Original Research Article

Study on parameters of severity in Dengue infection with both NS1 Antigen and Dengue IgM reactive on the same day, in a tertiary care hospital, Kolkata

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Abstract

Background: Dengue, an important arboviral disease in the tropics manifests with severe thrombocytopenia and deranged liver function. Detection of both NS1 antigen and Dengue IgM on the same day, during the first few days of fever increases the Dengue diagnostic severity. Therefore this study was conducted to study the changes in platelet count and level of hepatic enzymes along with other biochemical and haematological parameters to predict the severity of Dengue infection in these cases.**Methods:** This prospective study was conducted in the Department of Microbiology, NRS Medical College and Hospital, Kolkata from July 2018 to January 2019 for the simultaneous detection of NS1 antigen and Dengue IgM on the same day of febrile hospitalized patients in the age group of 13 to 60 years. The platelet count and hepatic enzymes along with other biochemical and haematological parameters were evaluated for these patients.**Results:** Of the total 284 blood samples received, 91 patients were Reactive to both NS1 antigen and Dengue IgM on the same day. Their mean age was 34 years, with male preponderance and maximum reactive on the 5th day of fever. Mean platelet count was 50,000 / mcL, SGOT and SGPT levels were raised with a mean of 215.60 units/litre and 152.7 unit/litre respectively.**Conclusion:** Presence of both NS1 antigen and Dengue IgM on the same day, associated with thrombocytopenia and deranged liver functions are important parameters for predicting disease severity and play a major role in determining the clinical outcome.

Key word : Dengue , NS1 antigen, IgM, SGOT/SGPT.

Introduction

Dengue virus is an important cause of acute febrile illness in tropical and subtropical settings causing Dengue Fever,Dengue Hemorrhagic Fever and Dengue Shock Syndrome, representing a broad spectrum of clinical illness varying from mild to severe symptoms leading to death. [1]Dengue virus is a member of the flaviviridae family which comprises West nile virus, Japanese encephalitis virus, yellow fever virus and Tick borne encephalitis virus among others.[2]Till now, Dengue Fever was believed to be caused by four different serotypes. The fifth variant DENV-5 was isolated in October 2013. This serotype follows the sylvatic cycle unlike the other four serotypes which follow the human cycle.[3] Mosquitoes belonging to the genus Aedes**(***Aedes aegypti, Aedes albopictus* and *Aedes polynesiensis***)** play an important part in transmission of Dengue. The primary and most important vector is *A aegypti***,** but *A albopictus* and *A polynesiensis* may act as vectors depending on the geographic location. [4] Up to 3.6 billion people are estimated to now live in tropical and subtropical areas where the dengue viruses have the potential to be transmitted.[5]

Global estimates vary, but regularly approximate 50 million to 200 million Dengue infections, 500,000 episodes of Severe Dengue (DHF/DSS), and over 20,000 Dengue related deaths occur annually.[6] Usually, Dengue infected people remain asymptomatic or only have mild symptoms such as uncomplicated fever; others have more severe symptoms and few have life threatening illness.[7] The incubation period ranges from 3-14 days but most often it is 4 to 7 days. The disease primarily features sudden onset fever, retro-orbital headache, severe muscle and joint pain and rash. The associated muscle and joint pains gives the name 'break-bone fever'.[8]This severe disease is marked by endothelial dysfunction and impaired blood clotting.[9]Extravasation from the blood vessels due to endothelial dysfunction leads to accumulation of fluid inside the chest and abdominal cavities. Bleeding complications are a resultant of clotting abnormalities. Increased viraemia and multi organ involvement specially the liver are associated with more severe

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and complicated disease.[10]Deregulated host immune response against the virus and direct effect of viremia on liver cells result in hepatic impairment which is usually seen in dengue infection.Hence, thrombocytopenia and deranged liver functions are important manifestations of Dengue severity. This in the presence of both NS1 and Dengue IgM reactivity on the same day in the first few days of fever are important diagnostic parameters. This study was conducted to assess the severity of Dengue infection with both NS1 antigen and Dengue IgM reactive on the same day along with changes in platelet count and level of hepatic enzymes.

