Original Article

Dengue Fever Outbreak in Delhi, North India: A Clinico-Epidemiological Study

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ABSTRACT

Background: Dengue viruses, single-stranded positive polarity ribonucleic acid (RNA) viruses of the family *Flaviviridae*, are the most common cause of arboviral disease in the world. We report a clinico-epidemiological study of the dengue fever outbreak of 2010 from a tertiary care hospital in Delhi, North India. **Objectives:** Objectives of the study were to know the incidence of laboratory-confirmed dengue cases among the clinically suspected patients; to study the clinical profile of dengue-positive cases; and to co-relate the above with the prevalent serotype and environmental conditions. **Materials and Methods:** Four thousand three hundred and seventy serum samples from clinically suspected cases of dengue infection were subjected to μ-capture enzyme-linked immunosorbent assay (ELISA) for detection of dengue-virus-specific IgM antibodies. Virus isolation was done in 55 samples on C6/36 cell mono-layers. Clinical and demographic details of the patients were obtained from requisition forms of the patients or from treating clinicians. **Results:** Out of the 4,370 serum samples, 1,700 were positive for dengue-virus-specific IgM antibodies (38.9%). Prevalent serotype was dengue virus type-1. Thrombocytopenia and myalgia was seen in 23.1% and 18.3% of the 1,700 dengue IgM-positive patients, respectively. Also, 10.3% of 1,700 were dengue hemorrhagic fever (DHF) patients; and the mortality in serologically confirmed dengue fever cases was 0.06%. **Conclusions:** A change in the predominant circulating serotype, unprecedented rains, enormous infrastructure development, and increased reporting due to improved diagnostic facilities were the factors responsible for the unexpected number of dengue fever cases confronted in 2010.

Keywords: Dengue virus, prevalent serotype, μ-capture ELISA

Introduction

Dengue viruses, single-stranded positive polarity ribonucleic acid (RNA) viruses of the family *Flaviviridae*, are the most common cause of arboviral disease in the world. Dengue viruses have four serotypes, designated dengue types 1-4; and are transmitted mainly by bite of *Aedes aegypti* mosquito and also by *Aedes albopictus*. More than two-fifths of the world's population (2.5 billion) live in areas potentially at risk for dengue.[1,2] The global incidence of dengue fever (DF) and dengue hemorrhagic fever (DHF) has increased dramatically in recent decades, and has turned this disease into a serious public health problem, especially in the tropical and sub-tropical countries.[3-5]

Dengue infection is endemic in many parts of India. In India, the first epidemic of clinical dengue-like illness was recorded in Madras (now Chennai) in 1780. The first virologically proven epidemic of DF in India occurred in 1963-1964, outbreaks have been reported from different parts of the country at regular intervals.[6-12]

Delhi, a city in North India, is endemic for dengue infection and has experienced eight outbreaks of dengue virus infection since 1967; with the last reported in 2006.[11-13] We report the experience of All India Institute of Medical Sciences (AIIMS), a tertiary care hospital in Delhi city, in the 2010 dengue outbreak.

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The objectives of the study were to know the incidence of laboratory confirmed dengue cases among the clinically suspected patients, to study the clinical profile of dengue-positive cases, and to co-relate the above with the prevalent serotype and environmental conditions.

Materials and Methods

The study included clotted blood specimens received in virology laboratory, from clinically suspected cases of dengue infection, from 1st May 2010 to 31st December 2010. Serum was separated aseptically and was stored at –70°C until further processing.

Serotype identification

For the identification of serotype, virus isolation followed by indirect fluorescent antibody assay (IFA) was done. As isolation could be done only in the acute phase samples for which proper cold chain was maintained throughout the transport, it was done in only 55 samples which were collected within 6 days of fever from the suspected dengue cases and were transported to the virology laboratory in ice. Virus isolation was carried out in the C6/36 clone of *Aedes albopictus* cell lines as described earlier.[11] IFA was performed using specific monoclonal antibodies to dengue virus types 1-4 (provided by Dr. D.J. Gubler, then at CDC, Atlanta, during the 1996 outbreak).[14]

Diagnosis of dengue infection

The serum samples from patients having ≥ 5 days of fever (n = 4370) were tested for dengue-specific IgM antibodies. μ-capture dengue IgM enzyme-linked immunosorbent assay (ELISA) kit was used (supplied by the National Institute of Virology, Pune; under the National Vector Borne Disease Control Program). Manufacturer's instructions were strictly followed for performing the test and interpreting the results. Optical Density (O.D) was measured at 450 nm using ELISA reader (BioTek^R, Winooski, United States).

