

A Study on Prevalence and Seasonal Distribution of Dengue at a Tertiary Care Centre of North India

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Abstract:

Introduction: Dengue virus infection is a major public health issue prevalent in tropical and sub-tropical countries all over the world mostly in urban and semi-urban areas. Over 2.5 billion people (40%) of the world's total population are at a risk. The present study is aimed to study the prevalence and seasonal distribution of dengue disease during three consecutive years from 2016-2018 at a tertiary care centre of North India. **Method:** This is an observational retrospective study conducted on total 6,481 (Six thousand four hundred and eighty one) clinical suspected cases referred from indoor and outdoor departments of Medicine and Pediatrics of Sarojini Naidu Medical College, Agra during the period from 1st January 2016 to 31st December 2018. Serum samples collected from suspected cases were collected and subjected to ELISA for detection of Non Structural Protein1 (NS1 antigen) and Immunoglobulin M (IgM) Antibodies. **Results:** From the analysis, this study reflects that the numbers of dengue cases in 2016 are maximum and outnumbered the dengue cases among three consecutive years from 2016 to 2018. Most of the cases were in the age group 0-30 years with a male preponderance. The outbreak occurred during the months of August to November indicating vector transmission in the monsoon and post-monsoon season. In 2016 overall prevalence rate of dengue was found to be 16.66% with prevalence rate of 12.92% for Dengue NS1 antigen and 20.94% for Dengue IgM antibodies. In 2017 overall prevalence rate of dengue was found to be 14.77% with prevalence rate of 11.77% for Dengue NS1 antigen and 16.29% for Dengue antibodies. In 2018 overall prevalence rate of dengue was found to be 13.56% with prevalence rate of 12.92% for Dengue NS1 antigen and 11% for Dengue antibodies. The maximum positivity was recorded in the year 2016 (16.66%), followed by 2017 (14.07%) and 2018(13.56%). Our study shows male preponderance with maximum cases in the year 2018 was recorded in the month of October (22.75%) whereas the lowest in the month of May (1.96%). **Conclusion:** In our study both NS1 Antigen and IgM ELISA tests were useful for the laboratory diagnosis and confirmation of dengue cases. NS1 in combination with IgM ELISA offers most sensitive diagnosis for dengue. As this disease affects the population in the monsoon and post monsoon months therefore continuous monitoring of dengue infection is important during the post-monsoon season. The peak in dengue positivity was observed during September to October.

Key words: Dengue, ELISA, IgM, NS1, WHO

Introduction:

Dengue virus infection is a major public health issue prevalent in tropical and sub-tropical countries all over the world mostly in urban and semi-urban areas.

Dengue virus is a positive-strand RNA virus of the Flaviviridae family with 4 distinct serotypes (DEN-1,

DEN-2, DEN-3 and DEN-4) and it is transmitted to humans by several species of Aedes mosquito. Over 2.5 billion people (40%) of the world's total population are at a risk. WHO estimates that about 50-100 million dengue infections occur worldwide every year.

WHO had classified the symptomatic dengue virus infection into Dengue Fever (DF), Dengue

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Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS).^[1] In 2009, WHO has categorized the dengue patients according to clinical manifestations such as dengue without warning signs, dengue with warning signs (abdominal pain, vomiting, mucosal bleeding, fluid accumulation, lethargy, liver enlargement, increased hematocrit with decreasing platelets) and severe dengue.^[2,3]

In India an estimated 33 million cases had occurred in 2010.^[4,5] In 2016 more than 100,000 laboratory confirmed cases of dengue were reported by NVBDCP.^[6] Dengue in India has been drastically growing over the last few decades with rapidly changing epidemiology.^[7-9] It has become more frequent, especially in urban parts.^[10-11]

