

Myocarditis in Dengue Fever - A Retrospective Review from a Tertiary Care Hospital in Pakistan

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ABSTRACT

Dengue fever is an important public health problem with diverse manifestation. One of the complication is myocarditis. In current study, we assessed the clinical, electrocardiographic and echocardiographic features of Dengue fever related myocarditis and compared it with similar published studies. All adult patients with Dengue fever transferred to medical ICU of Ittefaq Hospital during the epidemic of dengue fever from July 2011 to October 2011 were included. Patient admitted in ICU with hypotension were classified in to four sub groups: Hypovolemic shock, cardiogenic shock, Dengue hemorrhagic shock and Dengue leakage shock. Patients with cardiogenic shock were analyzed for demographic details, clinical and laboratory features. A total of 24 patients were identified as having Myocarditis. 20 (83.3%) were male and 3(12.5%) were female. Mean age of the patients was 32 years. Most common clinical features were shortness of breath (100%), fatigue (100%), palpitations (100%) and hypotension(100%). Electrocardiography revealed Sinus tachycardia in 21(87.5%), Atrial fibrillation in 2(8.3%), Ventricular tachycardia in 1(4.1). Echocardiogram revealed global hypokinesia, low ejection fraction and biventricular enlargement in all patients(100%). Cardiac biomarker like Troponin T and Creatinine Kinase were elevated in all 24(100%) patients. 20(83.3%) patients expired and 4(16.6%) improved completely and discharged. So we can conclude that dengue fever associated myocarditis is poorly reported but an important complication associated with high mortality in our patient. Clinical, electrocardiographic and echocardiographic findings are nonspecific and high degree of the clinical awareness is required from the physician for the timely diagnosis.

Keywords: Dengue fever, myocarditis, echocardiography

INTRODUCTION

Dengue, an arthropod-borne viral infection, is an important public health problem. *Aedes aegypti* mosquito is responsible for transmission of the four dengue virus serotypes: dengue-1, -2, -3 and -4¹. Symptoms starts with fever, headache, retro-orbital pain, rash, severe myalgia and arthralgia. Dengue haemorrhagic fever/dengue shock syndrome (DHF/DSS) are the serious clinical manifestations characterized by increased vascular permeability, thrombocytopenia (platelets <100,000), bleeding tendency and hypovolemic shock^{2,3}.

Most of the time Dengue infections are asymptomatic. The clinical disease is divided into three phases: the febrile phase, the critical phase, and the recovery phase. The critical phase of the infection is associated with a falling platelet count, leukopenia. The critical phase is characterized by the occurrence of features of plasma leakage with rising hematocrit, fluid leakage in third space and, hypotension^{4,5}. Atypical presentations also have been described such as hepatitis (27%)⁶, altered consciousness (25%), renal impairment (7%), cardiac

involvement (8%), pulmonary changes (9%), acalculous cholecystitis (9%), hemophagocytic syndrome (2.5%), pancreatitis (1%), and acute abdominal pain (11%)⁷.

Cardiac involvement is seen in centers with large patient turn over. Cardiac involvement ranges from asymptomatic disease to arrhythmias, hypotension, myocarditis, myocardial depression with symptoms of heart failure and pericarditis^{8,9,10,11}. In the last dengue epidemic in Lahore Pakistan, in our tertiary care center, Myocarditis was identified as the major cause of the morbidity and mortality. All the patient with clinical diagnosis of Myocarditis were initially treated for hypovolemic shock but later on clinical deterioration were suspected of having myocarditis.

The purpose of this study was to analyze the clinical features, Electrocardiographic and the echocardiographic features of our patients and compared it with similar studies published in the literature.

PATIENTS AND METHODS

All adult patients with Dengue fever transferred to medical ICU of Ittefaq Hospital during the epidemic of dengue fever from September 2011 to October 2011

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were included. Ittefaq hospital is a 550 bed hospital with attached medical college and fully equipped multidisciplinary critical care unit approved by Pakistan medical and dental council. Patient admitted in ICU with hypotension were classified in to four sub groups: Hypovolemic shock, cardiogenic shock, Dengue haemorrhagic shock and Dengue leakage shock. Patients with cardiogenic shock were analyzed for Demographic details, clinical and laboratory features. Statistical Analysis was carried out using Statistical package for social sciences.

