Original Research Article

Clinicopathological profile of dengue like illness in children – A prospective study

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A B S T R A C T

Keywords

COD
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To assess and compare the clinical manifestations of DENGUE like illness with rapid serological test in children <18 yrs. To determine the frequency of primary and secondary dengue infection through separate determination of Ig G and Ig M. Study design: cross sectional study. Setting: Tertiary referral centre. Participants: 175 children in the age group of 1-18 yrs of either sex (98 males, 77 females) with features suggestive of dengue as per WHO criteria were included. Methods. All clinically suspected cases of dengue fever aged <18 yrs according to WHO criteria were included in the study. Blood samples for dengue serology IgM and Ig G antibodies and NSI Ag , platelets were drawn after informed consent. The clinical manifestations were correlated with the laboratory results. Results. A total of 175 serum samples were collected from pediatric patients <18yrs of age , who presented with clinical signs of dengue like illness .All the 175 cases had fever. Children who presented with clinical signs of chills, abdominal pain, body pain, vomiting, rash, hepatomegaly, bleeding manifestations, pleural /abdominal effusion had high titres of IgM , IgG and NS1 Ag titres(p value was between 0.015 to 0.837 which was statistically significant). Conclusion. Detection of Ig M antibodies coupled with thrombocytopenia and fever indicate high level of definitive diagnosis of dengue/ dengue hemorrhagic fever when compared to Ig G antibodies or NS1 antigen alone. Keywords: dengue fever, thrombocytopenia, NS1Ag – non structural surface Ag, ICT immunochromatographic test.

Introduction

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Participants: 175 children in the age group of 1-18 yrs of either sex (98 males, 77 females) with features suggestive of dengue as per WHO criteria were included. Methods. All clinically suspected cases of dengue fever aged <18 yrs according to WHO criteria were included in the study. Blood samples for dengue serology IgM and Ig G antibodies and NSI Ag , platelets were drawn after informed consent. The clinical manifestations were correlated with the laboratory results. Results. A total of 175 serum samples were collected from pediatric patients <18yrs of age , who presented with clinical signs of dengue like illness .All the 175 cases had fever. Children who presented with clinical signs of chills, abdominal pain, body pain, vomiting, rash, hepatomegaly, bleeding manifestations, pleural /abdominal effusion had high titres of IgM , IgG and NS1 Ag titres(p value was between 0.015 to 0.837 which was statistically significant). Conclusion. Detection of Ig M antibodies coupled with thrombocytopenia and fever indicate high level of definitive diagnosis of dengue/ dengue hemorrhagic fever when compared to Ig G antibodies or NS1 antigen alone. Keywords: dengue fever, thrombocytopenia, NS1Ag − non structural surface Ag, ICT immunochromatographic test.

Materials and Methods

Source of data collection. serum samples from patients <18 yrs presenting to the hospital with dengue like illness were tested for NS1 antigen, Ig G, , Ig M dengue antibodies.

Study design : cross sectional study.
Sample size :175
setting : tertiary care hospital

All clinically suspected cases of dengue fever aged <18 yrs according to WHO criteria were included in the study. Age >18yrs and Patients with slide positive malaria or ICT positivity for malaria, urinary tract infection , enteric fever , liver abscess and pneumonitis are excluded.Patients demographic characteristics were collected in a predesigned proforma. Blood samples for dengue serology (IgG , IgM) ,NS1 Ag, platelets were drawn after informed consent. The clinical manifestations were correlated with the laboratory results.

Instrument used

SD BIOLINE dengue duo cassette.

This device is based on the immunochromatographic principle (ICT) that allows simultaneous detection of dengue NS1 antigen and IgG/M antibody. Positive samples produce a pink line both in test and control position. Negative samples produce a pink line only at the control position . The assay is performed according to the manufacturer's guidelines and results are recorded. A positive control will be tested for quality control.

Rationale for sample size

Clinically suspected dengue fever cases (80%) are likely to be confirmed by detection of antigen and or antibody by immunochromatographic test ICT [8]. Considering the above diagnostic accuracy and keeping the absolute precision of +_6 and with a desired confidence interval of 95% it is estimated that nearly 175 clinically suspected dengue fever cases need to be studied to achieve the objectives of the study.

Statistical analysis

Quantitative data was summarized in terms of mean and standard deviation. Qualitative data expressed as percentages. Association of NS1 Ag, IgM, IgG with various clinical manifestations were assessed through chi square test of significance. $P \leq 0.05$ was taken for statistical significance.

Results and Discussion

A total of 175 sera samples were collected from pediatric patients less than18yrs of age , who presented with clinical signs of dengue like illness. Among them , 77 were females and 98 were males. M:F ratio (1:0.78).

All the 175 cases had fever, hence the p value for NS1Ag was not applicable. The p value for NS1 Ag in patients with clinical signs of chills, abdominal pain, body pain, vomiting, rash, hepatomegaly, bleeding manifestations, pleural /abdominal effusion were found to be between 0.015 to 0.837 which was statistically significant.