In the early 2000s, dengue was endemic in a few southern (Maharashtra, Karnataka, Tamil Nadu and Pondicherry) and northern states (Delhi, Rajasthan, Haryana, Punjab and Chandigarh). The total number of dengue cases has significantly increased in India since 2001. It has recently spread to many states, including the union territories.^[12] From 2010 onwards, the states of Assam, Bihar, Jharkhand, Orissa and Uttarakhand and some union territories including Andaman and Nicobar Islands, Dadra and Nagar Haveli, and Daman and Diu have become endemic for dengue. India experienced the highest dengue incidence in 2012 (about 41 per million population), 2013 (61 per million population) and 2014 (32 per million population). Since 1998-2014, the highest dengue incidence was reported in Pondicherry (372.92 per million population), followed by Dadra Nagar Haveli (176.31 per million population) and Delhi (102.15 per million population). Similarly, a high dengue incidence ranging between 21 and 50 per million, was reported from the states of Punjab, Gujarat, Karnataka, Kerala, Tamil Nadu and Orissa.

The disease shows seasonal pattern as the cases peak after monsoon. India receives 75% of its rainfall during the southwest monsoon period from June to September.^[13] The disease is transmitted by the bite of several species of mosquitoes within the aedes genus, primarily being *Aedes aegypti*. According to various studies, both *Aedes aegyptia* and *Aedes albopictus* are the competent vectors for dengue virus in India.^[14] Indian monsoon rainfall provides ample breeding habitats for *Ae. aegypti*, thus leading to high vector densities.^[14] The infection causes flu-like illness

and occasionally develops into a potentially lethal complication called dengue hemorrhagic fever (DHF) and Dengue shock syndrome (DSS).

In the present scenario all the 4 serotypes are prevalent in almost every state of India.^[8,10,15] One serotype of dengue produces lifelong immunity against re-infection but for other serotypes, only partial or temporary immunity is produced. On the basis of the endemicity of dengue, World Health Organization (WHO) has kept India under category A, considering dengue as an epidemic where outbreaks occur every year and attributes to the leading cause of hospitalization and deaths among children, hyper-endemicity with all the four serotypes circulating in urban areas and spread to rural areas.^[16]

Diagnosis of dengue virus infection at an early stage is important and is performed by serological based ELISA test. NS1 antigen detection test is conducted for suspected cases having 0-5 days of fever history and IgM antibody test is conducted for suspected cases having more than 5 days of fever history. This study is conducted at a tertiary care centre in northern part of India among clinically suspected dengue patients to report the sero-prevalence of dengue for a period of three consecutive years and to study the seasonal epidemiology and demographic profile of the disease.

Method:

This is an observational retrospective study conducted in Sarojini Naidu Medical College, Agra a tertiary care centre of North India. Blood samples from the clinically suspected cases of dengue were collected in serology laboratory of Department of Microbiology from Out-patient Departments of Medicine, Pediatrics as well as patients admitted in various wards over a period of 3 years from 1st January 2016 to 31st December 2018. Around 2-3 ml of blood samples was collected from the patients having clinical signs and symptoms consistent with dengue and samples were centrifuged at 4000 rpm for 5 minutes. Serum was separated aseptically using standard methods and transported to the virology laboratory for further processing if not tested within 3 days, the serum was transferred to a sterile vial and stored frozen at -20°C. A Performa was filled for each patient that includes personal as well as clinical history. The suspected cases having a fever history of 0-5 days were considered for Dengue NS1 Antigen

ELISA (as per Dengue NS1 Ag MICROLISA J.Mitra & Co. Pvt.Ltd., Recombilisa Dengue Ag Kit M/S CTK Biotech Inc.) Whereas, those having a fever history of more than 05 days were screened and tested for IgM antibodies (as per National Institute of Virology-DEN-IgM Capture ELISA kit, NIV, Pune) as per NVBDCP (National Vector- Borne Disease Control Programme) guidelines. ELISA test for detection of NS1 antigen and IgM antibodies was conducted as per the manufacturer's instructions. Ethical clearance for the study was not required as samples were referred to the laboratory for routine diagnostic purposes and not for research purpose.

Results:

Out of total 6,481 samples collected over a period of 3 years from 1st January 2016 to 31st December 2018 in Sarojini Naidu Medical College, Agra a tertiary care centre situated in north India, 973(15%) had confirmed dengue.

