Chikungunya: a reemerging infection spreading during 2010 dengue fever outbreak in National Capital Region of India

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Abstract Chikungunya fever is an important reemerging arbovirus illness, which is transmitted by the same vector as of dengue virus. Many cases of concurrent infections with multiple dengue virus serotypes have been reported in many countries. Also, concurrent infection with Chikungunya virus and dengue virus has been reported in the past in Delhi. Therefore, this study was done to detect Chikungunya IgM antibodies in suspected dengue fever patients. In this study, 1666 serum samples suspected of dengue fever and collected during the outbreak period (August 2010–December 2010) were tested for dengue IgM antibodies, of which 736 tested negative. Of the 736 dengue IgM negative sera, 666 were tested for Chikungunya IgM antibodies. The demographic profile and essential laboratory investigations were recorded. Chikungunya IgM was detected in 9.91 % of the patients. During the post-monsoon period though dengue dominated in numbers, the number of Chikungunya fever cases increased gradually followed by an abrupt decrease with the onset of winter. The Chikungunya IgM positive patients were suffering from fever of more than 5 days duration and had thrombocytopenia. Due to similarity in clinical features and vector transmitting dengue and Chikungunya virus, continuous surveillance of both dengue fever and

Chikungunya fever is desirable for better management and epidemiological assessment.

Keywords Aedes · Chikungunya · Dengue · Post-monsoon · Reemerging

Chikungunya fever is an acute febrile illness caused by an arthropod-borne alphavirus, Chikungunya virus (CHIKV). CHIKV was first recognized as a human pathogen during the 1950s in Africa, and since then, cases have been identified in many countries in Africa and Asia [8]. In Asia, CHIKV is mainly transmitted within an urban cycle in an inter-human transmission by the human-biting *Aedes aegypti* and the less anthropophilic *Aedes albopictus*, which is usually found in suburban and rural areas. CHIKV, mainly causing high grade fever and arthralgia, was of limited public health concern before its emergence in the Indian Ocean in 2005 [18].

In India, epidemics of Chikungunya fever were reported during the twentieth century viz, Kolkata in 1963, Chennai in 1965 and Barsi in 1973 [11]. Thereafter, sporadic cases occurred specially in Maharashtra state during 1983 and 2000. During an epidemic outbreak of Chikungunya fever in 2006, more than 1.39 million suspected cases of Chikungunya fever affecting 210 districts in 13 states were reported. Maximum number of cases was recorded from Andhra Pradesh, Karnataka, Kerala, Tamil Nadu, Gujarat, Madhya Pradesh and Maharashtra [11].

In Asia, the CHIKV affected areas overlap with Dengue virus (DENV) endemic areas, thereby providing opportunities for mosquitoes to become infected with both viruses [5]. Co-infection with 2 dengue viruses (DENV-1 and DENV-4) was first reported in Puerto Rico in 1982 [7]. Since then, many cases of concurrent infections with

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multiple DENV serotypes have been reported in other regions [2, 4, 12]. Co-infection of CHIKV and DENV was reported in Vellore, India, in 1964 [10]. CHIKV and DENV nucleic acids were detected from clinical samples obtained during dengue fever outbreak of 2006 in Delhi [5]. Subsequently, co-infection of DENV and CHIKV were again reported from Delhi in 2014 and from Odisha and Maharashtra in 2015 [1, 13]. The present study was undertaken to examine CHIKV infection in patients with suspected dengue fever during dengue outbreak in 2010 in Delhi.

The study was conducted in the virology laboratory of a 1500-bedded tertiary care teaching hospital in New Delhi. Ethical approval certificate for the study was obtained from the institutional ethical committee. Written informed consent from the study subject was obtained in each case. A total of 1666 serum samples from clinically suspected cases of dengue fever collected during the 2010 dengue outbreak (August 2010–December 2010) were included in the study. All the serum samples of patients who presented with fever of more than 5 days duration were subjected to dengue IgM serology using the dengue IgM antibody capture ELISA [NIV Dengue IgM Capture ELISA KIT (version 2.4), National Institute of Virology, Pune, India]. The samples negative for dengue IgM were tested for CHIKV IgM antibodies using the IgM antibody capture ELISA [NIV CHIK IgM Capture ELISA KIT (version 3.4), National Institute of Virology, Pune, India]. The demographic profile of each patient and essential laboratory investigations were also recorded.

During the study period, our lab received 1666 cases suspected of dengue fever, out of which 930 samples tested positive and 736 tested negative for dengue IgM antibodies. Of the 736 dengue IgM negative sera, 666 were tested for Chikungunya IgM antibodies. Rest of the 70 samples could not be tested due to limited availability of CHIKV IgM antibody capture ELISA kits. Out of 666 dengue IgM negative sera, 66 (9.91 %) were positive for Chikungunya IgM antibodies with 57 (86.36 %) of the patients being adults and 9 (13.64 %) being children under 12 years of age. Of the 66 Chikungunya IgM positive patients, 39 (59.09 %) were males and 27 (40.91 %) were females. Clinically the patients were suffering from fever of more than 5 days duration and thrombocytopenia. Other symptoms encountered were rashes and arthralgia involving knees, ankles, wrists, hands and feet. A seasonal weekly distribution of number of cases depicting change in occurrence of dengue fever and Chikungunya fever cases is shown in Fig. 1.

