Chandipura virus infection causing encephalitis in a tribal population of Odisha in eastern India

BHAGIRATHI DWIBEDI, JYOTSNAMAYEE SABAT, RUPENANGSHU K. HAZRA, ANU KUMAR, DIWAKAR SINGH DINESH, SHANTANU K. KAR

ABSTRACT
Background. The sudden death of 10 children in a tribal village of Kandhamal district, Odisha in eastern India led to this investigation.

Methods. We conducted a door-to-door survey to identify cases. Antibodies for Chandipura, Japanese encephalitis, dengue, chikungunya and West Nile viruses were tested by ELISA in probable cases. Chandipura virus RNA was tested from both human blood samples and sand flies by reverse transcriptase polymerase chain reaction. We conducted vector surveys in domestic and peri-domestic areas, and collected sand flies.

Results. Entomological investigations revealed the presence of Phlebotomus argentipes and Sergentomyia sp. Thirty-five patients presented with fever, 12 of them had altered sensorium including 4 who had convulsions. The blood samples of 21 patients were tested; four samples revealed Chandipura virus-specific IgM antibody.

Conclusion. Chandipura virus infection causing encephalitis affected this tribal population in eastern India at 1212 m above sea level.


INTRODUCTION
Chandipura virus (CHPV) is a vesiculovirus of the Rhabdoviridae family. It was isolated in 1965 in Chandipur in the Nagpur region of India from two adults with a febrile illness during an outbreak caused by dengue and chikungunya viruses. Several outbreaks of CHPV encephalitis have been reported in India. These have been characterized by rapid onset of fever, involvement of the central nervous system and a high case-fatality rate. Most studies from India in outbreak and surveillance settings between 1975 and 1999 indicated that Japanese encephalitis virus (JEV) was the most common virus in acute encephalitis syndrome (AES), but studies after 2000 have shown a predominance of CHPV and Enterovirus. We investigated the cause of sudden death of 10 children in a village in Kandhamal district of Odisha, in eastern part of India, during the second half of September 2009.

METHODS
Two children presented with altered sensorium and died suddenly in Gudrigaon village, Daringibadi block, Kandhamal district in the third week of September 2009. The area is in the eastern Ghat, 4000 feet (1212 m) above sea level, at a latitude of 19.9° N and longitude of 84.1° E. The average annual rainfall in the area is 1597 mm and the atmospheric temperature varies from 0 °C (December) to 35 °C (May). The affected village, inhabited by the Kandha tribal community, had a population of 195 covering 37 households.

We screened all households by a door-to-door visit and recorded the cases and deaths. We examined patients admitted to the district headquarters hospital and recorded hospital case reports including the detailed clinical presentation and outcome, i.e. recovery or death.

A probable case was defined as a person presenting with sudden onset of fever, altered sensorium, motor weakness, convulsion, abdominal pain, headache, vomiting or head reeling as a single symptom or in any combination.

Blood samples were collected within 5 days of the onset of illness from 21 patients. These included patients admitted to hospital, stored samples of those who had died as well as those procured during the household survey. Written consent was obtained from patients, parents/guardians before enrolment and sample collection.

We collected convalescent phase sera from the 11 survivors in the third week of illness. The samples were sent to the laboratory at Regional Medical Research Centre, Bhubaneswar and tested for IgM antibody by ELISA for JEV, dengue, chikungunya and West Nile viruses.

Samples for CHPV antibody were tested at the National Institute of Virology, Pune (Maharashtra, India) on the basis of an antigen-capture ELISA method described by Chadha et al. in 2005. The test was validated by running the sample with negative and positive controls. Serum from age-matched, apparently healthy children from an area not affected by the outbreak, and serum and cerebrospinal fluid from children with flavivirus infection other than CHPV, were also tested. The test was considered valid if the negative control value was <0.100 OD and the positive control value was in the range 1.000–1.500 OD.

We conducted a vector survey in the domestic and surrounding areas and collected sand flies. CHPV RNA was tested from both human blood samples and sand flies by reverse transcriptase polymerase chain reaction (RT-PCR) following the method described by Rao et al.

RESULTS
A total of 35 cases recorded from the village were clustered in 18 of 37 households. The number of family members affected in these households varied from one to seven. The cases occurred over 8 days (17–24 September) from the first reported case (Fig. 1). Fourteen patients (40%) were below 10 years of age, nine
between 10 and 18 years (25.7%) and 12 were above 18 years of age (34.2%, Table I).

