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RESEARCH ARTICLE

A STUDY TO ASSESS CARDIAC MANIFESTATIONS OF DENGUE FEVER AND ITS CORRELATION WITH WARNING SIGNS

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ABSTRACT

Aims and Objectives: To assess cardiac manifestations in patients of dengue fever and to find out the correlation of cardiac manifestations with prognosis/warning signs of dengue fever.
Methods: It was conducted at Rohilkhand Medical College and Hospital, Bareilly in the Department of Medicine in the month of July to September 2016. Fifty patients of age 20 years or more with positive dengue serology were interviewed and examined after taking an informed consent. ECG was done for all patients and few suspected patients underwent echo evaluation. The data was analyzed using statistical significance tests
Results: 12 patients had no warning signs, 38 patients had one warning sign or the other. Nine patients had severe dengue. The minimum pulse rate was 34 beats/minute. The most common cardiac abnormalities noted were rhythm abnormalities of which the commonest was sinus bradycardia, found in 32 percent. There was statistically significant correlation between cardiac manifestations and all the warning signs except persistent vomiting. Among severe dengue, fluid accumulation causing respiratory distress was found to have a significant correlation with the cardiac manifestations
Conclusion: The most common cardiac manifestations noted were transient rhythm abnormalities, of which sinus bradycardia was the commonest. There was no evidence of myocarditis in any of the patients. There was statistically significant correlation between cardiac manifestations and all the warning signs except persistent vomiting. Among severe dengue, fluid accumulation causing respiratory distress was found to have a significant correlation with the cardiac manifestations

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INTRODUCTION

Arboviruses represent a serious public health problem in tropical and subtropical regions of the world. Dengue virus (DENV), the most important arthropod borne diseases is transmitted to humans by mosquitoes of the *Aedes* family (Rice et al., 1996). All four dengue virus serotypes (DENV- 1, DENV - 2, DENV-3 and DENV-4) can cause the disease which can present as a mild self-limiting illness, dengue fever (DF), or as the more severe forms of the disease, dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS) (Sam et al., 2003). The World Health Organization (WHO) 2009 guidelines classify patients into three groups; dengue without warning signs, dengue with warning signs and severe dengue (World Health Organization et al., 2009). Cardiac manifestations in dengue virus infection can range from asymptomatic bradycardia to life threatening myocarditis (Daniel et al., 2005 and Wiwanikit et al., 2008).

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Various studies have quoted several cardiac manifestations of dengue infection sinus bradycardia, transient AV blocks, transient ventricular arrhythmias, myocarditis and pericardial effusion. We performed this study with the objective of studying the cardiac manifestations of dengue and to study the correlation of the cardiac manifestations to the severity of dengue.

Aims and Objectives

- To study cardiac manifestations in patients of dengue fever presenting to our hospital.
- To find out the correlation of cardiac manifestations to the warning signs of dengue fever.

MATERIAL AND METHODS

Study design: Cross-sectional study

Setting: The present study comprises of 50 patients, conducted in the Department of Medicine, Rohilkhand Medical College

and Hospital, Bareilly on patients presenting with dengue fever from July 2016 to September 2016.

Inclusion Criteria

- 1.Age group of ≥ 20 years
- Confirmed cases of dengue fever (ELISA positive)
- Fulfilling the WHO criteria for dengue

Exclusion Criteria

- Previous history of any type of cardiac illness.
- E.C.G. suggestive of old M.I. or on medications affecting the heart rate (e.g., β-blockers, β-agonists, calcium channel blockers, antiarrythmic drugs)

Ethical clearance was obtained prior to the study and written informed consent was obtained from the participating patients.After physical examination, systemic examination and a group of tests that included:

- Complete blood count
- Platelet count
- Electrocardiography
- 2D Echocardiography

Three serial ECGs were taken on;

Day one, day three and day Seven or day of discharge (Whichever was earlier). All the patients were evaluated using two-dimensional echocardiography. Dengue patients positive for one of the following investigations with or without clinical features were considered as cardiac involvement.

- Features suggestive of rhythm disturbance
- Heart rate changes like sinus tachycardia or bradycardia
- Abnormal ECG an ECHO were considered for cardiac manifestations.
- ECG changes included sinu tachycardia, sinus bradycardia,
- non-specific ST-T wave changes, inverted T waves, first degree heart block and right bundle branch block

Echocardiography changes were interpreted as

- ***Systolic dysfunction***–Refers to impaired ventricular contraction.
- ***Diastolic dysfunction*** – Refers to an abnormality in the filling during diastole.
- ***Ejection fraction*** – The fraction of the blood pumped out of a ventricle with each heart beat (Normal value – 67 ± 12%)
- ***Pericardial effusion*** – An abnormal accumulation of fluid in the pericardial cavity.

