World Health Organization

ZIKA EPIDEMIOLOGY UPDATE

JULY 2019

Global overview

As of July 2019, a total of 87 countries and territories have had evidence of autochthonous mosquito-borne transmission of Zika virus (ZIKV), distributed across four of the six WHO Regions (African Region, Region of the Americas, South-East Asia Region, and Western Pacific Region).[1] In 2018, Ethiopia was the only new country added to the list of countries with evidence of autochthonous, mosquito-borne transmission, based on a publication of a 2014 study.[2]

Incidence of ZIKV infection in the Americas peaked in 2016 and declined substantially throughout 2017 and 2018.[3] Zika virus transmission has been found in all countries in the Region of the Americas except mainland Chile, Uruguay, and Canada.[3] Although epidemiologic data from the African, South-East Asian, and Western Pacific Regions are more limited, new scientific evidence continues to accumulate and advance our understanding of global ZIKV transmission and its associated complications.

Recent studies have provided new information on the incidence, prevalence, and patterns of ZIKV transmission worldwide. For example, in Indonesia, a retrospective population-based serosurvey found approximately 9% of children had evidence of prior ZIKV infection by the age of 5 years.[4] In Lao People's Republic, evaluation of specimens from asymptomatic adult blood donors in 2015 found nearly 10% had evidence of prior ZIKV infection.[5] Thailand demonstrated seasonal patterns of ZIKV transmission that coincided with those of dengue virus, which share common mosquito vectors.[6] India reported a ZIKV outbreak in Rajasthan State in 2018.[7] New evidence identified that the ZIKV strain found in the Americas had spread to Angola and was associated with a cluster of microcephaly in 2017-2018.[8,9,10] Cases of Zika-associated congenital malformations, microcephaly, and foetal death have been identified in countries in Asia.[11,12,13] These and other recent epidemiologic data are summarized below according to WHO region.

Globally, 61 countries and territories in six WHO regions have evidence of established competent *Aedes aegypti* vectors but have not yet documented ZIKV transmission.[1] Therefore, there is still the potential risk for ZIKV to spread to additional countries. It is also possible that some of these countries have or have had transmission that has not yet been detected or reported. All areas with prior reports of ZIKV transmission have the potential for re-emergence or re-introduction.

Infection with ZIKV continues to carry the risk of Guillain-Barré Syndrome and adverse pregnancy outcomes including increased risk of preterm birth, foetal death and stillbirth, and congenital malformations collectively characterized as congenital Zika syndrome (CZS), including microcephaly, abnormal brain development, limb contractures, eye abnormalities, brain calcifications, and other neurologic manifestations. The provision of long-term care for affected children and families remains a substantial need of healthcare systems and community-based programs.

ZIKV genetic sequence analyses have been important in elucidating patterns of global spread.[14-18] Two major lineages of ZIKV, known as the Asian and African lineages, have been identified. The Asian

lineage was first identified in Asia and subsequently spread to the Pacific Islands and then to the Americas. The 2015-16 epidemic in the Americas was caused by a strain of the Asian lineage commonly referred to as the American strain. For the purpose of this report, the strain of the Asian lineage that had been and continues to circulate in Asia will be referred to as the "Asia lineage-Asian strain" or the "older" Asian strain.

The differences in the epidemic potential and pathogenicity of these viral lineages and strains are not fully understood. The 2018 ZIKV outbreak in India was due to the Asian lineage-Asian strain, demonstrating the epidemic potential of this older Asian strain.[19] Cases of congenital Zika syndrome, microcephaly, and foetal death have been confirmed in women infected with Asian lineage virus, both the American and Asian strains, providing new evidence that adverse birth outcomes are not limited to the strains that caused the epidemic in the Americas.[11,12] Studies have demonstrated that ZIKV has circulated in Africa for decades, but no case reports or human studies have yet investigated effects of the African lineage on pregnancy and birth outcomes. Studies of the African lineage *in-vitro* and in animal models suggest the potential for increased pathogenesis in pregnancy compared with the Asian lineage, causing foetal loss rather than birth defects[20,21] The effects of Zika African lineage viruses on birth outcomes remains an area of needed research.[22]

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. 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 systems are challenging due to limitations of available diagnostic tests.[23,24,25]

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. 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.

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 congenital Zika syndrome 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 mosquito-borne viruses and other emerging and re-emerging threats to public health.

- Read "WHO guidelines for the prevention of sexual transmission of Zika virus"
- Read "Information for travellers visiting countries with Zika virus transmission"
- See map "Countries and territories with current or previous Zika virus transmission"
- See list "Countries and territories with current or previous Zika virus transmission, July 2019."

