Seroprevalence and Trend of Dengue Cases Admitted to a Government Hospital, Delhi – 5-Year Study (2006-2010): A Look into the Age Shift

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Original Article

ABSTRACT

Background: Diagnosis of dengue infection is easily and best accomplished by demonstration of specific IgM antibodies in blood. We analyzed retrospectively the dengue IgM seropositivity available for samples obtained over a period of 5 years (2006–2010) from patients with suspected dengue fever (DF)-like illness to investigate whether there was an overall increase in the dengue IgM prevalence over this period.

Methods: Blood samples were collected from patients with DF-like febrile illnesses attending the Pediatric, Medicine, and Fever clinics of a Government hospital, Delhi. A total of 8138 individuals (suspected dengue cases) obtained over 5 years were tested for dengue specific IgM antibodies. Year wise, month wise, and age wise data on geographic distribution and clinical manifestations were analyzed.

Results: Of the 8138 samples, 1600 (19.66%) were positive for dengue specific IgM. The year 2006 had the highest number of reported cases, 761 (46.23%). In our study, the age group most commonly affected of all 5 years was 11–20 years. Out of the total 1600 cases admitted to the hospital between 2006 and 2010, 279 (58.9%) had DF, 178 (37.6%) had dengue hemorrhagic fever, and 16 (3.38%) had dengue shock syndrome. We found a high burden of dengue in young children and late adolescents in both rural and urban communities at a magnitude greater than previously described.

Interpretation and Conclusion: We observed an increase in the dengue positive cases every alternate year, thereby indicating a possible role of herd immunity in northern India. We did not find a steady increase in the number of cases over 5 years. We found an increase in the number of positive cases in children and young adolescents.

Key words: Delhi, dengue infection, herd immunity

INTRODUCTION

Dengue is emerging as an important mosquito-borne arboviral disease in the world. Once known to occur sporadically, epidemics

of dengue have now become a regular occurrence. It is estimated that about 50–100 million individuals are infected with dengue worldwide per year with up to 500,000 people being admitted to hospital.[1] Worldwide epidemiology is changing. Delhi has experienced seven outbreaks of dengue virus infection since 1963 with the last outbreak reported in 2006.[2-5] The 1996 epidemic in India was mainly due to the virus DEN-2.[2] In 2006, all four serotypes of dengue viruses were found in co-circulation.[5,6]

Early diagnosis of dengue virus infection is important for treatment as well as aversion of complications like Dengue Shock Syndrome (DSS) and Dengue Hemorrhagic Fever (DHF). Treated DHF/DSS is associated with 3% mortality whereas untreated is associated with 20% mortality. Dengue virus-specific IgM antibodies appear as early as 3 days of dengue viral fever and can persist up to 30–60 days whereas IgG antibodies rise at about 7 days, peak at 2–3 weeks, and these persist for life.[7] IgM antibodies are useful in providing a provisional diagnosis from a single serum sample. Detection of dengue IgM antibodies is simple, easy, and a less time-consuming method of diagnosing dengue fever (DF) as compared with other classical serological methods like hemagglutination inhibition, neutralization, and complement fixation tests.[7]

There are numerous studies from the Indian subcontinent investigating outbreaks of DF or DHF in various parts of the country.[7-13] Existing national surveillance systems are often passive and are designed to monitor trends and to detect disease outbreaks. There are no studies investigating the overall prevalence of dengue in India on a long-term basis.

In the various studies reporting epidemics, it was seen that children <15 years of age were quite severely affected, but majority of infection occurred in active adults in the age group of 21–60 years.[3,5,6,14] Certain common signs and symptoms such as fever, headache, myalgia, arthralgia, and bleeding manifestations have also been observed. However, a few other studies have depicted differences in age distribution and clinical presentation.[5,15] The present study was done to analyze the trend of the disease over the years along with the clinical features, complications, and outcome of cases admitted to a Government hospital situated in North Delhi.

METHODS

The study was carried out at Hindu Rao Hospital (HRH), a 980-bedded hospital in North Delhi, India. Dengue IgM seropositivity status was determined from the samples obtained over a period of 5 years (2006-2010) from patients with probable dengue. Blood samples were collected from patients with probable dengue attending the pediatric, medicine, and fever clinics of the hospital. The clinical basis for diagnosing the patients as having dengue virus infection was based on WHO definitions.[8] DF, DHF, and DSS are defined by WHO as:

Probable DF is defined as acute febrile illness with two or more of the following manifestations: headache, retro-orbital pain, myalgia, arthralgia, rash, hemorrhagic manifestations, and leucopenia. In addition, a supportive serology - a positive IgM antibody test on a late acute or convalescent-phase serum specimen or occurrence at the same location and time as other confirmed cases of dengue fever. Confirmed DF is a case confirmed by laboratory criterion.

