Original Research Article

Study of clinical profile of dengue fever and correlation with NS1 antigen and IGM antibody test

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Abstract

Background: Dengue fever, an infection caused by several arthropod borne Viruses, is characterised by biphasic fever , myalgia or arthralgia , rash , leucopenia and lymphadenopathy. Dengue is the most common arboviral illness transmitted worldwide caused by 4 serotypes of dengue virus DEN 1, DEN 2, DEN 3, DEN 4, family flaviviridae, genus flavivirus. Dengue is transmitted by mosquitoes of genus Aedes, aedes aegypti being most important vector in subtropical and tropical areas of world. **Aims and Objective:** 1. To study clinical presentation of dengue fever and its correlation with NS1 antigen and dengue IGM Antibody. 2. To detect NS1 antigen positivity among the study population. 3. To compare IgM capture ELISA with NS1 antigen detection for diagnosis of dengue. **Methodology:** Prospective study of 210 patients with dengue infections done at civil hospital, Ahmedabad carried out from August 2015 to November 2017. Patients included in this study are according to case definition of dengue fever in paediatric ward (1 month to <12yrs). **Result:** Dengue is common preventable vector born disease with incidence 1.67% among hospital indoor patients and almost equally distributed in both sexes. Only 12% of patients had severe dengue and most common presentation was dengue hepatitis (6.2%) and least occurring presentation is myocarditis (2.4%). Fever was the predominant symptom seen in 96.7% of cases followed body aching, nausea vomiting. Most common sign was tachycardia seen in 51.9 % followed by maculopapular rash and hepatomegaly. NS1 Ag was positive in 95% patients presented in 1st to 5th day of Illness while serum IgM was positive in 97% of patients presented after 10 days of Illness.
Key Word: NS1 antigen, IGM antibody test.

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INTRODUCTION

Dengue fever is a severe flu like illness that affects the infants, children's, adolescents, and adults. Dengue is one of the most serious and the most common mosquito borne viral infections of the man affecting mainly the tropical and subtropical countries in the world and caused by the bite of Aedes group of mosquitoes especially Aedes aegypti. Dengue is an acute viral disease caused by a virus (serotype 1-4) belonging to the broad group of Arbo-viruses, family Flaviviridae, subfamily Flavivirinae and genus Flaviviruses. Dengue virus has a positive sense, ss RNA viral genome. In order to detect dengue fever, there are various tests available like antigen detection tests (Non- structural 1 antigen- NS1 antigen), Antibody detection tests like Dengue IgM and Dengue IgG, virus isolation in cell culture, immunofluorescence or by detection of viral RNA by nucleic acid amplification tests (NAAT). NS1 antigen detection and Dengue IgM and Dengue IgG detection which detects dengue infection are easy to do and cheap. Moreover they detect the disease early so that and prompt treatment can be given. According to WHO the incidence of dengue globally shoot up 30 fold in the past 50 years , estimated that India had largest number of dengue cases, with about

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33 million apparent and another 100 million asymptomatic infections occurring annually. According to directorate of national vector borne disease control programme, India in 2017 has seen 11,832 more cases of dengue compared with 2016. The overall estimate of the prevalence of laboratory confirmed dengue infection based on testing of more than 200,000 clinically suspected patients was 38.3%. With the increasing incidence of dengue infection, the early diagnostic confirmation of dengue infection in patients allows for timely clinical intervention, etiological investigation, and disease control, hence, diagnosis of dengue disease during the acute phase should be a priority and is a public health concern.

AIMS AND OBJECTIVES

1. To study clinical presentation of dengue fever and its correlation with NS1 antigen and dengue IGM Antibody .
2. To detect NS1 antigen positivity among the study population.
3. To compare IgM capture ELISA with NS1 antigen detection for diagnosis of dengue.

MATERIAL AND METHODS

Prospective study of 210 patients with dengue infections done at civil hospital, Ahmedabad carried out from August 2017 to August 2018. Patients included in this study are according to case definition of dengue fever in paediatric ward (>1 month to <12 yrs). Who Defines Dengue Fever as acute febrile illness of 2-7 days duration with two or more of the following manifestations includes retro orbital pain or ocular pain, headache, rash, myalgia, arthralgia, hemorrhagic manifestations. Their history and examination findings were received in details, all investigation specially NS 1 and Ig M was done in all patients and treatment details were recorded and analysed.

Dengue Haemorrhagic Fever

A. A case with clinical criteria of dengue fever plus

B. Haemorrhagic tendencies evidenced by one or more of the following

- Postive tourniquet test
- Petechiae ,ecchymoses or purpura
- Bleeding from mucosa , gastrointestinal tract, injection sites or other sites plus

C. thrombocytopenia (<100000 cum per cmm)

D. evidence of plasma leakage due to increased vascular permeability , manifested by one or more of the following

- A rise in average haematocrit for age and sex > 20%
- A more than 20% drop in haematocrit following volume replacement treatment compared to baseline.
- Signs of plasma leakage (pleural effusion, ascites, hypoproteinemia)

Dengue Shock Syndrome (Dss): All the above criteria for DHF with evidence of circulatory failure manifested by rapid and weak pulse and narrow pulse pressure (<20% mm hg) or hypotension for age, cold and clammy skin and restlessness.