African Region

Overview

Evidence of ZIKV transmission has been identified in several countries in the African Region;[1,26-28] those with evidence of transmission prior to the 2015 epidemic include Burkina Faso,[29] Burundi,[30] Cameroon,[31] Central African Republic,[32] Côte d'Ivoire,[33] Gabon,[34] Nigeria,[35] Senegal, Sierra Leone,[26-27] and Uganda.[36-38] Information on the incidence and trends of ZIKV transmission in the African Region remains limited. Information from some countries with newly-detected transmission and events since 2015 are highlighted below.

Angola

In 2016, two cases of ZIKV infection were confirmed by RT-PCR, one in an Angola resident and one in a returning traveller.[39] In December 2017, 42 infants with microcephaly were reported with a suspected association with ZIKV infection;[40] additional microcephaly case reports continued through the following year. In February 2018, a confirmed case of congenital Zika syndrome was reported in an infant born to a mother who was a resident of Angola, with no other travel history, who delivered in Portugal. ZIKV genome analysis confirmed infection with the Asian lineage found in the Americas.[9] A separate study of stored specimens and of suspected microcephaly cases confirmed additional cases infected with the American strain based on full virus genome analysis.[10] These studies confirmed introduction of mosquito-borne transmission of the ZIKV strain from the Americas into continental Africa.

Cabo Verde

During the 2015-2016 epidemic, 7580 suspected cases of ZIKV disease and 18 cases of ZIKV-associated microcephaly were reported. Viral sequence analysis conducted in March 2016 demonstrated evidence of infection with the same Asian strain that was found in the Americas.[41,42]

Guinea-Bissau

In 2016, four cases of ZIKV infection were confirmed by RT-PCR.[43,44] Preliminary results of viral sequence analysis from 2016 suggested infection with the ZIKV African lineage. (*unpublished data, Institut Pasteur, Dakar)*. Subsequent investigations of 15 infants with microcephaly identified 13 mothers and/or their infants positive for ZIKV IgG and neutralizing antibodies by plaque reduction neutralization test (PRNT); no samples tested positive for ZIKV RNA or IgM.[45] In 2018, 16 cases of microcephaly were reported. Among those with available specimens, four tested positive for ZIKV IgG and neutralizing antibodies by PRNT; none tested positive for RNA or IgM.[46] Causal association between microcephaly and maternal ZIKV infection in these cases remains unknown. Enhanced surveillance for

detection and investigation of acute rash/fever illness is underway to ascertain if there is ongoing ZIKV transmission.

Ethiopia

A community-based household survey evaluating yellow fever seroprevalence was conducted in five areas of Ethiopia in 2014 and published in 2018. Yellow fever IgG-positive specimens were tested for dengue, West Nile, and ZIKV infections. Seven specimens were ZIKV IgG positive and infection was confirmed by PRNT, representing the first known evidence that ZIKV transmission has occurred in Ethiopia.[2]

Region of the Americas

Overview

The WHO Regional Office for the Americas (AMRO)/Pan American Health Organization (PAHO) maintains reports of cases of ZIKV infection and congenital Zika syndrome.[3] 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 reported number of cases of Zika virus disease by country and sub-region and a Zika epidemiologic summary are maintained on the AMRO/PAHO website.

The ZIKV outbreak in the Americas peaked during the first half of 2016. Incidence subsequently declined in essentially all countries and territories throughout 2017 and 2018.[3] In 2018, a total of 31,587 suspected, probable, and confirmed cases of ZIKV disease were reported in the Region of the Americas. Of these, 3,473 (11%) were laboratory confirmed. In general, transmission persists at low levels in some areas and is not uniformly distributed within countries. Some countries and territories, particularly relatively smaller island states and territories appear to have interrupted transmission or low levels of transmission below levels of detection. Some island states have maintained strong surveillance programs that indicate that transmission is likely interrupted, but surveillance and reporting are not uniform or consistent across the region.[47] Ongoing vigilance remains important to ensure early detection of potential re-emergence or re-introduction of transmission.

Results of case reports for 2018 are summarized below. Reporting practices vary across the region; 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 directly comparable. In 2018, Brazil reported 19,020 cases, representing 60% of all reported cases in the region, of which 7% were laboratory confirmed. Some countries with the highest number of cases and incidence in 2018 include Panama with 2,752 suspected cases (incidence of suspected cases 66/100,000 population) and Bolivia with 1,736 suspected cases (incidence of suspected cases 15/100,000 population). In the Caribbean, Cuba reported 873 confirmed cases, the highest number in

the Caribbean (estimated incidence of confirmed cases 7.6/100,000 population). Canada, mainland Chile and Uruguay have never reported autochthonous, vector-borne transmission of ZIKV and this pattern has remained unchanged to date.

