

Zika Virus - A New Global Threat

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Abstract

In the early 2015, numerous cases of patients presented symptoms of mild fever, rash, conjunctivitis and arthralgia were reported in the northeastern Brazil. Although all patients lived in a dengue endemic area, molecular and serological diagnosis for dengue resulted negative. Chikungunya virus infection was also discarded. Subsequently, Zika virus (ZIKV) was detected by reverse transcription-polymerase chain reaction from the sera of eight patients and the result was confirmed by DNA sequencing. Phylogenetic analysis suggests that the ZIKV identified belongs to the Asian clade. This is the first report of ZIKV infection in Brazil. Ongoing research describes the phenotypic spectrum of potential Zika virus-core related congenital infections and the observations of new cases are really more important. Furthermore medications like pain relief and antihistamines are being used for fever and rash. As there is no specific treatment, they should get plenty of rest, should drink enough fluids and the pain and fever are treated with common medicines. In case the symptoms get worst, they should consult physician and take advice. No vaccines are available till now.

Keywords: Zika Virus; Global threat; No vaccine

Introduction

Zika virus is a rising mosquito-borne flavivirus very much similar to dengue virus and firstly isolated from a rhesus monkey which was found in Zika forest [1].

Zika virus disease is a virus infection caused by Zika virus (ZIKV) which is transmitted to people by the bite of an infected mosquito from Aedes genus. People with this disease have a mild febrile illness with maculo-papular rash. Spread of virus and a few outbreaks were reported earlier than 2007 in tropical Africa and in some part of Southeast Asia. Since 2007, many islands of the Pacific region had traced outbreaks. ZIKV disease was first time appeared in South America in 2015.

During large outbreak in French Polynesia in 2014, a numerous number of patients suffered from Guillain-Barre syndrome (GBS) was reported. Atypical raise of congenital microcephaly was notified in some part of north eastern Brazil in 2015. Sexual transmission of Zika virus is currently under investigation. There is no specific treatment or vaccine currently available for ZIKV infection. Therefore, the best way of prevention is protection against mosquito bites [2].

Historical Account

The last 20 years, numerous ZIKV isolated to have been found from Aedes spp. Now Africa (Ae. africanus) and Malaysia (Ae. aegypti), exposed these species as an epidemic or enzootic way [3-5].

Numerous ZIKV in human to have been also found between the 1960s and 1970s from West and East Africa in predictable parvovirus survey studies in the absence of disease [6-8].

Further serologic survey studies in the 1950s and 1960s found ZIKV infections among beings in Pakistan, Thailand, North Vietnam, Egypt, Nigeria, Uganda, India, Malaysia, Indonesia, and the Philippines [9].

All these statistics suggest as strongly to widespread of ZIKV from Africa to Southeast Asia north and west of the Wallace line. In 1977, ZIKV infection has been confirmed with 7 patients in Indonesia and Central Java in an acute fever [10].

Statistics with these 7 ZIKV circumstances and numerous previously survey studied on human infections mentioned that characteristics of clinical feature create infection with ZIKV involved anorexia, fever, headache, malaise, stomach pain, dizziness, and rash, in all cases infection appeared relatively mild, self-limiting, and nonlethal [11-14].

The disease spread-out likely epidemiology in April 2007, conjunctivitis, and arthralgia have renowned through physicians in Yap State, Federated States of Micronesia [15].

A rapid assay suggested in the Laboratory testing through that a dengue virus (DENV) has the instrumental cause. In June 2007, the samples have been referred for testing to the Arbovirus Diagnostic Laboratory at the Centers for Disease Control and Prevention (CDC, Fort Collins, CO, USA). By the testing of serological with immunoglobulin (Ig) M-capture ELISA with DENV antigen established current flavivirus infection in numerous patients. Tough by reverse transcript-PCR (RT-PCR) through flavivirus harmony primers DNA fragment is generated, which once exposed to nucleic acid sequencing, confirmed 90% nucleotide distinctiveness through ZIKV. These observed reported that ZIKV has the instrumental representative of the Yap epidemic. We explosion serologic limitations of the protecto-reaction amongst ZIKV-infected patient, statistics on predictable intensities of vermeil, and the comprehensive coding counting nucleic acid categorization of ZIKV attendant through the epidemic.

Properties and strains of Zika virus

Polygenetic analyses

These three methods of phylogenetic implication (NJ, ML and MP) recognized two major lineages (African and Asian). The most recent common ancestor of MR 766 (Uganda, 1947) deviated first, followed by deviation of the most recent common forefather of the ArD 41519 (Senegal, 1984) and IbH 30656 (Nigeria, 1968) strains, the P6-740 stress (Malaysia, 1966), and the EC Yap (Micronesia, 2007) and FS13025 (Cambodia, 2010) stresses.

