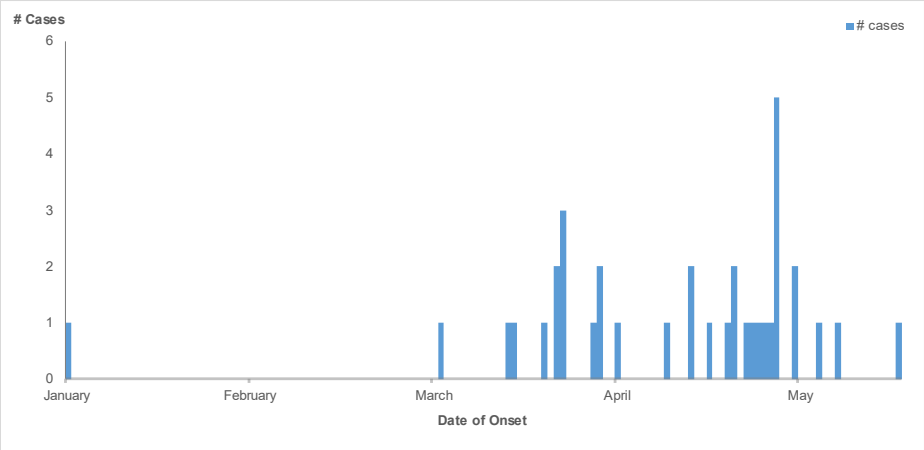
Feedback from operational stakeholders who manage or respond to outbreaks is that they are often too busy to review literature or obtain relevant background information to assist them with acute response. Unlike a traditional analytical outbreak investigation report, ***Watching Briefs*** *are intended as a rapid resource for public health or other first responders in the field on topical, serious or current outbreaks, and provide a digest of relevant information including key features of an outbreak, comparison with past outbreaks and a literature review. They can be completed by responders to an outbreak, or by anyone interested in or following an outbreak using public or open source data, including news reports.*

Watching brief

Title	An outbreak of West Nile Fever in Kerala, India, 2024
Authors	Abey Sushan, Mahesh N, Harikumar S
Date of first report of the outbreak	15th January 2024
Disease or outbreak	West Nile Fever
Origin (*country, city, region*)	Kozhikode district, Kerala, India
Suspected Source (specify food source, zoonotic or human origin or other)	West Nile Fever is a vector-borne disease caused by the mosquito borne virus (West Nile Virus) belonging to the Flaviviridae family (1).
Date of outbreak beginning	15 January 2024
Date outbreak declared over	Ongoing outbreak
Affected countries & regions	Kozhikode, Thrissur, Malappuram and Ernakulam districts of Kerala, India
Number of cases (specify at what date if ongoing)	We defined a case as an Acute Encephalitis syndrome case (AES) with viral detection by Reverse Transcription Polymerase Chain Reaction (RT-PCR) assay OR IgM antibody capture enzyme-linked immunosorbent assay

	(ELISA); PRNT is recommended to rule out cross reactions and confirmation OR Virus isolation by cell culture (2). Between 15 January 2024 and 30 May 2024, 36 cases (As on 15th July 2024) were reported from seven districts Kozhikode (14 cases), Thrissur (8 cases), Malappuram (6 cases), Ernakulam (4 cases), Idukki (2 cases), Palakkad and Kannur districts (1 case each). Most cases were reported during May 2024 (22 cases). Of these, 10 cases were confirmed through Plaque Reduction Neutralisation Test (PRNT).  *Figure 1. West Nile Fever cases by date of onset, Kerala, India, January – May 2024*
Clinical features	• The Incubation period is between 2 to 14 days but can be longer in older or immunocompromised persons (3). • Most infected persons are asymptomatic, but around 20% of infected persons develop West Nile Fever (4). The symptoms include fever, headache, body ache, maculopapular rash and swollen lymph glands. • But, in less than 1% of persons, West Nile Virus (WNV) infection can cause neuroinvasive disease that manifests as meningitis, encephalitis or acute flaccid myelitis (3). Neuroinvasive disease presents with headache, high-grade fever, neck stiffness, impaired consciousness, muscle weakness and paralysis, which can lead to coma and death (5). • Most cases presented with fever (n = 17; 46%) and neurological signs and symptoms such as seizures (n=3, 8%) and altered sensorium (n=11, 40%) suggestive of neuroinvasive disease such as acute encephalitis, and meningo-encephalitis. • The differential diagnoses of AES other than West Nile fever include Japanese Encephalitis (JE), Nipah, Herpes, Varicella, Dengue, Entero viral encephalitis, Malaria, Syphilis, Acute Tuberculous meningitis and Bacterial meningitis.

