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Research Article

Seroprevalence and Seasonal Trend of Dengue Virus Infection at a Teaching Hospital in Tumkur, India

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Abstract: Dengue fever is an acute febrile arbo-viral illness which is endemic in India. Continuous surveillance of Dengue infection at the regional level is essential for the proper and timely institution of vector control measures. This study was conducted with the purpose of assessing the seroprevalence and seasonal trend of Dengue virus infection in a tertiary care centre in Tumkur. Blood samples collected from patients presenting with acute febrile illness consistent with dengue infection from April 2013 to March 2014 were included in the study. The diagnosis of dengue was established using immunochromatographic principle to detect dengue NS1 antigen, IgG and IgM anti-dengue virus antibodies. Association between leucopenia and thrombocytopenia with dengue fever and the seasonal trend of dengue infection was also assessed. 278 blood samples were collected in the study period of which 91 were positive for one or more of the serological parameters of dengue infection. NS1 alone was positive in 49.45% of the cases emphasizing the need of inclusion of NS1 based assays for the routine diagnosis of dengue infection. Leucopenia and thrombocytopenia was found to be associated significantly with dengue fever and they can serve as useful accessory tools for the diagnosis of dengue infection. An increase in the dengue fever cases was noted in the monsoon and post-monsoon season corresponding to the increased breeding of mosquitoes.
Keywords: Dengue fever, Immunoglobulin G, Immunoglobulin M, NS1 antigen, seasonality

INTRODUCTION

Dengue fever is a mosquito borne acute viral illness transmitted by *Aedes aegypti* and *Aedes albopictus* in tropical and subtropical regions around the world [1]. Dengue virus (DENV) is a *Flavivirus* belonging to the family Flaviviridae. Infection is caused by four distinct serotypes of the virus DENV-1, DENV-2, DENV-3 and DENV-4. The spectrum of Dengue infection may range from asymptomatic infection to undifferentiated fever, Dengue fever (DF), Dengue Haemorrhagic fever (DHF) or Dengue Shock Syndrome (DSS) [2].

Dengue viral infection is endemic in the Indian sub-continent [3]. Recovery from infection provides lifelong immunity against that serotype but confers only partial and transient protection against subsequent infection by the other three serotypes [1]. Secondary infection with a serotype different from that causing primary infection may lead to Dengue Haemorrhagic fever and Dengue Shock Syndrome which can be fatal. Diagnosis of primary dengue is made by the detection of IgM anti-DENV antibodies which appear 5-7 days after the onset of illness and persist for 2-3 months whereas a secondary infection is characterized by production of IgG antibodies and a weak IgM response [3].

In view of the high mortality rate and to reduce the disease burden, it is imperative to have a rapid and sensitive laboratory assay for the early detection of the disease [4]. Dengue is a seasonal disease and is strongly influenced by rainfall and temperature [5]. The illness occurs throughout the year with a peak during monsoon and the post monsoon season due to high vector density [6]. This study was conducted with the purpose of assessing the seroprevalence and seasonal trend of Dengue virus infection in patients presenting to a tertiary care centre in Tumkur.

MATERIALS AND METHODS

This study was conducted in the Microbiology department of Shridevi Institute of Medical Sciences and Research Hospital, Tumkur which is a 350 bedded multi-specialty hospital. The study period was for one year from April 2013 to March 2014.

Blood samples collected from patients presenting to the hospital with dengue like illness for which dengue serology was requested were included in the study. Dengue serology for detection of NS 1 antigen, IgG and IgM anti-DENV antibodies were performed using Dengue Day 1 Test which is a rapid test based on immunochromatographic principle for the detection of Dengue NS1 Antigen and differential detection of IgM and IgG anti-DENV antibodies in human serum or plasma manufactured by J. Mitra & Co. Pvt. Ltd. The results were compared with platelet count and total count. The seasonal variation in the number of Dengue positive cases was also assessed. Statistical analysis was performed using Fisher's exact test and significance was assessed based on the two-tailed P value. A P value of < 0.01 was considered as significant.

RESULTS AND DISCUSSION

278 blood samples were received in the Microbiology department for Dengue serology. Of these 91 samples were positive for one or more serological parameters for Dengue. Maximum positivity was seen among young adults in the age group of 16 – 30 years. The incidence of Dengue was higher in males compared to females. Male to female ratio among the seropositive cases was 1.6:1 (Table 1, Figure 1). It has been established earlier that in many Asian countries, lower disease incidence in women may be a statistical artifact related to lower reporting and care-seeking for women and that determining sex differences requires well-designed studies considering both biological and social factors that influence the disease pattern in the community [7].

