Comparison of Serological and Hematological markers in Dengue: A Cross-sectional study

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Abstract

Dengue virus is the most common Arbo-virus found in India. It has four serotypes DEN-1 to DEN-4. Recently the fifth serotype (DEN-5) was discovered in 2013 from Bangkok. Dengue is one of the major causes of mortality and morbidity in India. Dengue is characterized by high fever, arthralgia, myalgia, hepatomegaly, and thrombocytopenia. Early diagnosis of dengue leads to decrease the mortality. Our study aimed to explore the early diagnostic methods for dengue fever. This is a cross sectional study conducted in Department of Microbiology in a period of April 2021-March 2022. Simultaneously blood samples were subjected to serological examination of NS1 antigen, IgM and IgG antibody by immune-chromatographic method and hematological examination by auto-analyser.

Totally 382 patients were suspected to dengue; on this 74 were serologically proven. Hematological investigation of patients shows thrombocytopenia, leucopenia, and raised hematocrit. On correlation, hematological investigation is better in early diagnosis of dengue fever (p value 0.014). Hematological investigation followed by serology will lead to early diagnosis of dengue fever. Dengue fever is an important public health problem in tropical countries like India. It can present varied clinical manifestations. Early recognition and prompt management are essential to reduce the morbidity and mortality associated with dengue.

Keywords: Dengue, dengue virus, thrombocytopenia, NS1 antigen, *Aedes albopictus*.

Introduction

Dengue fever is one of the most common arthropods borne viral disease. Dengue is an ssRNA virus belonging to *Flaviviridae* family. It is transmitted by the bite of *Aedes aegypti* and *Aedes albopticus* mosquitoes mostly in day time. Dengue is more prevalent in tropical and subtropical regions. It is also known as break bone fever and is characterized by biphasic fever, headache, myalgia, rash, arthralgia, leucopenia and varying degrees of thrombocytopenia[3]. The word "dengue" is derived from Swahili phrase ka-dinga pepo means "cramp like seizure". First clinical case was reported by Benjamin Rush in Philadelphia, who described dengue as "Break bone fever" because of symptoms of myalgia and arthralgia[4].

Dengue hemorrhagic fever (DHF) is characterized by four major clinical manifestations: high grade fever, hemorrhagic phenomena, hepatomegaly and circulatory failure. Such patients may develop hypovolemic shock resulting from plasma leakage. This is called dengue shock syndrome (DSS) and can be fatal[1]. WHO estimates 50-100 million cases of dengue each year. More than three hundred thousand cases of dengue hemorrhagic fever (DHF) are diagnosed each year resulting in 24,000 deaths per year. Dengue fever has been reported from India over a long time but DHF was first reported in 1963 from Calcutta[8]. Early diagnosis of dengue is important for provision of specific care which ensures marked reduction in the morbidity of the disease[10]. The main objective of the study was to observe the correlation between the hematological and serological parameters in dengue infected patients.

Material and Methods

The present study was conducted over a period of one year (April 2021 to March 2022) in Department of Microbiology, after approval from ethical committee of the institute. A total 382 suspected cases of dengue fever were admitted in Hospital during the above-mentioned period and were included in the study and were subjected to serological tests including antigen NS1 and antibody detection of dengue specific IgM and IgG with immuno-chromatographic method. Hematological findings of the patients were recorded. Haemogram profile was done on Automated Hematology analyzer Sysmex KX- 21.

Statistical analysis: Quantitative and qualitative data were expressed as percentages. Association of NS1 Ag, IgM, IgG with Platelet profile was assessed through Chi square test of significance. P<=0.05 was taken for statistical significance.

Results

Out of 382 patients, 74(19.38%) were serologically positive for dengue by ICT method. In this NS1 46 (62.17%), IgG 21(28.38%) and IgM 28 (37.83%) were shown in table 1. Laboratory investigations revealed that the most common hematological abnormality was thrombocytopenia in 240 (63.02%) patients (platelet count less than 1, 00,000/ cumm) followed by leucopenia (total leucocyte count < 4,000) in

245 (64.01 %) patients. However, in 85 (22.06%) patients, platelet count was below 50,000/cumm and only 10 (02.06%) cases had platelet count below 20,000/cumm at the time of presentation. Other hematological parameters are shown in tables 4 to 7.

The correlation of dengue serology reports with platelet count in all patients is presented in table 8. The p value for IgM, IgG, NS1 titers correlated well with the platelet count (p value 0.000-0.014). Dengue is usually accompanied with immune mediated destruction of platelet. The present study has also revealed an in-platelet count with positivity for NS1, IgM and IgG respectively. Some of patients showed thrombocytopenia with dengue serology negative which may due to some other cause.

Discussion

Dengue virus is the most common Arbo-virus found in India. It has four serotypes (DEN-1 to DEN-4). Recently the fifth serotype (DEN-5) was discovered in 2013 from Bangkok.