Nucleotide and amino acid sequence variation among African and Asian strains

Based on nucleotide and amino acid classification conformation, the African strains were the greatest divergent from the Asian stresses, and strains from the same topographical regions were the least divergent (Africa and Asia). There were several deduced amino acid modifications among the stresses, in the turn associated to topographical zone of virus assembly.

Genetic variation among three MR 766 sequences

There are two MR 766 stresses that had been formerly sequenced exhibited extensive genetic variation (6.3% nucleotide, 1.8% amino acid divergence). To investigate of this discrepancy; we were sequenced as an additional stress of MR 766 from the WRCEVA collection. The MR 766 sequence through accession number AY632535, has been ultimately selected for use in our studies due to the antiquity of its low passage, nucleotide and amino acid comparison to the high passage MR 766 stress that have sequenced (0.4% nucleotide and 0.6% amino acid divergence), and its situation next to the root of the MR 766 lineage in a tree comprising all three sequences (not shown).

Glycosylation site variation between African and Asian strains

Obliterations in a possible glycosylation area of several strains were observed following their arrangement. A 4-codon deletion was observed started at amino acid position 153 of the E-protein of the MR766 strain (GenBank accession number AY632535), a 6-codon deletion at position 156 of another MR 766 strain (GenBank accession number DQ859059), and a 6-codon deletion at position 156 of the IbH 30656 strain sequenced in this study. The MR 766 strain sequenced here did not exhibit any deletions in the expected amino acid sequence and provided indication of passage-associated alterations in hypothetical glycosylation site.

Replication of Zika Virus

By clarithrin mediated endocytosis or by apoptotic mimicry, it intermediates internalization into the host cell due to the connection of the viral envelope protein E to host receptors. A fusion of host endosomal membrane with virus membrane and into the cytoplasm RNA genome is discharged. All structural and non structural proteins for yielding the replication proteins, which is cleaved and is translated into a polyprotein by the positive -sense genomic ssRNA. In cytoplasm viral factories, in the surface of endoplasmic reticulum replication takes place. From the genomic ssRNA (+), dsRNA genome is synthesized. Viral mRNAs/new ssRNA (+) is replicated/transcribed by providing the dsRNA genome. At the endoplasmic reticulum there is an occurrence of virus assembly. Transportation takes place from the Virion buds via the host ESCRT complexes to the Golgi apparatus at the endoplasmic reticulum. Fusion competent is a process in which prM protein is cleaved in the Golgi by maturing the virion. By the process of exocytosis there is a discharge of new various [16].

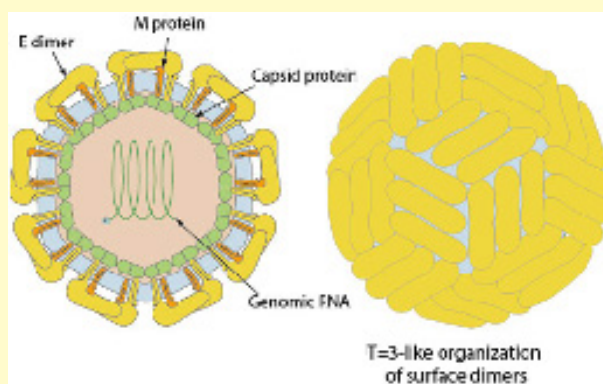


Figure 1: General Structure of Zika flavi virus virion.

Epidemiology

Through mosquito bites

Zika virus is transmitted to community mainly through the bite of an infected mosquito mainly Aedes species. These are similar to those mosquitoes that cause dengue and chikungunya viruses. Generally these mosquitoes lay eggs in and near stagnant water in things like buckets, bowls, flower jars, animal dishes, and vases. These mosquitoes prefer to bite people, and live close to people.

Mosquitoes that spread viruses i.e. chikungunya, dengue, and Zika are aggressive daytime biters. But they can also bite at nighttime. Mosquitoes turn into infected when they feed on a person previously infected with the virus. Infected mosquitoes are then able to spread the virus to further new people through bites.

Rarely, from mother to child

A mother previously infected with Zika virus near at the delivery time can transmit the virus to her baby around the time of birth, however this is rare.

Probably Zika virus can be transmit from mother to fetus at some stage in pregnancy. This mode of transmission is being examined.