<table>
<tr><td>Mode of transmission (dominant mode and other documented modes)</td><td>West Nile Virus is mainly transmitted to humans through the bite of infected Culicine mosquitoes. Cases of West Nile Virus transmission through organ transplantation (6), blood transfusion (7), and breast milk (8) have also been reported. West Nile Virus is transmitted between mosquitoes and wild birds in nature. Mosquitoes become infected when they feed on birds that have high levels of the virus in their blood. The mode of transmission in the current outbreak was not investigated.</td></tr>
<tr><td>Demographics of cases</td><td>All age groups were affected including infants and elderly. Males and Females were equally affected. Median (IQR) age of case patients in this outbreak was 34 (13-63) years.

Table 1. Age distribution of West Nile fever cases, Kerala, India, January - July 2024

<table><tr><th>Age group</th><th># cases (%)</th></tr><tr><td>< 18 years</td><td>12 (33%)</td></tr><tr><td>18 – 60 years</td><td>14 (39%)</td></tr><tr><td>> 60 years</td><td>10 (28%)</td></tr><tr><td>Total</td><td>36</td></tr></table>
None of the reported cases are classified as imported from other states/countries, and all cases are deemed autochthonous.</td></tr>
<tr><td>Case fatality rate</td><td>The case fatality is usually between 3 to 15% (9). Severe disease and death are more common among elderly and immunocompromised.

2 deaths have been reported among the reported cases, both of whom had severe comorbidities. The overall case fatality is 5.6%.</td></tr>
<tr><td>Complications</td><td>Approximately 1 in 150 infected persons will have a severe illness with central nervous system (CNS) involvement (10). The complications of West Nile Virus infection include meningoencephalitis, meningitis, encephalitis, and acute flaccid paralysis. Older persons and immunocompromised persons are at greater risk for developing severe disease and complications.

14 (39%) out of 36 cases presented with neurological complications such as seizures (n=3, 8%), altered sensorium (n=5, 14%) and encephalitis (n=3, 8%). The incidence of neurological complications in this outbreak is higher compared to the other similar outbreaks.</td></tr>
<tr><td>Available prevention</td><td>ChimeriVax-WN02 is a live, attenuated chimeric vaccine which has proven to be highly immunogenic (11). However, to date, no vaccines have been approved for use in humans (12). Prevention of West Nile Virus infection mainly depends on measures to reduce mosquito bites. The main preventive strategies include the use of personal protective measures such as the use of protective</td></tr>
</table>

	clothing, mosquito repellents and use of mosquito nets and community-level measures such as source reduction activities and the use of larvicides and insecticides. Screening of blood and organ donors prevents transmission through blood transfusion and organ donation.
Available treatment	Treatment is mainly supportive as no specific treatment is available for West Nile fever. Patients with severe symptoms or neurological symptoms require admission, intensive monitoring and management of symptoms like headache, vomiting, dehydration and seizures. Ventilatory support may be required for patients with encephalitis.

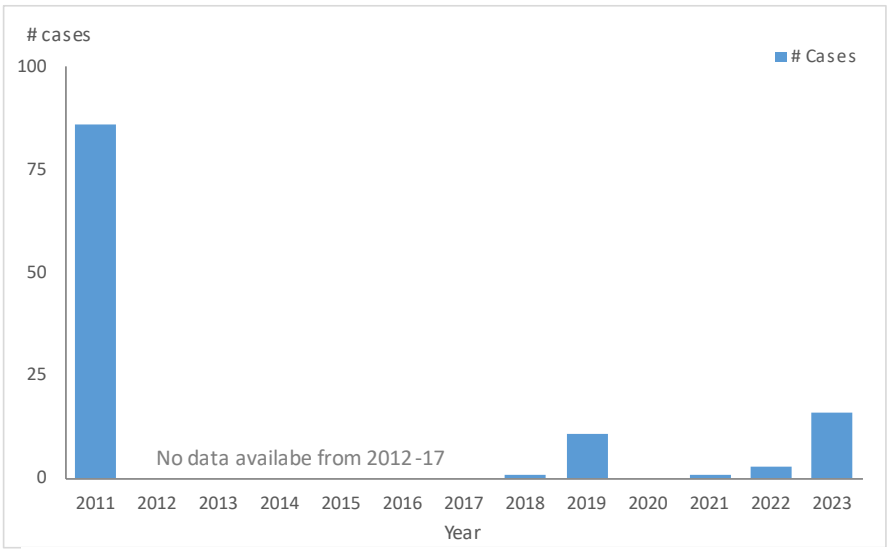


Figure 2. West Nile Fever cases, Kerala, 2011-2023

Comparison with past outbreaks

- From 2011 to 2023, 102 cases and 6 deaths were reported in Kerala, India. Most number of cases were reported in 2011 (86 cases).