In 2018, 73% of 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 56% of countries and territories had any report available in 2018. Nonetheless, data reported represented more than 98% of the population of the Region of the Americas.[47] Efforts are underway to strengthen Zika surveillance and reporting; in 2018, PAHO/AMRO updated and published *Guidelines for Surveillance of Zika Virus Disease and Its Complications*.[48] 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.

Eastern Mediterranean Region

No countries in the WHO Eastern Mediterranean Region (EMRO) have reported autochthonous transmission of ZIKV. The presence of *Aedes aegypti*, the primary competent mosquito vector for sustaining Zika transmission, has been documented in Djibouti, Egypt, Oman, Pakistan, Saudi Arabia, Somalia, Sudan and Yemen.[1,49] EMRO has implemented ZIKV preparedness plans and developed a framework for monitoring and evaluation.[50,51]

European Region

Although numerous cases of travel-associated ZIKV infections have been reported in European travellers, no countries in the region have reported autochthonous, mosquito-borne transmission of ZIKV.[1,52] *Aedes aegypti*, the primary competent mosquito vector, has been established in parts of Georgia, Portugal (Região Autónoma da Madeira), the Russian Federation and Turkey.[1,53-6] In December 2017, the Institute of Tropical Diseases and Public Health of the Canary Islands in Spain detected the presence of *Aedes aegypti* mosquitoes within a limited area on Fuerteventura; continued investigations are underway to determine if the vector is yet established.

South-East Asia Region

Overview

ZIKV has been circulating since at least the 1960s in several countries of the South-East Asia Region.[57] Despite this long history of ZIKV circulation in the region, information on the

epidemiology of ZIKV infection and its associated complications in the region remain limited. Prior to 2015, cases of ZIKV infection were identified in residents and returning travellers from Bangladesh,[58,59] Indonesia,[60,61] the Maldives,[62] and Thailand,[63] confirmed by serological and/or molecular testing. Thailand has reported confirmed cases of microcephaly due to an Asian lineage-Asian strain.[11] Detection of congenital Zika syndrome has been limited in the South-East Asia Region, potentially due to generally low levels of transmission in the general population or limited epidemiological data. 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

India first reported four cases of ZIKV infection in 2017; three were in Gujarat State (one which had occurred in late 2016), and one in Tamil Nadu.[64] In 2018, a ZIKV outbreak was detected in Rajasthan state.[7] Active case finding and screening of pregnant women were initiated, particularly in a 3 km radius of the Shastri Nagar area of Jaipur. As of December 2018, the India National Centre for Disease Control, Ministry of Health and Family Welfare reported 159 confirmed cases of ZIKV infection from Rajasthan state (including 63 pregnant women), 130 cases from Madhya Pradesh, and one case from Gujarat state.[65-67] An investigation of viral sequence analysis of five specimens from the Jaipur outbreak identified circulation of the Asia lineage-Asian strain, demonstrating the outbreak potential of the older Asian strain.[19]

Indonesia

Genomic sequence analysis of ZIKV obtained from a febrile patient in Jambi, Indonesia in 2014 showed circulation of the older Asian strain, consistent with circulation in Indonesia since 2000.[68] A study published in 2018 evaluated stored serum samples collected in 2014 for a population-based dengue seroprevalence survey in 14 provinces. Only specimens from children 1-4 years of age were included in the analysis to reduce the likelihood of specimens with cross-reactive dengue virus antibodies. Samples were assessed with ZIKV and dengue virus PRNTs. ZIKV seroprevalence was 9.1% in this under-5 population,[4] suggesting a relatively high incidence of ZIKV in this population.