Materials and Methods

This prospective study was conducted in the Department of Microbiology, NRS Medical College and Hospital, Kolkata from July 2018 to January 2019 for the simultaneous detection of NS1 antigen and Dengue IgM on the same day of a febrile hospitalized patient in the age group of 13 to 60 years. The platelet count and hepatic enzymes were evaluated for these patients. The inclusion and exclusion criteria's were as follows :

Inclusion criteria:

1. Age ≥13 years and ≤60 years.
2. Both NS1 antigen and Dengue IgM reactive on the same day by ELISA.
3. Patients in whom liver enzymes and platelet count were evaluated.
4. Patients complying the study through written informed consent.

Exclusion criteria:

1. All patients below the age of 13 years.
2. All patients above 60 years of age.
3. All patients who do not comply or refuse to participate in the study after informed consent.
4. Other febrile illness apart from dengue like malaria, typhoid and leptospirosis.
5. Cases reactive to HBsAg.

Results

Of the total 284 blood samples received,91 patients were reactive to both NS1 antigen and Dengue IgM on the same day.

The age distributions of patients reactive to both NS1 antigen and Dengue IgM on the same day are as depicted in the following pie chart. The mean age of occurrence was 34 years.

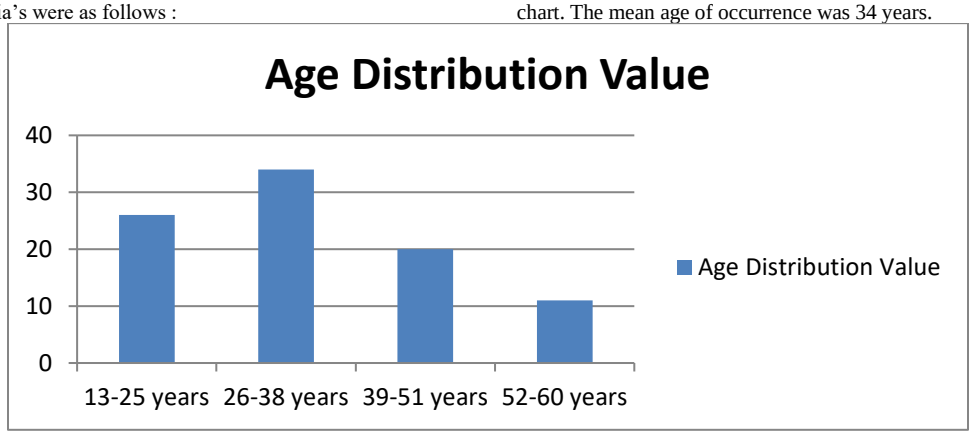

Fig 1: Age distribution of patients reactive to both NS1antigen and Dengue IgM on the same day.

There male: female ratio showed that there was male preponderance (63%) and female were (37%).

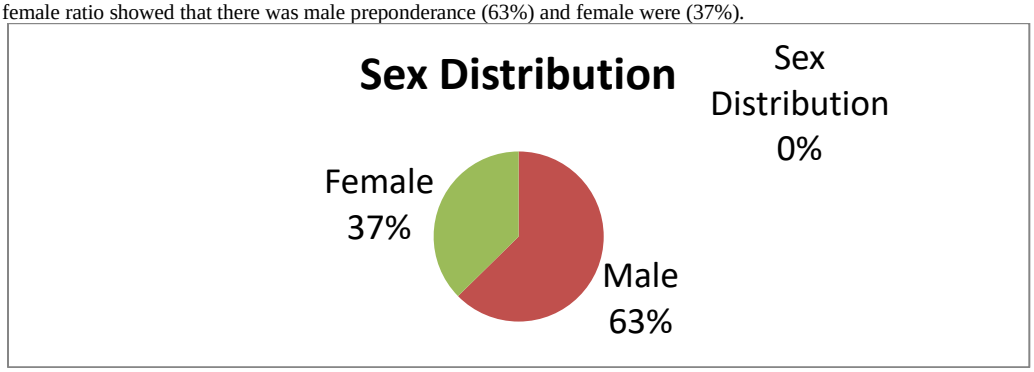

Fig 2: Sex distribution of patients reactive to both NS1antigen and Dengue IgM on the same day.

