Original Article

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Analysis of Trends in Dengue Infection among Patients Attending a Tertiary Care Teaching Hospital: A Retrospective Observational Study

Microbiology Section

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ABSTRACT

Introduction: Dengue, a common mosquito-borne arboviral infection in tropical countries, presents cyclical epidemics and seasonal variations with diverse clinical outcomes. Over the past three decades, it has become endemic in India, leading to a rising mortality trend, primarily due to its severity and antibody-dependent enhancement in secondary dengue cases. Therefore, understanding the trend of dengue infection in specific geographical areas is crucial for more efficient prophylaxis.

Aim: To provide a comprehensive overview of the seroprevalence of dengue virus infection in Surat district, including the trends in gender, age distribution, and seasonal variations of dengue infection from 2014 to 2021.

Materials and Methods: The present retrospective observational analysis was conducted in the Department of Microbiology, Government Medical College (tertiary care teaching New Civil Hospital), Surat, Gujarat, India. A total of 31,683 blood samples were received from patients with clinical suspicion of dengue-like illness from January 2014 to December 2021. Data collection took place from March 2022 to May 2022, and the analysis was conducted in June and July 2022. All samples underwent dengue infection detection using the Enzyme-linked Immunosorbent Assay (ELISA) method by Non structural 1 (NS1) antigen detection and Immunoglobulin M (IgM) antibody detection by Mac capture ELISA. Demographic and clinical details were obtained and recorded from laboratory request forms using a structured data sheet in using Microsoft Excel software version 2013. The data were entered and analysed using EpiInfo software version 3.5.1.

Results: Among the 31,683 blood samples tested, 5,994 (18.91%) cases were confirmed for dengue infection through ELISA testing. The highest number of positive cases (33.6%) was observed in the 20-29 years age group, with males outnumbering females in terms of dengue positivity at a ratio of 1.37:1. The maximum number of dengue cases occurred during the postmonsoon and early winter periods, with 96.5% of cases reported from Surat district, India.

Conclusion: The rising trend of dengue infection in different age groups over the years underscores the need for continued implementation of surveillance and preventive strategies before the monsoon, aiming to reduce severe dengue infections in the future.

Keywords: Demography, Enzyme-linked immunosorbent assay, Non structural antigen, Seropositivity

INTRODUCTION

Dengue (break-bone fever) is a viral infection transmitted from mosquitoes to people and is more common in tropical and subtropical climates. Approximately, half of the world's population is now at risk of dengue, with an estimated 100-400 million infections occurring each year [1]. The World Health Organisation (WHO) regions of Southeast Asia (SEA) and the Western Pacific represent about ~75% of the current global burden of dengue [1,2]. Over the past 50 years, there has been a 30-fold increase in the incidence of dengue fever, with geographic spread into new countries, including India. In the present decade, the disease has also spread from urban to rural settings [3]. Environmental atmospheric fluctuations, population growth, urbanisation, open water storage systems, inadequate waste disposal methods, poor sanitary measures, and the frequency of international travel all contribute to the hyperendemicity of dengue infection in India [4].

Dengue is an arboviral vector-borne infection transmitted by the bite of mosquitoes, primarily Aedes aegypti, followed by Aedes albopictus. These mosquitoes bite multiple individuals to complete a blood meal and often reside in domestic areas. Dengue belongs to the Flaviviridae family, and there are five distinct serotypes of dengue: DENV-1, DENV-2, DENV-3, DENV-4 and DENV-5 (discovered in 2013 from Malaysia) [5,6]. Recovery from one dengue infection is believed to provide lifelong immunity against that specific serotype. However, subsequent infections (secondary infections) by other serotypes in previously infected individuals increase the risk of severe dengue manifestations due to antibody-dependent enhancement. Thus, the clinical spectrum of dengue ranges from mild symptoms to dengue haemorrhagic fever and dengue shock syndrome [6]. Currently, there is no specific treatment for dengue infection. Early detection through serological tests and timely access to proper medical care facilities are crucial in preventing severe complications and reducing fatality caused by dengue. However, due to under reporting of dengue cases, lack of awareness in the community, delayed effective management and unavailability of a vaccine, dengue remains a major health crisis in India [7].

