

World Health ziка е Organization

ZIKA EPIDEMIOLOGY UPDATE

Global overview

As of December 2021, a total of 90 countries and territories have had documented evidence of autochthonous mosquito-borne transmission of Zika virus (ZIKV), distributed across five of the six WHO Regions (all except the Eastern Mediterranean Region).¹ Since the <u>last epidemiological update</u> in 2019, two countries have been added to the list of countries with evidence of autochthonous, mosquito-borne transmission, based on peer-reviewed published data. France was added following the report of autochthonous transmission recognized in late 2019, and Kenya was added after recent publications documented robust laboratory evidence of prior autochthonous transmission.^{2,3}

Since mid-2019, WHO and partner public health agencies have continued to review ZIKV epidemiological data by region. In the Region of the Americas, where incidence of ZIKV infection peaked in 2016 and declined substantially thereafter, transmission continues to be reported in some countries and it remains the WHO Region with the highest number of reported ZIKV disease cases annually.⁴ India reported an outbreak of ZIKV disease in Kerala State that occurred in July 2021, marking the first outbreak activity in the South-East Asia Region since the cluster in Jaipur, India, in 2018.⁵ In the European Region, although cases in travellers returning from endemic areas have been reported since 2016, the first autochthonous transmission in this region was reported in France in 2019.² In the African Region, several studies have been conducted to determine seroprevalence of ZIKV antibodies in specimens from either ill or asymptomatic patients; one such study demonstrated population seroprevalence indicative of autochthonous transmission in Kenya.³ In the Western Pacific Region, only descriptions of sporadic ZIKV disease cases and one probable case of ZIKV-associated neonatal microcephaly have been reported since mid-2019.⁶

Globally, 59 countries and territories in six WHO regions have evidence of established and competent *Aedes aegypti* vector populations, but have not yet documented autochthonous ZIKV transmission.¹ In addition, other countries have established populations of *Aedes albopictus*, which are competent to transmit ZIKV but to a lesser extent than *Aedes aegypti* and are thus less likely to propagate and sustain large-scale ZIKV outbreaks.⁷ The presence of either of these vector populations poses an ongoing risk for ZIKV spread to additional countries. It is also possible that ZIKV transmission occurs, or has occurred, in some of these countries without being detected or reported. All areas with prior reports of ZIKV transmission have the potential for re-emergence or re-introduction, although population immunity to ZIKV, and to the closely related Flavivirus DENV, likely reduce the likelihood and extent of re-emergence or re-introduction.^{8,9}

ZIKV infection is recognized as a cause of Guillain-Barré Syndrome, as well as adverse pregnancy outcomes that include increased risk of preterm birth, foetal death and stillbirth, and congenital malformations collectively characterized in their most severe form as congenital Zika syndrome (CZS).^{10,11} CZS includes microcephaly and other abnormal cranial morphologies, abnormal brain development, limb contractures, eye abnormalities, brain calcifications, and other neurologic clinical

features. The provision of long-term supportive care for children with CZS, as well as for their families, remains a substantial demand on healthcare systems and community-based programs.

Continued efforts in sequencing ZIKV isolates and gene fragments have been important in elucidating trends in endemic transmission and patterns of global spread. Through phylogenetic analysis ZIKV has been characterised into two major lineages namely the African and Asian lineages. ZIKV African lineage was isolated sporadically in non-human and human specimens since 1947.¹² Asian lineage viruses were first isolated in Malaysia in 1951 and later in the Pacific Islands from 2007 onwards, with some activity in other Western Pacific and Southeast Asia countries since that time. The 2015-16 epidemic in the Americas was caused by a strain of the Asian lineage commonly referred to as the American strain. Presence of the ZIKV Asian lineage has been documented in the African Region and was implicated in outbreaks in Angola and Cabo Verde which included microcephaly cases.^{13,14} More recently, ZIKV African lineage genomic sequences were identified in Brazil through novel automated sub-typing screening of NCBI databases; the specimens from which the RNA was obtained were of mosquito and non-human primate origin.¹⁵ The effect of introduction of these strains into areas where others have previously circulated is not known at this time.