Laboratory criterion for confirmation of DF includes any one of the following: isolation of dengue virus from serum or autopsy samples; demonstration of a four-fold or greater change in reciprocal IgG or IgM to one or more dengue virus antigens in paired serum samples or demonstration of dengue virus antigens in autopsy tissue, serum or cerebrospinal fluid samples by immunohistochemistry, immunofluorescence or ELISA; or detection of dengue virus genomic sequences in autopsy tissue, serum or cerebrospinal fluid samples by polymerase chain reaction (PCR).

DHF includes all the following criteria, i.e., fever or history of acute fever lasting 2–7 days, occasionally biphasic, along with hemorrhagic tendencies evidenced by at least one of the following: positive tourniquet test/ petechiae, ecchymoses or purpura/ bleeding from the mucosa, gastrointestinal tract, injection sites or other locations/ hematemesis or melena along with thrombocytopenia (100,000 cells per mm^3 or less) and increase in plasma leakage due to increased vascular permeability (manifested by at least one of the following - a rise in the hematocrit equal to or greater than 20% above average for age, sex, population or a drop in the hematocrit following volume replacement treatment equal to

or greater than 20% of baseline or signs of plasma leakage such as pleural effusion, ascites, and hypoproteinemia).

DSS is defined as all the above criteria for DHF plus evidence of circulatory failure manifested by: rapid and weak pulse, narrow pulse pressure (<20 mmHg [2.7 kPa]), which is manifested by hypotension for age and cold clammy skin.

In the present study, the samples were collected usually 5–10 days following the onset of illness but the exact date of sampling was not available for most of the patients. Approximately 5 mL blood was collected, serum was separated, and dengue-specific IgM antibodies were detected by dengue IgM antibody capture ELISA test issued by National Institute of Virology (NIV), Pune. All the tests were carried out as per the manufacturer's instructions.

RESULTS

During the study period (2006–2010), a total of 8138 serum samples were tested for dengue IgM antibodies. Of the 8138 samples, 1600 (19.66%) were positive for dengue specific IgM. Year-wise distribution of dengue IgM positive cases over the 5-year period is shown in Table 1. The year 2006 had the highest number of reported cases, i.e., 761, whereas lowest number was seen in 2009 with only 58 dengue positive cases. Dengue cases saw an uneven growth in these 5 years with increases seen in 2006 (761), 2008 (242), and 2010 (473). Regarding the total number of deaths, a decrease in mortality was seen from 2007 to 2010.

Month-wise distribution of positive cases in all the 5 years [Table 2] has shown a peak in the month of September 682 (42.2%), which is closely followed by October 656 (41%).

Out of the total 1600 cases admitted to the hospital between 2006 and 2010, 279 (58.9%) had DF, 178 (37.6%) had DHF, and 16 (3.38%) had DSS [Table 3].

In the present study, the age group most commonly affected of all 5 years was found to be 11–20 years followed by the age group 21–30 years [Table 4 and Figure 1].

Fever was seen in 1526 of patients (95.37%) followed by myalgia 597 (37.31%), vomiting 423 (26.43%) and abdominal pain 183 (11.43%) [Table 5]. In our study, the most common hemorrhagic manifestations were rash 522 (32.62%), melena 304 (19%), and petechiae 219 (13.68%).

Majority of the patients attending Hindu Rao Hospital belonged to North district (48.12%) and North-east districts (20.43%) of Delhi [Table 6].

DISCUSSION

Dengue has emerged as a global health problem. There is no effective vaccine to prevent this infection. The present study showed an increase in

Table 1: Year-wise distribution of cases from 2006–2010 at HRH

Year	Total no. of suspected dengue cases	Total no. of dengue positive cases	Total no. of deaths
2006	1646	761 (46.23%)	7 (0.91%)
2007	321	66 (20.56%)	1 (1.51%)
2008	569	242 42.53%)	1 (0.41%)
2009	366	58 (15.84%)	0
2010	5236	473 (9.03%)	1 (0.21%)
Total	8138	1600 (19.66%)	10 (0.62%)

Table 2: Month-wise distribution of cases from 2006–2010

Year	July	Aug	Sept	Oct	Nov	Dec	Total	%
2006	6	20	182	497	56	0	761	47.56
2007	0	4	56	6	0	0	66	4.12
2008	0	39	126	60	17	0	242	15.12
2009	0	6	8	31	13	0	58	3.62
2010	0	101	310	62	0	0	473	29.56
Total	6	170	682	656	86	0	1600	99.98