Up till now, there is no such information regarding infants getting Zika virus during lactation. So mothers are secure to breastfeed even in areas where Zika virus is found [17].

Through infected blood or sexual contact

Reports indicate that virus possibly spread through blood transfusion and through sexual contact [18].

Virology of Zika virus

ZIKV is RNA virus Comprised 10,794 nucleotides encoding 3,419 amino acids. is almost related to Spondweni virus; the 2 viruses are the only members of their clade within the mosquito-borne cluster of flaviviruses [19-22].

Another relatives include Ilheus, Rocio, and St. Louis encephalitis viruses; yellow fever virus is the prototype of the family, in addition includes dengue, Japanese encephalitis, and West Nile viruses [23,24].

Based on the research indicated Studies Zika viruses diseases Forest suggested blunted the viremia caused by yellow fever virus in monkeys stop st also does not stop transmission of yellow fever virus [25,26].

Pathogenesis of Zika Virus

1. Incubation period in mosquitoes is about 10 days.
2. The reservoirs of virus are primarily monkeys and humans.
3. The pathogenesis of the virus is investigated to begin with an infection of dendritic cells near the site of inoculation, bear by a spread to lymph nodes and the bloodstream. Flaviviruses mostly replicate in the cytoplasm, but Zika virus antigens have been infected the cell nuclei

The virus usually grows and developed Infection in which the head of an infected fetuswill will be small heads and brain damage in newborns (microcephaly).

The most critical period is the first trimester of Pregnancy in which most of the women doesn't realize they are pregnant. Professionals do not know how the virus penetrates the placenta and damages the growing brain of the embryos [27].

Clinical presentation

Till now there is no Effective drug or Vaccines

The co-infections with mosquito borne diseases are also considered along with differential diagnosis such as dengue fever, malaria and chikungunya.

The medication is appropriate and is mainly planted on pain relief, antihistamines for pruritic rash and fever reduction.

There is an increased risk of hemorrhagic syndrome documented with other flavivirus as well as the risk of reyes syndrome after viral infection in children and teenagers, so the treatment with acetylsalicylic acid and NSAIDS was dismayed [28].

In 1964 when Simpson explained his own professionally acquired ZIKV illness at age 28 it was considered as the umber one documented information of human ZIKV disease [29].

First symptoms appear as a light headache. The second day, amaculopapular rash painted his face, neck, trunk and upper arms, and also covers to his palms and soles. Enduring fever, malaise and back pain introduced. From the dusk of the 2nd day of illness he was a

febrile, the rash was piling away and he felt quite good. On the third day, he felt perfect, and now he had only rash which also evaporated over the next 2 days. From the serum collected, so far while he was febrile, ZIKV was isolated.

Laboratory acquired ZIKV illness in a man was documented with sudden appearance of fever, headache and joint pain but no rash [30]. From the first day of symptoms, serum was collected and ZIKV was isolated; in the first week the mans illness gets resolved. Among the 7 ZIKV case-patients in Indonesia, everyone have fever, but they were observed by hospital based supervision for febrile illness which was explained by Olson., *et al.* [31].

Other demonstration included mainly diarrhea, anorexia, constipation, abdominal pain and dizziness. Among them one of them had conjunctivitis but none of them had rash. Rash, conjunctivitis and Arthralgia were the epidemic characterization on Yap Island [32,33]. Other less frequent demonstration included headache, mylgia, retro orbital pain, edema and vomiting [34]. Due to main neurological conditions, Zika infection is considered as more serious issue. There are various researches being conducted to find out the effects of Zika on fetuses. A relationship has been established between an increase in cases of microencephaly in new borns and zika virus infections by Ministry of Health of Brazil. The preliminary analysis of the Research found out that the greatest risk of microencephaly and malformations appears to be associated with infection during first trimester of pregnancy. Various researches are being conducted to find out the aetiology, risk factors and complication of microencephaly [35].

Gullain-Barre syndrome; A rare ataxia where a person's own immune system harms the nerve cells, causing muscle fragile and sometimes paralysis [36].

Diagnosis

Still now no perfect diagnostic test is been developed for detection for zika. Most of the time its depends on the physical symptoms in most people, diagnosis is based on physical symptoms and epidemiological circumstances (such as Zika outbreak in the patient's area or trips to areas where the virus is circulating).

Laboratory Diagnosis of ZIKA Virus

Still now there is no widely accepted test for diagnosis for zika in most people, diagnosis is based on clinical symptoms and epidemiological circumstances (such as Zika outbreak in the patient's area or countries where the virus is circulating).