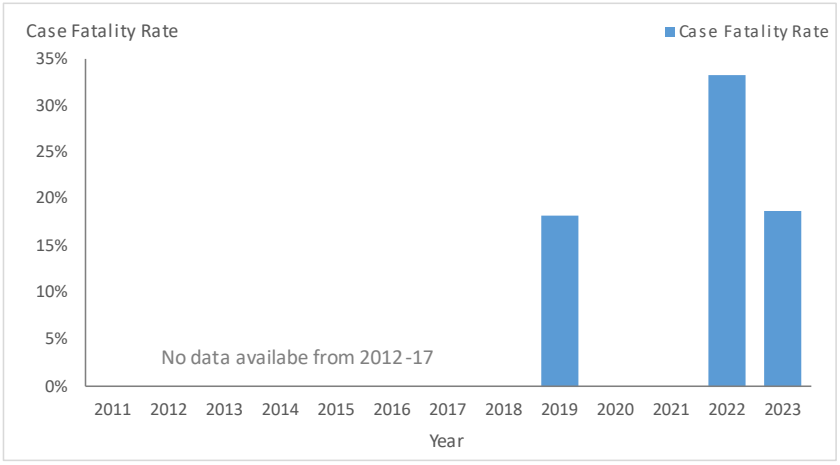


Figure 3. Case Fatality Rate of West Nile Fever, Kerala, 2011-2023

- The overall case fatality rate was 5.1%. Case Fatality Rate varied from 0% to 33% from 2019 to 2023. The highest case fatality was reported in 2022 (33%) (13).

Unusual features	A higher incidence of neurological complications like altered sensorium, seizures, and encephalitis was noted in patients during this outbreak. The case fatality was also higher.
Critical analysis	• WNV was first isolated in 1937 from the blood of an infected woman in the West Nile province of Uganda (14). The Virus was identified to cause severe meningoencephalitis during a 1957 outbreak in Israel. During the 1990s outbreaks were reported from Russia, Romania and Israel. WNV was first reported in the United States in 1999. • In India, antibodies against WNV was first identified in humans during the 1950s (15). Since, then outbreaks have been reported from Assam(16), West Bengal (17) and Tamil Nadu (18). WNV was first identified in Kerala during the AES outbreak in 2011 (19). • Kerala, a south Indian state, reported the first case of West Nile fever in 2011. Since then, 102 cases were reported from all districts till 2023. • The presence of the Virus in an environment which is endemic to closely related Japanese Encephalitis Virus (JEV) and other flavivirus including dengue and Kyasanur forest disease Viruses further warrants detailed investigation from public health aspect. • West Nile Encephalitis is indistinguishable from other causes of AES at clinical presentation and can only be confirmed through laboratory testing. Since JE, Nipah and other aetiological agents of AES are prevalent in Kerala, all AES cases should be subjected to laboratory testing for confirmation. WNV testing shall also be included in the viral panel for AES. • West Nile Virus does not replicate rapidly enough in humans and horses to infect a new mosquito to continue the natural cycle. Hence, humans are considered dead end hosts (20). However, WNV may circulate silently among birds and can lead to spill-over event to humans and/or horses. Mosquito survey and virological analysis, bird survey and serological analysis and other “One Health” approaches are necessary to understand the distribution and determinants of West Nile Virus distribution and factors associated with its incidence in humans and animals (21,22).

Key questions	1. What is the community incidence of West Nile Virus infection in Kerala, India? 2. Why is there a higher proportion of neurological complications in the present outbreak? 3. What is the distribution of the vector, Culicine mosquitoes, in Kerala? 4. Is there a concurrent increase in other diseases transmitted by Culicine mosquitoes in Kerala? 5. Are all the cases reported across various districts in Kerala epidemiologically related?
Ethics statement	This Watching brief was prepared as a health system response to a public health emergency using secondary information with the objective of describing the outbreak for public health responders to aid them in controlling the outbreak thereby reducing complications and mortality. Hence, ethical approval was not sought.