Figure 1 shows the distribution of dengue data from 2016-18 and it depicts that in 2016 out of total 2827 cases 471 (16.66%) were found positive for dengue. Based on the history of days of fever days, 1509 were categorized for testing for NS1 ELISA and 1318 for IgM ELISA, out of which 195(12.92%) cases were found positive for NS1 and 276(20.94%) were found positive for IgM. In 2017, total 1229 cases were tested out of which 173(14.07%) were found positive.

Out of these, 603 were NS1 cases, out of which 71 (11.77%) cases were found positive, whereas, out of 626 cases, 102(16.29%) were positive for IgM antibodies. In the same order, in the year 2018, a total 2425 cases were enrolled, out of which 329(13.56%) were dengue positive. A total of 1509 were detected positive for NS1 antigen and 101 (11%) out of 910 IgM cases, were found positive. The maximum positivity was recorded in the year 2016 (16.66%), followed by 2017 (14.07%) and 2018(13.56%).

Figure 2 shows gender-wise distribution of dengue positive cases. In 2016, 297(63 %) were males and 174 (37 %) were females. In 2017, 91 (53 %) were males and 82 (47 %) were females. In 2018, 203 (62 %) were males and 126 (38 %) were females. Our study shows male preponderance.

Figure 3 shows the age-wise distribution of dengue cases, we observed maximum cases in the age group 11-20 years (31.21%) in the year 2016. In the year 2017, the maximum case of dengue falls in the age group 21-30 (25.43%). In 2018, however, the maximum positivity was found in the age group 0-10 years (39.51%). Confining the data for the least positive cases, we observed that it lied in the age group 61-above in all the three years included in the study: 2017 (2.89%) followed by 2016 (2.12%) and 2018 (1.51%) in chronological order.

