

A Cross-Sectional Study of 50 Patients with Fever and Thrombocytopenia in a Tertiary Care Hospital and the Presence of Dengue Antibodies in Them.

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Abstract

Objective

The objective of the study is to detect the presence of dengue antibodies in 50 patients with fever and thrombocytopenia.

Materials and methods

This study was done on patients, who were admitted to Saveetha Medical College, Thandalam, Chennai. A series of 50 patients with fever and thrombocytopenia were collected.

Results

20 patients showed a positive result of IgG antibodies, and 14 patients had IgM antibodies to be positive. The remaining 16 patients had a positive result of NS1 antibody in them. The result (presence of dengue antibodies) was found to be positive in 39 patients and negative (absence of all three antibodies) in the remaining 11 patients included in the study.

Conclusion

From the study it is concluded that there were more number of patients who were diagnosed with secondary infection of dengue with the presence of IgG antibodies in them when compared to those with primary infection of dengue.

Keywords-*Aedes aegypti* mosquito, dengue antibodies, fever, IgG and IgM, thrombocytopenia.

INTRODUCTION

Dengue is a febrile condition caused by a flavivirus transmitted by mosquitoes. The illness is endemic in Asia, the Pacific, Africa and the America. Dengue is known to be the most rapidly spreading mosquito-borne illness caused by a virus. The two mosquito vectors responsible for causing dengue are *Aedes aegypti* and *Aedes albopictus*. There are four serotypes of dengue virus, all producing a similar clinical syndrome; type-specific immunity is life-long, but immunity against the other serotypes lasts only for a few months. The incubation period is 2-7 days and the prodromal symptoms include malaise and headache for 2 days. Clinical manifestations during the acute onset of the illness are fever, backache, arthralgia, headache, generalised pains, vomiting, bradycardia, depression, dysguesia, lymphadenopathy. Other complications include dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS) that occurs after the onset of fever in the critical phase. [1] An early and accurate laboratory diagnosis of dengue could assist clinical management. There is currently no licensed dengue vaccine available and the only means of prevention is through surveillance and vector control. There is also no effective anti-viral therapeutic on the market and supportive therapy such as fluid replacement is the only treatment for severe forms of the disease. [2] However diagnosis of dengue infection (DI) may be made by RT-PCR or by the isolation of virus from the blood in cell cultures. These gold standard tests for identification of DI are not within the reach of peripheral and even most tertiary care laboratories. Of late, non-structural protein 1 (NS1) antigen detection is available for diagnosis of DI. Serologic diagnosis depends on the demonstration of fourfold or greater rise (or fall) in

antibody titres. Detection of dengue specific IgM/IgG antibody has been the mainstay of diagnosis of DI. [3]

MATERIALS AND METHODS

This study was done on patients, who were admitted to Saveetha Medical College, Thandalam, Chennai. We collected a series of 50 patients with fever and thrombocytopenia.

Inclusion criteria

Patients admitted with fever and found to have thrombocytopenia are included in the study. Patients above 18 years were included.

Exclusion criteria

Patients with fever and no thrombocytopenia are not included. Patients with thrombocytopenia and no fever are not included. Patients below the age of 18 years were excluded from the study.

Method

The laboratory diagnosis for dengue was done by IgM and IgG ELISA test. Once the patients were admitted with fever and thrombocytopenia, a careful history was recorded and general physical examination was done. Detailed examination of various systems was done. Routine investigation and the specific and special investigations were done as and when indicated. Details of history, general physical examination and laboratory and technical investigation reports were noted down from time to time. Once the specific diagnosis was reached, patients were treated for it specifically and symptomatically. [4]

RESULTS

The samples were tested by ELISA method. From the data it was obtained that 20 patients showed a positive result of IgG antibodies, indicating the presence of secondary infection and 14 patients had IgM antibodies to be positive with primary infection of dengue. The remaining 16 patients had a positive result of NS1 antibody in them. Therefore, the presence of dengue was confirmed and the

result was found to be positive in 39 patients and negative (absence of all three antibodies) in the remaining 11 patients included in the study.

Dengue antibodies	IgG (+)	IgM (+)	NS1 (+)
Number of patients	20	14	16

Statistical Analysis**Case Processing Summary**

Result	Valid N (listwise)
Positive ^a	11
Negative	39

Larger values of the test result variable(s) indicate stronger evidence for a positive actual state.

a. The positive actual state is Negative.