RESULTS

A Total of 128 patients during Dengue Epidemic from July 2011 till October 2011, were shifted to Medical ICU because of complications of dengue such as shock, unconsciousness and multi-organs failure.

122(95.31%) patient were in shock and 6(4.68%) were unconscious (Table 1).

Dengue leakage shock was noted in 6(4.9%) patients. All these patients improved. 8(6.5%) cases were in Dengue Hemorrhagic Shock(DHS). Out of these 8 patient 3(37.5%) expired and 5(62.5%) patients improved.

Cardiac Shock was noted in 24(19.67%) cases. The Demographic details, clinical and laboratory features are out lined in table 2 & 3. Most of these patients were male with average age of 30. Most common clinical presentation was hypotension (100%) and shortness of breath (100%). EKG abnormalities observed in these patients were sinus tachycardia (84%), aerial fibrillation (8%) Ventricular tachycardia (8%). Echocardiographic findings revealed Global hypokinesia (100%), Ejection fraction less than 40(100%) and Biventricular dilatation (100%).

Table1: Medical ICU admissions during Dengue epidemic(n= 128)

Dengue Fever with Shock n= 122 (95.31%)				Dengue Fever with Unconsciousness n=6(4.68%)		
Hypovolemic	Cardiogenic		Dengue Hemorrhagic Shock	Dengue Leakage shock	Dengue Encephalitis	Dengue Multi-organ Failure
84 (68.8%)	24 (19.67%)		8(6.5%)	6 (4.9%)	4(66.66%)	(33.33%)
All patients	Expired	Recovered	Expired	Recovered	All recovered	
Recovered	20(83.3%)	4(16.6%)	3(37.5%)	5(62.5%)		

Table 2: Clinical and Laboratory features in Dengue virus induced myocarditis

Clinical features	n
Fever	24(100)%
Shortness of breath	24(100%)
Palpitation	22(91.6)
Fatigue	24(100%)
Hypotension	24(100%)
Tachycardia	24(100%)
Raised Jugular venous pressure	2(8.3%)
Bilateral chest crepts	24(100%)
S3 Gallop	2(8.3%)
Lower limb pitting edema	2(8.3%)
Tender Hepatomegaly	0

Laboratory features

Lab feature	Average value
Hgb	15gm/dl
Hct	41%
Total white cell count	1858/cumm3
Platelet count	60,000/cumm3
Dengue virus serology	IgM positive in all cases
Troponin T	6.75 ug/l (0-0.01)
Creatinine kinase	950 u/l (0-225)

Table 3: Summary of Electrocardiographic and echocardiographic findings (n=24)

Electrocardiographic findings	n
Sinus tachycardia	21(87.5%)
Atrial fibrillation	2 (8.3%)
Ventricular tachycardia	1(4.1)
Echocardiography Findings	
Global hypokinesia	24 (100%)
Ejection fraction less than 40%	24(100%)
Biventricular Dilatation	24(100%)

DISCUSSION

Cardiac involvement in dengue is common and is seen in centers handling large numbers of cases^{8,9,10,11}. The pathophysiology of cardiac involvement in dengue is not clear. Both direct viral invasion of Myocardium and cytokinemediated immunological injury have been postulated^{12,13}. Myocarditis, pericarditis, and cardiomyopathy after dengue have been reported in the literature but no large report on adult patients have been seen from Pakistan^{8,9,10}.