The maximum incidence of both NS1 antigen and Dengue IgM reactivity on the same day was seen on 5th day of illness. The mean platelet count was 50000 per microliter of blood.

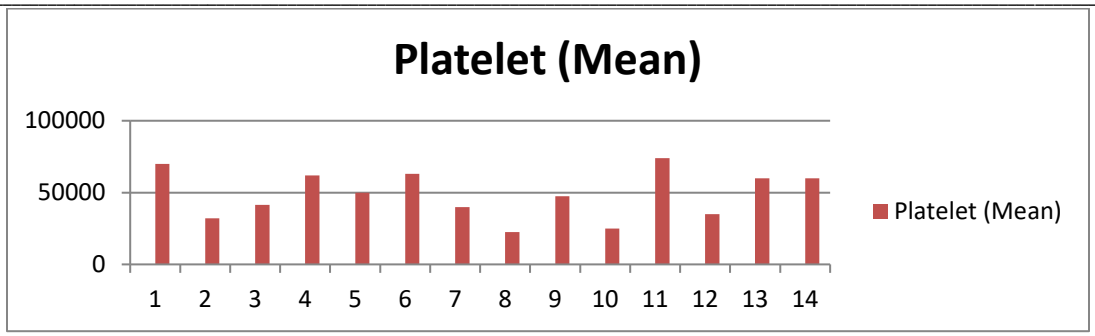

Fig 4: Distribution of platelet count

SGOT and SGPT levels were raised with a mean of 215.60 units/litre and 152.7units/ litre with both NS1 Antigen and Dengue IgM reactive on the same day respectively.

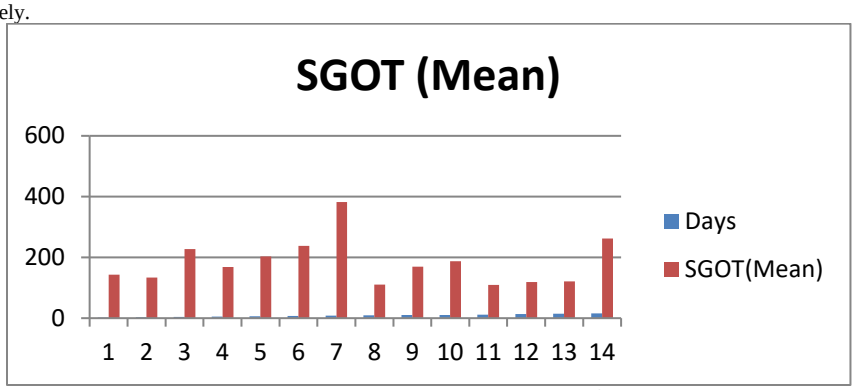

Fig 5 : SGOT levels as seen with duration of illness.