Figure 1: Distribution of Dengue data from 2016-2018

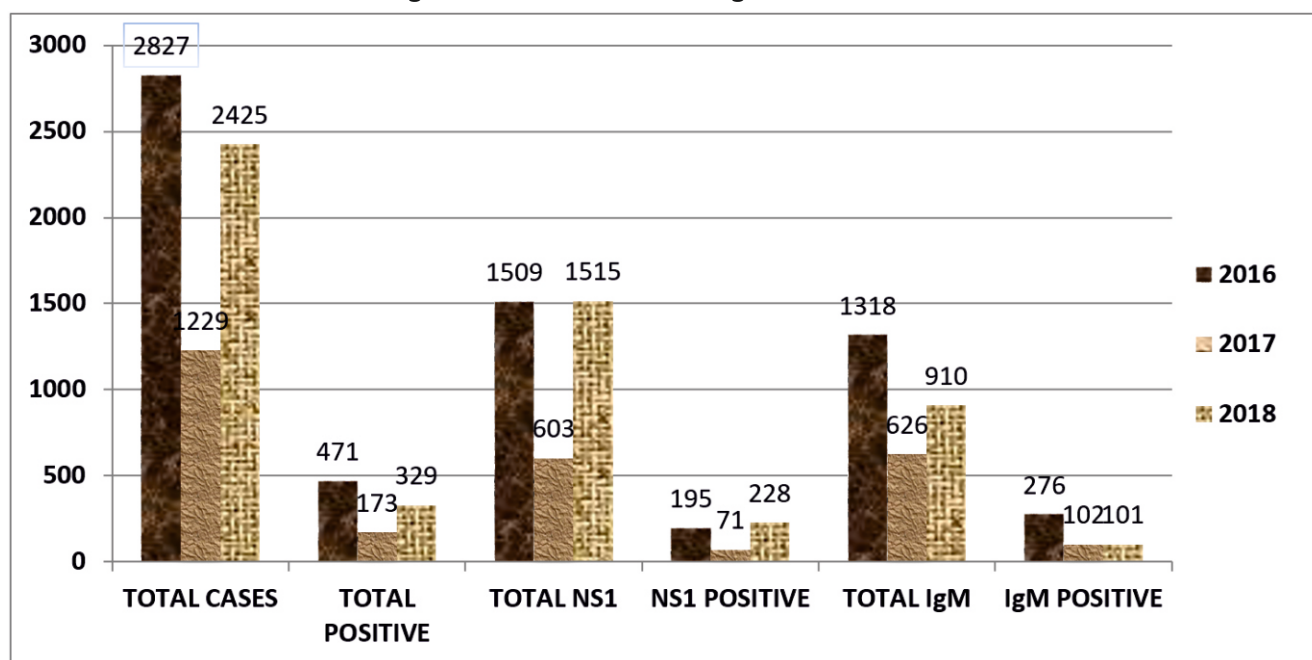


Figure 4 depicts monthly distribution of total suspected Dengue cases received during 2016-2018 and Figure 5 shows monthly distribution of Dengue Positive cases reported during 2016-2018. According to monthly analysis, it was found that in the year 2016, the highest dengue load was found to be in the month of October (19.92%) and lowest in the month of December (06%) In the year 2017, the highest dengue positive cases were recorded in the month of November (21.33%) and lowest in July (2.38%). The maximum cases in the year 2018 was recorded in the month of October (22.75%) whereas the lowest in the month of May (1.96%).

Discussion:

Dengue is a globally emerging major public health problem in the tropical and sub-tropical since the last decade. Dengue has been appearing repeatedly with regular periodic surges.^[17]

The present study was conducted at a tertiary care centre of north region involving total 16.6% serologically confirmed cases in 2016, 14% in 2017 and 13.5% in 2018. Total Dengue NS1 positive cases were 12.9% in 2016, 11.7% in 2017 and 15% in 2018. Total Dengue IgM positive cases were 20.9% in 2016, 16.2% in 2017, and 11% in 2018. On an average, more NS1 cases (494) were reported as compared to IgM

Figure 2: Gender-wise distribution of Dengue Positive cases

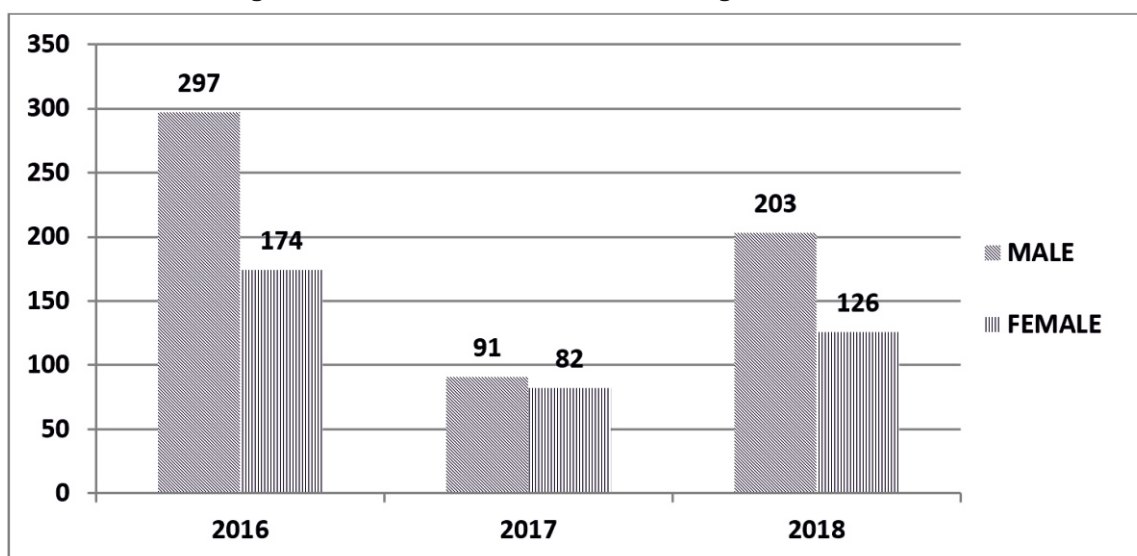
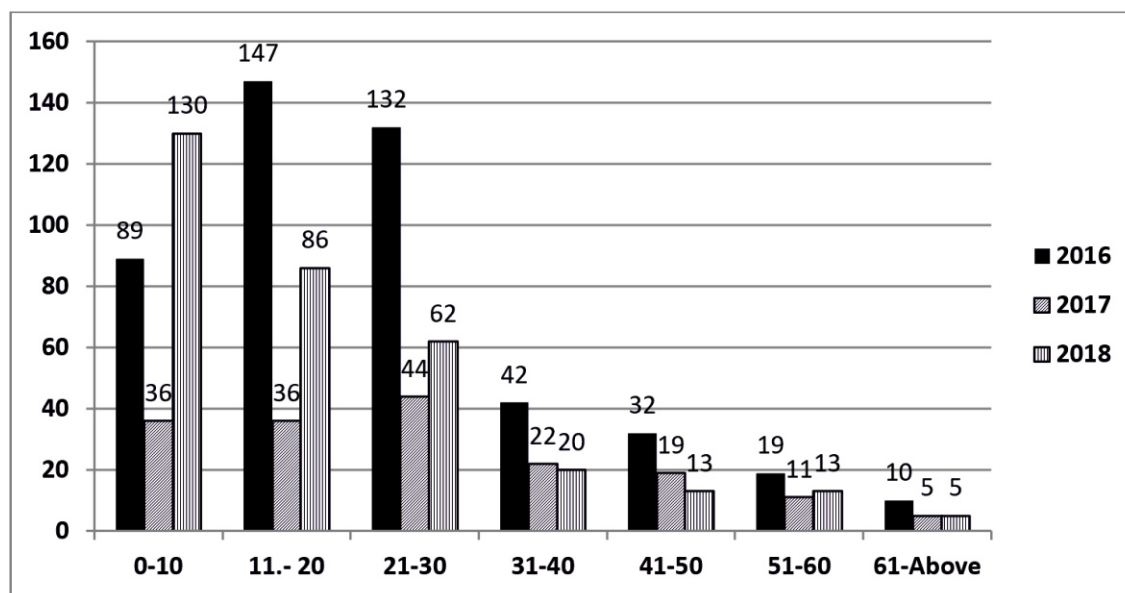