*No cases were reported from January to June from HRH

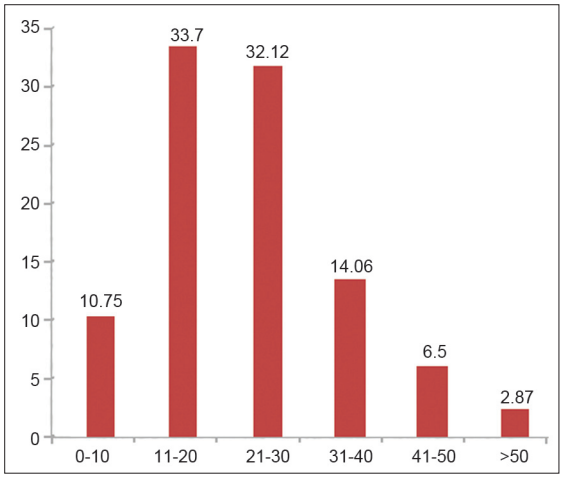

Figure 1: Age-wise distribution of cases from 2006–2010

Table 3: Age-wise distribution of cases (2006–2010)

Age-wise (years)	2006 (%)	2007 (%)	2008 (%)	2009 (%)	2010 (%)	Total	%
0–10	92 (12.08)	5 (7.57)	19 (7.85)	3 (5.17)	53 (11.2)	172	10.75
11–20	259 (34.03)	30 (45.45)	78 (32.23)	20 (34.48)	152 (32.13)	539	33.7
21–30	222 (29.17)	24 (36.36)	86 (35.53)	19 (32.75)	163 (34.46)	514	32.12
31–40	102 (13.4)	5 (7.57)	36 (14.87)	12 (20.68)	70 (14.79)	225	14.06
41–50	54 (7.09)	1 (1.51)	20 (8.26)	3 (5.17)	26 (5.49)	104	6.5
>50	32 (4.2)	1 (1.51)	3 (1.23)	1 (1.72)	9 (1.9)	46	2.87
Total	761	66	242	58	473	1600	100

Table 4: Year-wise distribution of cases and outcomes

Year	DF	DHF	DSS	Total cases
2006	441 (57.9)	294 (38.6)	26 (3.4)	761
2007	38 (57.57)	26 (39.39)	02 (3.03)	66
2008	145 (59.9)	88 (36.36%)	9 (3.7)	242
2009	31 (53.4)	25 (43.10)	02 (3.4)	58
2010	279 (58.9)	178 (37.6)	16 (3.38)	473
Total	934	611	55	1600

Table 5: Signs and symptoms of the cases (n = 1600)

Signs	No. of cases	%
Fever	1526	95.37
Myalgia	597	37.31
Vomiting	423	26.43
Abdominal pain	183	11.43
Rash	522	32.62
Petechiae	219	13.68
Gum bleed	171	10.68
Hematuria	15	0.93
Melaena	304	19
Hematemesis	158	9.8
Epistaxis	274	17.12
Conjunctival hemorrhage	17	1.06
Hemoptysis	32	2

dengue virus activity (as evidenced by dengue IgM positivity) in Delhi during 2006 with the minimum positive cases seen in 2009. A study from Delhi reported 260 positive cases in 2005.[6] Delhi, considered endemic for dengue, was reported as being hyper-endemic by another study.[16]

Dengue cases saw an uneven growth in these 5 years from 2006 to 2010 [Table 1] with the highest number of cases being reported in 2006, i.e., 761 and lowest in 2009 ,i.e., 58. Decrease in the number of dengue positive cases was seen in the years 2007 and 2009, i.e., 66 and 58 cases, respectively. A study from Thailand reported that greater the incidence of dengue infection of the previous year's epidemic, the milder the subsequent year's disease severity. This raises the interesting possibility that herd immunity is an important contributor to disease severity.[17] This may be possible either by replacing the subsequent year's predominant circulating dengue serotype(s) by a new circulating dengue virus serotype because of protective antibody or by changing the host immune response to experience milder illness.

The seasonal variation of transmission of dengue with increased activity in the post-monsoon season was seen.[18] The data on month-wise prevalence of dengue for the past 5 years reveals that the number of cases increased from July to October, confirming the active transmission period is during monsoon and post-monsoon period every year [Table 2]. Similar results were seen in a study from Delhi for the years 2004, 2005, and 2008.[5,16] This can be explained by the stagnant water sources following heavy rainfall, which could favor breeding of the mosquito vector resulting in an increased post-monsoon incidence of dengue, thereby maintaining the vector population throughout the year. This again emphasizes the need for appropriate vector control measures to be implemented during this period to reduce the case incidence. These findings also indicate that preventive measures against dengue infection should probably come into full swing during the post-monsoon months. No dengue cases were reported in the months of January–June from our institution in the years 2006–2010.

