International Journal of Entomology Research
www.entomologyjournals.com
ISSN: 2455-4758
Received: 16-07-2024, Accepted: 15-08-2024, Published: 30-08-2024
Volume 9, Issue 8, 2024, Page No. 222-225

Zika virus: A persistent global health threat and its impact on pregnancy

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Abstract
The Zika virus has emerged as a significant threat to public health, causing concern due to its potential to cause serious health complications, particularly in pregnant women and their unborn children. The primary mode of transmission is through infected Aedes mosquitoes, commonly found in tropical and subtropical regions. Recent outbreaks in Pune, Maharashtra, highlight the need for preventive measures. While most infected individuals do not show symptoms, those who do may experience mild symptoms such as rash, fever, and joint pain. The real concern lies in the potential birth defects associated with Zika virus infection during pregnancy, such as microcephaly. To prevent the spread of the virus, it is crucial to eliminate mosquito breeding sites, use insect repellent, wear protective clothing, use mosquito nets, and seek medical advice for symptoms. Understanding the risks and taking preventive measures are essential in protecting oneself and communities from the threat of Zika.

Keywords: Zika virus, public health, Aedes mosquitoes, microcephaly, insect repellents

Introduction

The Zika virus is a mosquito-borne virus that was discovered in 1947 in Uganda in a Rhesus macaque monkey. In the 1950s, evidence of infection and illness in people was found in various African nations. Human infections were found sporadically throughout Asia and Africa during the 1960s and 1980s. On the other hand, Zika virus epidemics have been documented in Africa, the Americas, Asia, and the Pacific since 2007 [1].

While there were no recorded hospitalizations or fatalities, the first confirmed epidemic was in 2007 on Yap Island in the Western Pacific.After that, 2 ZIKV made its way to the South Pacific and French Polynesia in 2013 before, most likely, making its way to Brazil in late 2015. When a strong epidemiological correlation was found with a rise in microcephaly cases, the Zika outbreak in Brazil attracted international attention. The WHO then deemed ZIKV to be a Public Health Emergency of International Concern in 2016. As of December 2020, there has been over 5.8 million Zika infections documented since the virus's debut in the Americas6, with over 7452 cases being reported in only 2020. ZIKV cases from French Polynesia were documented in 87 countries and territories as of July 2019 [2].

The Zika virus (ZIKV) is an arbovirus, which is a type of virus carried by arthropods. The main mosquito species via which ZIKV is spread is the Aedes genus. The majority of ZIKV transmission has been linked to the Aedes aegypti mosquito species. But ZIKV has also been discovered to be present in the Aedes albopictus species (Stegomyia albopicta) [3].

The virus belongs to the genus Flavivirus and the family Flaviviridae. There is very little genomic divergence observed when compared to other viruses in the same genus. ZIKV is a single-stranded, positive-sense RNA. Its 10.7 kb genome encodes only one polyprotein. Ten proteins are produced by additional cleavage: three structural (c, prM/M, and E) and seven non-structural (NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS5) [3].

Fig 1: Asian tiger mosquito Aedes albopictus, one of the species that can carry the Zika virus, begins its blood meal. (Image credit: James Gathany, CDC)

Transmission

Congenital transmission of the Zika virus occurs when a pregnant person shares the infection with her fetus, and perinatal transmission occurs around the time of delivery. Congenital or intrauterine (in utero) transmission of the Zika virus happens when an individual becomes infected with the virus before to childbirth, allowing the virus to infect the developing foetus [4].

When a pregnant individual contracts the Zika virus within two weeks of giving birth, the virus is transferred to the unborn child at or near the moment of delivery. This is known as perinatal transmission of the virus. An infant may experience symptoms like fever, arthralgia, conjunctivitis, and maculopapular rash if they contract the Zika virus during pregnancy.

Breast milk has been linked to the Zika virus. Although Zika virus transmission through breast milk has not been proved, possible infections with the virus have been found in newborns who are nursing [4].

A person who has an infection with the Zika virus can transmit the virus to their partner(s) through sexual contact.

Even when an individual is infected with the Zika virus, they may not exhibit symptoms at the time of sexual contact [4].

It can be transferred from an infected person before, during, and after the infected individual experiences symptoms. A person who possesses the virus but never shows any symptoms may also transfer the infection to others [4].

Impact of Zika virus on Pregnancy

Zika virus (ZIKV) infections during pregnancy have the potential to cause severe central nervous system defects and other teratogenic consequences when they are transferred transplacentally to developing fetuses. Congenital Zika syndrome (CZS) is the term for the group of congenitally infected kids that can experience mild, moderate, or severe unfavorable outcomes, despite the fact that the majority of fetuses with prenatal ZIKV exposure do not exhibit any discernible clinical defects [5].

Microcephaly

Infants with suspected or confirmed congenital ZIKV infection have been found to have low birth weight and intrauterine growth restriction; however, the relationship between this condition and the pathogenetic process remains unknown.

