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STUDY OF CARDIAC MANIFESTATIONS IN PATIENTS WITH SEROPOSITIVE DENGUE FEVER

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ABSTRACT

Aims and Objectives: To study the cardiac manifestations of the dengue fever. **Method:** This one year descriptive study was undertaken at SSIMS & RC,Davangere under the Department of Medicine. A total of 100 patients with either dengue NS1 or IgM or IgM and IgG were studied. The assessment of cardiac manifestations was done based on electrocardiogram, 2D echocardiography and cardiac enzymes. **Results:** Of the 100 patients, 64 (64%) were males and the male to female ratio was 1.7:1. The commonest clinical presentation was myalgia followed by fever On clinical examination 23% of the patients had bradycardia, 10% patients had tachycardia and 6% had hypotension at the time of presentation.94% patients had thrombocytopenia A raised CK-MB and Troponin I was observed in 51% and 11%. patients ECG findings revealed 5% of the patients had first degree heart block, 20% had sinus bradycardia. 9% had sinus tachycardia. 5% had ST segment changes, 2% had T wave changes. Cardiac manifestation was observed in 94% of the patients with a positive correlation with the severity of the dengue fever defined as by W.H.O. criteria. **Conclusion:** Patients with dengue fever are at high risk of developing myocarditis and rhythm disturbance and other cardiac manifestations therefore require a close cardiac monitoring.

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 mosquitos of the Aedes family.[1] 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).[2]

The World Health Organization (WHO) 2009 guidelines classify patients into three groups; dengue without warning signs, dengue with warning signs and severe dengue.[3]

Early laboratory confirmation of dengue infection is crucial. Among the methods available for dengue diagnosis, virus isolation provides the most specific test result. Detection of IgM or IgG antibodies is the standard for serologically confirming a dengue infection. The presence of IgM or high levels of IgG in acute serum collected from a suspected dengue case suggests a probable dengue infection.[4] An up-to-date test for early diagnosis of dengue infection is dengue NS1 antigen detection.[1]

Most cases of dengue are self- limited, and the course of the disease is a nonspecific febrile state, general malaise and weakness. Patients feel severe muscle pain and retro-orbital pain, with or without skin rash. Laboratory tests may reveal increased hepatic enzyme levels, leukopenia and thrombocytopenia, which are abnormalities consistent with but nonspecific for dengue fever.[1] The most severe forms of the disease are dengue shock syndrome and dengue hemorrhagic fever. The shock syndrome is due to an important alteration in capillary permeability and significant capillary leakage of plasma into extra-vascular spaces, and is associated with immune activation and high serum levels of tumor necrosis factor-a (TNF) receptor, interleukin (IL)-8, and other factors.

It is postulated that, dengue rarely affects the heart. Medical literature has reports of isolated cases of atrioventricular conduction disorders (junctional rhythm and atrioventricular block), supraventricular arrhythmias, and myocarditis. On the other hand, the ventricular dysfunction associated with the acute phase of dengue hemorrhagic fever has been described by several authors and is probably under diagnosed in clinical practice.[6]

Although cardiac manifestations specific to dengue are rare, depression of myocardial function is frequent in the hemorrhagic form of the disease or in the associated shock.

To-date very few studies have addressed the issues of cardiac manifestation in dengue fever. Hence the present study was planned to assess the cardiac manifestations of

denguefever &to identify subclinical/latent cardiac involvement.

MATERIAL AND METHODS

This study was performed under the Department of Medicine, S.S Institute of Medical Sciences and Research Centre, Davangere, Karnataka. The study design was a hospital based descriptive study and conducted for the period of 12 months from January 2015 to December 2015.Adult patients with clinical features suggestive of Dengue infection later confirmed by Dengue tests (NS$_1$, IgG and IgM ELISA) were included in the study. Mixed infections and Previous cardiac disease were excluded.

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

• Complete blood count
• Platelet count
• Electrocardiography
• 2D Echocardiography
• Cardiac enzymes – CK-MB and Troponin I

ECGs were taken on; Day one.All the patients were evaluated using two-dimensional echocardiography on day one CKMB and Troponin I was done on day of admission and values were interpreted as normal between 0 to </=4.3 ng/ML and 0 to </=0.05 ng/ML

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, raised CKMB and/or troponin I and abnormal ECG and ECHO were considered for cardiac manifestations.

ECG changes included sinus tachycardia, sinus bradycardia, non-specific ST-T wave changes, inverted T waves and first degree heart block

Echocardiography changes were interpreted as;
Pericardial effusion:An abnormal accumulation of fluid in the pericardial cavity.*Lv hypokinesia*: Refers to impaired ventricular contraction. *Ejection fraction*:The fraction of the blood pumped out of a ventricle with each heart beat (Normal value –67±12%) *Valvular abnormality:* Abnormality of valve leaflets or valve itself.