Severity of Dengue Fever

Patients who were seropositive for Dengue were classified on the basis of WHO Criteria[6,7] as follows:

- Dengue Fever (DF)
- Dengue Fever with unusual bleed (DFB) – bleeding tendencies not satisfying WHO criteria for DHF.
- Dengue Hemorrhagic Fever (DHF)

Four cardinal features of DHF as defined by WHO are as follows:

- Fever or history of fever lasting 2–7 days, occasionally biphasic
- A hemorrhagic tendency shown by at least one of the following: a positive tourniquet test; petechiae, ecchymoses or purpura; bleeding from the mucosa, gastro - intestinal tract , injection sites or other locations; or hematemesis or melena
- Thrombocytopenia [≤100,000 cells/mm3 (100×109/L)]
- Evidence of plasma leakage owing to increased vascular permeability shown by: an increase in hematocrit ≥20% above the average for age, sex and population; a decrease in the hematocrit after intervention ≥ 20% of baseline ;signs of plasma leakage such as pleural effusion, ascites or hypoproteinaemia.
- Dengue Shock Syndrome (DSS)
- For a case of DSS, all four criteria for DHF must be met, in addition to evidence of circulatory failure manifested by: Rapid and weak pulse and narrow pulse pressure (<20 mmHg or 2.7 kPa) manifested by Hypotension for age and Cold, clammy skin and restlessness or lethargy.

The categorical data was expressed as rates, ratios and proportions and comparison was done using chi-square test and Fisher's exact test. The continuous data was expressed as mean ± standard deviation (SD). A probability value ('p' value) of less than or equal to 0.05 at 95% CI was considered as statistically significant.

RESULTS

The mean age of our study group was 32 years. The youngest patient was 20 years old and the oldest patient was 72 years old. There were 27 males and 23 females in our study. 33 patients presented to us within the first week of fever, 17 were febrile at admission. Of the 50 patients studied all patients were dengue NS1 positive (ELISA). Of the 50 patients, 21 patients had persistent abdominal pain, 29 patients had persistent vomiting which was the commonest warning sign. 23 patients had mucosal bleeding, 6 had clinical evidence of fluid accumulation, 2 had restlessness, 4 had hepatomegaly >2 cm (Table 1).

Table 1. Patients of dengue fever with warning signs

Warning signs	Number of cases
Abdominal pain	21
Persistent vomiting	29
Mucosal bleed	23
Fluid accumulation	6
Lethargy/restlessness	2
Hepatomegaly >2 cm	4

The minimum platelet count of the study population was 8,000/ cubic mm. The mean platelet count was 30,000 ± 23,895 cubic mm. The maximum packed cell volume was 56 (Mean 43.6 ± 6.15). Of the 50 patients studied, one was found to be in shock, as evidenced by a systolic BP <90 mm of Hg. Six patients were observed to have fluid accumulation sufficient to cause respiratory distress. 2 patients had severe hepatic derangement as evidenced by SGOT and SGPT values above 1000 IU. The highest SGOT and SGPT values were 1384 IU/L and 1245IU/L

respectively. The maximum serum creatinine value noticed was 2.1 mg/dl (Table 2).

Table 2. Patients of dengue fever with severe dengue manifestations

Severe dengue	No. of cases
Shock	1
Fluid accumulation causing respiratory distress	6
Organ impairment	
SGOT or SGPT >1,000	2
Impaired consciousness	2

The mean pulse rate of the study population was 70/minute. The minimum pulse rate was 34 beats/minute and the maximum pulse rate was 140 beats/ minute. 11 patients had sinus bradycardia- it was the commonest rhythm abnormality noted. 2 patients had unexplained sinus tachycardia. Ventricular arrhythmias in the form of ventricular bigeminy, ventricular trigeminy and ventricular tachycardia were noted in one patient each. All these changes reverted back to sinus rhythm in 24 hours. AV dissociation with sinus node dysfunction was observed in one patient, which resolved in 24 hours. ST- T changes were noted in 4 patients. Echocardiographic evaluation was done in 18 patients. All the cardiac manifestations of dengue are summarised in Figure 4. 5 patients had systemic hypertension, 6 had type 2 diabetes mellitus. Of the 50 patients studied, two patients expired, they succumbed to ARDS. There was statistically significant correlation (p value< 0.05, Chisquare test) between cardiac manifestations and all the warning signs except persistent vomiting, which was the commonest warning sign noted (Table 3).Of the manifestations of severe dengue, only fluid accumulation causing respiratory distress was found to have a significant correlation (p value <0.05, Chi square test) with the cardiac manifestations of dengue (Table 4)

