

Patterns of ECG Manifestations in Dengue Infection

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Abstract:

Background: Dengue fever has emerged as one of the most common viral diseases in the world. The clinical manifestation ranges from mild febrile illness to severe disease such as dengue hemorrhagic fever and dengue shock syndrome. Dengue is known to affect various systems. So, different aspects of disease need to be explored. Cardiac involvement in dengue fever is not uncommon and has been reported in literature. ECG is widely used as a screening tool not only because it is easily available but also due to its ability to indicate cardiac involvement.

Objective: The aim of the study was to determine the patterns of ECG changes and their frequency in a cohort of patients with dengue fever (DF) and dengue hemorrhagic fever (DHF) along with the association of ECG changes with severity of dengue infection and clinical manifestation of cardiac involvement.

Method: We conducted a cross-sectional observational study involving 50 patients with dengue fever and dengue hemorrhagic fever, admitted in Medicine department of Dhaka Medical College Hospital, Dhaka from 1st October, 2017 to 31st March, 2018. Admitted patients with high grade fever and positive Dengue IgM, NS, AG or RT-PCR were included. Patients with electrolyte abnormalities, preexisting heart disease, drugs interfering with heart rhythm were excluded from study.

The Standard 12 lead ECG was carried out in study patients on 3rd day of disease onset and on the day of discharge after disease recovery. Frequency & pattern of ECG changes like heart rate, rhythm, P wave, T wave, ST segments and QRS complex were analyzed and recorded. Statistical analysis was done using SPSS 25 on windows 10. Categorical and numerical data's were expressed as frequencies and percentage. Cross tabulation was done between DF and DHF with different ECG findings. To establish the significance of various findings and association in between variables chi-square analysis, Pearson correlations were done in all cases. P value < 0.05 considered significant

Result: Total 50 patients with dengue fever were enrolled, 39 patients (78%) were diagnosed as dengue fever and 11 patients (22%) were diagnosed as dengue hemorrhagic fever (DHF). Mean age of the patient was 33.08 ± 9.79 years. Male – female ratio of 1.5:1 fever was noted in all 50 patients (100%), myalgia (94%), headache (84%), skin rash (82%), & retro-orbital pain(54%), vomiting (26%), only 3 patients (6%) complained about abdominal pain. Only 4 patients had cardiac symptoms. 3 patients complained about palpitation and only 1 patient had symptom of chest pain and dyspnea. In most of the patients, (34 in number, 68%) ECG was normal. Only 16 patients (32%) had abnormal findings in ECG. 9 patients (18%) had bradycardia, 3 patients (6%) had tachycardia, 2 Patient (4%) had T Inversion and 1 patient (2%) had ST elevation and 1 patient (2%) had ST depression. Among total 16 abnormal ECG, predominant finding was bradycardia (>50% of abnormal ECG). P value is <0.01.

Correlation of ECGs with clinical severity (Dengue fever and Dengue Hemorrhagic fever) found no statistically significant association (P value is 0.725).

Key words: Dengue fever, ECG manifestations, Bradycardia, Transient cardiac symptoms.

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Introduction:

One of the most important mosquito borne viral diseases in world is dengue infection. Dengue is a member of Flaviviridae family consisting of a single stranded RNA virus with four serotypes: DENV-1, DENV-2, DENV-3 and DENV4.¹

The natural history of dengue infection usually follows a clear pattern. Symptomatic disease follows an incubation period of four to seven days, and begins as an acute febrile illness with high temperature, malaise, retro-orbital headache, myalgia, backache, nausea, loss of appetite, and vomiting.² The critical phase is defined by the occurrence of features of plasma leakage, rising hematocrit, clinical or radiological evidence of third space fluid leakage, and, in some cases hypotension. A proportion of patients develop clinical shock, of which a minority proceed to develop severe intractable shock, coagulopathy with bleeding and multi-organ failure which can culminate in death.³

As the incidence of dengue increases, reports of atypical manifestations are also on the rise, although these may be underreported.⁴ Cardiac involvement is not uncommon and is encountered in centers handling large numbers of dengue cases. Relative bradycardia is a notable clinical feature of Dengue fever. Relative bradycardia was first reported from Singapore in 2005.⁵ Also Clinical manifestations of cardiac involvement can vary widely from silent disease to severe myocarditis resulting in death. Rhythm abnormalities, hypotension, arrhythmias, myocarditis, myocardial infarction and pericarditis has been reported.⁶

Still, the significance of cardiac involvement in dengue infection is not fully understood. According to the histopathological analysis, dengue virus has a direct action on myocardium through autoimmune response against cardiac epitopes.⁷ Evidence is increasing that dengue can cause myocardial impairment, arrhythmias and occasionally fulminant myocarditis. No antiviral agents are licensed for dengue and treatment remains supportive with judicious fluid replacement for patients with severe disease.⁸