In last dengue epidemic in Lahore Pakistan in 2011, in our tertiary care center, out of 122 patients of dengue fever with shock admitted in ICU, 24

patients were diagnosed as Myocarditis. Mortality due to haemorrhagic shock, dengue leakage shock and hypovolemic shock was not significant making Myocarditis as a major cause of mortality in our patient population. The high incidence and mortality of myocarditis in our study population may be related to dengue virus serotypes and their antigenicity, as seen in some studies^{8,9}. Kularatneet al described few cases of myocarditis caused by Dengue serotype 3 in Sri Lanka¹⁴. There are no reports of cardiac involvement seen with serotype 1 and 4, there is lack of evidence to link cardiac involvement with a particular serotype. Secondary infection by different serotype can lead to severe cases of dengue fever. It is not clear whether cardiac involvement in Dengue represents secondary infection by a different serotype¹⁵.

Myocarditis in dengue may have been under reported due to the lack of definite criteria to define cardiac involvement, and this was clearly observed in our patients. Most of our patients were admitted in ICU due to hypotension and shock, and were treated for hypovolemic shock but later on suspected of having myocarditis due to deterioration in clinical condition despite aggressive fluid management. Hypovolemia, shock, arrhythmias and pulmonary edema have all been seen in severe dengue infection¹⁶ and so if viral myocarditis was a primary event it was thought in our patients, it would be difficult to differentiate it from other causes of such manifestations like plasma leakage shock, occurring in Dengue fever thus, separating secondary cardiac effects from primary cardiac involvement is difficult, and this may have led to under-reporting of cardiac involvement in the past¹⁶. Clinical features, electrocardiographic abnormalities, abnormal cardiac biomarkers, and echocardiographic findings have been evaluated in various studies as possible markers of cardiac involvement in dengue^{8,9,10,11,14,15}.

The presence of electrocardiogram (ECG) abnormalities has been used to indicate cardiac involvement in dengue¹⁷. In our patient's sinus tachycardia was most commonly seen followed by atrial fibrillation and ventricular tachycardia. None of the rhythm disturbance, in our patient, is specific for myocarditis. Rhythm abnormalities observed include relative bradycardia¹⁸, sinoatrial block¹⁹ and disorders of atrioventricular conduction (junctional rhythm¹⁹, atrial flutter²⁰, and atrial fibrillation²¹). Electrocardiographic features resembling acute myocardial infarction have also been reported¹⁷.

Cardiac biomarkers such as Troponin T and CPK MB were elevated in all of our patients and this along with Supporting clinical feature of worsening hypotension despite aggressive fluid resuscitation

indirectly indicated cardiac involvement in our series. A prospective study in Sri Lanka showed that 25% have abnormal results in one or more biomarkers²² so it is difficult to establish a relationship between cardiac biomarkers and cardiac functions¹⁶.

Echocardiographic evidence of myocardial involvement in dengue has been clearly demonstrated. All patients in our study have global hypokinesia, dilated heart and poor ejection fraction (<40%) suggesting myocarditis. Constantine and colleagues²³ described echocardiographic features of myocarditis in 8 out of 37 adult and pediatric patients with dengue, and poor left ventricular ejection fraction (LVEF) below 60% was seen in four patients. Waliet al evaluated cardiac function using echocardiography and radionuclide ventriculography in 17 patients with dengue and low ejection fraction below 40% was found in 7 patients, and global hypokinesia in 12 patients²⁴. Satarasingheet al demonstrated echocardiographic evidence of myocarditis in 24% of patients with dengue. Cardiac dilatation was the most commonly observed echo evidence of Myocarditis predominantly seen in right ventricle (57%)²⁵.

The management of these patients with dengue associated myocarditis is also challenging. Initially our patients were treated with aggressive intravenous hydration but later on confirmation of the diagnosis were managed by supportive care including cautious intravascular fluids, diuretics and inotropic support. Other therapeutic modalities such as use of intravenous methyl prednisolone in a 14-year-old with dengue complicated by myocarditis was reported by Premaratnaet al, but this therapeutic modality was not considered in our series²⁶.

CONCLUSION

Dengue virus induced myocarditis is underreported but it is an important cause of the mortality in Dengue fever. Nonspecific clinical features and variable electrocardiographic and echocardiographic findings requires a high degree of clinical suspicion by the treating physician. Awareness is important for this entity to prevent the high mortality, as seen in our patients.

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