Among the affected patients (n=35), 12 had clinically severe manifestations with altered sensorium, indicating involvement of the central nervous system. These patients presented with sudden onset of head reeling or headache, sweating and vomiting followed by motor weakness (inability to walk or move the limbs) and spells of unconsciousness before becoming comatose and/or dying. Four patients presented with convulsions. Other associated symptoms were low-grade fever (9 patients), chest pain, burning sensation over the body, and irritability. Pain during movement of the eyes and unilateral deviation of the uvula was observed in one patient, indicating involvement of multiple cranial nerves. This patient recovered completely in a week. All the patients were admitted to hospital and were given symptomatic treatment with broad-spectrum antibiotics. All of them were investigated for malaria by blood smear examination, which was negative. Of these 12 patients, 10 died within 8–12 hours of onset of symptoms. The case-fatality rate was high in children below 10 years of age, contributing to 70% of all deaths.

The remaining 23 patients had mild symptoms, without involvement of the central nervous system. They presented with abdominal pain (78.2%), fever (70%), headache or head reeling (39%), nausea or vomiting (26%), palpitation (17.3%), chills (13%) and sweating (8.7%) in different combinations. The symptoms lasted for 2–5 days (mean 70 hours) followed by complete recovery.

The mean age of the survivors was 23.9 years and of those who died was 12 years. Most (92%) survivors had a mild clinical presentation without altered sensorium whereas all the patients who died had altered sensorium/motor weakness. The survivors recovered completely without any neurological deficit.

Samples from 21 patients were tested for CHP IgM antibody at the National Institute of Virology, Pune and 4 were found positive. Other viral markers such as IgM antibody to JEV, dengue, chikungunya and West Nile virus were negative in all the samples. Serum of all the patients was negative for CHPV RNA by RT-PCR.

In our investigation of domestic and peri-domestic areas, we found the presence of sand flies, *Phlebotomus argentipes* (*P. argentipes*) and *Sergentomysia sp.* from households and animal dwellings. *P. argentipes* collection was 1/trap/night and 0.5 per man-hour density in aspiration catch from human dwellings. We collected seven sand flies from the living area of the village that had several moist places such as termite mounds with crevices and small water streams flanked by thick vegetation, which were suitable for their breeding. The tribal population reared pig, goat and cattle as pet animals and their sheds were close to human dwellings. The sand flies tested by RT-PCR were negative for CHPV RNA.

### Table I. Age and gender distribution of patients, and those who died

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Patients</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>&lt;10</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>10–18</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>&gt;18</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>17</td>
<td>18</td>
</tr>
</tbody>
</table>

DISCUSSION

We believe this is the first report of CHPV infection causing encephalitis in Odisha on the eastern coast of India, an area outside the reported zone of CHPV infection. Many outbreaks of CHPV have been reported from other states in India.²,³,⁵,⁶ The presence of CHPV infection in Odisha indicates its spread from the bordering state of Andhra Pradesh, where the infection has been present since 2003.² In 2004, the outbreak afflicted a tribal population in the hilly areas of Gujarat.³ The outbreak in Daringibadi, Odisha was located at a higher altitude (1212 m), and shows that CHPV infection can occur at such altitudes too.

The clinical features observed in this outbreak were similar to those reported earlier, except pain abdomen and involvement of the cranial nerves. The case-fatality rates in different CHPV outbreaks in India were 55.6% (2003, Andhra Pradesh), 41% (2003, Nagpur), 78.3% (2004, Gujarat) and 54.4% (2005–6, Warangal, Andhra Pradesh), and mainly affected children.²,³,⁵,⁶ The present outbreak had a case-fatality rate of 28.6%. Our patients, who recovered from illness, were free from any neurological sequelae. Similar observations were made during the CHPV outbreak in Warangal district of Andhra Pradesh (2005–6) where no neurological sequelae were seen.⁶

Sand flies have been implicated as possible vectors for transmission of CHPV.⁷ We studied a limited number of sand flies and could not detect CHPV RNA, but their presence and the favourable environment for breeding could suggest their role in the emergence of the infection.

Our investigation indicated that the spread of CHPV infection to newer areas in eastern India was causing a high mortality among children in a different ecological setting, and could spread to newer geographical locations in the future. Thus, CHPV should be looked for in cases of acute encephalitis in children in sporadic or outbreak situations along with JEV, which is the major cause of viral encephalitis in the region.

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Conflict of interest. None

Contributions

BHAGIRATH DWIBEDI: Field investigation, Clinical examination, Data analysis and interpretation of results, manuscript preparation

![Fig 1. Day-wise appearance distribution of patients and deaths.](image)


References