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 various clinical manifestations. (p value, IgM, IgG and NS1 were 0.000,0.699 and 0.027 respectively). IgM titres were positive in all the 175 cases, (p value -0.000) hence it suggests that, IgM is the most specific marker for rapid diagnosis when compared to Ig G and NS1 antigen. The reason for this could be that the samples analyzed were from patients with history of 3-7 days of fever and IgM antibody appears quite early in the course

of illness (Fry et al., 2011).

There were 85 cases (45%) where in IgM and IgG titres were both elevated. These were the cases which were clinically sick and unstable (hypotension) and required longer ICU monitoring. These cases had severe clinical manifestations in the form of fever, pain abdomen, thrombocytopenia which correlated well with dengue serology .The reason for this could be the fact that since IgG and Ig M titres both were elevated, they were suffering from secondary infection. In secondary infections the strain of the virus which causes the second infection is different from the strain which has caused the primary infection. During the secondary infection, there is an exaggerated immune response due to the presence of antibodies that were produced during primary infection. Clinically it results in a leak syndrome where in the plasma leaks in to the free spaces of the body(pleural space/ abdomen) causing hypotension and shock. Dengue non structural protein 1 (NS1)has been identified as a useful early serum marker for primary and secondary dengue infections and is typically present between days one to nine after the onset of clinical signs with a peak from days 3-5 (Fry et al., 2011) . Thus detection of NS1 antigen would be a promising test to diagnose dengue in its early febrile illness (Shrivatsava et al., 2011).

However in the present study detection of NS1 antigen alone without considering the antibody status(IgM /IgG) could not be taken as positive for the diagnosis of dengue like illness in pediatric age group. The correlation of results of NS1 Ag with the clinical signs (i.e., fever, chills , vomiting , body pain, abdominal pain, effusion , hepatomegaly, bleeding in the present study are presented in the table 1.

Table.1 Association of NS1Ag with the various clinical manifestations

Clinical manifestations	NS1 Antigen						P value
	Positive		Negative		Total		
	N	Percent	N	Percent	N	Percent	
1.Fever	13	7.4	162	92.6	175	100	Not applicable
2. Chills present	4	3.7	9	13.6	13	7.4	0.015
absent	105	96.3	57	86.4	162	92.6	
total	109		66		175		
3.Vomiting +present	7	7.1	92	92.9	99	100	0.837
Absent	6	7.9	70	92.1	76	100	
Total	13		162		175		
4.Rash present+	4	20	16	80	20	100	0.023
Absent	9	5.8	146	94.2	155	100	
total	13		166		175		
5.Body_Pain Present	3	6.1	46	93.9	49	100	0.681
Absent	10	7.9	116	92.1	126	100	
Total	13		166		175		
7.Bleeding_manifestation present	1	16.7	5	83.3	6	100	0.380
Absent	12	7.1	157	92.9	169	100	
Total	13		162		175		
8.Hepatomegaly Present	5	6.2	76	93.8	81	100	0.557
Absent	8	8.5	86	91.5	94	100	
Total	13		162		175		
9.Pleural/Abdominal Effusion Present	2	4	48	96	50	100	0.274
Absent	11	8.8	114	91	125	100	
Total	13		162		175		

Table.2 Association of results of ICT with platelet count in pediatric patients.

		Platelet count			pValue
		Normal	Decreased	Total	
IgM	Positive	2	24	26	
	negative	68	81	149	0.000
	Total	70	105	175	
IgG	Positive	2	32	34	0.001
	negative	68	73	141	
	Total	70	105	175	
NS1	Positive	1	12	13	0.013
	negative	69	93	162	
		70	105	175	

In the present study all the 175 cases had fever and hence a positive result of NS1 Ag with fever could be considered as definitive diagnosis of dengue like illness (Lt Col Banerjee et al., 2008). Children who presented with non specific clinical signs such as nausea /vomiting , body pain with positive dengue serology, could not be considered as tool for definitive diagnosis of dengue like illness.

The correlation of results of NS1 Ag with clinical signs on examination (i.e. abdominal effusion, hepatomegaly, bleeding manifestations) is presented in table 1. There is strong association of the dengue serology reports with the clinical signs and hence in the presence of positive reports, the clinical signs could be considered as supporting evidence for the diagnosis of dengue like illness.

The correlation of dengue serology reports with platelet count in all patients is presented in table2. The p value for IgM, IgG, NS1 titres correlated well with the platelet count (p value 0.000-0.013). Dengue is usually accompanied with immune mediated destruction of platelet. The present study has also revealed a decrease in platelet count with positivity for IgM, IgG, NS1 respectively.

Detection of Ig M antibodies coupled with thrombocytopenia and fever indicate high level of definitive diagnosis of dengue/ dengue hemorrhagic fever when compared to Ig G antibodies or NS1 antigen alone.

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