Table 1
Serological investigation of Dengue

ICT method	No. of patients	% (percentage)
NS1	46	62.17
IgG	21	28.38
IgM	28	37.83

Table 2
Pattern of Seropositivity in Dengue

Seropositivity in Dengue	No. of patients
NS1/IgG/IgM	2
NS1/IgG	1
NS1/IgM	1
IgG/IgM	15

Table 3
Laboratory Investigation of Dengue

Lab Test	No. of Patients	% (Percentage)
Haemoglobin	54/382	14.1
Haematocrit	55/382	14.3
Total leucocyte count	245/382	64.1
Platelet profile	240/382	63.2
Immunochromatographic test	74/382	19.8

Table 4
Haemoglobin

Haemoglobin (gm/dl)	Results	% (Percentage)
<10.0	54/382	14.1
10-15	294/382	76.5
>15	34/382	9.4

Table 5
Haematocrit

Haematocrit (%)	Results	% (percentage)
<35	95/382	25.4
35-45	232/382	60.3
>45	55/382	14.3

Table 6
Total Leukocytes count

Total Leucocyte count (cells/cumm)	Results	% (Percentage)
<4,000	245/382	64.1
4000-11000	95/382	25.4
>11000	37/382	10.5

Table 7
Platelet profile

Platelet count (per cumm)	Results	% (percentage)
<20,000	10/382	2.6
21,000-50,000	85/382	22.2
51,000-1,00,000	145/382	37.5
1,00,000-1,50,000	95/382	25.4
>1,50,000	47/382	12.3

Table 8
Association of results of ICT with platelet count in Dengue patients

		Platelet count			pValue
		Normal	Decreased	Total	
IgM	Positive	3	25	28	
	Negative	139	215	354	
	Total	142	240	382	0.014
IgG	Positive	3	18	21	
	Negative	139	222	361	
	Total	142	240	382	0.000
NS1	Positive	5	41	46	
	Negative	137	199	336	
	Total	142	240	382	0.001

Dengue is one of the major causes of mortality and morbidity in India. Dengue is characterized by high fever, arthralgia, myalgia, hepatomegaly, and thrombocytopenia[2]. Early diagnosis of dengue leads to decrease the mortality. Our study aimed to explore the early diagnostic methods for dengue fever.

In our study, 74 patients were serologically positive to dengue by immune-chromatographic method. In that NS1 antigen reactive patients were found to be more in number when compared to seropositive IgM and IgG antibodies in patients. Anemia was associated with most of the patients with 14.5% dengue illness compared to other study conducted by Tejushree et al[11] showing significant difference in both studies. In our study hematocrit level was increased in patients whereas Mavilla et al[6] reported in 30% of patients.

By hematological investigation, thrombocytopenia is the most significant abnormality seen in most of the patients. This may be due to depression of bone marrow observed in acute stage of dengue virus infection. Other explanations are direct infection of the megakaryocytes by virus leading to increased destruction of the platelets or the presence of antibodies directed against the platelets[5]. Thrombocytopenia may result from destruction of peripheral platelet or bone marrow megakaryocytes by viruses which consequently reduce the platelet production. Haemorrhagic manifestations are very common with severe thrombocytopenia and severity of haemorrhagic tendency correlates with the platelet counts[10].

In our study, 63.3% of patients shows thrombocytopenia which has been correlated with other studies[1,3,7,8]. In our study, 64.1% of patients had a total leucocyte count of less than 4000/ µl. Rashmi[9] suggested that dengue infected patients were usually leukopenic and characterized by a reduction in the absolute number of neutrophils and monocytes. A rapid and accurate method for diagnosis of dengue fever is important both for the clinician and the patient to reduce the morbidity and mortality associated with dengue fever. In the present study, the titres IgM, IgG and NS1 correlated well with the platelet profile (p value, IgM, IgG and NS1 were 0.000,0.001 and 0.01 respectively). NS1 antigen is positive in 62.17% of cases (p value 0.000), hence it suggests that NS1 is the most specific marker for rapid diagnosis followed by IgM and IgG antibodies. A study conducted by Abishek et al[1] showed that IgM is most specific marker for rapid diagnosis of Dengue fever. The present study has also revealed decrease in platelet count with positivity for IgM, IgG, and NS1 respectively.

Infection with dengue fever offers lifelong immunity but the cross immunity is minimal and short lived. The main complication of the dengue fever is the development of dengue hemorrhagic fever[11]. Dengue fever is a self-limiting disease. Dengue hemorrhagic fever causes morbidity and mortality. No antiviral treatment is available hence fluid and electrolyte replacement and supportive therapy is the available modalities of treatment. Since there is no vaccine for this disease, vector control is the only way to check the transmission of disease.

Conclusion

Dengue is preventable if it is detected earlier. Hemogram is a simple method to diagnosis dengue. The hemogram is the most important guide to therapy and prognosis. Most of the cases in our study had thrombocytopenia and leucopenia.

These indicators, if rightly and timely assessed can be of value for better care of complicated cases. Inclusion of NS1, IgM and IgG in the diagnosis of dengue increases the detection rate significantly. Hematological investigation followed by serology will lead to early diagnosis of Dengue fever. Dengue fever is an important public health problem in tropical countries like India.

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