ECG abnormalities may be asymptomatic or go undetected. Clinical manifestations suggesting cardiac involvement in dengue are diverse and include chest pain, palpitations, pleurisy, and irregularities of pulse, bradycardia, hypotension, pulmonary edema, and features of shock.⁹

Patients with dengue fever are at risk of developing myocarditis and rhythm disturbance and therefore require a close cardiac monitoring.¹⁰ Studies relating cardiac involvement and ECG changes with Dengue fever in our country are scarce. Hence, this study was taken up to observe the pattern of heart rate and other electrocardiographic changes associated with Dengue fever.

Materials & methods:

We conducted a cross-sectional observational study involving 50 patients with dengue fever and dengue hemorrhagic fever, admitted in Medicine department of Dhaka Medical College Hospital, Dhaka from 1 October, 2017 to 31 March, 2018. Sampling was done by purposive sampling method & sample size was calculated by using a standard formula. Though calculated sample size was bigger but we enrolled 50 cases due to time & resource limitation.

Ethical clearance was taken from Institutional ethical review committee (ERC) of Dhaka Medical College. Admitted Patients with high grade fever with positive Dengue IgM / Dengue NS₁ AG /Dengue RT-PCR were included in the study. Patients with electrolyte abnormalities, preexisting heart disease, drugs interfering with heart rhythm were excluded from study.

The informed consent of the patients was taken by describing the objectives and purpose of the study. They were also given freedom to withdraw themselves from the study whenever they want and were ensured that the information obtained from them will be kept confidential.

Clinical evaluation was done by investigating the patients with complete blood counts including hemoglobin, hematocrit, platelet counts and serum Electrolytes.

After that all enrolled patient was asked in a guided way according to the questionnaire to evaluate clinical sign/symptoms. Their clinical presentation and examination findings were noted.

The Standard 12 lead ECG was carried out in study patients on 3rd day of disease onset and on the day of discharge after disease recovery. After proper positioning of the patient lying quietly in the supine position, leads were placed properly. Electrocardiogram data was checked; type of ECG changes like heart rate, rhythm, P wave, T wave, ST segments and QRS complex were analyzed and recorded.

Data Analysis:

Collected Data sheets were checked carefully for any error, processing works were done which include registration of schedules, coding and computerization, preparation of dummy tables, data analysis and matching.

All the data were entered in IBM Statistical package for Social Science (SPSS) 25 for Windows 10. Categorical & numerical data were expressed as frequencies & percentage. Cross tabulation was done between DF and DHF with different ECG findings. To establish the significance of various findings & association in between variables chi-square analysis, Pearson correlation were done and in all cases. P value < 0.05 considered significant.

Observations & Results:

Total 50 patients with dengue fever were enrolled. 39 patients (78%) were categorized as dengue fever and 11 patients (22%) were diagnosed as dengue hemorrhagic fever (DHF).

On the evaluation of the demographic profile, 19(38%) were between 21-30 years of age. Mean age of the patient was 33.08 ± 9.79 years (Table:1) Out of 50 cases 30(60%) patients were male and 20(40.0%) were female. In this study Male – female ratio was 1.5:1

Table 1: Age distribution of patients

		Frequency	Percent
Age	15-20	4	8.0
	21-30	19	38.0
	31-40	16	32.0
	41-50	9	18.0
	> 50	2	4.0
Total		50	100.0
Mean ± SD		33.08 ± 9.79	

The commonest clinical presentation was Fever, noted in all 50 patients (100%), followed by myalgia (94%), Headache (84%), Skin Rash (82%), Retro-Orbital pain (54%), vomiting (26%), only 3 patient (6%) complained about abdominal pain. (Figure:1).

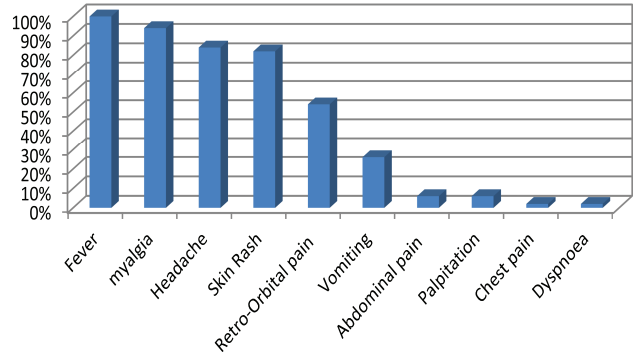


Figure 1: Distribution of clinical Symptoms in study patient (n=50)

Only 4 patients had cardiac symptoms, 3 patients (6%) complained about palpitation and only 1 patient had symptoms of chest pain (2%) and dyspnea (2%), (Figure:2).

