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Review Article

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Zika Virus- A Globally Threatening Illness

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ABSTRACT

Zika fever is an illness caused by the Zika virus, is a member arbovirus of the virus family Flaviviridae and the genus Flavivirus, transmitted by daytime-active Aedes mosquitoes, such as *A. aegypti* and *A. albopictus*. Symptoms are similar to other flaviviruses such as dengue fever or the alphavirus chikungunya, but are milder in form and usually last four to seven days. Most cases (60–80%) are asymptomatic. In May 2015, the Pan American Health Organization (PAHO) issued an alert regarding the first confirmed Zika virus infection in Brazil. The outbreak in Brazil led to reports of Guillain-Barré syndrome and pregnant women giving birth to babies with birth defects and poor pregnancy outcomes. There is currently no vaccine, but development is a priority of the National Institutes of Health. The virus is spread by mosquitoes, making vector control and avoidance an essential element to disease control.

Keywords: Zika fever, Zika Virus, Aedes mosquitoes, PAHO

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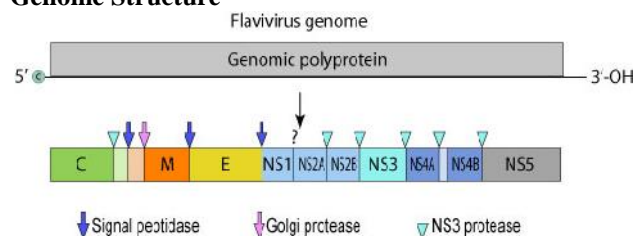
1. Introduction

Zika virus [1] is a mosquito-borne flavivirus closely related to dengue virus. Zika virus is spread to people through mosquito bites. Its name comes from the Zika Forest of

Uganda, where the virus was first isolated in 1947. [2] The illness is usually mild with symptoms lasting from several days to a week. Severe disease requiring hospitalization is

uncommon. The main clinical symptoms in symptomatic patients are low-grade fever, conjunctivitis, transient arthritis/joint pain (mainly in the smaller joints of the hands and feet) and maculopapular rash that often starts on the face and then spreads throughout the body.[1] Health officials studying the 2015 Brazilian outbreak suspect that the disease may undergo mother-to-child transmission in the womb and cause microcephaly, a major birth defect. [2] Hemorrhagic manifestations have been documented in only one instance, hematospermia (blood in semen). In November 2015, reports from the Brazilian Health Ministry alerted people to a previously unknown connection between the Zika virus and cases of newborn microcephaly in Northeastern Brazil based on two cases of severely affected fetuses in whom amniocentesis confirmed the presence of the Zika virus in the amniotic fluid. The ultrasound findings in these two fetuses, as reported on 5 January 2016, showed that both have a small head circumference (microcephaly) due to the destruction of different parts of the brain. The Brazilian Ministry later confirmed the previously suspected connection between Zika infection of pregnant women and newborn microcephaly, with at least 2,400 suspected cases of microcephaly in the country in 2015 as of 12 December, and 29 fatalities. According to a CNN report, Brazilian health officials were also recommending that parents consider putting off pregnancy due to the sharp increase in cases of microcephaly. A link has been established with neurologic conditions in infected adults, including Guillain-Barré syndrome^{3,4,5,6}. The first human cases were reported in Nigeria in 1954. A few outbreaks have been reported in tropical Africa and in some areas in Southeast Asia. There have been no documented cases of Zika virus in the Indian subcontinent. Surveys have found antibodies to Zika in healthy people in India which could indicate past exposure, though it could also be due to cross-reaction with other flaviviruses. Zika has since spread to more than 20 countries mostly concentrated in Central and South America and the Caribbean and it's expected to go much further.

Genome Structure



The Zika virus is a positive sense single-stranded RNA molecule 10794 bases long with two non-coding regions flanking regions known as the 5' NCR and the 3' NCR. The open reading frame of the Zika virus reads as follows: 5'-C-prM-E-NS1-NS2A-NS2B-NS3-NS4A-NS4B-NS5-3' and codes for a polyprotein that is subsequently cleaved into capsid (C), precursor membrane (prM), envelope (E), and non-structural proteins (NS). The E protein composes the majority of the virion surface and is involved with aspects of replication such as host cell binding and membrane fusion. NS1, NS3, and NS5 are large, highly-conserved proteins while the NS2A, NS2B, NS4A, and NS4B proteins are smaller, hydrophobic proteins. Located in the 3' NCR

are 428 nucleotides that may play a part in translation, RNA packaging, cyclization, genome stabilization, and recognition. The 3' NCR forms a loop structure and the 5' NCR allows translation via a methylated nucleotide cap or a genome-linked protein. It is most closely related to the Spondweni virus and is one of the two viruses in the Spondweni virus clade. [7,8,9]

