Original Research

Correlation Of Cardiac Manifestations With Severity Of Dengue Fever

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Abstract
Background: Dengue is most rapidly spreading mosquito borne viral disease in the world. In the last 50 years, incidence has been increased 30-fold with increasing geographic expansion to new countries and, in the present decade, from urban to rural setting. An estimated 50-100 million dengue infections occur annually and approximately 2.5 billion people live in dengue endemic countries.

Objective: To find out the correlation of cardiac manifestations with severity of Dengue fever.

Materials and Methods: The cross sectional study was conducted in patients with Dengue Fever admitted in Hospitals attached to Mysore Medical College and Research Institute, Mysore.

Results: Maximum number of cases were between 18 to 30-year age group. Males were more than female population. Fever was present in all patients followed by myalgia (28%) and vomiting (21%). Bleeding manifestation was present in 20% of patients. Thrombocytopenia was present in 91% of patients. No single symptom or sign was statistically significant with severity of dengue. Cardiovascular manifestations were present in 25 patients. Sinus tachycardia was most common ECG finding seen in 17 patients, followed by sinus bradycardia which was seen in 6 patients. 9 patients with cardiac manifestation had dengue fever with warning signs.

Conclusion: There was statistically significant (p=0.007) correlation between cardio-vascular manifestations with WHO criteria for severity of dengue fever.

Keywords: Severity of dengue fever, correlation, cardiac manifestations

Introduction:

The first outbreak of dengue fever recorded in India was in 1812, but they started to look for neurological evidence of dengue infection only in 1954, which showed that DENV-1 and DENV-2 were widespread. In1960, DENV-1 was isolated in Vellore, in the south, without any association with bleeding diathesis.[1,2] A double peak hemorrhagic fever epidemic occurred in India for the first time in Kolkatta between July- 1963 and March- 1964. DENV-2 virus strain was isolated from

patients with severe hemorrhagic manifestation during first peak.[3, 4]

In New Delhi, outbreaks of dengue fever were reported in1967, 1970, 1980. An explosive outbreak of dengue fever occurred between August to October in the year 1982. DENV-1 and DENV-2 were reported from 36 patients. There were no hemorrhagic manifestations or fatalities recorded during this episode.[5]

Dengue is one of the most important emerging viral diseases globally. Most symptomatic infections have a relatively benign course. However, few patients develop severe manifestations, including endothelial dysfunction with increased capillary permeability, bleeding, hypovolemic shock which can lead to cardiovascular collapse and organ impairment.[6,7] There is an increasing evidence that dengue can also cause myocardial impairment, arrhythmias and occasionally fulminant myocarditis. Currently dengue is one of the most important emerging infectious diseases in the world. The dengue virus (DENV), a member of the genus *Flavivirus* in the family *Flaviviridae*, is a single-stranded enveloped RNA virus, which has four distinct, but related, serotypes (DENV1–4).[8]

Dengue is transmitted by mosquitoes of the genus *Aedes*, and is reported in more than 100 countries, with a high incidence across South and Southeast Asia and increasing number of cases reported from Latin America.[7] Previously dengue was classified into dengue fever (DF) and dengue hemorrhagic fever (DHF) grades I – IV; DHF grades III and IV together comprised dengue shock syndrome (DSS). In 2009, the WHO revised the classification system owing to difficulties in applying the old system in clinical situations and several reports of severe cases that did not fit the criteria for DHF. Patients are now classified as having dengue with or without warning signs, or severe dengue. Age seems to influence the clinical picture of dengue, with shock occurring more frequently in children, and bleeding and organ impairment being more common in adults.[9]

The observation that severe dengue is more common in repeated infections with a different DENV serotype, and that severe manifestations occur late in the course of the disease, when the virus is being cleared from tissues and the peripheral blood, suggest an underlying immune driven pathogenesis, although the precise mechanisms remains unknown. [11]

Although the vast majority of DENV infections are either asymptomatic or result in mild disease, an estimated 1–5% of patients presenting to hospital develop complications, including plasma leakage from the capillaries, bleeding and organ impairment. In severe cases, plasma leakage can result in potentially fatalcardiovascular collapse, that is DSS.[6]

Material and Methods:

The cross sectional study was conducted in patients with Dengue Fever admitted in Hospitals attached to Mysore Medical College and Research Institute, Mysore during the study period of November 2017-May 2019.

