



# Emergence of Japanese encephalitis in nonendemic regions of India: a public health concern?

Utkarsh Singh, MBBS<sup>a</sup>, Bijaya K. Padhi, PhD<sup>c</sup>, Vinay Suresh, MBBS<sup>a</sup>, Himanshu Jindal, MBBS<sup>b</sup>, Ranjit Sah, MBBS, MD<sup>d,e,\*</sup>

## The case in Pune, India

The eve of 3 November 2022 witnessed the first case in about 3 years of the viral-borne disease Japanese encephalitis (JE) in the city of Pune, a nonendemic A region for the virus. A 4-year-old boy from the Wadgaonsheri area was admitted to the Pediatric ICU at Sassoon General Hospital with complaints of fever, convulsions, spastic paralysis, and altered sensorium. The child received treatment with little effect and was kept on ventilator support for 9 days. Blood and cerebrospinal fluid samples were sent for scrutinization to the National Institute of Virology (NIV), Pune. Considering suspicions of an infectious pathology, the sera of seven household members, 16 nearby residents, 18 dogs, and pigs were also sampled and reported. The samples tested positive for JE on 29 November 2022<sup>[1]</sup>. This raises concerns for a potential outbreak when considering the geographical, climatic, and sociocultural conditions of the population in the area.

## The disease

JE is a viral infection caused by the Japanese encephalitis virus (JEV), a member of the family *Flaviviridae*. This neurotropic virus has five genotypes (GI–GV), with the GIII variant seen in the India–Sri Lanka–Nepal region<sup>[2]</sup>. It transmits via the bite of *Culex* mosquito species and is amplified in hosts that include pigs and ardeid birds. Humans and cattle are dead-end hosts.

<sup>a</sup>King George's Medical University, Lucknow, <sup>b</sup>Ganesh Shankar Vidyarthi Memorial Medical College, Kanpur, Uttar Pradesh, <sup>c</sup>Department of Community Medicine and School of Public Health, Postgraduate Institute of Medical Education and Research, Chandigarh, <sup>d</sup>DY Patil Medical College, Hospital and Research Centre, Dr DY Patil Vidyapeeth, Pune, Maharashtra, India and <sup>e</sup>Tribhuvan University Teaching Hospital, Institute of Medicine, Kathmandu, Nepal

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\*Corresponding author. Address: Tribhuvan University Teaching Hospital, Kathmandu 44600, Nepal. Tel.: +977-9803098857. E-mail address: ranjitsah@iom.edu.np (R. Sah).

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JE mostly causes an asymptomatic infection, and rarely presents with clinical features that progress to a fulminant condition which include fever, altered sensorium, headache, excessive reflexes, seizures, and coma. Neuroimaging such as cranial computed tomography and MRI show bilateral thalamic changes suggestive of JE<sup>[3]</sup>. IgM capture ELISA on serum/cerebrospinal fluid is the preferred investigation of choice.

Currently, three vaccines against JE are available in India. The SA 14-14-2 is a live-attenuated cell culture–derived vaccine with a high seroconversion rate and minimal side effects. JEEV by Biological Evans India Ltd is recommended for travelers to JE endemic areas. JENVAC by Bharat Biotech is an inactivated Vero cell culture vaccine with very good seroprotection postexposure.

Treatment options for JE are quite limited, and only the complications are treatable. The administration of steroids or mannitol to manage elevated ICP is known to improve the prognosis in cases of sequelae such as seizures or status epilepticus. Good nursing and optimal electrolyte monitoring can take care of pressure sores, paralysis, and contractures<sup>[4]</sup>.

## Similar outbreaks in the past

In Assam, there were numerous outbreaks which resulted in 773 patients with clinically suspected viral encephalitis being admitted to various hospitals during June and August of 2000–2002<sup>[5]</sup>.

A similar outbreak occurred in Gorakhpur, from July to November 2005. It was the longest and deadliest pandemic in three decades, killing 1344 people and affecting 5737 people across seven districts of eastern Uttar Pradesh<sup>[6]</sup>.

Twenty-four fatalities were recorded in the Malkangiri district of Odisha between September and November of 2012 which marked the advent of the disease in the state after nearly two decades<sup>[7]</sup>.

