

## REVIEW ARTICLE

# Zika Virus Infection: A Global Health Emergency

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**ABSTRACT****Key words:****Arboviruses, Zika virus, microcephaly, Aedes mosquito, Brazil outbreak****\*Corresponding Author:**Ayman K. Johargy  
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*Zika virus is an arthropod-borne virus in the Flaviviridae family. It was first isolated in 1947 in Uganda. The main route of Zika virus transmission is through an infected Aedes mosquito bite. However, other routes of transmission were possible including vertical transmission from mother to fetus, sexual transmission and by blood transfusion. Infection is usually asymptomatic, and commonly reported symptoms include fever, maculopapular rash, arthralgia, conjunctivitis, headache and myalgia. However, Zika virus infection during pregnancy is a cause of microcephaly and other severe fetal brain malformations. For laboratory diagnosis of Zika virus infection a combination of serological and molecular techniques, along with clinical and epidemiological data can be used. There is no specific antiviral treatment or vaccine for Zika virus, meaning that prevention with proper education is the best protection against it. In this review, we focused on different aspects of Zika virus, including virological characteristics, epidemiology and routes of transmission, signs and symptoms, laboratory diagnosis, treatments, prevention and control measures.*

**Method:**

We conducted a review of the varied informations about Zika virus, including history and isolation, classification and structure, epidemiology and transmission, pathogenic mechanisms, clinical symptoms, laboratory diagnoses, treatments, prevention and control. A search of the papers was performed using PubMed and Google Scholar. We used the following keywords: 'Zika virus', 'epidemiology and routes of transmission of Zika virus', 'Zika virus clinical syndromes', 'treatment of Zika virus disease', 'prevention of Zika virus disease' and 'pregnancy and Zika virus. The timeline was set from January 1950 to December 2021.

**History and isolation:**

Zika virus was first isolated in 1947 in the Zika Forest of Kampala in Uganda, from which its name was derived<sup>1</sup>. However, the first described case of infection in humans was from a 10-year-old female from Nigeria in 1953<sup>2</sup>. Zika virus then spread geographically to different countries of Africa, Asia and the Americas<sup>3</sup>.

**Classification and structure:**

Zika virus is an arthropod-borne virus that is classified in the Flaviviridae family, which includes Zika virus, yellow fever virus, West Nile virus, dengue virus and hepatitis C virus<sup>4</sup>.

In structure, Zika virus consists of a positive-sense, single-stranded - 11 kb RNA genome in an icosahedral capsid with an outer enveloped shell. The genome encodes three structural proteins: capsid, envelope and membrane. In addition, there are seven nonstructural

proteins: NS1, NS2A, NS2B, NS3, NS4A, NS4B and NS5<sup>5</sup>.

**Epidemiology and transmission:**

Zika virus can be transmitted through an infected mosquito bite, from mother to fetus, by blood transfusion and by sexual transmission.

The most common route of transmission is by an *Aedes* mosquito bite, caused by various species of *Aedes*: *A. aegypti*, *A. albopictus*, *A. polynesiensis*, *A. vittatus*, *A. unilineatus* and *A. hensilli*<sup>6</sup>.

Vertical transmission from infected mother to fetus can occur because the virus can cross the placental barrier, resulting in intrauterine infection; intrapartum transmission can also happen<sup>7</sup>. Post-natal transmission of Zika virus infection through breastfeeding has not yet been defined, though viral RNA has been detected in breast milk<sup>8</sup>.

Blood transfusion is another likely route for Zika virus transmission. The possibility for transfusion-transmitted Zika virus was revealed in the French Polynesia outbreak of 2013–2014 where 2–8% of the asymptomatic blood donors screened using a nucleic acid test were positive for Zika virus RNA<sup>9</sup>, and in Brazil some cases were reported of transfusion-transmitted Zika virus infections<sup>10</sup>.

Sexual transmission is another route of Zika virus transmission; high viral loads have been conveyed from semen samples of infected individuals. Sexual transmission of Zika virus has been described in about 13 countries without concurrent mosquito-borne transmission. Most published cases report transmission from symptomatically infected men to women.

However, transmission from a symptomatic man to another man, from a symptomatic woman to a man and from an asymptomatic man to a woman have also been claimed<sup>11,12</sup>.