Inclusion Criteria:
Patients aged 18 years and above
Confirmed dengue fever cases with Dengue NS1 Ag / IgM positive or both Fulfilling WHO Criteria for Dengue fever

Exclusion Criteria:
Patients on medications affecting the Heart rate / rhythm Patients with history of preexisting heart disease
Patients with electrolyte abnormalities affecting the heart rate/rhythm Patients with history of Thyroid Disorders

The sample size in our study is 100, assuming the anticipated prevalence of cardiac manifestations in dengue to be around 50%, assuming an error 5% (Za = 1.96) and b error 20% (Zb = 0.842) and a power of 80%, with a precision of 5%, according to the following formula.

$$n = \frac{(Za + Zb)2 + p\ q}{d\ 2}$$

n = sample sizep
 = prevalence q
= 1 − p
d = precision

Statistical Analysis: Statistical method chi square test will be used to study correlation between the cardiac manifestations of dengue with the warning signs and with severe dengue. To study whether the correlation is statistically significant.

Results:

According WHO criteria 100 confirmed cases of Dengue were selected. Maximum number of cases were between 18 to 30-year age group. Males were more than female population. Fever was present in all patients followed by myalgia (28%) and vomiting(21%). Bleeding manifestation was present in 20% of patients. Thrombocytopenia was present in 91% of patients. No single symptom or sign was statistically significant with severity of dengue. Cardiovascular manifestations were present in 25 patients. Sinus tachycardia was most common ECG finding seen in 17 patients, followed by sinus bradycardia which was seen in 6 patients. 9 patients with cardiac manifestation had dengue fever with warning signs. 5 patients with cardiac manifestation had severe dengue. One patient had myocarditis LV systolic dysfunction with EF-40% with global hypokinesia with complete heart block with heart rate of 30bpm.. One patient had 2nd degree type 1 sinoatrial exit block (Wenckebach). There was statistically significant (p=0.007) correlation between cardio-vascular manifestations with WHO criteria for severity of dengue fever.
Electrocardiographic changes (ECG) changes were statistically significant with WHO criteria for severity of Dengue fever.

Table 1: Cross-Tabulation of ECG and WHO Criteria

ECG- classified		WHO CRITERIA			
		Dengue Fever	Dengue Fever with warning signs	Severe Dengue	Total
Complete heart block	Count	0	0	1	1
	Percent	0.0%	0.0%	10.0%	1.0%
Normal	Count	52	18	5	75
	Percent	82.5%	66.7%	50.0%	75.0%
Second degree SA exit block Type 1 (Wenckebach)	Count	0	0	1	1
	Percent	0.0%	0.0%	10.0%	1.0%
Sinus bradycardia	Count	2	3	1	6
	Percent	3.2%	11.1%	10.0%	6.0%
Sinus Tachycardia	Count	9	6	2	17
	Percent	14.3%	22.2%	20.0%	17.0%
Total	Count	63	27	10	100
	Percent	100.0 %	100.0%	100.0%	100.0 %
Chi-square value- 24.25					
P value- 0.007*					

*significant

Table 2: Cross-Tabulation of PCV and WHO Criteria

PCV- classified		WHO CRITERIA			
		Dengue Fever without warningsigns	Dengue Fever with warningsigns	Severe Dengue	Total
High	Count	5	3	0	8
	Percent	7.9%	11.1%	0.0%	8.0%
Low	Count	28	15	4	47
	Percent	44.4%	55.6%	40.0%	47.0%
Normal	Count	30	9	6	45
	Percent	47.6%	33.3%	60.0%	45.0%
Total	Count	63	27	10	100
	Percent	100.0%	100.0%	100.0%	100.0%
Chi-square value- 3.15					
P value- 0.53					

There was no statistical significance between hematocrit (PCV) and WHO criteria for severity of dengue.

Table 3: Cross-Tabulation of Total Count and WHO Criteria

Total Count- Classified		WHO CRITERIA			Total
		DengueFever	Dengue Feverwith warning signs	SevereDengue	
High	Count	5	3	3	11
	Percent	7.9%	11.1%	30.0%	11.0%
Low	Count	18	4	2	24
	Percent	28.6%	14.8%	20.0%	24.0%
Normal	Count	40	20	5	65
	Percent	63.5%	74.1%	50.0%	65.0%
Total	Count	63	27	10	100
	Percent	100.0%	100.0%	100.0%	100.0%
Chi-square value- 6.09					
P value- 0.19					

There was no statistical significance between total count and WHO criteria forseverity of dengue

Table 4: Cross-Tabulation of Platelet Count and WHO Criteria

Platelet count-classified		WHO CRITERIA			
		DengueFever	Dengue Feverwith warning signs	SevereDengue	Total
Low	Count	57	25	9	91
	Percent	90.5%	92.6%	90.0%	91.0%
Normal	Count	6	2	1	9
	Percent	9.5%	7.4%	10.0%	9.0%
Total	Count	63	27	10	100
	Percent	100.0%	100.0%	100.0%	100.0%
Chi-square value- 0.11					
P value- 0.94					

There was no statistical significance between platelet count and WHO criteriafor severity of dengue.