Table 3.Correlation of warning signs to cardiac manifestations

	Cardiac manifestations		P value
	No	Yes	
Abdominal pain	21	12	0.045
Persistent vomiting	29	14	0.37
Fluid accumulation	6	5	0.032
Mucosal bleed	23	13	0.005
Lethargy / Restlessness	3	3	0.018
Hepatomegaly >2 cm	4	4	0.017

Table 4. Correlation of severe dengue to cardiac manifestations

Correlation of severe dengue to cardiac manifestations	Cardiac manifestations		P Value
	No	Yes	
Shock	1	1	0.44
Fluid accumulation causing respiratory distress	1	4	0.048
Severe bleeding	3	3	0.356

DISCUSSION

Cardiac manifestations in dengue virus infection can range from asymptomatic bradycardia to life threatening myocarditis. Various studies have quoted several cardiac manifestations of dengue infection viz. sinus bradycardia, transient AV blocks, transient ventricular arrhythmias, myocarditis, systolic and diastolic dysfunction and pericardial effusion. Myocardial involvement may be the direct result of dengue virus infection in susceptible individuals or may be due to effects of cytokines / cellular mediators of immune response (Pelupessy et al., 1989). The present study was done with the aim of studying the cardiac manifestations of dengue and to study the correlation of the cardiac manifestations to the severity of dengue. The mean age of our study population was 32 years. 41 percent of the study population presented to us within the first week of fever. Of the 50 patients studied, 50 patients were Dengue NS1 positive (ELISA). In the study by Wichman et al (Wichmann, Kularatne, 2009). IgM and IgG dengue testing was done to make a diagnosis of primary dengue infection and secondary dengue infection, respectively. The most common warning sign observed was persistent vomiting, seen in 58 percent of the patients, whereas restlessness/lethargy was the least common warning sign noted, seen in 5% of the patients. 58 percent of the patients had one warning sign or the other. In the study by Thein, et al, [10] on 108 patients with confirmed dengue fever, persistent vomiting was noted in 39% and it was the most common warning sign. Hepatomegaly was the least common warning sign, seen in 2%, in their study. In their study also, 58% of the patients had one warning sign or the other. Three patients had shock, nine had fluid accumulation causing respiratory distress and nine had severe bleeding. Severe hepatic impairment was seen in four patients, renal impairment in four, ARDS in four and impaired consciousness in three patients. Two patients had severe hepatic derangement as evidenced by SGOT and SGPT values above 1000 IU. The highest SGOT and SGPT values were 1384 IU/L and 1245 IU/L respectively. One patient had renal impairment. The maximum serum creatinine value noticed was 2.1 mg/dl.

The mean pulse rate of the study population was 70 beats/minute. The minimum pulse rate was 34 beats/ minute and the maximum pulse rate was 140 beats/minute. The commonest rhythm abnormality noted was sinus bradycardia, found in 32%. Three patients had unexplained sinus tachycardia. AV dissociation with sinus node dysfunction was observed in one patient, which resolved in 24 hours. Ventricular arrhythmias in the form of ventricular bigeminy, ventricular trigeminy and ventricular tachycardia was noted in one patient each. All these changes reverted back to sinus rhythm in 24 hours. Echocardiographic evaluation was done in 18 patients. Echocardiographic evidence of myocarditis was not seen in any patient. There was statistically significant correlation between cardiac manifestations and all the warning signs except persistent vomiting, which was the commonest warning sign noted. Among severe dengue, fluid accumulation causing respiratory distress was found to have a significant correlation with the cardiac manifestations.

Conclusion

Of the 50 patients studied, 10 patients had no warning signs, 40 patients had one warning sign or the other. Nine patients had severe dengue. The most common cardiac abnormalities noted were rhythm abnormalities of which the commonest was sinus bradycardia, found in 32 percent. Ventricular arrhythmias in the form of ventricular bigeminy, ventricular trigeminy and ventricular tachycardia were noted in one patient each. AV dissociation with sinus node dysfunction was observed in one patient. All these changes reverted back to sinus rhythm in 24 hours. Of the 18 patients who underwent echocardiographic study. There was statistically significant correlation between cardiac manifestations and all the warning signs except persistent vomiting. Among severe dengue, fluid accumulation causing respiratory distress was found to have a significant correlation with the cardiac manifestations.

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