Given that the periodic display of seroprevalence of dengue infection is an important tool for effective control and preventive programmes. Hence, the present study was aimed to provide a comprehensive overview of the seroprevalence of dengue virus infection in Surat and other neighboring districts of South Gujarat, India, from 2014 to 2021. The study also intends to analyse the gender and age-wise distribution, as well as, the seasonal variations of dengue infection.

MATERIALS AND METHODS

The present retrospective observational analysis was conducted in the Department of Microbiology, Government Medical College (tertiary care teaching New Civil Hospital), Surat, Gujarat, India. Between January 2014 to December 2021, a total of 31,683 blood samples from suspected patients with dengue- like illness were received in the Microbiology Department. The dengue data were collected from the register for suspected cases of dengue

maintained in the department, and a master chart of all cases was created to extract information on age, sex, district, testing, result and date of report. Data collection occurred between March 2022 and May 2022, and the analysis took place in June 2022 and July 2022. The present study was time-bound, and therefore only the records available during the study duration were considered. The study protocol received approval from the Institutional Ethical Committee (Approval No: GMCS/STU/ETHICS/23466/19). Informed written consent was waived as the study involved retrospective data analysis.

Inclusion criteria: Blood samples (5 mL) were collected in plain vacutainers from patients of different age groups who presented with clinically suspected dengue-like illnesses, including sudden onset of fever, headache, retro-orbital pain and back pain along with severe muscle weakness, received in the Microbiology Department were included in the study. As this institute serves as a sentinel surveillance site for dengue testing, we not only provide health services to Surat but also to neighbouring districts such as Navsari, Valsad, Dang, Tapi, Vyara, Bharuch and Narmada. Therefore, blood samples were also received from various districts in South Gujarat and were included in the study.

Exclusion criteria: Patients with other co-infections such as malaria, typhoid, or other co-morbid diseases were excluded from the study.

Study Procedure

Blood samples, along with duly filled laboratory request forms, were received in the Microbiology Department. The blood samples were allowed to clot at room temperature and then centrifuged at 2000 RPM for 10 minutes. The separated serum sample was used for dengue testing. The detection of dengue infection was performed using the ELISA method. For patients with illness duration of less than five days, NS1 antigen detection was used. For patients with illness duration of more than five days, IgM antibody detection was performed using the NIV DEN IgM Capture ELISA kit from NIV, Pune, India, following the manufacturer's instructions. The results were recorded accordingly.

STATISTICAL ANALYSIS

Demographic and clinical details, including age, sex, residential status and days of fever, were obtained and recorded from the laboratory request forms. A structured data sheet was created using Microsoft Excel software version 2013. The data were entered and analysed using EpiInfo software version 3.5.1. The analysis was presented as frequency and percentage distributions. The data were retrospectively analysed to determine the trend of seropositivity for dengue infection, age and gender-wise distribution, seasonal variations and epidemiological distribution of dengue infection.

RESULTS

A total of 31,683 blood samples from suspected dengue cases were received in the Microbiology Department of a tertiary care teaching hospital in Surat between January 2014 and December 2021. Among these samples, 5,994 (18.91%) cases were confirmed for dengue infection through either NS1 antigen detection by ELISA or IgM antibody detection by capture ELISA.

Out of the 5,994 seropositive cases, 3,506 (58.49%) were positive by NS1 antigen ELISA and 2,488 (41.5%) were positive by IgM antibody ELISA. The choice of test (NS1 antigen or IgM antibody) was determined based on the request by the clinician, taking into consideration the number of days of fever. The total number of cases and the positivity rates for dengue infection are described in [Table/Fig-1].

Method used	Positivity, n (%)
Total samples (N=31683)	5994 (18.91)
Positive by NS1 antigen ELISA	3506 (58.49)
Positive by IgM antibody ELISA	2488 (41.5)

[Table/Fig-1]: Positivity of dengue by ELISA.