The differences in the epidemic potential and pathogenicity of these viral lineages and strains remain poorly understood. Although an earlier report postulated the association of a specific viral mutation of the Asian lineage with the observation of teratogenic effects of ZIKV infection following the outbreaks in French Polynesia and the Americas in 2015-2016, this hypothesis was challenged by the documentation of a case of microcephaly in Thailand after congenital infection with Asia lineage-Asian strain ZIKV without the mutation.¹⁶ In contrast, to date, adverse pregnancy outcomes and cases of CZS caused by ZIKV African lineage viruses have not been recognized and it is not known whether this is because they do not occur, or because of limitations of detection and surveillance. Studies of the African lineage *in-vitro* and in animal models suggest the potential for increased pathogenesis in pregnancy compared with the Asian lineage, suggesting a propensity to cause fetal loss rather than birth defects.¹⁷

Accurate and up-to-date epidemiologic data on ZIKV are limited in many areas of the world. The majority of ZIKV infections are asymptomatic, and when disease occurs, symptoms are generally mild and non-specific, and therefore may not be detected or reported. Many countries lack or have limited systems for routine surveillance, case detection and reporting of ZIKV disease cases. In the absence of large outbreaks, available information is often based on clinical case reports, traveller cases, and research studies. Even in settings with laboratory capacity, case detection and surveillance are challenging due to limited availability of diagnostic tests and difficulties with interpretation of serologic test results because of known cross-reactivity of ZIKV with related circulating flaviviruses, most notably DENV. Most recently, capacities to detect arbovirus transmission have been further hampered in many countries by the COVID-19 pandemic for reasons that include diversion of limited surveillance and response resources to address this ongoing public health emergency and reduction in healthcare seeking behaviour, particularly during periods of intense SARS-CoV-2 transmission. Pandemic mitigation measures may also have rendered certain settings more favorable for arbovirus transmission because of household crowding and an accumulation of mosquito breeding sites (e.g., containers) during stay-at-home orders.

Lack of detection or reporting of ZIKV transmission, therefore, cannot necessarily be equated with evidence that transmission is not occurring, particularly in areas with low levels of transmission. In

addition, transmission may have continued or started again and not been detected in areas where vector surveillance and control efforts have been impaired, particularly over the course of the COVID-19 pandemic. Decisions to guide family planning or travel to countries with a history of ZIKV transmission, particularly for pregnant women, women who may become pregnant, and their male partners, should be based on an assessment of information provided by country public health departments and consultation with the individual's healthcare provider.¹⁸

WHO remains committed to strengthening public health systems for early detection and response to emergence, re-emergence, and global spread of ZIKV infection and its complications, including monitoring for CZS and Guillain-Barré syndrome. WHO continues to work with regional and national health authorities to enhance health system capacity to detect, report, and respond to the continued threat of ZIKV transmission, as well as to other *Aedes*-borne arboviruses and other emerging and re-emerging threats to public health.

- Read "Prevention of sexual transmission of Zika virus"
- Read "Information for travellers visiting Zika affected countries"
- See map "Countries and territories with current or previous Zika virus transmission"
- See list "<u>Countries and territories with current or previous Zika virus transmission, February</u> 2022

African Region

Overview

Evidence of ZIKV transmission has been identified in several countries in the African Region; however, information on the current incidence and trends of ZIKV transmission remains limited. Since the last epidemiological update, the only country with newly detected serological evidence of autochthonous transmission is Kenya.

Kenya

A retrospective serologic study was conducted using blood specimens collected from a random sample of asymptomatic persons within village clusters in West Pokot and Turkana counties in 2016 and 2017.³ The estimated seroprevalence to various flaviviruses were heterogeneous across the two counties and the most common neutralizing antibodies detected were against yellow fever virus, West Nile virus, ZIKV and DENV. The overall seroprevalence for ZIKV in West Pokot was 7.11% and <1% in Turkana, consistent with circulation of ZIKV in Kenya. Two additional studies provide some possible supporting evidence of ZIKV circulation in Kenya, although additional confirmatory neutralizing antibody testing would be needed to exclude cross-reactive antibodies as the reason for the positive ZIKV results, as well as the need to exclude travel and yellow fever vaccination histories among the small number of possible cases identified.^{19,20}

Region of the Americas

Overview

The WHO Regional Office for the Americas (AMRO)/Pan American Health Organization (PAHO) maintains data on reported cases of ZIKV disease and CZS.⁴ Data from ongoing surveillance are reported by countries and territories directly to PAHO/WHO or collected from epidemiological bulletins posted on Ministry of Health websites. A summary of <u>reported case numbers by country</u> and sub-region and a <u>Zika epidemiologic summary</u>, most recently in the context of COVID-19, are maintained on the AMRO/PAHO website.²¹

The ZIKV outbreak in the Americas peaked during the first half of 2016. Incidence subsequently declined in most countries and territories from 2017-2020. In 2020, a total of 22,885 cases of ZIKV disease were reported in the Region of the Americas. Of these, 2,742 (12%) were laboratory confirmed.⁴ These data indicate that ZIKV transmission persists at low levels in several countries in the Americas, with observed heterogeneity across the region and within countries. Some reporting jurisdictions, particularly relatively smaller island and territories appear to have interrupted transmission. However, while some have maintained strong surveillance programs that indicate that transmission is likely interrupted, surveillance and reporting are not uniform or consistent across the region and in some cases may not be sufficiently sensitive to detect low levels of transmission. Ongoing vigilance remains key to ensure early detection of potential re-emergence or re-introduction of ZIKV transmission.