After the first isolation of Zika virus in humans in 1952, serosurveillance studies have identified an extensive distribution of Zika virus in several African and Asian countries. The first defined outbreak in the literature appeared in 2007 in the Federated States of Micronesia, Oceania<sup>13</sup>. Later, Zika virus spread to other parts of the continent. Subsequently, Brazil became the epicenter of an epidemic from mid-2014 to 2015<sup>14</sup>. Since then, Zika virus infections have troubled more than 80 countries, causing a pandemic. The infections are more commonly observed in situations that frequently accompany arbovirus transmission such as high population density, ideal climatological circumstances and a deficiency of infrastructure<sup>15</sup>.

#### **Pathogenic mechanism:**

The Zika virus transmission cycle begins when an *Aedes* mosquito bites an infected person and ingests blood containing the virus. The saliva of the mosquito becomes infected after an incubation period of 10 days. When infecting humans, the virus contaminates the dermal fibroblasts, epidermal keratinocytes and immature dendritic cells<sup>16</sup>. Interferon alpha and beta are formed by the infected cells but can be evaded by viral proteins. Zika virus then infects and spreads through various cell types and tissues to finally cross protective barriers around the immune-privileged fetus, interfering with the development of the fetal brain and eyes. The pathogenesis of the virus in adults is hypothesized to continue with a spread to lymph nodes and the bloodstream leading to various clinical symptoms<sup>17</sup>.

#### **Clinical symptoms:**

Zika virus infection is asymptomatic in about 80% of cases, and most patients present with only mild symptoms. Commonly reported symptoms include fever, maculopapular rash, arthralgia, conjunctivitis, headache and myalgia. The clinical disease is generally mild with symptoms lasting for less than a week<sup>18</sup>. Usually, Zika virus infection is not fatal. However, Zika virus-associated encephalitis and other related fatalities were reported in some cases<sup>19,20</sup>.

In addition, an association between Zika virus infection and Guillain-Barré syndrome has been noticed<sup>21</sup>. Moreover, Zika virus infection during pregnancy is a cause of microcephaly and other severe fetal brain malformations<sup>22</sup>.

#### **Laboratory diagnosis:**

For the laboratory diagnosis of Zika virus, different patients' samples can be used including blood (whole blood, serum or plasma), urine, saliva and cerebrospinal fluid. Molecular tests can be used for the detection of

Zika virus RNA by using reverse transcriptase polymerase chain reaction (RT-PCR). For serological tests, detection of Zika virus-specific immunoglobulin M (IgM) and immunoglobulin G (IgG) is recommended. A confirmation of positive IgM results, especially in pregnant women, can be performed using a plaque reduction neutralization test<sup>23</sup>.

An appropriate laboratory diagnosis for Zika virus comprises a combination of serological and molecular techniques, along with clinical and epidemiological data, specifically for pregnant women and children born with Zika congenital syndromes<sup>24</sup>.

Because Zika virus is a nationally notifiable condition, any laboratory-confirmed cases should be reported to the national health authority<sup>25</sup>.

#### **Treatment:**

There are no specific antiviral drugs for Zika virus infection. Analgesics and antipyretics drugs can be given to patients to reduce signs and symptoms. Patients are advised to rest and drink plenty of fluids. Aspirin and other non-steroidal anti-inflammatory drugs should be avoided before dengue is ruled out because of the increased risk of haemorrhage<sup>26</sup>.

#### **Prevention and control:**

Because no specific treatment is available for Zika virus disease, prevention is the best way to protect against it. For all mosquito-borne diseases, preventive procedures are similar and include mosquito and vector control programs<sup>27</sup>. Currently, there are no vaccines for Zika virus prevention, although substantial research into developing a Zika virus vaccine is underway, including mRNA-based, live-attenuated, killed and subunit vaccines<sup>28</sup>.

As a result, most countries should emphasize suitable education of the public, prevention, early detection in pregnant woman and appropriate management along with contact tracing to prevent an outbreak in the future<sup>29</sup>.

## **CONCLUSION**

With the recent pandemic of SARS-Cov-2, its quite significant to expect global outbreaks. Zika virus infection has emerged as an important risk to public health make it a potential applicant for a global health problem. Therefore, active surveillance studies combined with reliable and fast diagnosis and the development of specific antivirals and vaccines, could be better prevention and control of this emergent disease.

This manuscript has not been previously published and is not under consideration in the same or substantially similar form in any other reviewed media. I have contributed sufficiently to the project to be

included as author. To the best of my knowledge, no conflict of interest, financial or others exist. All authors have participated in the concept and design, analysis, and interpretation of data, drafting and revising of the manuscript, and that they have approved the manuscript as submitted.

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