RESULTS AND OBSERVATION

Total no of indoor patients	Total no of dengue cases	Incidence
12585	210	1.67%

Out of 12585 patients were admitted in civil hospital, Ahmedabad over period of 2 year from august 2016 to August 2018, total no of dengue cases were 210. Thus the incidence of dengue in this study among the hospitalised patients in paediatric ward at civil hospital, Ahmedabad was 1.67%.

Sex	No (n=210)	Percentage
Male	112	53.3%
Female	98	46.7%

In present study male: female ratio is 1.14:1. No significant sex different was noted in present study. It was observed almost equally in both sexes. A study done by Mishra *et al* shows sex ratio of 1.14:1 and study done by pothapregada *et al* shows sex ratio of 1.21:1.The present study showed increased in higher age group. This could be because subsequent infections are more severe and requiring admission. In a study by pothpregada *et al* 6-12 year age group was affected.

Age	No of patients	Percentage
<1 month	6	2.85%
1mnth - 1 yr	30	14.2%
1yr - 3 yr	42	20%
3yr - 6yr	54	25.7%
6yr -9yr	53	25.2%
9yr -12 yr	25	12%

In present study, most common presentation was fever(96.7%) followed by body ache, vomiting , abdominal pain, headache and rash. In study by Mishra *et al* fever was present in 100%, myalgia in 76.8% and in pothapregada *et al* fever in 94.6% and myalgia in 81.9%.. Non specific symptoms like cough/ cold and myalgia were also found in significant no of cases. Breathlessness, yellow discoloration of eyes and urine, body swelling, oliguria and convulsion are the symptoms of severe dengue and its complications. In present study, most common sign in dengue fever was tachycardia, probably associated with fever followed by maculopapular rash and hepatomegaly. A sign of complications like ascites, edema, pleural effusion, jaundice, bradycardia and comatose state is found in less number of patients. The higher incidence of patients of dengue fever with warning signs could be because these patients required hospital admission and thereby became a part of this study. Which is same as study done by Mishra *et al* which show 54.6% patients presented with dengue fever with or without warning signs.

Dengue fever	No of cases	Percentage
Dengue fever without warning signs	53	25%
Dengue fever with warning signs	132	63%
Severe dengue fever	25	12%

S Ig M was postive in 135 patients. NS 1 antigen test was positive in 75 patients.

Test	No of patients N =210	Percenta ge
NS 1 antigen test	75	35.7%
S . Ig M	135	64.3%

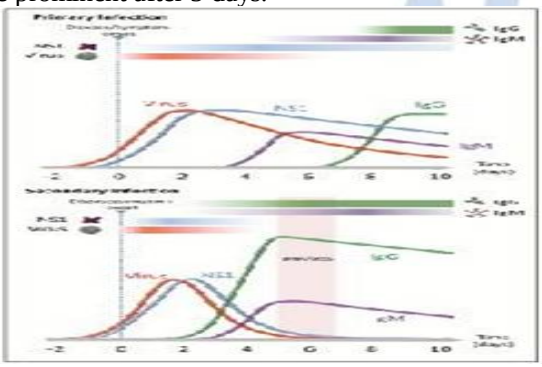
Day of illness on admissi on	No. of patient s	Positiv e NS1Ag report	Positiv e S.IgM report	P value
1-5 day	58	55	3	0.002
6-10 day	76	18	58	0.001
11-15 days	34	2	32	0.003
>16 days	42	-	42	0.003

As we have consider significant p value for correlation is 0.05. In present study, NS 1 antigen assay and S Ig M assay, both has been done in all suspected patients to compare sensitivity of the tests with the duration of illness. Out of 58 patients admitted on 1 to 5 day of fever most of the patient had positive NS1Ag test (95%) and only 3 patients had positive S. IgM report.(p value 0.002). In patients admitted after 10 day of fever, 97% of the patients had positive S.IgM report (p value 0.003). In patients admitted on 6 to 10 day of fever approximately 24% patients had positive NS1Ag report and rest 76% had positive S. IgM report. So it can be concluded that sensitivity of NS1Ag is more in initial 5 days of fever. In a study done by wang *et al* in first 7 days NS1 antigen was detected in 69.5% and in 8-15 days in NS1 is 29% whereas in initial days of illness according to study done by babaliche *et al* sensitivity of NS1 compared to IGM was 92.6% and specificity was 90%.

