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Review Article

Why Zika virus infection has become a public health concern?

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Abstract

Prior to 2015, Zika Virus (ZIKV) outbreaks had occurred in areas of Africa, Southeast Asia, and the Pacific Islands. Although a causal relationship between Zika infection during pregnancy and microcephaly is strongly suspected, such a connection has not yet been scientifically proven. In May 2015, the outbreak of ZIKV infection in Brazil led to reports of syndrome and pregnant women giving birth to babies with birth defects and poor pregnancy outcomes; the Pan American Health Organization (PAHO) issued an alert regarding the first confirmed ZIKV infection in Brazil. Currently, ZIKV outbreaks are ongoing and it will be difficult to predict how the virus will spread over time. ZIKV is transmitted to humans primarily through the bite of infected mosquitos, Aedes aegypti and Aedes albopictus. These mosquitoes are the principle vectors of dengue, and ZIKV disease generally is reported to include symptoms associated with acute febrile illnesses that clinically resembles dengue fever. The laboratory diagnosis can be performed by using reverse-transcriptase polymerase chain reaction (RT-PCR) on serum, viral nucleic acid and virus-specific immunoglobulin M. There is currently no vaccine and antiviral treatment available for ZIKV infection, and the only way to prevent congenital ZIKV infection is to prevent maternal infection. In February 2016, the Taiwan Centers for Disease Control (Taiwan CDC) activated ZIKV as a Category V Notifiable Infectious Disease similar to Ebola virus disease and MERS.

Keywords: microcephaly; transmission; Zika virus

1. Introduction

Zika virus (ZIKV) is a single-stranded RNA virus, an arthropod-borne flavivirus distributed throughout much of Africa and Asia. Other mosquito-borne flaviviruses previously determined to be of public health importance include yellow fever, dengue, St. Louis encephalitis, West Nile and Japanese encephalitis viruses. ZIKV is transmitted to humans primarily through the bite of an infected *Aedes* mosquito species, first isolated from a monkey in the Zika forest of Uganda in 1947.[1] Subsequently, sporadic human infections were reported in Africa and Asia, and the first documented ZIKV outbreak was reported from Yap State, Federated States of Micronesia in 2007.[2] The Asian lineage of the virus reappeared in French Polynesia in October 2013, and thereafter between November 2013 and February 2014, with an increased incidence of neurological complications, including 42 cases of Guillain-Barré syndrome; these complications were a unique and worrisome feature of the outbreak that warrants further study.[3] ZIKV disease is generally reported with characteristics of acute febrile illnesses that clinically resembles dengue fever. The most common symptoms are fever, joint pain, rashes, and conjunctivitis, with symptoms lasting from several days to a week.

2. Countries with current active Zika virus infection

As of February 4, 2016, the ZIKV epidemic has continued to spread in most of the countries where its presence was

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indicated, and evidence of local ZIKV infection cases has been reported from 31 countries within the past 2 months, and 36 countries in the past 9 months.[4] Ultimately, ZIKV may be spread globally into additional environments where mosquitos can live and breed. The geographical range of ZIKV infection has increased in 2015 and 2016, with 26 countries and territories in the Americas now reporting autochthonous transmission of ZIKV.[5]

3. Mode of transmission

ZIKV is transmitted to humans primarily through the bite of infected mosquitos, namely: *Aedes aegypti and Aedes albopictus)*, which are found throughout much of the Americas, including part of the United States. These mosquitoes are the principle vectors of dengue, chikungunya, Zika, and yellow fever.[6,7] These vectors are aggressive day time biters that breed in domestic water holding containers, and feed primarily in the outdoors and indoors near dwellings. During the outbreaks, anthroponotic (human-to-vector-to-human) transmission can occur. Mosquitoes become infected when they bite a person already infected with the virus. Infected mosquitoes can then spread the virus to other people through bites. To date, infected ZIKV RNA has been detected in blood, urine, semen, saliva, cerebrospinal fluid, amniotic fluid, and breast milk. Regarding transmission of the virus through the mother and to her baby during pregnancy, blood transfusion and sexual contact have been reported; however, there is currently no evidence that the virus is transmitted to babies through breast feeding.[7–10] However, the mechanism by which some mothers can pass the virus to their babies is still under study.