The seroprevalence of dengue infection varied each year with variations in age and gender distribution. Throughout the study period, the highest number of suspected cases, 6,829 (21.6%), and seropositivity, 1,763 (29.4%), were noted in the year 2019. In the remaining years, there was a rising trend in dengue positivity [Table/Fig-2]. The number of suspected dengue cases declined in 2020 due to the Coronavirus Disease 2019 (COVID-19) pandemic, as there was a lockdown period and reduced activity/ mobilisation.

Year	No. of the suspected dengue cases, N=31683, n (%)	No. of the ELISA positive cases, n=5994, n (%)
2014	2379 (7.5)	460 (7.7)
2015	3040 (9.6)	480 (8)
2016	3379 (10.7)	666 (11.1)
2017	3900 (12.3)	675 (11.3)
2018	4917 (15.5)	942 (15.7)
2019	6829 (21.6)	1763 (29.4)
2020	2148 (6.8)	241 (4)
2021	5091 (16)	767 (12.8)

[Table/Fig-2]: Year-wise data of suspected dengue cases and ELISA positive cases.

Males were more commonly affected than females, with a ratio of 1.37:1. The positivity rate among males was 3,466 (57.8%), which was higher compared to females, with 2,528 (42.2%) positive cases. The seropositivity among different age groups remained similar throughout the study period, with the highest rate observed in the age group of 20-29 years, with 2,011 (33.6%) cases, followed by teenagers aged 10-19 years, with 1,490 (24.8%) cases [Table/Fig-3]. Among the gender-wise positive cases, the highest dengue seropositivity was observed in males, with 1,081 (31.2%), and females, with 932 (36.9%), in the age group of 20-29 years [Table/Fig-4].

Variables	No. of the suspected dengue cases, n=5994, n (%)	No. of the ELISA positive cases, n=5994, n (%)
Gender		
Male	16220 (51.2)	3466 (57.8)
Female	15463 (48.8)	2528 (42.2)
Age group (years)		
≤9	5394 (17)	918 (15.3)
10-19	6029 (19)	1490 (24.8)
20-29	10519 (33.2)	2011 (33.6)
30-39	5034 (15.9)	937 (15.6)
40-49	2595 (8.2)	394 (6.6)
50-59	1239 (3.9)	147 (2.5)
≥60	873 (2.8)	97 (1.6)
District		
Surat	30449 (96.1)	5784 (96.5)
Other	1234 (3.9)	210 (3.5)

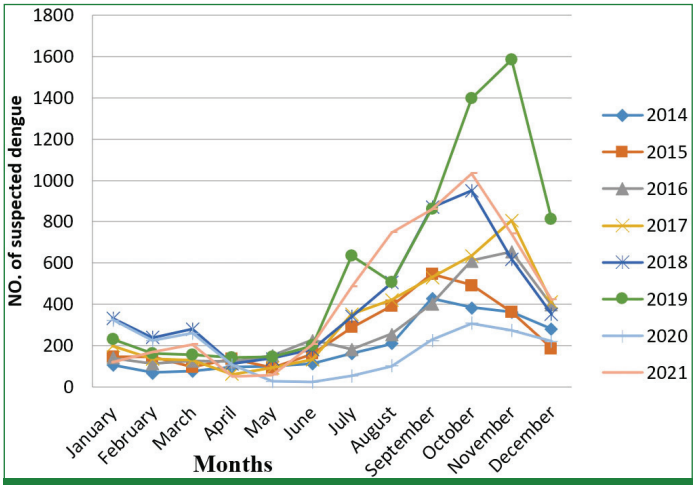
[Table/Fig-3]: Demographic distribution of dengue suspected cases with positivity.

The majority of samples were received from Surat District. Out of the total 31,683 samples, 30,449 (96.1%) were from Surat District, and 5,784 (96.5%) of these samples tested positive for dengue IgM antibody or/and NS1 antigen by ELISA during the period of 2014-2021 [Table/Fig-3]. A total of 1,234 (3.9%) samples were received from other districts in South Gujarat, out of which 210 (3.5%) samples tested positive for IgM antibody or/ and NS1 antigen detection by ELISA [Table/Fig-3].