Results of case reports for 2020 are summarized below. There is variability in reporting practices by country or territory; some countries, such as Mexico, report only laboratory-confirmed cases, while others also report suspected and probable cases. Therefore, data from different countries and territories are not comparable. In 2020, Brazil reported 18,941 cases, representing 83% of all reported cases in the region, of which 14% were laboratory confirmed. Brazil's cumulative incidence of suspected cases was 9.08 per 100,000 population. The overall cumulative incidence of ZIKV disease in the Region of the Americas in 2020 was 2.34 per 100,000 population. Some countries had a higher cumulative incidence compared with the overall regional incidence including Brazil (mentioned above), Paraguay with 8.60 suspected cases per 100,000 population (n=593 cases), Bolivia with 6.49 suspected cases per 100,000 population (n=728 cases), and Guatemala with 5.24 suspected cases per 100,000 population (n=904 cases). In the Caribbean, Barbados had the highest incidence in the region of 14.69 suspected cases per 100,000 population (n=42 cases). Bermuda, Bonaire, Canada, mainland Chile, Saint Eustatius and Saba, and Uruguay have never reported autochthonous, vector-borne transmission of ZIKV.

In 2020, 15 (29.4%) of the countries and territories in the Region of the Americas had at least one Zika surveillance report available. The sub-region with the lowest reporting was the Caribbean where only two (7%) of the countries and territories had any report available in 2020. Nonetheless, the cumulative populations of the reporting countries represent more than 98% of the population of the Region of the Americas.²¹ Efforts are underway to strengthen ZIKV surveillance and reporting. Throughout the Region of the Americas, multiple pregnancy cohorts and registries continue to follow pregnant women and their infants to advance understanding of ZIKV infection, maternal-fetal transmission, pathogenesis, and child outcomes.²²

Eastern Mediterranean Region

No countries in the WHO Eastern Mediterranean Region (EMRO) have reported autochthonous transmission of ZIKV. However, because of the documented presence of *Aedes aegypti* populations in several countries in the region, EMRO has developed ZIKV preparedness plans and developed a framework for monitoring and evaluation of their implementation.²³ In addition, half of the countries in the region participated in the WHO global external quality assessment programme for molecular arbovirus diagnostics, demonstrating generally good proficiency.²⁴

European Region

Although numerous cases of travel associated ZIKV infections were reported in European travellers from 2015-2018, no autochthonous cases were documented. In 2019, however, autochthonous, mosquito-borne transmission of ZIKV was identified in the Var department in South-eastern France.² To maintain vigilance about areas at risk for introduction and autochthonous transmission of ZIKV and other mosquito-borne arboviruses, the distribution of mosquito vectors in the European region is regularly updated.²⁵

France

On 9 October 2019, the French authorities reported a case of autochthonous ZIKV disease in Hyeres, Var department, France.² No travel history to ZIKV endemic countries was reported for the patient or their partner. During the case investigation, two additional probable autochthonous ZIKV cases were identified from the same area and timeframe (onset of symptoms for the three cases ranged from 6 to 15 August 2019); all patients recovered. It is likely that the three cases resulted from vector-borne transmission of ZIKV in late July/early August. Vector control activities and epidemiological investigations were implemented to detect the vector and additional cases. No additional cases were reported after this initial cluster.

South-East Asia Region

Overview

ZIKV has been circulating since at least the 1960s in several countries of the South-East Asia Region. The region as a whole remains at risk for ZIKV transmission because of the presence of competent vectors, often in high densities. Improved surveillance and epidemiologic investigations are needed to better ascertain the incidence of ZIKV infection in the South-East Asia region and its impact on birth outcomes.

India

In July 2021, India reported an outbreak of ZIKV disease in Kerala State, marking the first outbreak activity in the South-East Asia Region since the outbreak in Jaipur, India, in 2018.⁵ Infection was initially detected in a pregnant woman in Trivandrum district, Kerala state, with febrile rash illness. Expanded testing within the community identified at least seventy PCR-confirmed cases of ZIKV disease by August, 2021. This is the first time that cases of ZIKV disease have been confirmed in Kerala and Maharashtra states (South-western coast) in India, although Gujarat (North-west of the

country) and Rajasthan (North) states in India reported ZIKV disease cases in 2017 and 2018 respectively. Given the wide distribution of the primary mosquito vector, *Aedes aegypti*, and less competent vector, *Aedes albopictus* in Kerala and Maharashtra states, where DENV and chikungunya virus disease cases are reported annually, the ecological and epidemiological conditions are favourable for ZIKV epidemic transmission and potential endemicity.