Table 1: Dengue positivity by age and sex

Age group	Male	Female	Total (%)
0 – 15	6	3	9 (9.89)
16 – 30	34	16	50 (54.94)
31 – 45	10	6	16 (17.56)
46 - 60	5	8	13 (14.29)
61 – 75	1	0	1 (1.10)
>75	0	2	2 (2.20)
Total	56	35	91 (100)

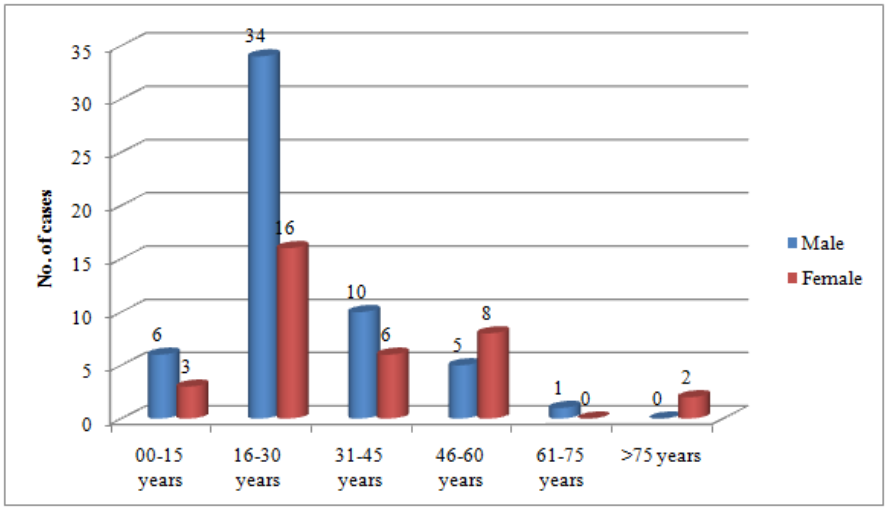

Fig. 1: Age and sex distribution of Dengue positive cases

91 samples were positive to one or more of the serological markers of Dengue infection. 45 samples (49.45%) were positive only for NS 1 antigen, 5 (5.49%) were positive for IgM only 29 (31.87%) were positive for IgG. The remaining 12 samples were positive for more than one serological parameter (Table 2). The most common serological marker to be positive was NS 1 antigen in comparison to the other serological markers (P value = 0.0074). NS 1 (Non-structural protein 1) is a highly conserved glycoprotein that is essential for the viability of DENV. It circulates uniformly in all serotypes of dengue virus at high levels during the first few days of illness. [4]. NS1 is shown to be a highly specific viral marker making it extremely reliable parameter for the diagnosis of dengue infection from day 1 of fever [8]. Appearance of antibodies occurs after 5-10 days after onset of illness in primary infection and 4-5 days in case of secondary dengue virus infection [4].

In this study, only NS 1 antigen was positive in 49.45% of the cases. These cases would have been failed to be detected at that time if only antibody based assays are used for the laboratory diagnosis of Dengue.

Similar findings were observed in other studies in which the sensitivity of detection of Dengue infection increased when both antigen and antibody based assays were used as diagnosis [4,9]. Anti-Dengue IgG positivity is seen in secondary Dengue infection or in cases of past infection. Differentiation requires the use of serological tests based on IgM capture and IgG capture ELISA in which the cut off value of the IgG is set to discriminate between high levels of IgG (characteristic of secondary dengue infections) and lower IgG (characteristic of primary/past infection) [2]. The differentiation between primary and secondary dengue infection is important as secondary dengue infections are more commonly associated with Dengue Haemorrhagic fever and Dengue Shock Syndrome with higher rates of morbidity and mortality.

Table 2: Sero-positivity for Dengue infection

Serological marker	No. positive (%)
NS 1	45 (49.45)
Ig M	05 (5.49)
Ig G	29 (31.87)
NS 1 + Ig M	02 (2.2)
NS 1 + Ig G	06 (6.6)
Ig G + Ig M	02 (2.2)
NS 1 + Ig G + Ig M	02 (2.2)
Total	91 (100)

The incidence of leucopenia (total count < 4,000 cells/Cumm) and thrombocytopenia (platelet count <1,00,000 cells/Cumm) was compared in Dengue positive cases. The 187 Dengue negative cases with acute febrile illness served as controls. Leucopenia was found to be significantly higher in the Dengue positive cases as against the Dengue negative controls (P value = <0.0001). Similarly thrombocytopenia was also found to be significantly higher in the Dengue positive cases than the Dengue negative controls (P value = <0.0001) (Table 3). These findings were consistent with other studies which also found a significant association between thrombocytopenia and dengue infection [5, 8].

Myelosuppression in Dengue Fever leads to leucopenia and thrombocytopenia occurs due to autoantibody induced phagocytosis of platelets. These laboratory data can play a complementary role in prompting the suspicion and facilitating the timely diagnosis of Dengue, even before the results of the serological tests are available [9].