An occipital head circumference (OHC), which is measured between the occipital protuberance and the glabella, that is two standard deviations (SDs) smaller than the average for gestational age (GA) or corrected GA has been the traditional definition of microcephaly. An OHC of less than 3 SDs is considered severe microcephaly. Either a fundamental anomaly present from birth or a secondary head growth failure developing over time can be the cause [6].

Ocular anomalies

Approximately 25% of newborns diagnosed with CZS had abnormalities in their eyes, a percentage significantly greater than the 6–7% frequency in the general population. Macular abnormalities, localized pigmentary retinal alterations, chorioretinal atrophy, and abnormalities of the optic nerve, such as optic nerve hypoplasia, an elevated cup-disk ratio, and pallor, were among the findings. Coloboma, subretinal hemorrhages, vascular tortuosity, aberrant retinal arteries with focal vascular dilatation, and pigmentary clumping were among the other alterations. Some infants also have iris colobomas, microcornea, microphthalmia, cataracts, intraocular calcification, congenital glaucoma, strabismus, and nystagmus. The CZS eye discoveries did not progress. Thirty percent of newborns with CZS had visual loss, with cortical visual impairment being the most likely cause. Thirty percent of CZS cases had significant visual impairment. When the related ocular findings were taken into account, the rate of vision impairment rose to 84% [7].

Congenital contractures

Fetuses and newborns with suspected or confirmed congenital ZIKV infection have been documented to develop congenital contractures involving one or more joints (arthrogryposis multiplex congenita or arthrogryposis [6].

Fig 2: A new report in the journal JAMA Pediatrics highlights the range of damage Zika infection can cause a developing fetus. Photo: JAMA Pediatrics

Pregnancy outcome

The results of the pregnancy included either a live birth (with or without defects) or the loss of the pregnancy due to miscarriage, early pregnancy termination, or stillbirth. Miscarriage was defined as intrauterine fetal death that transpired before to a gestational age of 20 weeks in order to facilitate comparison with other studies. Intrauterine fetal mortality at or after a gestational age of 20 weeks or intrapartum death during delivery were considered stillbirths [8].

Diagnosis

Tests for serology: These assays identify antibodies generated in reaction to the Zika virus. Plaque reduction neutralization tests (PRNT) and enzyme-linked immunosorbent assays (ELISA) are the two main serological assays [9].

ELISA: This test finds anti-Zika IgM and occasionally anti-Zika IgG antibodies. It is helpful in the diagnosis of acute or recent infections. False positive results from ELISA tests, however, might occasionally result from antibodies from different flavivirus illnesses, such dengue.[9]Accuracy: ELISA's sensitivity and specificity can differ. Although it may have cross-reactivity with other flavivirus infections, it typically has a high sensitivity for identifying Zika virus infection [9].

PRNT: This is a more specific test that measures the ability of antibodies to neutralize the virus in a laboratory setting. It is considered the gold standard for confirming Zika virus infection due to its high specificity.

- **Accuracy**: PRNT is highly specific and can differentiate between Zika and other flavivirus infections, but it is more complex and time-consuming than ELISA [10].

Viral RNA can be found in blood, urine, and other bodily fluids using PCR (Polymerase Chain Reaction) tests. When viral RNA is detected in the early stages of sickness, it can be utilized to diagnosis acute Zika virus infection. Accuracy: PCR is a very sensitive and specific method for identifying RNA from the Zika virus. Due to the decrease in viral RNA, it is less efficient in later stages of infection,but it can accurately detect an acute infection. Limitations: If the RNA levels are too low or the test is conducted too late in the infection process, PCR may not be able to identify the virus since it requires specialist laboratory equipment [11].

Imaging Studies: Although imaging cannot be used to provide a direct Zika virus diagnosis, it can be used to evaluate how the virus affects the central nervous system, particularly in infants who have congenital Zika syndrome. Ultrasound: Fetal ultrasound in pregnant women can identify abnormalities such brain calcifications or microcephaly that are linked to Zika virus infection. Accuracy: Although ultrasound is a useful diagnostic tool for spotting structural problems, it cannot detect the Zika virus itself.

Diagnostic and surveillance strategies
Conflict with additional viral infections
Problem: In regions where Zika is also prevalent, symptoms of other viral infections including dengue and chikungunya can often be confused with those of the Zika virus. Differential diagnosis may become challenging as a result [13]
Variability in the Specificity and Sensitivity of Diagnostic Tests:

Challenge: The sensitivity and specificity of Zika diagnostic procedures, like PCR and serological testing, might vary. False negatives or positives may result from cross-reactivity with other flavivirus infections [14].

Difficulties with serological testing Challenge: Because antibodies to the Zika virus may cross-react with those of the dengue virus, serological tests may provide difficulties that make an accurate diagnosis more difficult [15].
Monitoring mosquito populations, especially Aedes mosquitoes, which are the main carriers of the Zika virus, is the goal of vector surveillance. Techniques: Involves mosquito capturing, surveys of larvae, and observation of environmental factors influencing mosquito reproduction [1].

Effectiveness: Assists in locating possible risk zones and regions with high mosquito populations. Personalized control methods can result from efficient vector surveillance [1].