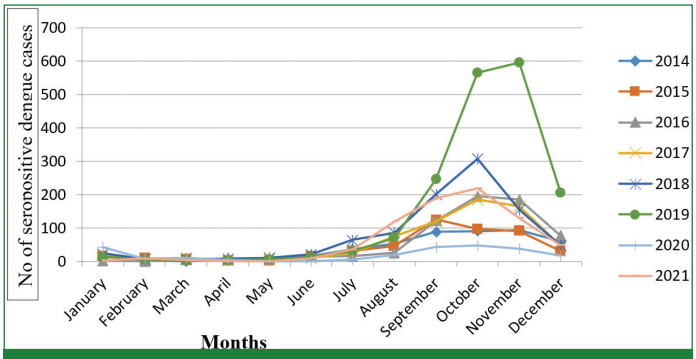
Age groups (years)	No. of the ELISA positive cases in males, n=3466, n (%)	No. of the ELISA positive cases in females, n=3466, n (%)
0-9	523 (15.1)	395 (15.6)
10-19	1010 (29.1)	478 (18.9)
20-29	1081 (31.2)	932 (36.9)
30-39	534 (15.4)	404 (16)
40-49	194 (5.6)	200 (7.9)
50-59	82 (2.4)	65 (2.6)
≥60	42 (1.2)	54 (2.1)

[Table/Fig-4]: Age-wise gender distribution of dengue positive cases.

As the monsoon in South Gujarat starts from June and lasts until October, suspected cases of dengue start rising towards the end of June, reach their peak in August and September, and begin to decline from December every year [Table/Fig-5,6]. The positivity of dengue fever also starts increasing from early July until November every year. A seasonal peak of dengue virus infection is recorded around 6-8 weeks after the arrival of rain every year until early winter.



[Table/Fig-5]: Month-wise distribution of dengue suspected cases.



[Table/Fig-6]: Month-wise distribution of dengue positive cases.

DISCUSSION

Dengue is an emerging viral infection and a major health problem in India. The WHO has declared dengue to be hyperendemic in India, and periodic epidemics of dengue are becoming more frequent. The spectrum of clinical illness varies from patient to patient, making the clinical diagnosis difficult. The detection of NS1 antigen within the first five days of fever and IgM antibody detection after five days of fever by ELISA remains the mainstay for early detection and management of dengue infection.

The present study analysed the trend in the prevalence of dengue in South Gujarat, India in the most recent years from 2014 to 2021. Panwala T and Mulla S conducted a study on the trends of dengue infection from 2010 to 2013 [8]. The present study was aimed to further elucidate the trend of dengue infection from 2014 to 2021. Dengue seropositivity rates are presented by sex, age group and seasonal variation, aiding in the demographic understanding of the prevalence of dengue infection. In the present study, a total of 31,683 dengue-suspected patients were tested from January 2014 to December 2021. Out of these, 5,994 patients were seropositive, with 3,506 (58.49%) detected by NS1 Antigen (Ag) using ELISA, and 2,488 (41.5%) detected by IgM antibody using ELISA. The NS1 Ag assay, when combined with MAC-ELISA on a single serum sample of a suspected case, has the ability to improve the diagnostic algorithm, contributing significantly to the clinical treatment and control of dengue viral infections [9,10].

Overall, the seroprevalence of dengue infection during the current study period was 18.91%, which is slightly lower (20.41%) than previously reported in year 2010-2013 a study by Panwala T and Mulla S in the same geographical area [8]. This strongly indicates the impact of preventive strategies implemented by the municipality in reducing dengue cases over the years. Similar surveillance studies on the seroprevalence of dengue infection conducted by Poddar N et al., reported 25%, while Sood S reported 18.99%, which is consistent with the findings of the present study [11,12]. The study by Murhekar M et al., noted a prevalence of 28.4% among different regions of India [13].