Table 5: Cross-Tabulation of AST And WHO Criteria

AST-classified		WHO CRITERIA			
		DengueFever	Dengue Feverwith warning signs	SevereDengue	Total
High	Count	47	17	9	73
	Percent	74.6%	63.0%	90.0%	73.0%
Normal	Count	16	10	1	27
	Percent	25.4%	37.0%	10.0%	27.0%
Total	Count	63	27	10	100
	Percent	100.0%	100.0%	100.0%	100.0%
Chi-square value- 2.92					
P value- 0.23					

There was no statistical significance between AST, ALT and WHO criteria forseverity of dengue.

Discussion

The present study was conducted to know the cardiovascular manifestations in dengue fever and their correlation with severity of Dengue fever. There are very few studies which correlate cardiovascular manifestations with severity of dengue fever.
This study was done on 100 patients with NS1 and IgM positive Dengue fever cases admitted to the hospitals attached to Mysore Medical College and Research Institute, Mysore
The mean pulse rate noted in our study was 82.87. The minimum pulse rate was 30/min and maximum pulse rate was 140/min. In a study done by S Sheetal and Elizabeth Jacob, mean pulse rate was 70/min and minimum pulse rate was 34/min and maximum pulse rate of 140/min.[12] In a study by Thein, Leo et al minimum pulse rate was 34/ min and maximumpulse rate was 140/min.[82] In a study by Latheef et al mean heart rates were significantly lower in denguegroup (87.6/min) compared to controls.[13]

In this study ECG was done in all patients, out of 100 patients normal sinus rhythm was present in 98 patients. Sinus tachycardia was present in 17 patients followed by sinus bradycardia in 6 patients. Rhythm abnormality was present in two patients who had severe Dengue. One patient had complete heart block who required Temporary Pacemaker Insertion (TPI) and one patient had second degree sinoatrial exit block Type1 (Wenkebach), which resolved spontaneously. In a study by Yacoub et al. (2012), in Vietnam, ECG abnormalities were present in 18 /51(35%) patients assessed. 3/10 (30%) in dengue, 11/32 (34%) in dengue with warning signs and 4/9 (44%) in the severe group. The abnormalities included 1st degree AV block, sinus bradycardia, T wave changes and ST segment abnormalities.[14]

In a study by La orkun et al, in 35 hospitalized children in Thailand, cardiac rhythm abnormalities were found in ten patients (29%), including sinus pause, first-degree and Mobitz type I second-degree AV block (Wenckebach), and atrial and ventricular ectopic beats.[15]
In a study done by S Sheetal and Elizabeth Jacob, the most common ECG changes noted were rhythm abnormalities of which the commonest was sinus bradycardia, found in 32%. Ventricular arrhythmias in the form of ventricular bigeminy, ventricular trigeminy and ventricular tachycardia was noted in one patient each. AV dissociation with sinus node dysfunction was present in one patient.[12]
Kaushik et al have described atrioventricular dissociation and sino-atrial exit block in a child with dengue fever.[16]

Virk Hu et al have described complete heart block in a 32-year female patient.[17] In a Study by Goutam Dutta and Pratik Mitra in Calcutta, 128 patients studied Fifteen patients had cardiac complications. Bradyarrhythmias were commonest cardiac manifestations. There were eight

patients (6.6%) having different types of bradyarrhythmia. Four patients had sinus bradycardia with varying heart rate between 40 to 50 beats/minute. Three patents had junctional bradycardia. one patient had 2:1 AV nodal block.[18]

In our study 2D echo was done in 7 patients. It was normal in 7 patients. One patient had LV systolic dysfunction and LV global hypokinesia suggestive of myocarditis, whose ECG showed complete heart block.