Figure 3: Age-wise distribution of Dengue Positive cases



cases (479) by ELISA from the serum samples of the suspected patients. In our study more cases were diagnosed by NS1 ELISA test as compared to IgM ELISA as it detects both primary and secondary dengue infections before the appearance of IgM antibodies.^[2,18-21] This is due to awareness of patients and clinicians for testing of dengue during febrile phase of infection.

Initially, dengue was considered an urban disease because of rapid development of urban areas resulted in unplanned colonization, improper proper supply and wastewater management system create ideal conditions for the proliferation of the vector.^[10,22,23] The

outbreak of dengue is reported continuously from the large cities of India like Delhi, Lucknow, Bangalore, Gwalior, Vellore, Calcutta, and Pondicherry.^[10,24-30]

In our study, on a comparison of the data obtained from three consecutive years of dengue recurrence at a tertiary care hospital situated in north India we found that there was a gradual decrease in the number of cases reported positive from the year 2016-2018. According to the study, 16.66% were positive in 2016 whereas 13.56% were found positive in the year 2018. While in the year 2017 the positive cases were reported as 14.07%. These findings are consistent with other studies from India.^[13,16]

Figure 4: Monthly distribution of total suspected Dengue cases received during 2016-2018

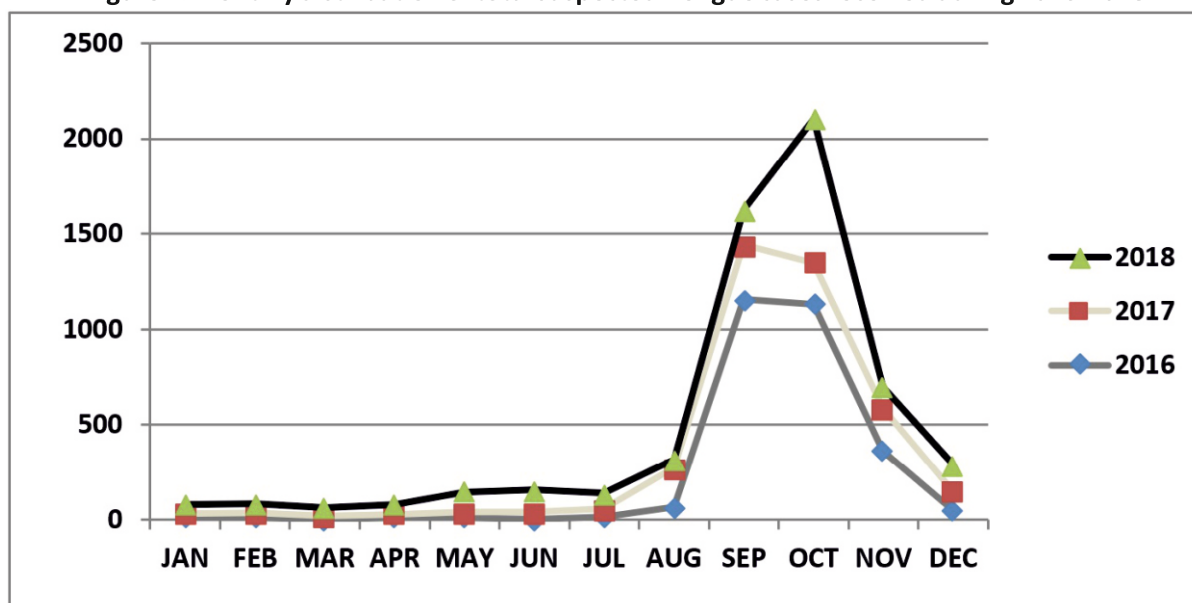
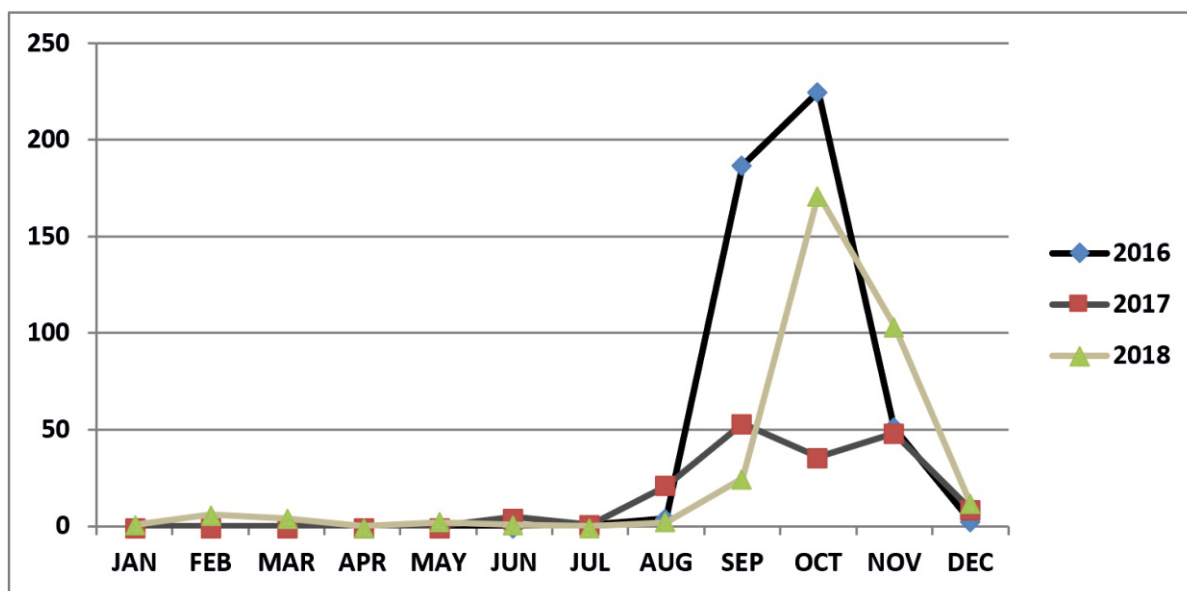


Figure 5: Monthly distribution of Dengue Positive cases reported during 2016-2018