Myanmar

A retrospective study published in 2018 provided evidence of ZIKV infections in two distinct areas in Myanmar since at least 2006. The study identified evidence of ZIKV infection among suspected dengue patients in Mandalay (2004-2015) and asymptomatic healthy persons in Yangon (2017).[69]

Thailand

Since 2016, Thailand Ministry of Public Health has maintained case-based surveillance and reporting for ZIKV infection among children, adults, pregnant women, infants with

congenital Zika syndrome (CZS), and cases of Guillain-Barré syndrome. Confirmed cases require positive ZIKV RT-PCR; CZS cases are confirmed by ZIKV RT-PCR or IgM. A total of 1,121 confirmed cases were reported in 2016 and 577 cases in 2017, with demonstrated seasonality in both years. ZIKV cases peaked approximately 3 weeks following peak dengue virus transmission in both years. A total of 121 confirmed cases were identified in pregnant women in 2016-2017, 45% of which were asymptomatic infections.[6,70,71] These data provide strong evidence of established, endemic ZIKV transmission in Thailand and likely other countries in Asia. Phylogenetic analysis of ZIKV strains collected from patients with PCR-confirmed infection provide evidence of ZIKV circulation in Thailand since at least 2002.[72] Thailand has implemented prospective cohort studies of pregnant women and investigations of novel methods for ZIKV sentinel surveillance, including use of specimens from the measles/rubella surveillance program, to evaluate use of common reporting systems that use similar case definitions.[6]

Western Pacific Region

Background

Prior to the 2015-2016 epidemic in the Americas, outbreaks of ZIKV infection were reported in the Federated States of Micronesia (2007), French Polynesia (2013), Cook Islands (2014), and New Caledonia (2014).[15] Laboratory-confirmed cases of ZIKV infection in travellers returning from Malaysia[73] and Viet Nam[74] were reported in 2015. Evidence of transmission prior to 2015 has been confirmed by serological and/or molecular investigations of humans or mosquitoes in Cambodia,[75,76] Lao People's Democratic Republic,[77] Malaysia,[78,79] Papua New Guinea[80] and the Philippines.[81]

During the period of 2015-2016 epidemic, eight additional countries and territories of the Pacific Islands reported laboratory-confirmed cases of ZIKV infection for the first time, including American Samoa,[82] Fiji, Samoa, Solomon Islands, Vanuatu,[83] Marshall Islands,[84] Palau[85] and Tonga.[86] Information on the incidence and trends of ZIKV transmission in the Western Pacific Region remains limited. Some country updates are highlighted below.

Lao People's Democratic Republic

A study published in 2019 summarized a retrospective seroprevalence survey of 359 asymptomatic blood donors in 2003-2004 and 687 blood donors in 2015 who were screened for ZIKV IgG and infection confirmed by virus neutralization tests. ZIKV seroprevalence was found to be 4.5% in 2003-2004 and 9.9% in 2015.[5]

Singapore

In August 2016, the Ministry of Health (MOH) and National Environment Agency (NEA) in Singapore reported the country's first case of locally-transmitted ZIKV infection.

Retrospective testing identified a cluster of cases in Kallang-Aljunied and 14 smaller clusters and sporadic cases were reported in 2017.[87] No cases have been reported since January 2018.

Viet Nam

Following the detection of local cases of Zika virus infection in March 2016, local authorities intensified Zika virus disease surveillance and control measures. As of March 2017, 23 laboratory-confirmed cases of Zika virus infection had been identified in Viet Nam. In June 2016, an infant was born with congenital Zika syndrome in Dak Lak Province, confirmed by PRNT of mother and infant. Additional laboratory investigations identified evidence of recent ZIKV infection in four family members as well as two neighbours, suggesting a recent cluster or outbreak, and indicating the potential difficulty in detecting smaller outbreaks of asymptomatic or mild ZIKV infections.[88]

Zika virus and microcephaly in the Western Pacific Region

The ZIKV outbreak in French Polynesia in 2013-2014 is estimated to have infected over half of the general population. A retrospective analysis identified eight microcephaly cases during the period of the outbreak.[89]

In 2016, the Marshall Islands reported a case of microcephaly linked to ZIKV infection during pregnancy.[90] In Viet Nam, two cases of ZIKV infection in pregnancy with adverse foetal outcomes occurred in 2016 and were reported in 2017. The first was a case of probable ZIKV-associated microcephaly diagnosed serologically.[13] In the second case, maternal infection resulted in intrauterine foetal demise. ZIKV infection was confirmed by PCR in both foetal and placental samples; the husband of the pregnant woman also had travel history to Malaysia. Viral sequence analysis revealed an Asian lineage ZIKV strain, closely related to strains from Malaysia and French Polynesia;[12] however, the sequence comparison fragment is not described.

Limited detection of congenital Zika syndrome in the region may be due to low levels of transmission in the general population or limited systems for surveillance and disease detection. Improved surveillance and epidemiologic investigations are needed to better ascertain the incidence of ZIKV transmission in the Western Pacific Region and its impact on birth outcomes.

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