Western Pacific Region

Background

Sporadic cases of ZIKV infections have been reported by health ministries in countries across the Western Pacific Region (Malaysia, Singapore); however, in general, information on the incidence and trends of ZIKV transmission in the Region remains limited. Since the last epidemiological update, a literature review identified a case of ZIKV infection in a traveller returning from Kiribati and a publication on one probable case of ZIKV-associated neonatal microcephaly in Lao People's Democratic Republic.^{26, 6}

Kiribati

A traveller who had spent several months in Kiribati in April 2015, became ill 2 days after returning to New Zealand and had molecular evidence of ZIKV infection.²⁶ The travel itinerary suggested this case was possibly a sentinel indicator of autochthonous transmission in Kiribati, however, autochthonous transmission has not been detected through surveillance or testing of suspect arboviral disease cases in Kiribati.

Lao People's Democratic Republic

A probable case of CZS was reported in 2020 when a boy was born with microcephaly in Vientiane to a woman who reported a rash illness during the 12th week of gestation.⁶ At the time of the rash, tests for DENV, cytomegalovirus, toxoplasmosis, rubella and Herpes simplex viruses 1/2 were negative, but neither molecular nor serologic testing for ZIKV infection were performed. After delivery, ZIKV IgG was detected in blood collected from the mother and IgM and IgG in blood from the infant. While PRNT₉₀ revealed ZIKV titres of 1/320 in the baby and 1/640 in the mother, cross-neutralization tests with other flaviviruses could not be performed due to limited volumes. For DENV, only rapid tests for IgM and IgG antibodies could be performed, and results were negative. For this reason, the case remained a probable rather than a confirmed case of CZS.

References

- 1. WHO. Countries and territories with current or previous Zika virus transmission. Updated February 2022. Accessible at: [insert hyperlink]
- Giron Sandra, Franke Florian, Decoppet Anne, et al. Vector-borne transmission of Zika virus in Europe, southern France, August 2019. *Euro Surveill*. 2019;24(45):pii=1900655. Accessible at: <u>https://doi.org/10.2807/1560-7917.ES.2019.24.45.1900655</u>
- Chepkorir E, Tchouassi DP, Konongoi SL, et al. Serological evidence of Flavivirus circulation in human populations in Northern Kenya: an assessment of disease risk 2016-2017. Virol J. 2019;16(1):65. Published 2019 May 17. Doi:10.1186/s12985-019-1176-y

