Increased utilization of treatment centre facilities during a dengue fever outbreak in Kolkata, India

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Abstract
An outbreak of febrile illness occurred in Kolkata (formerly Calcutta), India, which led to an increased utilization of treatment centre facilities during August – September 2005. The etiological agent was confirmed to be dengue by analysing 308 acute-phase clinical specimens for virus-specific IgM antibodies.

Keywords: Dengue fever; Outbreak; Treatment centres.

Background
In dengue-hyperendemic countries such as Indonesia, Thailand, the Philippines and Viet Nam, the circulation of multiple virus serotypes is well-established, regular dengue outbreaks occur, and the severe form of the disease is a common problem readily recognized by experienced clinicians. In contrast, in South Asian countries such as India, Bangladesh, and Sri Lanka, dengue is considered as an emerging disease and epidemics have been more recently recognized. Clinicians have less experience with dengue, and laboratory confirmation of the etiology of the viral disease is urgently needed to highlight this problem. Recently, an increasing number of outbreaks have been reported from various parts of India. We report a laboratory-confirmed outbreak of dengue fever in an urban slum community of Kolkata during the course of a community-based fever surveillance study.

Methods
Kolkata is the third largest city in India and is one of the world’s most densely populated cities; 13 million residents live within an area of 1450 sq. kms. Kolkata has three seasons,
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the cool dry months from November to February, the hot dry period from March to May, and the monsoon season from June to October. As part of a typhoid fever vaccine trial, we conducted a community-based passive surveillance for febrile illness in a well-defined urban slum population of about 60,000 individuals living in Wards 29 and 30. Blood samples were collected from patients residing in the study area who presented to treatment facilities in the study area with fever of 3 days or longer[10]. The blood samples were used to inoculate Bactec Plus Aerobic bottles (Becton Dickinson, New Jersey, USA) for bacterial culture, to make thick and thin blood films for malaria diagnosis, and preserved as sera for serological testing. A detailed description of the methods is presented elsewhere[10]. The study was approved by the Institutional Ethics Committee of the National Institute of Cholera and Enteric Diseases, the Ministry of Health Screening Committee of the Government of India, and the Institutional Review Board of the International Vaccine Institute.

An alarming increase in febrile episodes was noted in 2005 (Figure). The number of fever episodes evaluated in August and September 2005 was 1637, nearly double the 935 cases evaluated in August and September 2004. The possibility of a dengue outbreak was investigated using a Commercial Pathozyme Dengue IgM kit (Omega Diagnostics Limited, Omega House, Carsebridge Court, Whins Road, Scotland, UK)[11]. This is an in vitro diagnostic test based on an indirect enzyme immunoassay for screening dengue IgM antibody in infections caused by all four serotypes. Briefly, diluted sera (after absorption of IgG antibody) were added to the wells coated with dengue-specific antigen. After a thorough wash, peroxidase conjugated

Figure: The number of fever episodes evaluated and confirmed malaria, typhoid and paratyphoid fever from January 2004 to December 2005, Ward 29 and 30, Kolkata, India
antihuman IgM followed by specific substrate were added. A colour development indicated the presence of human anti-dengue antibody. The reaction was stopped by the addition of diluted sulphuric acid and absorbance was measured. Positive and negative controls supplied with the kit were used during each run. We compared the characteristics of patients with and without dengue IgM. We used the chi-square test for comparison of categorical variables and the Wilcoxon rank sum test for comparison of medians. Statistical significance was designated as a p-value less than 0.05 (2-tailed).

Results

From 1 August to 30 September 2005, a total of 1637 residents in the study area presented to a treatment centre with fever of 3 days or more. Of these 1637 fever cases, 471 (29%) presented with fever of 5 days or longer, and 308 (65%) were tested for dengue. 87/308 (28%) were positive for dengue IgM antibodies, suggestive of primary dengue infection. The ages ranged from 3 years to 60 years for those who tested positive and 1 year to 77 years for those who were negative. The characteristics of the patients with a positive and negative test for dengue IgM were compared (Table). The patients who had a positive dengue IgM test had a slightly lower median age and were more likely to have vomiting. There were no significant differences in the other characteristics between the two groups.