In a study by Wali et al, Global hypokinesia was present in 12/17 patients and mean LV ejection fraction was 39.63%, which was comparable to our study.[19]

In a study by Goutam Datta and Pratik Mitra, four patients had left ventricular dysfunction and in that two of them presented with heart failure.[18]

In a study by Kabra et al, on 54 children with dengue LVEF was <50% in 16.7% of patients, and <35% in 3.7% of patients.

In our study Troponin I was done in 3 patients and it was negative in all of them.

In a study by Sheetal, Elizabeth J, Troponin T was done in 18 patients and it was negative in all which is comparable to our study.[12]

In a study by Goutam Datta and Pratik Mitra, quantitative Troponin was not elevated in any of the patients.[18]

Conclusion:

There was statistically significant (p=0.007) correlation between cardio-vascular manifestations with WHO criteria for severity of dengue fever.

References

1. World Health Organization, Dengue hemorrhagic fever: Diagnosis, Treatment and Control, Geneva; World Health Organisation; 1986

2. Carey DE, Myers RM, Reuben R, Rodrigue FM. Studies on dengue in Vellore, South India. Am J Trop Med Hyg. 1996; 15:580-7.

3. Khurana SK, Thergaonkor A, Talib VH. Dengue DHF: Indian scenario. In: Talib VH, editor. Dengue hemorrhagic fever (symposium). Pune: 1997: p.23-28.

4. Rao MCVR. Dengue fever in India (Annotational). Indian J Pediatr. 1987;54(1):11-14.

5. Balaya S, Paul SD, D' lima LV and Pavri KM. Investigations on an outbreak of dengue in Delhi in 1967. Indian J Med Res. 1969 April;57(4):765-774.

6. Sophie Yacoub, and Bridget Wills, et al. Predicting outcome from dengue. BMC Medicine 2014, 12:147 10.1186/s12916-014-0147-9.

7. Dengue: guidelines for diagnosis, treatment, prevention and control. Geneva: World Health Organization; 2009.

8. Kuhn RJ, Zhang W, Rossmann MG, Pletnev SV, Corver J, Lenches E, et al. Structure of dengue virus: implications for flavivirus organization, maturation, and fusion [Internet]. Cell. U.S. National Library of Medicine; 2002 [cited 2019Nov23]. Available from: https://www.ncbi. nlm.nih.gov/pmc/articles/PMC4152842/

9.   The TD, Thu TLT, Minh DN, Van NT, Tinh HT, Vinh CNV, et al. Clinical Features of Dengue in a Large Vietnamese Cohort: Intrinsically Lower Platelet Counts and Greater Risk for Bleeding in Adults than Children. PLoS Neglected Tropical Diseases. 2012;6(6).

10. Yacoub S, Mongkolsapaya J, Screaton G. The pathogenesis of dengue. Current Opinion in Infectious Diseases. 2013;26(3):284–9.

11. Simmons CP, Farrar JJ, Nguyen VC. & Wills B. Dengue. N. Engl. J. Med. 366, 1423–1432 (2012).

12. Sheetal S, Jacob E: A Study on the Cardiac Manifestations of Dengue. JAPI. 2017 May; 64:30-34.

13. Lateef A, Fisher DA. & Tambyah PA. Dengue and relative bradycardia. Emerg. Infect. Dis. 13, 650–651 (2007).

14. Yacoub S, Griffiths A, Chau TT, Simmons CP, Wills B, Hien TT et al. Cardiac function in Vietnamese patients with different dengue severity grades. Crit.Care Med. 2012; 40:477–483

15. La-Orkhun V, Supachokchaiwattana P, Lertsapcharoen P. & Khongphatthanayothin A. Spectrum of cardiac rhythm abnormalities and heart rate variability during the convalescent stage of dengue virus infection: a Holter study. Ann. Trop. Paediatr. 31, 123–128 (2011).

16. Kaushik JS, Gupta P, Rajpal S. & Bhatt S. Spontaneous resolution of sinoatrial exit block and atrioventricular dissociation in a child with dengue fever. Singapore Med. J. 51, e146–e148 (2010).

17. Virk HU, Inayat F, Rahman ZU. Complete Heart Block in Association with Dengue Hemorrhagic Fever. Korean Circ J. 2016;46(6):866–869. doi:10.4070/kcj.2016.46.6.866.

18. Datta G, Mitra P. A study on cardiac manifestations of Dengue. JAPI. 2019July; 14-16.

19. Wali J, Biswas A, Chandra S, Malhotra A, Aggarwal P, Handa R, et al. Cardiac involvement in Dengue Haemorrhagic Fever. International Journal of Cardiology. 1998;64(1):31–6.