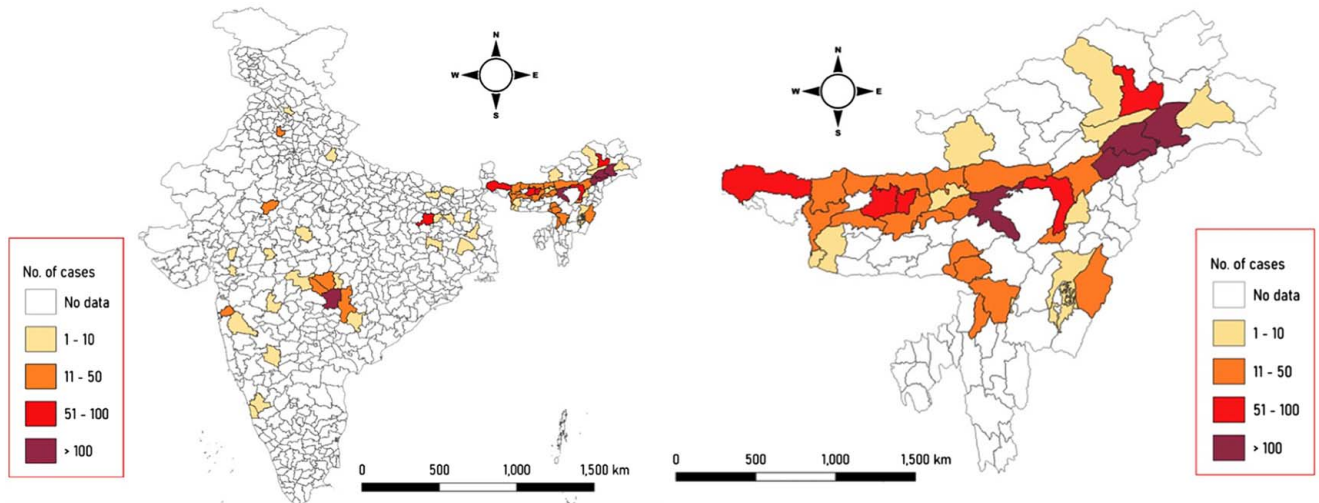
Another large outbreak broke out in the northern districts of the state of West Bengal in July 2014, infecting as many as 398 while claiming the lives of 115 citizens<sup>[8]</sup>.

A large number of affected districts and a higher caseload suggest that the Northeast has been the most severely impacted region over the past decade. The figure represents a choropleth map of India and the North-Eastern States that details acute encephalitis syndrome outbreaks caused by JEV (Fig. 1).

The timeline in the figure shows similar outbreaks that have spread to various Indian states (Fig. 2).

## Concerns to be raised

As JE is a vector-borne disease, open drainage in urban areas and stagnant irrigation in waterlogged fields are major concerns as



**Figure 1.** Choropleth maps of acute encephalitis syndrome – Japanese encephalitis outbreaks across India (left) and specifically the North-Eastern states (right).