Discussion

Our surveillance detected an outbreak of dengue fever during the rainy season in a densely-populated area of India, where dengue has not traditionally been considered a local cause of fever. The principal vector for dengue fever is the female Aedes aegypti which breeds around human dwellings, in water containers, vases, cans, old tyres and other discarded objects,[12], which are common in the study site. The presence of this vector in Kolkata has been documented. Ae. aegypti prevalence coincides with the rainy season which sets in Kolkata from July to September[13], the same months when this dengue outbreak occurred.

We confirmed acute dengue fever in our study area with no evidence of severe manifestations (i.e. plasma leakage, haemorrhage, shock). There are four dengue

<table>
<thead>
<tr>
<th></th>
<th>Positive for dengue IgM (n = 87)</th>
<th>Negative for dengue IgM (n = 221)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females (%)</td>
<td>48 (55%)</td>
<td>101 (46%)</td>
<td>N.S.</td>
</tr>
<tr>
<td>Median age in years</td>
<td>17</td>
<td>20</td>
<td>0.05</td>
</tr>
<tr>
<td>Median number of days fever</td>
<td>5</td>
<td>6</td>
<td>N.S.</td>
</tr>
<tr>
<td>With continuous fever (%)</td>
<td>24 (28%)</td>
<td>56 (25%)</td>
<td>N.S.</td>
</tr>
<tr>
<td>With nausea (%)</td>
<td>27 (31%)</td>
<td>56 (25%)</td>
<td>N.S.</td>
</tr>
<tr>
<td>With vomiting (%)</td>
<td>17 (20%)</td>
<td>18 (8%)</td>
<td>0.01</td>
</tr>
<tr>
<td>With abdominal pain (%)</td>
<td>15 (17%)</td>
<td>21 (10%)</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

N.S.: Not significant
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serotypes. Infection with one provides life-long immunity against the same serotype, but not against the other serotypes. The risk of severe disease is increased about 15-fold during repeat infection due to a serotype different from a previous dengue infection[14]. Thus, populations previously infected by one or more dengue serotypes are at an increased risk for more severe manifestation during subsequent dengue episodes due to other serotypes.

The observations made in Kolkata in 2005 are consistent with a population with little to no pre-existing, anti-dengue immunity and where dengue is an emerging disease. Although the illnesses in the current outbreak were self-limiting, the sudden increase in consultations was an unexpected burden to the existing treatment facilities. Furthermore, there is the potential for more severe disease manifestations in future outbreaks. The proportion of febrile episodes caused by dengue during the coming years warrants further investigation. It would also be important to follow any changes in signs and symptoms of the disease, particularly the occurrence of severe manifestations.

We did not perform virological confirmation of the disease and therefore could not evaluate the circulating dengue serotype(s). We were not able to check for other etiologies, especially other flaviviruses with potential diagnostic cross-reaction. Our serological diagnosis of dengue infection relied on the presence of IgM antibody. By day five of illness, 80% of dengue cases had detectable IgM antibody, and by day six to ten, 93 to 99% of cases have detectable IgM that may persist for over 90 days[15]. We were unable to check for dengue IgG antibodies in the acute sera, nor did we collect convalescent sera to assess a rise in IgG antibody titre. However, we believe that the test for IgM antibodies among those with fever of 5 days or longer is appropriate to confirm an outbreak, particularly in this relatively dengue-naïve community.

The realization that dengue fever is an increasing cause of febrile disease in South Asia suggests the urgent need for preventive interventions. A safe, highly protective, long-lasting vaccine at an affordable price for large populations at risk in the tropical regions of Asia and the Americas would be the ideal control strategy. Meanwhile, preventive activities have to focus on vigorous vector control.

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References


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