SUMMARY

Dengue is an endemic viral disease affecting tropical and subtropical regions around the world. Dengue infection presents with non specific fever that mimics other viral illnesses. However, according to WHO case definition dengue fever (DF) is defined as acute febrile illness with two or more manifestations among headache, retro-orbital pain, myalgia, athralgia, rash, haemorrhagic manifestations and leucopenia. Dengue haemorrhagic fever (DHF) is defined as 2- 7 days of acute febrile illness with bleeding, thrombocytopenia and evidence of plasma leakage. When all the features of DHF are present along with circulatory failure then the patient is categorized as dengue shock syndrome (DSS). The major diagnostic methods currently available are viral culture, viral RNA detection by RT-PCR and serological tests such as IgM capture ELISA. Serological test by antibody detection as IgM ELISA capture. Antibody response to infection differs according to the immune status of the host. First antibody to appear I g M. Its levels peak at 2 weeks after the onset of symptoms. Declines to undetectable levels

over 2 to 3 months. Secondary antibody is Ig G is detectable at low titres at the end of 1st week of illness, increasing slowly thereafter and is still detectable after several months and even for life. Current strategy under National Vector Disease Control Program(NVBDCP) suggests that diagnosis of a particular flavi virus should always be made taking into account the clinical presentation, the performance of serological tests and the knowledge of the flavi virus circulating in that particular geographic region. Tests for antigen and antibody detection are widely used for confirmation of dengue infection. However, performance of tests depends upon specificity and sensitivity of the test kits used. High specificity is important if the tests are being used to confirm dengue as the cause of the outbreak whereas sensitivity is very important if the tests are to be used to support clinical diagnosis and for case management. Following the bite of an infected aedes mosquito, dengue virus replicates quickly before the development of signs and symptoms. NS1 Ag circulates uniformly in all serotypes of dengue virus and circulates at high level during the 1st few days of illness. This is the reason for high detection rate of NS1Ag in acute phase sera, there after decreases gradually and antibody detection becomes more prominent after 5 days.



CONCLUSION

Dengue fever, common in developing countries like India causes significant morbidity and mortality, presents like any other viral illness. Hence these patients should be diagnosed early for prompt treatment. The present study showed that NS1 antigen detection along with IgM and IgG tests have can started. The result revealed that both NS1 and IgM have a very high specificity. Although early detection is important and it is possible with NS1 Ag as it is more sensitive in first 5 days of life, Ig M was more specific and sensitive in later days of life. Thrombocytopenia, rising hematocrit and clinically petechiae and positive tourniquet test provide supportive evidence in early detection. So NS 1 Ag and liver function test plays important role in early diagnosis, early detection of complication and as a prognostic marker for outcome in dengue fever. Our finding suggest that the NS1 antigen capture ELISA is very useful and specific tool for the diagnosis of acute dengue infection .However, the sensitivity of the NS1 assay is depended on the level of viremia and host humoral immune response Therefore, a combine use of NS1 antigen with dengue IgM test could significantly improve diagnostic sensitivity of dengue infection. Hence if we do both NS1 antigen detection test and IgM/IgG antibody detection test, we can diagnose dengue fever early so that the morbidity and mortality can be reduced and hence we conclude that the serological tests do have significant role in the early diagnosis of dengue fever.

REFERENCES

1. Nelson textbook of pediatrics 18th edition
2. Clinical Profile of Dengue Fever in Children: A Study from Southern Odisha, India , scientific Shubhankar Mishra, * Ramya Ramanathan, and Sunil Kumar Agarwalla Published online 2016 Apr 24.
3. Clinically profiling pediatric patient of dengue. Sriram pothapregada ,banupriya kamalakannan , journal of global infectious diseases , 2016 , volume 8 , issue 3 , page 115-120
4. The Study of Detection of Dengue NS1 Antigen and IgM Antibody by ELISA in and around Aurangabad, India. M. M. Duthade*, A.S. Damle, J. B. Bhakre, A. A. Gaikwad, J.A.Iravane, Arjun Jadhav and Anuja Samale , International journal of current microbiology and applied sciences ,Volume 4 Number 10 (2015) pp. 416-422
5. Catching dengue early; clinical features and laboratory markers of dengue virus infection. Prakash Babaliche, Darshan Doshi, journal of the association of physicians of India, volume 63, may 2015
6. Evaluation of a Commercial SD Dengue Virus NS1 Antigen Capture Enzyme-Linked Immunosorbent Assay Kit for Early Diagnosis of Dengue Virus Infection. Seok Mui Wang and Shamala Devi Sekaran , journal of clinical microbiology , 2010 June 23
7. Textbook of pediatric infectious disease
8. Clinical handbook of pediatric infectious disease
9. Nelson's pediatric antimicrobial therapy
10. Dengue WHO guidelines 2018
11. National Guidelines for clinical management of dengue fever.

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