Table 3: Dengue positivity Versus Total count and Platelet count

Dengue serology	Total count (<4,000 cells/Cumm)	Platelet count (<1,00,000 cells/Cumm)	Total
Dengue positive (n = 91)	50 (54.95%)	33 (36.26%)	83
Dengue negative (n = 187)	06 (3.21%)	08 (4.28%)	14
Total	56	41	

The association of the presence of the individual serological markers and thrombocytopenia was also assessed. Though the incidence of thrombocytopenia was observed to be high when NS 1 antigen was detected, this association was not found to be statistically significant (P value = 0.3223). NS 1 antigen is also considered as an indicator of disease severity. A very high concentration of NS 1 antigen within 72 hours of illness can be used to identify patients at high risk of developing Dengue Hemorrhagic Fever [4, 10]. Dengue Ig G was found to be least associated with thrombocytopenia. (Table 4).

Table 4: Comparison of positivity to serological parameters and platelet count

Serological parameter	Total positive	Platelet count (<1,00,000 Cells/Cumm)
NS 1	55	26 (47.27)
Ig G	39	12 (30.77)
Ig M	11	06 (54.55)

The seasonal trend of Dengue over one year was also assessed. Rain, temperature and humidity are reported as the major climatic factors which can cause epidemics either alone or in combination [6]. We found an increase in the dengue cases from the month of July with a peak in the month of October, followed by a decline in cases (Table 5, Figure 2). The increased incidence of cases coincided with the monsoon and

post-monsoon season. These results were consistent with other studies which also found an increased incidence of dengue infection in the monsoon and post monsoon season [5, 6, 11, 12].

Table 5: Seasonal distribution of Dengue positivity

Month	Total tested	Total positive
April 2013	2	1 (1.1%)
May 2013	1	1 (1.1%)
June 2013	2	0 (0.0%)
July 2013	31	9 (9.9%)
August 2013	51	13 (14.29%)
September 2013	53	17 (18.68%)
October 2013	50	23 (25.27%)
November 2013	28	10 (10.99%)
December 2013	17	2 (2.2%)
January 2014	6	3 (3.3%)
February 2014	20	5 (5.5%)
March 2014	17	7 (7.7%)
Total	278	91 (100%)

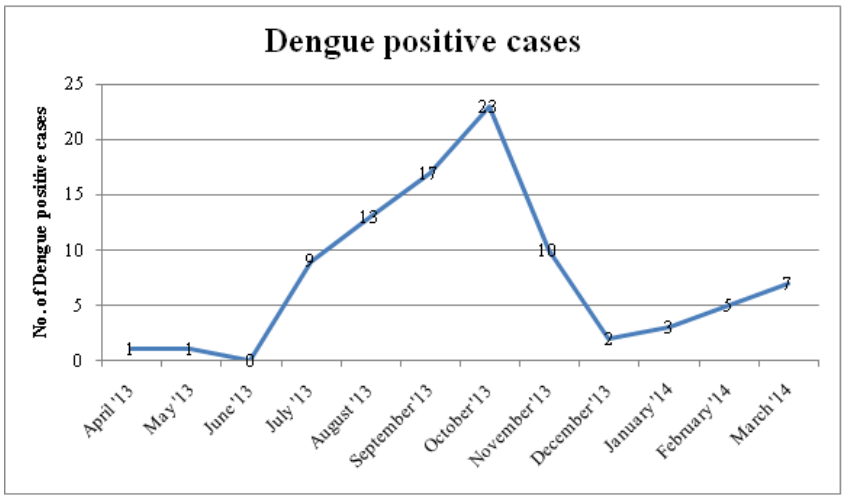

Fig. 2: Monthly distribution of dengue infection cases

CONCLUSION

The current study was conducted with the purpose of assessing the seroprevalence and seasonal trend of Dengue infection in a tertiary care centre in Tumkur. The incidence of dengue infection was found to be higher in young adults and in males compared to females. This study re-emphasizes the need for the inclusion of NS 1 antigen detection based assays for the early and accurate diagnosis of Dengue virus infection. Sensitivity of detection of dengue infection increases with the inclusion of NS1 antigen assays in the laboratory. Thrombocytopenia and leucopenia was significantly associated with dengue infection in comparison with patients presenting acute febrile illness other than dengue. Reduced platelet count and total leucocyte count can be used as a useful and cheap laboratory investigation prompting a high suspicion of dengue infection, especially in resource poor settings where serological tests for dengue may not be available. Dengue shows a seasonal trend of distribution and the incidence increases in the monsoon and post monsoon period, due to artificial collections of water that serve as breeding ground for mosquitoes.

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