Dengue affects humans of all age groups worldwide and poses a pediatric public health problem in some parts of the world.[19] During the present study, comparison between the different age groups revealed that adults were infected disproportionately to children from 2006 to 2010 [Table 3]. We found a high burden of dengue in young children and late adolescents in both rural

Table 6: District-wise distribution of dengue cases

Districts of Delhi	Cases	%
North	770	48.12
North-east	327	20.43
North-west	84	5.25
West	112	7
South	30	1.9
East	20	1.25
South-west	89	5.56
Central	50	3.12
NCR	118	7.37
Total		100

NCR = National Capital Region

and urban communities at a magnitude greater than previously described. There was an increase in the total number of cases in 2006 and 2010 within the age groups 11–20 years and 21–30 years. Studies from Singapore, Indonesia, and Thailand suggest that exposure to multiple serotypes over a period of time results in development of immunity, i.e., multitypic immunity in adults. The shift in the age preponderance can be partly explained by the accumulation of multitypic immunity in the adult population.[20-22] It is suggested that over a period of time as the length of time of co-circulation of multiple serotypes of dengue in a particular geographic area increases, adults have a lower probability of remaining susceptible to infection. This results in the young population to become completely susceptible individuals. Therefore, monotypically immune individuals are more likely to be from younger age groups.[16] Dengue was first reported from Kolkata in 1963, which means the dengue virus has been in circulation for the last 38 years.[23] This circulation resulted in the accumulation of immunity in older individuals, driving the average age of primary and secondary infection towards younger age groups. The present study showed maximum number of dengue positive cases were from the age group 11–20 years. Similar results were seen in a study from other parts of India,[17,20,24,25] but our observation differs with other reported studies from Delhi where the burden of dengue was formed by the age group 21–30 years.[4,6] A study from Malaysia reported patients above 12 years were the most affected age group throughout the 5 years of study (1999–2003) for reasons being unknown.[26] Another study from North India found the age group of 0–15 years to be highly affected.[27]

Studies reported that the year 2006 showed co-circulation of all four serotypes along with high percentage of concurrent infections.[24] DEN-1 was the predominant type in the year 2008.[5] Studies from Thailand reported DEN-1 to be associated with milder form of disease, whereas DEN-2 and DEN-3 were reported to cause dengue with severe hemorrhagic manifestations.[28] There were almost constant number of patients diagnosed with DF and DHF in all 5 years [Table 3]. Although we did not determine the serotypes, comparison with the known data suggested no such association of serotypes with disease severity. We emphasize that the association of concurrent infections with severe forms of disease (DHF/DSS) needs further studies.[25,28-30]

Fever was the most common presenting symptom seen in 1526 of the patients (95.37%). Similar studies in and around India have also substantiated fever as being the most common presenting symptom.[21] Retro-orbital pain, generally considered as a cardinal feature of dengue fever, was not seen in our patients.[21] Rash, melena, and epistaxis were the common hemorrhagic manifestations seen. Another study from Delhi saw epistaxis and melena to be the most common manifestations whereas a study from South India reported rash and petechiae to be the common ones.[5,21]

Majority of the Dengue patients attending our hospital clinics belonged to North district (48.12%) and North-east districts (20.43%) of Delhi [Table 6]. We found that the cases were not confined to the urban areas of Delhi only, but also in the neighboring rural areas. It is therefore necessary to implement vector control measures such as source reduction in rural areas as well. Ours is the first study which shows the district-wise distribution of dengue positive cases, which came to our hospital in Delhi.

There was an increase in the total number of samples received in the laboratory for dengue serology in 2010 as compared with the previous years [Table 2]. This may be owing to a higher rate of suspicion amongst clinicians since this area saw an above average rainfall this year. Rain, temperature, and relative humidity are suggested as important factors attributing towards the growth

and dispersion of this vector and potential of dengue outbreaks.[1,4,18,24] Also, construction work was in full throttle since Delhi was preparing itself for the Commonwealth Games.

There are certain limitations of our study. Since our data analysis is based on laboratory-confirmed cases, we can assume them to be the tip of the iceberg in the overall pattern of dengue spread, and that the distribution of under-reported cases will follow the one of laboratory-confirmed cases. Also the actual contribution of asymptomatic cases to the local spread of dengue is unknown, in part due to the uncertainty about their potential to infect *Aedes aegypti* mosquitoes while viremic. No molecular studies were done to find the circulating serotypes. Research on the circulating serotypes and their genotypes may be of help in addressing the probabilities of DSS/DHF incidence in future.

Our findings increase the understanding of this disease and the full burden of infection. This study, in fact, has important public health implications on planning public health responses to dengue for the next decade. If the age shift represents the transition from endemicity to hyperendemicity, similar shifts in age are likely to be observed in the rest of India and other regions in Asia where dengue has emerged more recently. Although further studies are required, to the best of our knowledge, this is the first study from North India to report the age shift in the dengue patients from being in adults (21–30 years) to children and young adolescents (11–20 years). This finding may be of help to the epidemiologists, pediatricians, and dengue prevention and control measure authorities for early diagnosis and to plan out and implement various measures targeting the young population.

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