Lethargy	12	12
Hepatomegaly	3	5
Swollen Sock	2	0
Respiratory distress	5	1

In dengue patients, correlation between ECG changes and warning signs were demonstrated in table 3. There was statistically significant correlation between

ECG abnormalities and abdominal pain and mucosal bleed.

The presence of plasma leakage was observed among 77 (96.3%) patients. Proportion of echocardiography abnormalities were higher among patients with plasma leak 6 (30%) as compared to without plasma leak 9 (15%), this difference was not found to be statistically significant (Table 4).

Table 4: Association of Echocardiography Abnormalities with Plasma Leak

Observation	Total (N=80)	Plasma Leak Present (N=20)	Plasma Leak Absent (N=60)	χ^2	P
Echocardiography Abnormalities	15 (19%)	6 (30%)	9 (15%)	1.872	0.231

DISCUSSION

Epidemics of an illness resembling dengue have been known to have occurred in 1779, 1780 across three continents of Asia, Africa and North America. The first epidemic of DHF in recent times occurred in Manila, Philippines 1953. In India dengue virus was first isolated in Calcutta in 1945 and the epidemic of DHF first occurred in Calcutta in 1963. Since even epidemics of dengue fever have been reported from

various parts of India and mostly attributed to strains DEN 2 and DEN 3.

Features of encephalitis such as seizures and coma are rare in DHF but have been observed during study procedure. These may occur as a result of prolonged shock and bleeding within internal organs. Inappropriate use of water in treatment leading to hyponatremia may cause features of encephalopathy. Subdural effusions have been observed in some cases. Febrile convulsions may be seen in infants. Fetal

cases of encephalitis have been reported. Acute liver failure and renal damage usually occur at the terminal stage and may be associated with encephalopathy features. There is a marked rise in AST and ALT in these cases. Renal failure and haemolytic uremic syndrome are observed in some cases. Some of the cases were seen in patients with underlying factors such as G6PD or hemoglobinopathy causing an intravascular hemolysis.

Out of 80 patients, 26 (32%) had abnormal electrocardiography and 54 (68%) patients had normal one. Likewise, the finding of the current study various other studies like Tarique et al were also noticed abnormal ECG among patients suffering from dengue infection but incidence was slightly higher than our study (67.24%) [8].

Abnormal ECG were also noticed in other studies like Tarique et al, but incidence was slightly higher than our study (67.24%) [8]. In current study, relative bradycardia was found in 14, tall t waves in 2 and ventricular ectopics in 1 patient. In study done by Aisha Lateef et al., similar incidence of relative bradycardia was found [9]. Similar to our study, in the study done by Tarique et al. [8], abnormal ECG findings e.g. supraventricular tachycardia, poor progression of R wave, left bundle branch block, tachycardia, bradycardia, ST depression, were noted. In our study 15 patients has echocardiography changes, in similar to this finding Wali et al [10] also documented that patients of dengue haemorrhagic fever had electrocardiography changes.

Abdominal pain (50%) and Vomiting (43%) was the most common warning sign in this study. In a similar fashion fever and persistent vomiting was noted in 39% of cases documented by Thien et al [11] and was most common warning sign. Similar result was also documented by Kumar S et al [12].

Despite the fact that the present study findings have potential clinical implications but also have certain limitations. Quantitative assay of

biomarkers and evaluation of cardiac markers could not be assessed. Because of poor compliance of the patients towards follow-up repeated electrocardiographic and echocardiographic evaluation not done. Further studies to assess impact of management following cardiac abnormality detection are warranted.

CONCLUSION

In all type of Dengue infections incidence of cardiac involvement was quite high. Due to the overlapping clinical manifestations such as capillary leak associated with dengue infection, tachycardia, pulmonary edema, and hypotension as well as due to the low index of clinical suspicion cardiac involvement in dengue fever is often underdiagnosed. Dengue affects pericardium, myocardium, endocardium as well as electrical conduction system of the heart. In dengue viral fever patient, sinus bradycardia was the most common electrocardiographic change, which resolved spontaneously over period of 36 to 48 hours.

Declaration of Conflicting Interests

The author declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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REFERENCES

1. Gubler DJ. Dengue and dengue hemorrhagic fever. Clin Microbiol Rev 1998;11(3):480-96.
2. Rice CM. Flaviviridae: The viruses and their replication. In: Virology Fields BN, Knipe DM, Howley PM Eds. 3ed., Philadelphia:

- Lippincott-Raven Publishers, 1996. P.931-59.
3. Willis BA, Oragui EE, Stephens AC, et al. Coagulation abnormalities in dengue hemorrhagic Fever: Serial investigations in 167 Vietnamese children with Dengue shock syndrome. Clin Infect Dis 2002; 35(3):277-85.
 4. Sheetal S, Jacob E. A Study on the Cardiac Manifestations of Dengue. JAPI. 2016; 64:30-5.
 5. Wichmann D, Kularatne S, Ehrhardt S, Wijesinghe S, Brattig NW, Abel W, et al. Cardiac involvement in dengue virus infections during the 2004/2005 dengue fever season in Sri Lanka: Southeast Asian J Trop Med Public Health. 2009;40:727- 30.
 6. Pesaro AE, D'Amico E, Aranha LF. Dengue: cardiac manifestations and implications in antithrombotic treatment. Are Bras Cardiol 2007; 89:e12-5.
 7. Yadav RK, Kumar S. To study cardiac manifestations in patients presenting with dengue infection and to find out the correlation of cardiac manifestations to warning signs of dengue. Int J Adv Med 2017;4:323-8.
 8. Tarique S, Murtaza G, Asif S, et al. Electrocardiography manifestations in dengue infection. Annals 2013;19:4.
 9. Lateef A, Fisher DA, Tambyah PA. Dengue and relative bradycardia. Emerg Infect Dis 2007;13(4):650-651.
 10. Wali JP, Biswas A, Chandra S, et al. Cardiac involvement in dengue haemorrhagic fever. Int J Cardiol 1998; 64(1): 31-36.
 11. Thein S, Aung MM, Shwe TN, Aye M, Zaw A, Aye K, et al. Risk factors in dengue shock syndrome. Am J Trop Med Hyg. 1997;56:566-72.
 12. Kumar S, Suman S, Ranjan R. A clinical and biochemical study of dengue fever in Kosi region of Bihar, India. Int J Adv Med 2017;4:964-7.

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