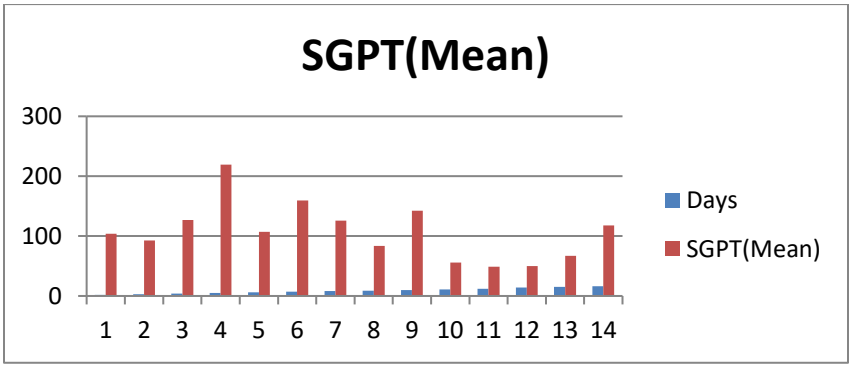

Fig 6: SGOT and SGPT levels as seen with duration of illness

Table 1:Standard Deviation for individual days are as follows

Days	No of Patients	PLATELET	SGOT	SGPT
2	1	0	0	0
3	5	17204.65	44.44502	65.03353
4	6	20686.15	120.0927	58.07897
5	23	29238.61	128.1062	594.1918
6	20	22790.35	382.219	209.956
7	21	23222.09	209.6444	199.118
8	6	30743.11	506.3275	98.92323
9	2	9185.587	47.76505	36.12997
10	2	27556.76	62.46199	32.45574
11	1	0	0	0
12	1	0	0	0
14	1	0	0	0

15	1	0	0	0
16	1	0	0	0

Discussion

Dengue fever is one of the most important arboviral infections and is a major global public health problem. In this study focus was on patients reactive to both NS1 antigen and Dengue IgM on the same day.Of the total 284 blood samples received, 91 patients were reactive to both NS1 antigen and Dengue IgM on the same day. In a similar study conducted by SC Arya et al among the 678 NS1-positive, 394 were exclusively positive for NS1, 145 were also positive for IgM. [12]In our study the mean age of occurrence was 34 years. This is in correlation with study by Eggar JR et al. where the results suggest that the risk for clinical disease after primary dengue infection is relatively low throughout childhood and then increases rapidly through adolescence and early adulthood. [13]

In our study there was significant male preponderance which is in concordance with the study by Anker M et al, based on reported dengue cases from national surveillance systems, found a consistent and significant excess of Dengue cases among males ≥ 15 years of age. [14]The study conducted by Ng DH et al showed that sixty-nine percent of the study population were male with a median age of 34 years which correlates with our findings.[15]In a study by Muham-mad Suleman et al, found during their study period (2013–2015), a total of 1270 serum samples were tested for NS1 antigen and dengue IgM antibodies of them 86% (1097/1270) were positive by one or two diagnostic test. Of the 1270 total samples, 68% (866/1270) were from male and 32% (404/1270) from female; the male to female ratio was 2:1. Young adults in the age group of 16–30 years were most affected. The maximum incidence of both NS1 antigen and Dengue IgM reactivity on the same day were seen on 5th day of illness but studies with similar findings are scarce. Thrombocytopenia is observable in several dengue cases and those with severe thrombocytopenia $<3x10^9$/L would need hospitalization and platelet transfusion. In adults, a platelet count of $5 \times 10^9\,L^{-1}$ and packed cell volume >50 are significantly associated with bleeding manifestations. However, a study by Chaudhary R et al enrolling 245 dengue patients showed no correlation between clinical bleeding and platelet count, and 81 non bleeding patients had counts of less than $20 \times 10^9\,L^{-1}$. [17] In contrast, another study by Makroo RN et al enrolling 225 dengue patients suggested that bleeding occurred more often in patients with platelet counts below $20 \times 10^9\,L^{-1}$. [18]In our study, SGOT and SGPT levels were raised with a mean of 215.60 units / Litre and 152.7 units / Litre respectively. As suggested in a study by Kalayanarooj S et al, SGOT/AST level tend to be greater than SGPT/ALT level.[19] Similar findings were seen in study by Uchadadia S et al. This pattern is similar in alcoholic hepatitis but not present in other cases of viral hepatitis. Studies have suggested that it maybe due to excessive release of AST from damaged myocytes during dengue infection. [20]

Conclusion:

Dengue is probably the most important arthropod borne viral disease worldwide. It poses major clinical, social and treatment challenges. Our study shows presence of both NS1 antigen and Dengue IgM on the same day, associated with thrombocytopenia and deranged liver functions which are important parameters for predicting disease severity and thus play a major role in determining the clinical outcome.