- 4. WHO Region of the Americas/Pan American Health Organization. PLISA Health Information Platform for the Americas: Cases of Zika virus disease, by country or territory. Accessible at: <u>https://www3.paho.org/data/index.php/en/?option=com_content&view=article&id=524:zika-weekly-en&Itemid=352</u>
- 5. WHO. Zika virus disease India. Disease Outbreak News. Accessible at: https://www.who.int/emergencies/disease-outbreak-news/item/zika-virus-diseaseindia#:~:text=On%208%20July%202021%2C%20a,case%20ever%20reported%20from%20Kerala
- 6. Calvez E, Vetsaphong P, Somlor S, et al. First probable case of congenital Zika syndrome in Lao People's Democratic Republic. *Int J Infect Dis*. 2021;105:595-597. doi:10.1016/j.ijid.2021.03.019
- Tham HW, Balasubramaniam V, Ooi MK, Chew MF. Viral Determinants and Vector Competence of Zika Virus Transmission. Front Microbiol. 2018;9:1040. Published 2018 May 23. doi:10.3389/fmicb.2018.01040
- 8. Rodriguez-Barraquer I, Costa F, Nascimento EJM, et al. Impact of preexisting dengue immunity on Zika virus emergence in a dengue endemic region. *Science*. 2019;363(6427):607-610. doi:10.1126/science.aav6618.
- 9. Katzelnick LC, Bos S, Harris E. Protective and enhancing interactions among dengue viruses 1-4 and Zika virus. *Curr Opin Virol*. 2020;43:59-70. doi:10.1016/j.coviro.2020.08.006
- Halani S, Tombindo PE, O'Reilly R, et al. (2021) Clinical manifestations and health outcomes associated with Zika virus infections in adults: A systematic review. *PLoS Negl Trop Dis* 15(7): e0009516. <u>https://doi.org/10.1371/journal.pntd.0009516</u>
- 11. Moore CA, Staples JE, Dobyns WB, et al. Characterizing the Pattern of Anomalies in Congenital Zika Syndrome for Pediatric Clinicians. *JAMA Pediatr*. 2017;171(3):288-295. doi:10.1001/jamapediatrics.2016.3982
- Haddow AD, Schuh AJ, Yasuda CY, Kasper MR, Heang V, et al. (2012) Genetic Characterization of Zika Virus Strains: Geographic Expansion of the Asian Lineage. *PLoS Negl Trop Dis*. 6(2): e1477. doi:10.1371/journal.pntd.0001477
- Hill SC, Vasconcelos J, Neto Z, et al. Emergence of the Asian lineage of Zika virus in Angola: an outbreak investigation. Lancet Infect Dis. 2019;19(10):1138-1147. doi:10.1016/S1473-3099(19)30293-2
- Faye O, de Lourdes Monteiro M, Vrancken B, et al. Genomic Epidemiology of 2015-2016 Zika Virus Outbreak in Cape Verde. *Emerg Infect Dis*. 2020;26(6):1084-1090. doi:10.3201/eid2606.190928
- 15. Kasprzykowski JI, Fukutani KF, Fabio H, et al. A recursive sub-typing screening surveillance system detects the appearance of the ZIKV African lineage in Brazil: Is there a risk of a new epidemic?. *Int J Infect Dis.* 2020;96:579-581. doi:10.1016/j.ijid.2020.05.090
- 16. Grubaugh ND, Ishtiaq F, Setoh YX, Ko AI. Misperceived Risks of Zika-related Microcephaly in India. *Trends Microbiol*. 2019;27(5):381-383. doi:10.1016/j.tim.2019.02.004
- Aubry F, Jacobs S, Darmuzey M, et al. Recent African strains of Zika virus display higher transmissibility and fetal pathogenicity than Asian strains. Nat Commun. 2021;12(1):916. Published 2021 Feb 10. doi:10.1038/s41467-021-21199-z
- 18. WHO guidelines for the prevention of sexual transmission of Zika virus. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO
- 19. Kisuya B, Masika MM, Bahizire E, Oyugi JO. Seroprevalence of Zika virus in selected regions in Kenya. *Trans R Soc Trop Med Hyg*. 2019;113(12):735-739. doi:10.1093/trstmh/trz077
- 20. Hunsperger E, Odhiambo D, Makio A, et al. Zika Virus Detection with 2013 Serosurvey, Mombasa, Kenya. *Emerg Infect Dis.* 2020;26(7):1603-1605. doi:10.3201/eid2607.191363
- 21. Pan American Health Organization / World Health Organization. Epidemiological Update: Arboviruses in the context of COVID-19. 2 July 2021, Washington, D.C. PAHO / WHO. 2021 Accessible at: <u>https://iris.paho.org/handle/10665.2/54497</u>

- 22. Wilder-Smith A, Wei Y, Araújo TVB, et al. Understanding the relation between Zika virus infection during pregnancy and adverse fetal, infant and child outcomes: a protocol for a systematic review and individual participant data meta-analysis of longitudinal studies of pregnant women and their infants and children. *BMJ Open*. 2019;9(6):e026092. Published 2019 Jun 18. doi:10.1136/bmjopen-2018-026092
- Establishing syndromic surveillance and event-based surveillance systems for Zika, dengue and other arboviral diseases. Cairo: WHO Regional Office for the Eastern Mediterranean; 2020. Licence: CC BYNC-SA 3.0 IGO. Accessible at: https://www.who.int/publications/i/item/9789290223443
- 24. Squires RC, Oxenford CJ, Cognat S, Konings F. Performance of Eastern Mediterranean Region laboratories in the World Health Organization external quality assessment programme for arbovirus diagnostics. *East Mediterr Health J*. 2020;26(5):616-619. Published 2020 May 21. doi:10.26719/emhj.20.015
- 25. Maps of surveillance activities and current known distributions of mosquito species in Europe and neighbouring regions. Accessible at: https://www.ecdc.europa.eu/en/disease-vectors/surveillance-and-disease-data/mosquito-maps
- Leder K, Grobusch MP, Gautret P, et al. Zika beyond the Americas: Travelers as sentinels of Zika virus transmission. A GeoSentinel analysis, 2012 to 2016. *PLoS One*. 2017;12(10):e0185689. Published 2017 Oct 3. doi:10.1371/journal.pone.0185689