IgG antibodies- Result**Crosstab**

			Result		Total
			Positive	Negative	
IgG antibodies	Positive	Count	20	0	20
		% of Total	40.0%	.0%	40.0%
	Negative	Count	19	11	30
		% of Total	38.0%	22.0%	60.0%
Total	Count	39	11	50	
	% of Total	78.0%	22.0%	100.0%	

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	9.402 ^b	1	.002		
Continuity Correction ^a	7.386	1	.007		
Likelihood Ratio	13.261	1	.000		
Fisher's Exact Test				.002	.001
Linear-by-Linear Association	9.214	1	.002		
N of Valid Cases	50				

a. Computed only for a 2x2 table

b. 1 cells (25.0%) have expected count less than 5. The minimum expected count is 4.40.

IgM antibodies- Result**Crosstab**

			Result		Total
			Positive	Negative	
IgM antibodies	Positive	Count	14	0	14
		% of Total	28.0%	.0%	28.0%
	Negative	Count	25	11	36
		% of Total	50.0%	22.0%	72.0%
Total	Count	39	11	50	
	% of Total	78.0%	22.0%	100.0%	

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	5.484 ^b	1	.019		
Continuity Correction ^a	3.848	1	.050		
Likelihood Ratio	8.375	1	.004		
Fisher's Exact Test				.022	.016
Linear-by-Linear Association	5.375	1	.020		
N of Valid Cases	50				

a. Computed only for a 2x2 table

b. 1 cells (25.0%) have expected count less than 5. The minimum expected count is 3.08.

NS1 Antibodies- Result**Crosstab**

			Result		Total
			Positive	Negative	
NS1 antibodies	Positive	Count	20	0	20
		% of Total	40.0%	.0%	40.0%
	Negative	Count	19	11	30
		% of Total	38.0%	22.0%	60.0%
Total	Count	39	11	50	
	% of Total	78.0%	22.0%	100.0%	

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	9.402 ^b	1	.002		
Continuity Correction ^a	7.386	1	.007		
Likelihood Ratio	13.261	1	.000		
Fisher's Exact Test				.002	.001
Linear-by-Linear Association	9.214	1	.002		
N of Valid Cases	50				

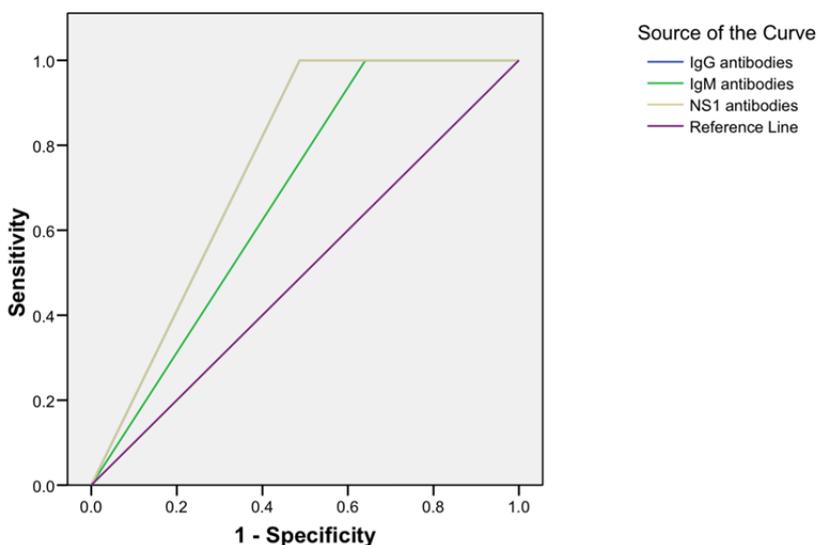
a. Computed only for a 2x2 table

b. 1 cells (25.0%) have expected count less than 5. The minimum expected count is 4.40.

Cross tabulation of the results of IgG, IgM and NS1 antibodies

IgG antibodies		IgM antibodies		Result		Total
				Positive	Negative	
Positive	Negative	NS1 antibodies	Positive	Count	7	7
			% within NS1 antibodies	100.0%	100.0%	
		Negative	Count	13	13	
	% within NS1 antibodies	100.0%	100.0%			
	Total		Count	20	20	
	% within NS1 antibodies	100.0%	100.0%			
Negative	Positive	NS1 antibodies	Positive	Count	8	8
			% within NS1 antibodies	100.0%	100.0%	
		Negative	Count	6	6	
		% within NS1 antibodies	100.0%	100.0%		
		Total		Count	14	14
		% within NS1 antibodies	100.0%	100.0%		
	Negative	NS1 antibodies	Positive	Count	5	5
			% within NS1 antibodies	100.0%	.0%	
		Negative	Count	0	11	
		% within NS1 antibodies	.0%	100.0%		
		Total		Count	5	16
		% within NS1 antibodies	31.3%	68.8%		

ROC Curve



Diagonal segments are produced by ties.