In the study, 7 Patients (14 %) had Petechiae, 3 patients (6%) had ascites, 2 patient (4%) had pleural effusion, 2 patients (4%) had Gum bleeding, 1 patient (2%) had Epistaxis and 1 patient had (2%) fresh per rectal bleeding.

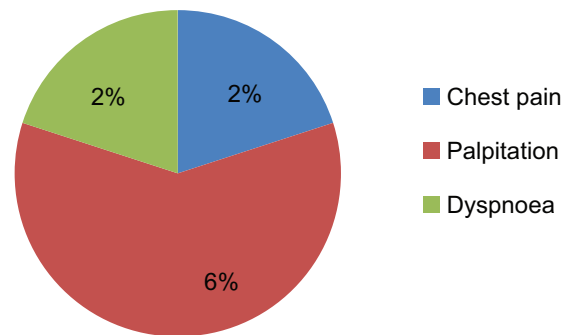


Figure 2: Patterns of Cardiac Symptoms in study patients (n=50)

Out of 50 patients 16 patients (32%) had abnormal finding in ECG, 34 (68%) had normal ECG (Figure: 3).

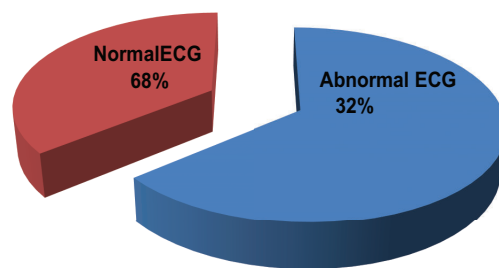


Figure 3: Total Abnormal ECG findings of study subject

We found that, 9 patient (18%) had bradycardia, 3 patient (6%) had tachycardia , 2 Patient (4%) had T Inversion and 1 patient (2%) had St elevation and 1 patient(2%) had ST depression (Table:2)

Our analysis shows that, among total 16 abnormal ECG, predominant finding was bradycardia (>50% cases of abnormal ECG) (Figure 4). Statistically bradycardia, as most common finding is strongly significant. P value is <0.01.

Table 2: Distribution of ECG findings of the patient.

	Frequency	Percent
Normal ECG	34	68.0
Abnormal ECG	16	32.0
Bradycardia	9	18.0
Tachycardia	3	6.0
T Inversion	2	4.0
ST Elevation	1	2.0
ST Depression	1	2.0

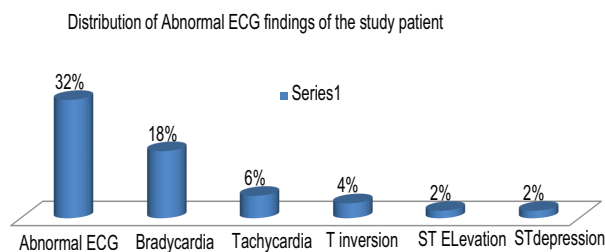


Figure 4: Distribution of Abnormal ECG findings of the study patient (n = 50)

In our analysis, we compared ECG changes with clinical severity, out of 39 patients of Mild Dengue Fever, 12 had abnormal ECG, 27 had normal ECG. In 11 cases suffering from severe Dengue Hemorrhagic Fever, ECG was abnormal in 4 patients, where 7 patients had normal ECG. There was no statistically significant association with clinical severity of the disease (P value 0.725, which is not significant).

Out of 9 patients with bradycardia, none of the patients had any cardiac symptoms. Three patients complained about palpitation and had tachycardia in their ECG. One

Patient with ST elevation presented to us with chest pain and dyspnea and was later diagnosed as acute MI. ECG changes are noted in both symptomatic and asymptomatic patients.

At the time of discharge, ECG was carried out again in patients with abnormal ECG and showed that the changes were normalized in patients with abnormal ECG, indicating transient rhythm changes due to Dengue fever. One patient with chest pain with ST elevation later proved as a case of acute MI. All patients were discharged and no death was occurred.

Discussion:

Maximum number of patients, 19(38%) were between 21-30 years of age, 16(32%) patients were in the age group of 31-40 years. Minimum infected patients, 2 patients (4%) belonged to >50 years of age. Mean age of the patient was 33.08 ± 9.79 years. In the study conducted by Shandana et al¹¹ mean age was 32.88±14.6years.

Out of total 50 cases, 30 patients (60%) were male and 20 patients (40.0%) were female. In the study Male – female ratio was 1.5:1. In the study done by Dr. Rakesh et al¹², most of the patients are males (64) in comparison to females (36) and ratio was 1.7:1.