Signs and Symptoms

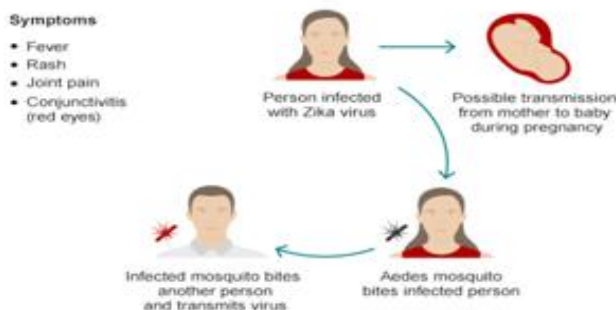
The most common signs and symptoms of Zika fever are fever, rash, joint pain, conjunctivitis (red eyes), muscle and joint pain and headache, which are similar to signs and symptoms of dengue and chikungunya fever. The incubation period, or time from exposure to the virus from a mosquito bite to onset of symptoms, is not well characterized as yet but is probably a few days to a week. Even more worryingly, there's compelling evidence that Zika is linked to a terrible birth defect called microcephaly, which is characterized by a shrunken head and incomplete brain development. The disease lasts for several days to a week and is sufficiently mild that hospitalization is not usually required. Death is rare.



Transmission

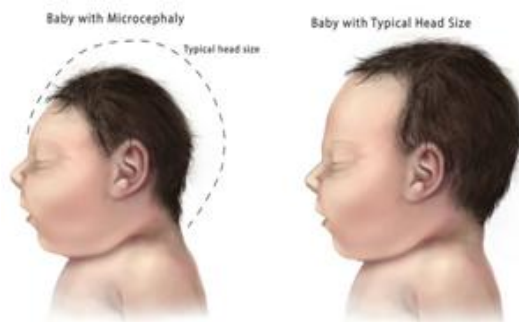
Transmission is via the bite of mosquitoes from the *Aedes* genus, primarily *Aedes aegypti* in tropical regions. It has also been isolated from *A. africanus*, *A. coarctatus*, *A. luteocephala*, *A. vittatus* and *A. furcifer*. During the 2007 outbreak on Yap Island in the South Pacific, *Aedes hensilli* was the vector, while *Aedes polynesiensis* spread the virus in French Polynesia in 2013. There have also been confirmed reports of two cases of sexual transmission and cases of vertical perinatal transmission. Like other flaviviruses it could potentially be transmitted by blood transfusion and several affected countries have developed strategies to try and screen blood donors.

Zika virus transmission cycle

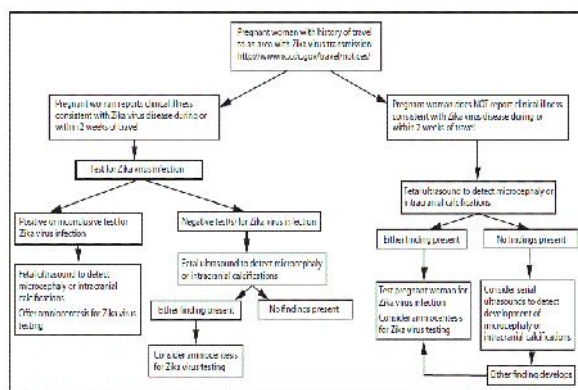


2. Effect of Zika in Pregnant Women

The difficulty with Zika is that many people who get the virus are never diagnosed — yet it might still potentially damage fetuses. This fact has put pregnant women and would-be moms in an awful bind. In some places in Latin America, women are being told to avoid having children for months or even years because of Zika. This isn't easy: In many of these countries, family planning is nonexistent, condoms are out of reach for some, and abortion is illegal. [10,11]. Meanwhile, American women who are pregnant have been advised to stay out of countries where the Zika virus is circulating. The Centers for Disease Control and Prevention also issued guidance on how to care for pregnant women during a Zika outbreak, and whether to get tested for Zika. If you're trying to get pregnant, proceed with caution if visiting these areas. The CDC recommends consulting your doctor before your trip and following steps to prevent mosquito bites during the trip.



If you'd like to get pregnant in the more distant future, however, there appears to be no need to worry. Zika virus does not seem to pose a risk of birth defects for future pregnancies. As best researchers can tell, the virus clears itself from the body pretty quickly, remaining in the blood for only about a week after infection.