Recording clinical and demographic details of patients

Clinical and demographic details of the patients were obtained from the patients' requisition forms, or from treating clinicians if required. The details were recorded in microsoft-excel sheets and those of dengue IgM ELISA-positive patients were analyzed to discern the pattern.

Results

Prevalent dengue serotype

Out of 55 specimens subjected to virus isolation, 33 (60.0%) were positive for dengue-1, while one specimen (1.8%) was positive for dengue-2. Thus, the prevalent serotype (97.1% of the 34 culture-positive DF cases) was dengue virus (DENV) serotype-1.

Demographic profile of the dengue IgM antibodies-positive cases

Dengue IgM antibody test was done on a total of 4,370 samples, of which 1,700 were positive for DENV-specific IgM antibodies (38.9%). In the 1,700 serologically confirmed dengue cases, male-to-female ratio was 1.6:1. The largest number of positive samples (30.8%) was from the age-group 21-30 years [Table 1]. The youngest patient was a 1-month-old male child and the oldest was an 87-year-old male patient.

Clinical profile and month-wise distribution of dengue cases [Table 2]

Out of 1,700 serologically confirmed dengue cases, 175 (10.3%) were DHF patients, of which 158 (9.3%) were DHF Grade I/II, and 17 (1.0%) were DHF Grade III/IV (dengue shock syndrome). Only one serologically confirmed dengue patient died (0.06%). Thrombocytopenia (platelet count < 100,000 cells per microliter of blood) was seen in 393 (23.1%) dengue IgM-positive patients and 311 (18.3%) patients presented with myalgia.

The first dengue IgM sero-positive case was in the last week of May, a 5-year-old male child from Jharkhand — a state in east-central India. Indigenous cases from Delhi appeared from third week of June. Maximum number of specimens was received in September (n = 1745; 39.9% of 4,370), followed by October (n = 1330; 30.4% of 4,370). The maximum cases diagnosed were also in September (n = 782; 46.0% of 1,700), followed by October (n = 448; 26.4% of 1,700). Percentage positives of the suspected cases peaked in September and August (44.8% and 44.2%, respectively).

Discussion

In the year 2010, four years after the last epidemic of 2006, India witnessed a massive wave of dengue fever, involving almost all states, except those in the extreme north and extreme north-east. The total number of serologically confirmed dengue cases from all over

Table 1: Age-wise distribution of dengue-positive patients

Age (years)	IgM ELISA-positive dengue cases (%)
0-10	248 (14.6)
11-20	393 (23.1)
21-30	524 (30.8)
31-40	273 (16.1)
41-50	131 (7.7)
>50	131 (7.7)
Total	1700 (100)

ELISA: Enzyme-linked immunosorbent assay

Table 2: Clinical profile and month-wise distribution of dengue-positive patients in 2010

Month	Samples tested (%of 4370)	IgM positive (%of 1700)	Percentage positives	Platelets <100,000	DHF	DSS	Myalgia
May	16 (0.4)	1 (0.06)	(6.3)	0	1	0	0
June	30 (0.7)	5 (0.3)	(16. 7)	2	1	0	1
July	97 ((2.2)	30 (1.8)	(30.9)	13	1	1	13
August	701 (16.0)	310 (18.2)	(44.2)	68	34	2	68
September	1745 (39.9)	782 (46.0)	(44.8)	212	71	9	132
October	1330 (30.4)	448 (26.4)	(33.7)	75	41	5	72
November	371 (8.5)	111 (6.5)	(29.9)	18	6	0	23
December	80 (1.8)	13 (0.8)	(16.3)	5	4	0	2
Total	4370 (100.0)	1700 (100.0)	(38.9)	393 (23.1)	158 (9.3)	17 (1.0)	311 (18.3)

Figures in the parentheses indicate percentage; DHF: Dengue hemorrhagic fever, DSS: Dengue shock syndrome

India in 2010 was 28,066, the highest on records. Total dengue IgM-positive cases from Delhi were 6,259 (22.8% of 28,066), considerably higher than those reported in the previous years (548, 1312, and 1153 in 2007, 2008, and 2009, respectively).[15] As per the epidemiological definition, as the number of dengue fever cases clearly exceeded all previous records, which was definitely greater than expected, it constituted an outbreak.