Area Under the Curve

Test Result Variable(s)	Area
IgG antibodies	.756
IgM antibodies	.679
NS1 antibodies	.756

The test result variable(s): IgG antibodies, IgM antibodies, NS1 antibodies has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

DISCUSSION

The diagnosis of dengue and the differentiation between primary and secondary infections are important not only for monitoring the spread of the epidemic but also for identifying the risk of severe forms of the disease. The detection of immunoglobulin IgM and IgG antibodies is the main technique for the laboratory diagnosis of dengue. A few days after the onset of fever, IgM appears as the initial immune response to a primary infection. Soon after IgM detection, IgG also appears on days 5-7 of the disease, reaching the highest titres during the third week of the disease. [5]

Dengue IgM antibody is a marker of recent infection, detection of which is easy, simple and less time-consuming as compared with other serological method. Though dengue IgM detection is a commonly performed test for diagnosis of dengue, it has limitations due to cross-reactivity between other circulating flaviviruses. [6]

The dengue virus NS1 (Non-structural protein 1) is a highly conserved glycoprotein that is essential for the viability of dengue virus and is produced both in membrane-associated and secretory forms by the virus. Enzyme-linked immunosorbent assays (ELISA) directed against NS1 antigen (NS1 Ag) have demonstrated its presence at high concentrations in the sera of dengue virus infected patients during the early clinical phase of the disease. [7]

There is an alarming increase in the incidence of fever with thrombocytopenia. Infections like malaria, dengue, leptospirosis, typhoid, viral fever are some of the common causes of fever with thrombocytopenia. A well organised systematic approach that is carried out with an awareness of causes of fever with thrombocytopenia can shorten the number of investigations and bring out diagnosis. From certain studies it was found that, dengue was one of the commonest cause for the incidence of fever and thrombocytopenia to occur. [8]

Incidence of dengue has increased 30 fold with an expanded geographic distribution of both the viruses and mosquito vectors to new countries and from urban to rural settings. The new challenge is recurrence of dengue haemorrhagic fever with higher severity, even twenty years after primary infection. [9]

CONCLUSION

From the study it is concluded that there were more number of patients who were diagnosed with secondary infection of dengue with the presence of IgG antibodies in them when compared to those with primary infection of dengue. Therefore, detection of dengue specific IgM/IgG antibody is essential and has been the mainstay for the diagnosis of dengue infection.

REFERENCES

1. Davidson's Principles and Practice of Medicine, 22nd edition.
2. Scott R. Fry et al, *The Diagnostic Sensitivity of Dengue Rapid Test Assays Is Significantly Enhanced by Using a Combined Antigen and Antibody Testing Approach*, *PLOS Neglected Tropical Diseases*, June 2011 | Volume 5 | Issue 6 | e1199.
3. Deepaali Danave et al, *Sero-Prevalence of Dengue in A Sub-Urban Region*, *International Journal of Contemporary Medical Research*, Volume 3 | Issue 4 | April 2016 | ICV: 50.43.
4. Shankar R. Raikar et al, *Clinical and Laboratory Evaluation of Patients with Fever with Thrombocytopenia*, *Indian Journal of Clinical Practice*, Vol. 24, No. 4, September 2013.
5. José Rubens Costa Lima et al, *Interpretation of the presence of IgM and IgG antibodies in a rapid test for dengue: analysis of dengue antibody prevalence in Fortaleza City in the 20th year of the epidemic*, *Revista da Sociedade Brasileira de Medicina Tropical*, 45(2):163-167, mar-apr, 2012.
6. Sanghamitra Padhi et al, *A three year retrospective study on the increasing trend in seroprevalence of dengue infection from southern Odisha, India*, *Indian Journal of Medical Research*, 140, November 2014, pp 660-66.
7. M.M. Duthade et al, *The Study of Detection of Dengue NS1 Antigen and IgM Antibody by ELISA in and around Aurangabad, India*, *International Journal of Current Microbiology and Applied Sciences*, 2015) 4(10): 416-422
8. Nikalje Anand et al, *Clinical Outcomes of Patients Presenting As Fever with Thrombocytopenia in Marathwada Region*, *International Journal of Science and Research (IJSR)*, Index Copernicus Value (2013): 6.14 | Impact Factor (2014): 5.611.
9. Saroj Goliae et al, *Serodiagnosis of dengue using NS1 antigen, dengue IgM, dengue IgG antibody with correlation of platelet counts*, *International Journal of AJ Institute of Medical Sciences* 1 (2012), 112-117.