The role of environmental factors in infectious diseases is well known. Most of the countries reported dengue epidemics during warm, humid and rainy seasons, which favor abundant mosquito growth and shorten the extrinsic incubation period as well.^[31-32] To identify the seasonal variation of the disease analysis of the data on monthly basis were done. As a tertiary care centre, the samples of suspected dengue cases were received throughout the year and therefore present study reports the continuous occurrence of dengue cases with variability. Number of positive cases was low from January to June. As rainy season starts by end of June and our study reported the maximum cases in the month of August to November during all three consecutive years of the study with a positivity varying around 19.92% to 22.75%. The correlation with occurrence of dengue infection and monsoon season is clearly evident in this study and it is further supported by similar findings from previous studies.^[33-35] As Agra is situated on the bank of Yamuna river, therefore there are lots of marshy places which provide excellent mosquito breeding places, due to rapid urbanization. *Aedes aegypti* mosquito is the primary vector and lives in proximity to human habitations in urban areas and breeds mostly in man-made containers. The vector of this disease is a day time feeder and it bites in the morning. The transmission of dengue with increased activity in monsoon and post-monsoon season was evident in the present study, in accordance with the reported patterns of dengue transmission.^[36]

Significant numbers of dengue positive cases were reported in different age groups. In 2016 majority of cases were reported in 11-20 years (31.2%) followed by 21-30 years (28.0%) age group. In 2017 majority of cases were reported in 21-30 years (25.4%) followed by 01-10 years (20.8 %) and 11-20 years (20.8%) age group. In 2018 majority of cases were reported in 01-10 years (39.5%) followed by 11-20 years (26 %) and 21-30 years (18.8%) age group. Overall the maximum dengue cases were from the age group 0-30 years. The shift from pediatric/adolescent population to young adults getting affected reflects the presence of non-immune adult population falling prey to the circulating serotype of dengue virus. The age group of 0-10 years was highly affected with dengue and these findings are not consistent with other Indian studies, as most of the Indian studies have reported 15 to 45

years as the most affected age group.^[35,37-38] In some international studies dengue has been reported to mainly a pediatric public health problem.^[39-40] Whereas the age group 20-30 years in the year 2017 which is consistent with other Indian studies.^[7,37,41]

The higher prevalence of dengue infection was noted among males than females. The male female ratio was noted to be 1.7:1, 1.10:1 and 1.61:1 in the year 2016, 2017 and 2018 respectively. The prevalence of the disease in males could be higher as a result of their indulgence in more outdoor activities as compared to females resulting in more exposure to the daytime biting of *Aedes*. The lower case positivity rates in females may be attributed to lower reporting rate and as they remain at home and are less exposed to risk of vector borne infection.^[22,29,42,43] Dengue is thus being spread irrespective gender or age group and emerging as a global challenge over the years.

Huge amount of infrastructure development have made growth environment favorable for breeding of mosquitoes and secondly due to improvement in the diagnostic facilities in the health care settings the reporting of cases is increased.

The present study has the limitations that clinical and mortality data is not available for the cases and the cases were not distinguished in to primary and secondary infection. Serotyping for dengue virus was not performed due to resource limitations.

Conclusion:

In 2016 overall prevalence rate of dengue was found to be 16.66% with prevalence rate of 12.92% for Dengue NS1 antigen and 20.94% for Dengue IgM antibodies. In 2017 overall prevalence rate of dengue was found to be 14.77% with prevalence rate of 11.77% for Dengue NS1 antigen and 16.29% for Dengue IgM antibodies. In 2018 overall prevalence rate of dengue was found to be 13.56% with prevalence rate of 12.92% for Dengue NS1 antigen and 11% for Dengue IgM antibodies. The maximum positivity was recorded in the year 2016 (16.66%), followed by 2017 (14.77%) and 2018(13.56%). Our study shows male preponderance with maximum cases in the year 2018 was recorded in the month of October (22.75%) whereas the lowest in the month of May (1.96%). The peak in dengue positivity was observed during September to October. The males as well as the pediatric population were most affected probably due to their more exposure during the

predominant biting hours of the mosquitoes. Thus in the absence of specific antiviral therapy and protective vaccine for dengue fever effective measures must be taken to control the transmitting vectors to prevent dengue outbreaks. Mortality from dengue fever can also be prevented by its early diagnosis and timely management, therefore this study emphasizes the need of epidemiological and entomological surveillance to monitor trends in distribution and seasonal patterns of dengue.

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Declaration:

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Conflict of Interest: Nil

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