References	1. CDC. West Nile Virus. 2024 [cited 2024 May 27]. About West Nile. Available from: https://www.cdc.gov/west-nile-virus/about/index.html 2. Ministry of Health and Family Welfare. Case definitions: Integrated Disease Surveillance Programme [Internet]. 2019 [cited 2023 Jul 4]. Available from: https://idsp.mohfw.gov.in/WriteReadData/l892s/4216524651671001411.pdf 3. CDC. West Nile Virus. 2024 [cited 2024 Oct 4]. Clinical Signs and Symptoms of West Nile Virus Disease. Available from: https://www.cdc.gov/west-nile-virus/hcp/clinical-signs/index.html 4. West Nile virus- Barbados [Internet]. [cited 2024 Oct 4]. Available from: https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON538 5. Santini M, Haberle S, Židovec-Lepej S, Savić V, Kusulja M, Papić N, et al. Severe West Nile Virus Neuroinvasive Disease: Clinical Characteristics, Short- and Long-Term Outcomes. Pathogens. 2022 Jan 2;11(1):52. 6. Kusne S, Smilack J. Transmission of West Nile virus by organ transplantation. Liver Transpl. 2005;11(2):239–41. 7. Pealer Lisa N., Marfin Anthony A., Petersen Lyle R., Lanciotti Robert S., Page Peter L., Stramer Susan L., et al. Transmission of West Nile Virus through Blood Transfusion in the United States in 2002. N Engl J Med. 2003;349(13):1236–45. 8. Possible West Nile Virus Transmission to an Infant Through Breast-Feeding --- Michigan, 2002 [Internet]. [cited 2024 May 28]. Available from: https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5139a1.htm 9. Ford-Jones EL, Fearon M, Leber C, Dwight P, Myszak M, Cole B, et al. Human surveillance for West Nile virus infection in Ontario in 2000. CMAJ Can Med Assoc J. 2002 Jan 8;166(1):29–35. 10. Sampathkumar P. West Nile Virus: Epidemiology, Clinical Presentation, Diagnosis, and Prevention. Mayo Clin Proc. 2003 Sep;78(9):1137–44. 11. Biedenbender R, Bevilacqua J, Gregg AM, Watson M, Dayan G. Phase II, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study to Investigate the Immunogenicity and Safety of a West Nile Virus Vaccine in Healthy Adults. J Infect Dis. 2011 Jan 1;203(1):75–84. 12. Kaiser JA, Barrett ADT. Twenty Years of Progress Toward West Nile Virus Vaccine Development. Viruses. 2019 Sep 5;11(9):823. 13. Data on Communicable Diseases – dhs [Internet]. [cited 2024 Oct 5]. Available from: https://dhs.kerala.gov.in/en/data-on-communicable-diseases/

14. Smithburn KC, Hughes TP, Burke AW, Paul JH. A Neurotropic Virus Isolated from the Blood of a Native of Uganda. 1940 Jul 1 [cited 2024 Jun 23]; Available from: https://www.ajtmh.org/view/journals/tpmd/s1-20/4/article-p471.xml

15. Banker D. Preliminary observations on antibody patterns against certain viruses among inhabitants of Bombay city. Indian J Med Sci. 1952;6(733):46.

16. Khan SA, Dutta P, Khan AM, Chowdhury P, Borah J, Doloi P, et al. West Nile virus infection, Assam, India. Emerg Infect Dis. 2011 May;17(5):947–8.

17. Khatun T, Chatterjee S. Emergence of West Nile virus in West Bengal, India: a new report. Trans R Soc Trop Med Hyg. 2017 Apr 1;111(4):178–84.

18. Risbud AR, Sharma V, Rao CV, Rodrigues FM, Shaikh BH, Pinto BD, et al. Post-epidemic serological survey for JE virus antibodies in south Arcot district (Tamil Nadu). Indian J Med Res. 1991 Jan;93:1–5.

19. Anukumar B, Sapkal GN, Tandale BV, Balasubramanian R, Gangale D. West Nile encephalitis outbreak in Kerala, India, 2011. J Clin Virol. 2014 Sep 1;61(1):152–5.

20. Rizzoli A, Jimenez-Clavero MA, Barzon L, Cordioli P, Figuerola J, Koraka P, et al. The challenge of West Nile virus in Europe: knowledge gaps and research priorities. Euro Surveill Bull Eur Sur Mal Transm Eur Commun Dis Bull. 2015 May 21;20(20):21135.

21. McLean RG, Ubico SR, Bourne D, Komar N. West Nile virus in livestock and wildlife. Curr Top Microbiol Immunol. 2002;267:271–308.

22. Muñoz J, Ruiz S, Soriguer R, Alcaide M, Viana DS, Roiz D, et al. Feeding Patterns of Potential West Nile Virus Vectors in South-West Spain. PLOS ONE. 2012 Jun 22;7(6):e39549.