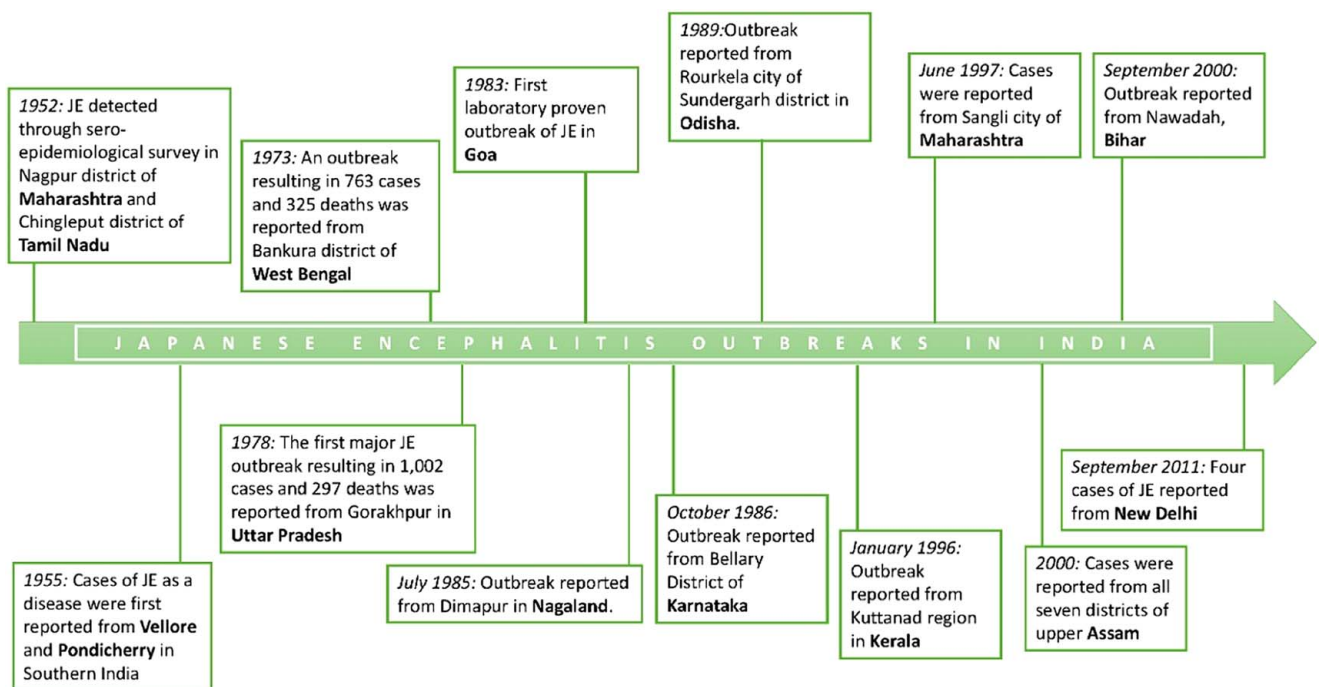
they provide excellent mosquito breeding grounds. Pigs near these mosquito breeding hotspots raise serious epidemiological concerns. The huge population of pigs in Pune is attributed to their commercial breeding, lack of slaughterhouses, and community opposition to slaughter.

Since no anti-JEV treatments exist, prevention against JE is of utmost importance. It is mostly based on three strategies: vector control, pig immunization, and human immunization. In India, prevention is mainly based on vector control, however, vaccination is the method of choice for obtaining long-term, effective protection against JE.

There exists no effective treatment for this disease, and therefore prophylaxis in the form of vaccination is recommended. Future research prospects should include developing a vaccine that is safe, economical, and able to provide life-long immunity with a single dose.

### The way forward

Following the reporting of sporadic JE and Zika cases, Pune saw the implementation of many surveillance measures, including a fever survey programme covering 480 households and an



**Figure 2.** Japanese encephalitis (JE) outbreaks in India (timeline).

entomological survey to check for *Culex* (primarily *Culex tritaeniorhynchus*) mosquito breeding sites in commercial complexes and housing societies<sup>[9]</sup>. To curtail the spread of the disease, many Indian states have implemented public health measures like community education campaigns, vector control measures, as well as efficient surveillance under the aegis of the National Vector Borne Disease Control Program (NVBDCP).

Following the sporadic JE and Zika cases, Pune is set to immunize over 11 lakh children in the age group 1–15 years due to the district's continued *Culex* infiltration through a first-of-its-kind immunization drive in the state of Maharashtra. The Pune Municipal Corporation (PMC) is one of three municipal corporations in the state to participate in the immunization program, the others being Parbhani, and Raigad<sup>[10]</sup>.

Keeping in mind the nature of recent events, clinicians and biologists should collaborate to develop tests that can invariably identify cases, to begin treatment protocols as soon as possible, while also participating in active research and trials to develop new drugs and vaccines with potential anti-JEV activity.

## Conclusions

JE is the most important cause of viral encephalitis in Asia which has resulted in multiple deadly outbreaks in the Indian sub-continent. One positive case of JE, such as the one reported in Pune could lead to an upsurge in the number of cases and subsequently an outbreak. It is imperative to take measures that preclude the development of an outbreak, such as vector control and vaccination drives. The management mostly comprises supportive treatment, as no potential cure exists.

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