Severity of Dengue Fever: Patients who were seropositive for Dengue were classified on the basis of WHO Criteria[8,9] 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:

1. Fever or history of fever lasting 2–7 days, occasionally biphasic
2. 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
3. Thrombocytopenia ≤100,000cell/mm^3
4. 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 data obtained was coded and entered into Microsoft Excel Worksheet (Annexure III). 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:

Among the 100 patients studied, 3% had an age of less than 20 years. 55% were in the age group of 20-29 years. 26% in the age group of 30-39 years, 12% in the age group of 40-49 years with 4% having an age of more than 50 years. Out of 100 patients 64% were males and 36% females.
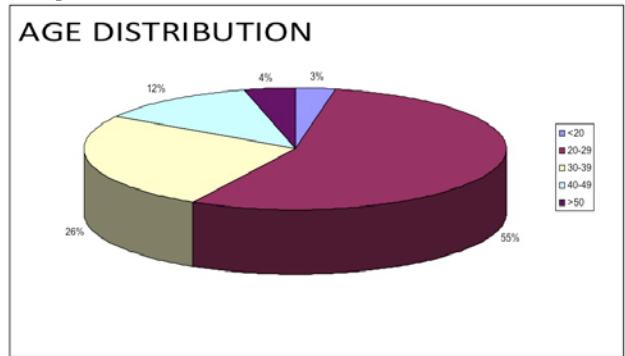
23% of the patients had bradycardia. 10% had tachycardia while 67% had a normal pulse rate at the time of examination.CVS findings in the 100 patients-8% had loud S1,2% had muffled heart sounds,10% had tachycardia,23% had bradycardia. 4% had systolic murmurs.2% had S3 &50% had a normal CVS examination.
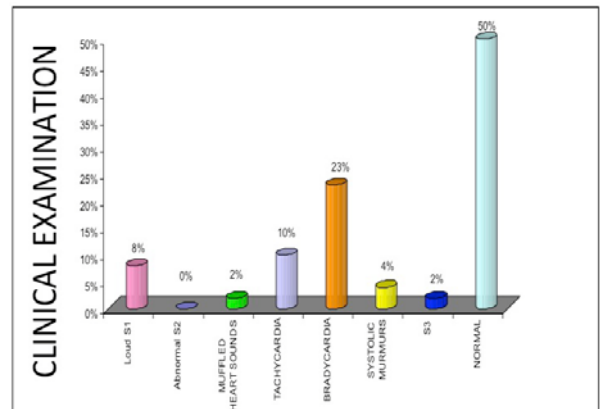

In ECG findings 5% of the patients had first degree heart block, 20% had sinus bradycardia. 9% had sinus tachycardia. 5% had ST segment changes, 2% had T wave changes.

CK-MB(ng/ml)	Frequency	Percent
</=4.3	49	49.0
>4.3	51	51.0
Total	**100**	**100.0**

51% had positive CK- levels of more than 4.3NG/ML.11% had Troponin I values positive while the remaining 89% had negative Troponin I values.theabnormal 2D ECHO findings found in 8 of the 100 patients- 50% of the 8 had

incidental findings of Mitral Valve Prolapse and pleural effusion. 25% of the 8 had reduced LV function. 13% of the 8 had LV hypokinesia and a further 12% of the 8 had evidence of pericardial effusion.
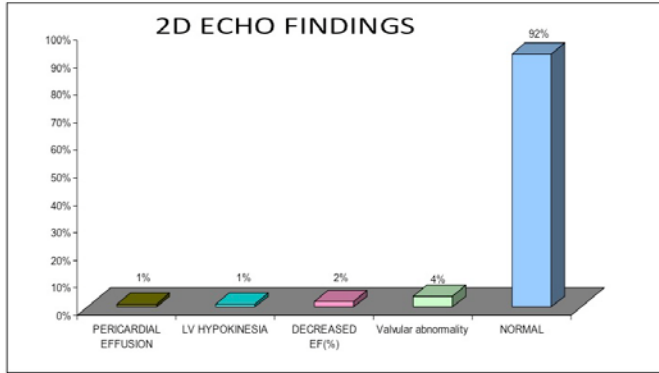
The correlation between troponin I levels and platelet count in the study- showing that 27.3% of the patients with positive Troponin I had platelets of less than 20,000 cells/mm3 while 63.6% of the patients with Troponin I positive had platelet counts of 20,000-50,000 cells/mm3.With a significant p-value, this shows that patients with higher Troponin I levels had a higher degree of thrombocytopenia in our study.
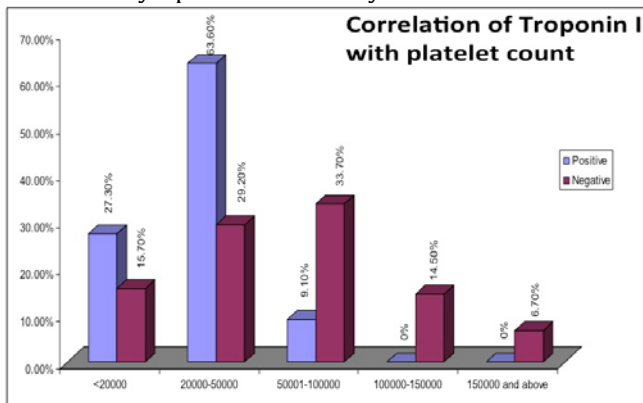

It was found that the 4 patients who had pericardial effusion, LV hypokinesia and reduced LV function(2) respectively all had high troponin I values while 86 of the 92 patients with a normal 2DECHO had negative Troponin I values. With a significant p value, this proves that 2D ECHO abnormalities was strongly associated with positive Troponin I values.