4. Clinical signs and symptoms

Signs and symptoms of ZIKV infection are relatively mild. Although the illness develops in only one in five persons, severe disease requiring hospitalization is uncommon and case fatality is very low.[11] The symptoms typically occur approximately 2 to 12 days after the mosquito bite, presenting most commonly with fever, maculopapular rash, conjunctivitis, and joint pain, and the clinical illness lasts for several days to a week. Other symptoms include muscle pain and headache, but abdominal pain, nausea, diarrhea, mucus membrane ulcerations, and pruritus are rarely observed.[12] There is a possible association between ZIKV and microcephaly in newborn babies with maternal ZIKV infection,[4,13] and some infected adults with neurologic conditions like Guillain-Barré syndrome (GBS) were also reported.[14] By the first week of February, 2016, 4783 suspected cases of microcephaly have been reported in Brazil; of these cases, 1132 (24%) were investigated and classified. If was found that 404/1132 (36%) cases had confirmed microcephaly and/or central nervous system malformations, and 17/404 (4%) were positive for ZIKV infection.[4] In July 2015, Brazil reported 76 cases with ZIKV infection with neurologic syndromes in Bahia state, and 42 of those cases were confirmed to have GBS.[5] In late January 2016, 104, 2, 1, and 255 cases of GBS were reported from El Salvador, Martinique, New Zealand, and Venezuela, respectively. French Polynesia also reported one imported case of ZIKV with neurological symptoms in February 2016.[4] Some countries, including Colombia and Suriname, reported ZIKV infection with deaths involving GBS or chronic medical illness.[15]

5. Diagnosis

The primary diagnosis of ZIKV infection is based on the patient's typical clinical features, places and dates of travel and activities. During the first week after onset of symptoms, laboratory diagnosis can be performed by using reverse-transcriptase polymerase chain reaction (RT-PCR) on serum or plasma to detect virus, viral nucleic acid,[16] or virus-specific immunoglobulin M and neutralizing antibodies.[17,18] During the acute illness period of ZIKV infection in patients, symptoms such as fever, rash, conjunctivitis, and serological testing can confirm the presence of ZIKV virus. However, there are no good laboratory tools with the capacity to confirm what occurs during the other months. Cross-reaction with some related flaviviruses, such as dengue 1,2,3, and 4, and with yellow fever and West Nile viruses is common, creating a circumstance where proper diagnosis of ZIKV may be difficult to achieve.[19] Then, a plaque-reduction neutralization testing can be performed to measure virus-specific neutralizing antibodies and differentiate between cross-reacting antibodies in primary flavivirus infections.[17,18] Due to a routine cross-reaction that is common in patients with dengue virus, patients with ZIKV infection should be evaluated for possible dengue virus infection. Dengue virus infection usually presents with high fever, severe headache, pain behind the eyes, muscle and joint pains, nausea, vomiting, swollen glands or rash. Dengue fever usually occurs after an incubation period of 4-10 days after the bite of the infected mosquito, and symptoms usually last for 2–7 days.[20] Unlike ZIKV infection, dengue typically is not associated with conjunctivitis (Table 1).

6. Management and Prevention of Zika virus infection

There is presently no vaccine and no specific antiviral treatment for ZIKV infection. Treatment is often supportive, and symptoms can be generally treated with fluids, rest and oral analgesics and antipyretics (e.g., acetaminophen) for fever and pain relief, while aspirin and others nonsteroidal anti-inflammatory drugs (NSAIDs) should be used only when dengue has been ruled out because of the risk of bleeding.[21] However, NSAIDs are not typically used during pregnancy.[22]

7. Prevention of mosquito bite

During the first week of ZIKV infection, the infected patient should avoid further mosquito bite because the ZIKV can be found in the blood and pass from an infected person to a mosquito. Consequently, an infected mosquito can then spread the virus to another person. Preventing further mosquito bite