References

1. Gibbons RV, Vaughn DW. Dengue: an escalating problem. Bmj. 2002 ;324(7353):1563-6.
2. Lindenbach BD, Rice CM. Molecular biology of flaviviruses. Advances in virus research. 2003 ;59:23-62.
3. Mustafa MS, Rasotgi V, Jain S, Gupta V. Discovery of fifth serotype of dengue virus (DENV-5): A new public health dilemma in dengue control. Med J Armed Forces India. 2015;71(1):67-70.
4. Malavige GN, Fernando S, Fernando DJ, *et al*.Dengue viral infections Postgraduate Medical Journal 2004;80:588-601.
5. Ferreira GL. Global dengue epidemiology trends. Rev Inst Med Trop Sao Paulo. 2012;54(Suppl 18):S5–S6.
6. Shepard DS, Coudeville L, Halasa YA, Zambrano B, Dayan GH. Economic impact of dengue illness in the Americas. Am J Trop Med Hyg. 2011;84(2):200–207.
7. Whitehorn J, Farrar J. Dengue. British medical bulletin. 2010;95(1):161-73.
8. Chen LH, Wilson ME. Dengue and chikungunya infections in travelers.Current opinion in infectious diseases. 2010 ;23(5):438-44.
9. Varatharaj A. Encephalitis in the clinical spectrum of dengue infection. Neurology India. 2010 ;58(4):585.
10. Martina BE, Koraka P, Osterhaus AD. Dengue virus pathogenesis: an integrated view. Clinical microbiology reviews. 2009;22(4):564-81.
11. George R. Clinical spectrum of dengue infection.Dengue and dengue hemorrhagic fever. 1997:89-113.
12. Arya SC, Agarwal N, Parikh SC, Agarwal S. Simultaneous Detection of Dengue NS1 Antigen, IgM plus IgG and Platelet Enumeration during an Outbreak. Sultan QaboosUniv Med J. 2011;11(4):470-6.
13. Egger JR, Coleman PG. Age and clinical dengue illness. Emerg Infect Dis. 2007;13(6):924-5.
14. Anker M, Arima Y. Male-female differences in the number of reported incident dengue fever cases in six Asian countries. Western Pac Surveill Response J. 2011 ;2(2):17-23.
15. Ng DH, Wong JG, Thein TL, Leo YS, Lye DC. The Significance of Prolonged and Saddleback Fever in Hospitalised Adult Dengue.PLoS One. 2016 ;11(12):e0167025
16. Muhammad Suleman, Rani Faryal, Muhammad MasroorAlam, Salmaan Sharif, ShahzadShaukat, Uzma Bashir Aamir, Adnan Khurshid, MeharAngez, MassabUmair, Mian Muhammad Sufian, YasirArshad, GhulamMujtaba, Syed SohailZahoor Zaidi,NS1 antigen: A new beam of light in the early diagnosis of dengue infection,Asian Pacific Journal of Tropical Medicine,2016;9(12):1212-1214.
17. Chaudhary R, Khetan D, Sinha S, Sinha P, Sonker A, Pandey P, Das SS, Agarwal P, Ray V. Transfusion support to dengue patients in a hospital based blood transfusion service in north India. Transfusion and apheresis science. 2006 ;35(3):239-44.
18. Makroo RN, Raina V, Kumar P, Kanth RK. Role of platelet transfusion in the management of dengue patients in a tertiary care hospital.Asian journal of transfusion science. 2007;1(1):4.
19. Kalayanarooj S, Vaughn DW, Nimmannitya S, Green S, Suntayakorn S, Kunentrasai N, Viramitrachai W, Ratanachu-Eke S, Kiatpolpoj S, Innis BL, Rothman AL. Early clinical and laboratory indicators of acute dengue illness.Journal of Infectious Diseases. 1997; 176(2):313-21.
20. Uchadadia S, Ghodke B, Bhuta K, Kejriwal A, Ghanekar J. Degree of impairment of liver function in dengue fever correlates to the severity of its complications. MGM J Med Sci. 2015;2(3):115-9.

Conflict of Interest: Nil

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