The Commonest clinical presentation was Fever noted in all 50 patients (100%), followed by myalgia (94%), Headache (84%), Skin Rash (82%), Retro-Orbital pain (54%), vomiting (26%), only 3 patients (6%) complained about abdominal pain. Only 4 patients had cardiac symptoms, 3 patients (6%) complained about palpitation and only 1 patient had symptom of chest pain (2%) and dyspnea (2%). 7 Patients (14 %) had Petechiae,3 patients (6%) has ascites, 2 patient (4%) had pleural effusion, 2 patients (4%) had Gum bleeding, 1 patient (2%) had Epistaxis and 1 patient had (2%) fresh per rectal bleeding. These findings are comparable with other studies. A study by Islam et al¹³, reported similar type of clinical presentation in his study of 50 cases of dengue syndrome. In this study the most frequent findings were fever in all patients (100%), Skin rashes, Retro-orbital pain, back pain, myalgia & other constitutional symptoms. Diarrhea, abdominal pain, organomegaly, ascites, and pleural effusion were infrequent complaints. Petechiae, positive tourniquet test and epistaxis were the most frequent hemorrhagic manifestations in DHF cases. Study conducted by Shandana

et al¹¹ reported cardiac symptoms like chest pain, dyspnea and palpitations in minimum number of patients.

In most of the patients (34 in number, 68%) ECG was normal. 16 patients (32%) had abnormal finding in ECG. Bradycardia was the predominant feature, 18% (9 patients) cases had bradycardia, 3 patients (6%) had tachycardia, 2 Patient (4%) had T Inversion and 1 patient (2%) had ST elevation and 1 patient (2%) had ST depression. More than 50% of total abnormal ECGs had bradycardia, which is the most frequent abnormal finding. All these findings are consistent with other study. Study conducted by Rajiv et al¹⁴ showed similar results, where bradycardia was a predominant ECG abnormality amongst total of 149 cases of Dengue fever analyzed. Study done by Shandana et al¹¹ also reported that commonly noted findings are bradycardia and ST elevation.

In our study, there was no association between abnormal ECG findings with clinical spectrum of the disease. Out of 39 patients of Dengue Fever, 12 had abnormal ECG, 27 had normal ECG. In 11 cases suffering from DHF, ECG was abnormal in 4 patients, where 7 patients had normal ECG. There was no statistically significant association (P value is 0.725, which is not significant).

In a similar study conducted by Mohit et al¹⁰ study, 85 (70.83%) had dengue hemorrhagic fever, 20 (16.67) had dengue fever and only 15 (12.5%) patients had dengue shock syndrome. The incidence of cardiac manifestations was found to be higher in patients with dengue shock syndrome (53.33%). Although the difference was not statistically significant (p=0.325)

Our study showed that only 8% patients had some sort of cardiac symptoms, against ECG changes in 32% of the sample. Most of the patients with abnormal findings in ECG were asymptomatic. ECG changes were noted in both symptomatic and asymptomatic patients.

Study done by Shandana et al¹¹ also noted similar result. In their study cardiac symptoms like chest pain, palpitations were identified but also asymptomatic patient showed ECG abnormality. In a study done by Gupta et al¹⁵, no patient had any cardiac symptom but they had ECG changes like tachycardia and bradycardia.

At the time of discharge, repeat ECG showed that the changes were normalized in patients with abnormal ECG,

indicating transient rhythm changes due to Dengue fever. One patient with chest pain with ST elevation later proved as a case of acute MI. All patients were discharged and no death was occurred.

Mohit et al¹⁰ did serial ECG in his study and report showed transient ECG abnormality as on the discharge day all cases with cardiac involvement showed normal ECG finding

Limitations of the study:

- Sample size was small in this study due to time & resource limitation.
- Cardiac manifestations are often transient and require serial electrocardiographic and echocardiographic evaluation to see myocardial involvement. In this study we could repeat ECG at the time of discharge but Echocardiography & other cardiac markers such as troponins and quantitative assay of biomarkers could not be assessed to all patients in our study due to financial constraint & because of poor compliance of the patients towards follow-up and repeated investigations.

Conclusion:

Cardiac involvement may occur in dengue infection and may be sub-clinical in presentation. Transient ECG changes were noted in both symptomatic and asymptomatic patients. There were no statistically significant association between ECG changes and severity of illness. The rhythm abnormalities in dengue fever tend to be benign and self-limited, and resolve in the majority of patients. A thorough evaluation is warranted in symptomatic patients as well as non-resolving/worsening rhythm disturbances.

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