Over the last one and half decades, outbreaks and sporadic cases have been ascribed to different serotypes of dengue virus. The 1996 epidemic was mainly due to dengue-2 virus.[11,12] In 2003 outbreak, all four DENV serotypes were found to be co-circulating.[13] In 2005, dengue-3 was identified as the predominant serotype in Delhi.[16] In the year 2010, the predominant serotype found was dengue-1, which seemed to have replaced the previous circulating serotype. It is known that infection with one dengue serotype provides lifelong homologous immunity, but only transient cross-protection against other serotypes. The change in prevalent serotype is the major factor responsible for the enormous number of dengue cases witnessed, as the exposed population was by and large non-immune and thus susceptible to serotype-1.

Dengue affects humans of all age-groups. In 1996, maximum number of cases was in the 5-20 year age-group, while in 2003, maximum number of positive cases was in 21-30 year age-group.[11-13] In our study, maximum dengue cases (524; 30.8% of 1,700) were from the age group 21-30 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.

Classical DF is characterized by sudden onset of high grade fever, accompanied by headache, retro-orbital pain, myalgia, and thrombocytopenia. In our study, myalgia was seen in 18.3% and thrombocytopenia in 23.1% cases. Thus, most of dengue cases were clinically indistinguishable from other febrile illnesses, and could be missed lacking the clinical suspicion and timely diagnosis.

The risk of developing DHF/DSS is greatest following an anamnestic dengue infection, particularly if the most recent infection was with dengue-2 virus.[17,18] Dengue-2 virus was the predominant serotype in 1996 outbreak of DF/DHF/DSS, and was responsible for the witnessed severity and mortality (10.8%). In 2003, a mortality of 1.3%was reported from AIIMS; and in 2006, 1.5% mortality was reported from India.[11,13,19,20] In 2010, total number of deaths was 110 all over India (mortality 0.4% of 28,066 cases), with 8 from Delhi (mortality 0.13% of 6,259 cases).[15] At AIIMS, with only one death, the mortality was even lower (0.06%). And, 10.3% of the cases were of DHF of which only 1.0% were DSS. This suggests that the present dengue outbreak was larger in scale, but lesser in severity.

The role of environmental factors in infectious diseases is well-known. In most countries, dengue epidemics are reported to occur, during the warm, humid, and rainy seasons, which favor abundant mosquito growth and shorten the extrinsic incubation period as well.[21-23] In our study, the largest proportion of serologically positive cases was recorded in the post-monsoon period, which is in agreement with previous studies.[22,24]

The reason for large number of DF cases can also be related to the fact that in 2010, Delhi witnessed one of the wettest monsoons recorded. Delhi obtained 997.2 millimeters (mm) of rainfall between July 1 and September 30. The total rainfall in these three months in 2010 was not only notably higher than that of the previous 4 years (412.1 mm, 408.2 mm, 268.3 mm, and 468.2 mm in 2006, 2007, 2008, and 2009, respectively) but also appreciably exceeded the 25-year average of 530.8 mm (1981-2005).[25] The prolonged and heavy rains led to a rise in mosquito growth, thus increasing transmission of mosquito-borne infections.

The huge amount of infrastructure development which took place prior to Commonwealth Games (October 2010), may also have made growth environment more

conducive for mosquitoes. Another factor which would have contributed to the number of dengue cases could be an increase in the reporting of cases due to improvement in diagnostic settings.

Conclusion

We report our experience of the dengue fever outbreak of 2010. The event was of a large magnitude, but was comparatively less severe. A change in the predominant circulating serotype, unprecedented rains, enormous infrastructure development, and increased reporting due to improved diagnostic facilities all accounted for the observed multitude of people affected.

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