Between 2014 and 2021, the number of dengue virus infection cases increased, showing a rising trend in both age-specific and gender-specific incidences. Almost all age groups were affected, with consistent seropositivity rates throughout the study period. The age group most commonly affected was 20-29 years, with a seropositivity rate of 33.6%. Among teenagers aged 10-19 years, the positivity rate was 24.8%, and for individuals aged 30-39 years, it was 15.6%. In the paediatric age group (0-9 years), seropositivity was 15.3%, consistent with the study by Panwala T and Mulla S (15.61%) [8].

Current study findings contradict some other Indian studies that reported the maximum burden of dengue infection in children. Deshkar ST et al., reported a positivity rate of 40.5% in the paediatric age group of 0 to 10 years, and Devaleenal B et al., reported a rate of 36% in the 5-14 years age group [14,15]. The higher prevalence in the paediatric age group leads to more severe secondary exposure in the form of dengue haemorrhagic fever and dengue shock syndrome, which is concerning. General protective measures such as using mosquito nets, repellents, mosquito stickers, and sprays play an important role in preventing dengue infection in children.

In the present study, the positivity rate among males was 57.8%, higher than that among females, which was 42.2%. Male patients showed a higher prevalence of this disease, and the male-to-female ratio was 1.37:1. Deshkar ST et al., reported a male-to-female ratio of 1.55:1 [14]. This observation may be due to the fact that males acquire mosquito bites during the daytime at their workplaces or while traveling, compared to females who mostly work as housewives [11,16]. The lower dengue incidence in women may be a demographic error related to the under reporting of women seeking treatment at hospitals.

Almost 96% of suspected cases and significantly confirmed dengue cases were from Surat district, compared to other districts in South Gujarat. This signifies that dengue is a disease of urban areas where industrialisation has led to the growth of Aedes aegypti mosquitoes, the principal urban vectors of dengue [13]. Improper disposal of solid waste, water leakages from air conditioners and air coolers, water accumulation in flower pots, and water containers for birds contribute significantly to mosquito breeding.

Although dengue cases occurred throughout the year, the incidence showed a uniform trend across all eight years. There has been a steady rise in the number of dengue cases every year with seasonal variations [14,15]. Cases start rising from the end of June, peak in September and October, and start declining from December

every year. This indicates that cases start rising during the monsoon period, reach their peak in the postmonsoon season, and start declining by winter until the next monsoon.

During the postmonsoon period, stagnant water reservoirs collected during the rainy season act as favourable breeding sites for the vectors, increasing the transmission of dengue infection. The association between the occurrence of dengue in the postmonsoon period of October to December is further supported by similar findings from other places in India [13,15,17,18].

This seasonal outbreak of disease transmission in the community is important at the local level for effective control measures, emphasising the implementation of preventive measures during water stagnation periods, mainly after the early monsoon phase and particularly in the postmonsoon phase [13,18]. Continued surveillance is essential to determine epidemiological and seasonal trends, so that preventive approaches can be targeted more effectively [19].

Limitation(s)

A major drawback of the present study is the inability to detect the circulating dengue virus serotype in the positive patients' serum samples using Polymerase Chain Reaction (PCR), which is a valuable tool for epidemiological and research purposes.

CONCLUSION(S)

The present hospital-based study may not accurately represent the true scenario, as it only includes highly suspected cases that were reported to the hospital. There has been an increasing trend in dengue infections, with a slightly higher proportion of cases among males compared to females. Adults are the most commonly affected age group. The seasonal distribution of cases was consistent throughout the study period, with the postmonsoon period showing higher positivity rates due to the formation of stagnant pools from the rains and the impact of climate change, which facilitate the breeding of Aedes aegypti mosquitoes. This information is vital for the local government and municipality in developing preventive and control strategies. Increased social awareness and improved early diagnostic facilities, especially those that are more sensitive and specific, can significantly impact the management of such severe infections. Regional tertiary care hospitals should be equipped with facilities for serotyping and genotyping dengue. Furthermore, regular publication of data pertaining to investigations and clinical outcomes is essential to enhance our understanding of and approach to the disease.

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