Diagnosis

It is difficult to diagnose Zika virus infection based on clinical signs and symptoms alone due to overlaps with other arboviruses that are endemic to similar areas. Zika virus can be identified by RT-PCR in acutely ill patients. However, the period of viremia can be short and the World Health Organization recommends RT-PCR testing be done on serum collected within 1 to 3 days of symptom onset or on saliva or urine samples collected during the first 3 to 5 International Journal of Current Trends in Pharmaceutical Research

days. Later on, serology through detection of specific IgM and IgG antibodies can be used. IgM can be detectable within 3 days of the onset of illness. Serological cross-reactions with closely related flaviviruses such as dengue and west Nile fever as well as vaccines to flaviviruses are possible. Commercial assays for Zika are available from Euroimmun (www.euroimmun.com). The US Centers for Disease Control and Prevention advises that "based on the typical clinical features, the differential diagnosis for Zika virus infection is broad. In addition to dengue, other considerations include leptospirosis, malaria, rickettsia, group A streptococcus, rubella, measles, and parvovirus, enter virus, adenovirus, and alphavirus infections (e.g., Chikungunya, Mayaro, Ross River, Barmah Forest, O'nyong-nyong, and Sindbis viruses)."

3. Prevention

There is currently no vaccine, but development is a priority of the National Institutes of Health. The virus is spread by mosquitoes, making vector control and avoidance an essential element to disease control. The US Centers for Disease Control recommends that individuals:

- Cover exposed skin by wearing long-sleeved shirts and long pants.
- Use an insect repellent
- Always follow product directions and reapply as directed:
- If you are also using sunscreen, apply sunscreen first, let it dry, then apply insect repellent.
- Follow package directions when applying repellent on children. Avoid applying repellent to their hands, eyes, or mouth.
- Stay and sleep in screened-in or air-conditioned rooms.
- Use a bed net if the area where you are sleeping is exposed to the outdoors.

CDC guidelines for the important surveillance and elimination of the white-striped-legged vector mosquitoes are available for professionals in the USA and for e.g. homeowners emphasising sealing, draining and/or scrubbing anything holding water in or near homes; weekly scrubbing off sticky eggs from water containers is needed.

Treatment

There is currently no specific treatment for Zika virus infection. Care is supportive with treatment of pain, fever, and itching. Some authorities have recommended against using aspirin and other NSAIDs as these have been associated with hemorrhagic syndrome when used for other flaviviruses. Additionally, aspirin use is generally avoided in children when possible due to the risk of Reye syndrome. Zika virus had been relatively little studied until the major outbreak in 2015, and no specific antiviral treatments are available as yet. Advice to pregnant women is to avoid any risk of infection so far as possible, as once infected there is little that can be done beyond supportive treatment. One *in vitro* study found that Zika virus may be sensitive to interferon treatment, which is commonly used against other viral infections, however these results have not been tested in animals or humans.

Table 1: Case Studies Linked With Zika Virus Infection in Brazil (as of January 2016)

S.No	Date of report location	Clinical findings	Laboratory findings
1	17 november 2015 Paraiba state	Foetus with ultra sound exams.30.1 weeks gestation Head circumference<2.6SD Observed lesions: <ul style="list-style-type: none"> Brain atropy with calcifications involving the white matter of the frontal lobes, including the caudate. Enlarged cisterna magna 	RT-PCR Zika virus positive in amniotic fluid [12]
2	17 november 2015 Paraiba state	Foetus with ultra sound exams.30.1 weeksgestation Head circumference<3.1 SD Observed lesions: <ul style="list-style-type: none"> Cerebral hemispheres were markedly asymmetric Thin pons and brainstem 	RT-PCR Zika virus positive in amniotic fluid [12]
3	28 november 2015 Ceara state	New born Born on 18 november 2015 No measurement of head circumference at birth Weight:945grams at birth Died within 5minutes from birth Observed lesions: <ul style="list-style-type: none"> Microcephaly Polydramnios 	Presence of zika virus genome in blood and tissue samples of newborn
4	5 January 2016 Rio grande do north state	Case: miscarriage, Foetus with malformation Mother reported rash & fever during pregnancy	Positive PCR test for zika virus on foetal sample in samples of the placenta
5	15 janaury 2016 Hawai (USA)	Case: baby with congenital microcephaly who was born recently on oahu island, hawai. Mother had a probable exposure to zika virus when she was residing in brazil in may 2015.	Laboratory confirmation of a past zika virus infection [13]

4. Conclusion

In the past few weeks, the world has mobilised to tackle the latest threat to global health security-Zika virus, now spreading rapidly in the Americas. Worldwide concern over Zika virus and its temporal and geographical association with clusters of birth and neurological conditions escalated, with WHO declaring a Public Health Emergency of International Concern. As neither treatment nor vaccines are available, prevention is based on personal protection measures similar to the measures that are applied against dengue and chikungunya infections. Increase awareness among obstetricians, paediatricians and neurologists in the EU/EEA that zika virus infections should be investigated for patients presenting with congenital central nervous system malformations, microcephaly and Guillain-Barre syndrome (GBS). Strengthen laboratory capacity to confirm suspected zika virus infections in order to differentiate zika virus infections from other arboviral infections.

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