2D ECHO	Troponin 1		Total	X2 value	'p' value
	Positiv	Negative			
Pericardial Effusion	1	0	1	35.049	<0.001
	9.1%	.0%	1.0%		
Hypokinesia	1	0	1		
	9.1%	.0%	1.0%		
Reduced LVF	2	0	2		
	18.2%	.0%	2.0%		
valvular abnormality	1	3	4		
	9.1%	3.4%	4.0%		
Normal	6	86	92		
	54.5%	96.6%	92.0%		
Total	11	89	100		
	100.0%	100.0%	100.0%		

In patients with both NSlAg and IgMAb positivity Of a total of 19 patients with both NSlAg and IgMAb positive. 13 patients(68.4%) had ECG changes, 1(5.2%) had ECHO findings, 5(26.3%) had Troponin I positivity and 11 (57.9%)had CK-MB positivity indicating an increased risk

of cardiac manifestations in patients with both NSlAg and IgMAb positivity.
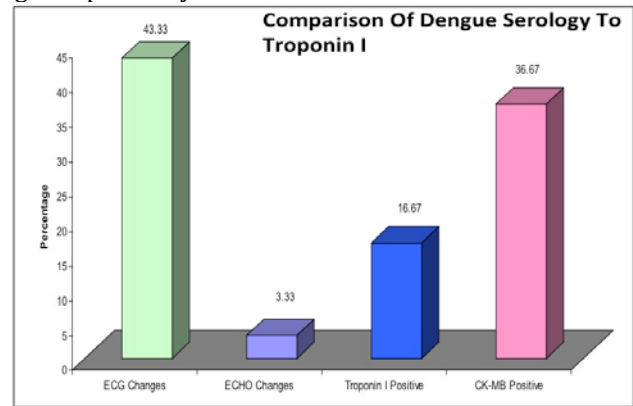
DISCUSSION

In this study, the age distribution was maximum between the ages of 20-29 years(53%) as compared to a study by Vishal Kumar Gupta et al where the mean age was 30.4 years.This study had a gender distribution of 64% males and 36% females which was as comparable to a study by Vishal Kumar Gupta which had the same sex distribution.23% of the patients in this study had bradycardia and 10% had tachycardia on pulse examination compared to a study by Kularatne SA who showed that 67% of the patients had either bradycardia or tachycardia.CVS examination findings in our case showed 1 patient with muffled heart sounds, 2 patients with a S3 and 4 patients with a systolic murmur when compared to a study by Antonio Eduardo Pesaro where only one patient had clinical evidence of cardiac involvement in dengue fever.In our study, abnormal ECG findings such as bundle branch blocks, ST segment and T wave changes, sinus bradycardia and heart blocks were seen in 50% of our patients which was comparable to the 62.5% of patients with abnormal ECG findings in a study by Kularatne SA[3].The 2D ECHO in our study showed that 2 patients had reduced LV systolic function while 1 patient had pericardial effusion and LV global hypokinesia respectively which was similar to a study by Carlos Henrique Miranda[2] where 2 patients had reduced LV function, two had LV segmental hypokinesia and one had pericardial effusion.Cardiac markers in our study revealed high CK-MB levels in 51% of our patients and positive troponin I levels in 11% while a study by Carlos Henrique Miranda had 15% of troponin I positivity.Further, in this study the p values for correlation between troponin I positivity and low platelet count, abnormal ECG findings and ECHO evidence of abnormalities consistent with dengue was significant suggesting that Troponin I positivity carries a greater risk of cardiac involvement in dengue fever, clinical or sub clinical. This was also found in patients in a study by Vishal Kumar Gupta which showed that 50% of patients with high troponin I had abnormal ECHO findings while 80% had abnormal ECG findings.

CONCLUSION

This study of the cardiac manifestations in 100 patients with dengue fever,demonstrated that the cardiac manifestations ranged from elevated biomarkers such as CK-MB and Troponin I with normal ECG and ECHO.

As the ECG findings in dengue fever may vary from rate abnormalities such as sinus bradycardia, conducting system abnormalities such as bundle branch and AV blocks to evidence of myocardial ischemia such as ST segment changes and T wave inversions

Thus we can conclude that cardiac manifestations in dengue are common and may present sub-clinically and therefore any primary care physician dealing with dengue fever must be vigilant for such changes and use cardiac biomarkers as a baseline investigation to identify early cardiac involvement along with the standard ECG and 2D ECHO cardiography.

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