Human case surveillance
Tracks human cases of Zika virus infection in order to determine the virus's prevalence and geographic dissemination [1].
Methods: consists of tracking clinical symptoms, reporting and testing probable instances, and epidemiological studies.[1]
Effectiveness: Offers information on trends and infection rates. Aids in the detection of epidemics and the assessment of their effects on public health [1].

Serological surveys
Establishes the percentage of the populace that has been infected with the Zika virus.
Techniques: Uses blood testing to find antiviral antibodies. Effectiveness: Provides information about the magnitude of previous infections and community immunity, which is essential for estimating risk in the future [4].

Birth defects surveillance
Goal: Tracks the incidence of birth abnormalities such microcephaly linked to Zika virus infection.
Methods: Gathers information on babies with birth abnormalities from clinics, hospitals, and registries.
Effectiveness: Essential for figuring out how Zika affects mother and child health and for directing treatment plans.[4]

Effectiveness
Early Detection: Early detection of outbreaks by surveillance programs enables timely control and intervention.

Targeted Interventions: Public health campaigns and targeted mosquito control are made possible by data from surveillance systems. Population Awareness: Assists in informing the general population about health dangers and precautions to take in relation to the Zika virus [16].

Prevention and Control Measures [1]

A. Avoid Mosquito Bites
Use Insect Repellent: Spray clothing and exposed skin with repellent that contains DEET, picaridin, or oil of lemon eucalyptus. As instructed, reapply, particularly after perspiring or swimming.
Put on Protective Clothes: To reduce skin exposure, put on long sleeve shirts, long pants, socks, and shoes.

B. Pregnant Women
Avoid Travel: Due to the possibility of birth abnormalities, pregnant women should refrain from visiting regions where the Zika virus is active. Consult Healthcare Providers: For individualized guidance and oversight, consult healthcare providers on a regular basis.

C. Environmental Control
Eliminate Standing Water: Zika-carrying mosquitoes breed in still water. Fill buckets, pots, and birdbaths with clean, empty water on a regular basis. Appropriate Waste Management: Make certain that garbage is disposed of appropriately and that empty containers don't hold water.

D. Community and Public Health Measures
Programs for Vector Control: Use of Insecticides: Put into action community-wide insecticide spraying initiatives, especially in regions with dense populations of mosquitoes. Public Education: Spread knowledge and instruction about mosquito control and preventive measures.

Healt monitoring
Track and Report Cases: To successfully control outbreaks, put in place mechanisms for tracking and reporting Zika cases.

Research and future directions
The Zika virus, which is mainly spread by Aedes mosquitoes, has been the focus of extensive investigation since it has been linked to serious birth deformities and neurological issues. Here is a summary of current studies and their future directions.

Vaccine development
Development of several vaccine candidates is ongoing at different levels. For example, the National Institutes of Health (NIH) and collaborators have been developing vaccines based on DNA and using particles that resemble viruses.

The challenge lies in guaranteeing both safety and long-term protection, particularly in light of the virus's mutation and possible cross-reactivity with other flaviviruses such as dengue [17].

Antiviral Therapies
The goal of this research is to create targeted antiviral medications that prevent the Zika virus from replicating or infecting host cells.
Advances: Research has looked into antiviral drugs and substances such as favipiravir. Safety and clinical efficacy must still be established, though [1].

Future Directions [4]

1. **Integrated Vaccine Approaches**
   - **Combination Vaccines**: Developing vaccines that provide cross-protection against Zika and other flaviviruses like dengue and yellow fever.
   - **Global Collaboration**: Strengthening international partnerships to pool resources and knowledge for vaccine development and deployment.

2. **Enhanced Vector Control Strategies**:
   - **Integrated Pest Management**: Combining genetic, chemical, and environmental control methods to create more effective and sustainable vector control strategies.
   - **Novel Techniques**: Research into new approaches like sterile insect techniques or parasitoids.

3. **Long-Term Epidemiological Studies**
   - **Impact Monitoring**: Tracking the long-term health effects of Zika virus infections on individuals and populations.
   - **Predictive Models**: Developing sophisticated models to predict outbreak risks and potential future patterns.

4. **Improving Diagnostics**
   - **Rapid Tests:** Creating more accessible, rapid, and accurate diagnostic tests for Zika virus to facilitate timely intervention.
   - **Cross-Reactivity Issues:** Addressing challenges in differentiating Zika from other flavivirus infections.

5. **Public Health Infrastructure**
   - **Preparedness**: Strengthening health systems to respond effectively to outbreaks, including improving community engagement and response strategies.
   - **Education and Awareness**: Enhancing public awareness about prevention measures and symptoms of Zika virus infection.

Conclusion
The Zika virus exemplifies how emerging infectious diseases can have profound and lasting effects on global health, particularly for vulnerable populations such as pregnant women and their unborn children. While significant progress has been made in understanding and combating the virus, ongoing efforts are crucial to mitigate its impact and prevent future outbreaks. The global health community must remain proactive in research, prevention, and response strategies to address this persistent threat and safeguard maternal and infant health.

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