In the past decade, dengue has become an important health concern in India, especially in the urban setting. With an unpredictable pattern of dengue fever outbreaks, Delhi suffers frequent spikes of dengue fever cases every 4–8 years [6]. The dengue fever outbreak of 2010 was

preceded by a massive wave of dengue fever in the year 2006 [5]. In 2006, CHIKV nucleic acid was detected from 17 clinically suspected cases of DENV/CHIKV co-infection at AIIMS, Delhi, of which 6 were co-infected with DENVs [5]. A study carried out in 2010 showed the ability of *Aedes* species from La Reunion Island, Indian Ocean, to replicate simultaneously autochthonous strains of DENV-1 and CHIKV provided in the same blood-meal, and to be able to deliver both of the infectious viral particles in their saliva. Also the same group succeeded in inducing a secondary infection with CHIKV after a gap of 7 or 13 days following a first infection with DENV-1 virus [18]. Hence their findings substantiated the plausibility of co-existence of CHIKV and DENV in the same host.

The year 2010 witnessed large number of dengue fever cases. In our study 930 (55.82 %) samples were found to be dengue IgM positive. However, it was found that during the post-monsoon period though dengue dominated in numbers, the number of Chikungunya fever cases increased gradually followed by an abrupt decrease with the onset of winter. A considerable fraction (9.91 %) of dengue IgM negative cases turned out to be positive for CHIKV infection. Similar findings were reported from different parts of the National Capital Region (NCR) in the same year, indicative of the expanding nature of this phenomenon [3, 14].

This study was carried out at the largest tertiary care hospital of east Delhi, catering to a large population of eastern NCR. The eastern NCR consist of mainly 3 administrative units—East Delhi and North East Delhi which belong to the state of Delhi, and Ghaziabad which is part of neighboring state of Uttar Pradesh. In our analysis, cases were seen not only from Delhi, but also from neighbouring states (Ghaziabad, Uttar Pradesh). As per surveys, these are among the most densely populated regions of Delhi (http://censusindia.gov.in/2011-prov-results/prov_data_products_delhi.html). Because of long duration of viremia and asymptomatic cases characteristic of dengue fever, people's mobility becomes an important factor in the disease transmission [17]. The census of 2011 has shown that the rate of growth of population in these areas was much higher in 2011 compared to 2001 due to migration from various parts of India (http://censusindia.gov.in/2011-prov-results/prov_data_products_delhi.html). Thus lack of urban planning with respect to changing demographic trends can further complicate the transmission of diseases like Chikungunya fever and dengue fever, whose vector has unique property of urban predilection. It is therefore pertinent to include the population mobility along with vector dynamics in developing control measures for Chikungunya fever and dengue fever.

The clinical differentiation of Chikungunya fever and dengue fever is difficult especially during outbreak period.

Fig. 1 Weekly distribution of Dengue IgM positive and Chikungunya IgM positive in Dengue IgM negative cases, from 01-01-2010 to 07-12-2010. Maximum number (152) of Dengue IgM positive cases were encountered towards end of September. The number of Chikungunya IgM positive cases started increasing from mid-October, and peaked (13 cases) in October end. Thereafter the number of Chikungunya IgM positive cases diminished

It has been documented that arthritis caused by CHIKV is the differentiating feature and that arthralgia can persist for long duration causing severe morbidity [16]. A retrospective study carried out in 2007 by Nagpal et al. showed that there was lack of Chikungunya fever case management facilities, trained manpower, essential supplies and record keeping in surveyed health facilities located in high incidence wards of Delhi. The same study also noted that there was lack of awareness in the stakeholders regarding the availability of diagnosis and treatment facilities in Delhi [11]. This points to the fact that most cases of Chikungunya fever may have been lost due to lack of proper diagnosis. Hence there is an urgent need to encourage the laboratory diagnosis of Chikungunya fever especially in endemic areas to confirm the aetiology.

The currently circulating strains of CHIKV in northern India are different from 1963 strains which belonged to Asian genotype. The currently circulating strain of CHIKV in northern India including Delhi had its origin from the 2006 epidemic strain of South India that moved towards northern India via the western central India between 2006 and 2010 in a phased manner with dominance of the East Central South African (ECSA) genotype, and it is closely related to 2006 Reunion island strain [15]. The clinical features seen during the present outbreak were different from those during outbreak of 1963. From 1963 to 1973, the common symptoms were fever, rash, severe and crippling arthritis, lymphadenopathy, gingivitis and bleeding gums [16]. In the current outbreak, fever, rashes, arthralgia and severe joint pain involving knees, ankles, wrists, hands and feet have been reported. Although the government of India has not

attributed, any death directly to Chikungunya fever, Mavalankar et al. have suggested that increase in death in the city of Ahmedabad during 2006 Chikungunya fever epidemic can be attributed to CHIKV on the basis of epidemiological evidences; however, due to lack of proper diagnosis other causes cannot be ruled out [9].

This study suggests that Chikungunya virus is continuously adapting itself and is reemerging as a potential infection in Indian subcontinent. Because of similar incubation periods, overlapping clinical signs and symptoms, and lack of awareness, it is likely that Chikungunya fever is under-diagnosed or is misinterpreted as dengue fever. Due to increased population density and influx of migratory population, chances of carrying both dengue and Chikungunya viruses becomes high. Hence co-circulation of both viruses may provide a diagnostic challenge for hospitals carrying out dengue serology alone. There is a dire need for regular surveillance of Chikungunya fever and dengue fever, especially in areas endemic for both the viruses, laying emphasis on diagnosis and better management of both the diseases. Vector-control measures have to be fine-tuned depending on the extent of the vector-pathogen association and its seasonal differences.

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