Diagnostic tests for ZIKA infection: PCR- Nucleic acid detection by reverse transcriptase-polymerase chain reaction (RT-PCR) targeting the non-structural protein 5 genomic region is the primary means of diagnosis. It is generally useful in the first 3-5 days after the beginning of symptoms.

Serological Test: An ELISA has been developed to detect IgM to ZIKA only after five days. Because it is closely related to dengue and yellow fever, it may cross-react with antibody tests for those viruses.

Nucleic acid amplification test: Nucleic acid amplification test (NAT) for detection of viral RNA can also be performed.

Plaque reduction neutralization assay: The Plaque reduction neutralization assay generally has improved specificity over immunoassays, but may still yield cross-reactive consequences in secondary flavi-virus infections [37,38].

Differentiating Zika Virus infectivity from Other Diseases

Zika virus infection exhibits through wide range analytic symptoms shared with multiple different diseases from the Flaviviridae Virus family, so sometime its common that's why physician may think Zika as the following disease [39]. Dengue fever, Malaria, Lep-tospirosis, Parvovirus, Enterovirus, Adenovirus, Alphavirus, Rickettsia, Group A Streptococcus, Rubella, Measles, Chikungunya, Yellow fever, West Nile virus, Japanese encephalitis, Ross River virus, Barmah Forest virus.

Patients bitten by mosquitoes may be parallel infected with Zika virus and other mosquito-borne infections, and this type of infection is also raising some other type of side infection. Zika virus infection is clinically distinct from similar diseases by its own genre mild symptoms like headache, low-grade fever, and mild joint pain [40]. Zika virus infection-related complications, such as microcephaly which distinguish Zika virus infection from other *flavi virus* disease [41].

Differentiating Zika Fever from Dengue Fever

The following table summarizes the distinguishing and common features between Zika fever and Dengue fever:

	Dengue Fever	Zika Fever
Common Clinical Features	Biphasic fever pattern, maculopapular rash, arthralgia, headache, and signs of hemorrhage	Fever, maculopapular rash, conjunctivitis, and headache
Hemorrhage Common?	Yes	No
Symptom Severity	May be severe	Usually mild
Symptom Duration	2 to 7 days	4 to 7 days
Incubation Period	4 to 10 days	3 to 12 days
Endemicity	Americas, Africa, Southeast Asia	Americas, Africa, Southeast Asia
Vector	Aedes mosquito	Aedes mosquito
Laboratory Findings	Leucopenia, rising hematocrit (suggestive of impending hemorrhage), thrombocytopenia, elevated liver function tests	Leucopenia but normal hematocrit, platelet count, and liver function tests
Diagnosis	RT-PCR or ELISA	RT-PCR or ELISA
Treatment	Supportive care, avoid aspirin and other NSAIDs	Supportive care

Treatment

Treatment consists of relieving pain, fever, and any other symptom that hassle the patient. To prevent dehydration, it is recommended to control the fever, rest, and drink plenty of water. There is no vaccine or specific drug for this zika virus infection. Still now Treatment is directed primarily at relieving symptoms using anti-pyretic and analgesics [42].

Infection Control, Personal Protection and Prevention

Prevention is also based on protection against mosquito bites. Due to lack of specific drugs prevention is the best way to stay protect from Zika infection. Therefore personal protection measures should be applied all day long and especially during the hours of highest mosquito activity. Personal protection, cover the exposed skin with long sleeves cloths and avoid mosquito bites especially in the evening and early morning. Using repellents and wearing long-sleeved shirts and long pants especially during the hours of highest mosquito activity, using long-lasting insecticidal treated mosquito bed nets which are essential to prevent mosquito.

Avoid accumulating garbage: Put it in closed plastic bags and keep it in closed containers.

Avoid allowing standing water in outdoor containers (flower pots, bottles, and containers that collect water) so that they do not become mosquito-breeding sites.

Removing mosquito breeding sites in close outdoor/indoor premises.

Repellent use must be strictly done in accordance with the instructions indicated on the product label.

For newborn children under three months of age, repellents are not recommended.

Travelers, especially children, pregnant women, and people with immune disorders or severe chronic illnesses, should consult their doctor or seek advice from a travel clinic to receive personalized recommendations on use of repellents and protection before travelling [43].

Vaccine: According to WHO, Zika virus transmission is raising in the Americas. It might affect Africa and Asia. But still, there is no vaccine available.

There are two promising vaccines namely “recombinant and inactivated” on which India based biotechnology industry is currently working. An inactivated vaccine is developed as a result of pathogen death in such a way that the host immune system can identify it [44].

Recommendation

- a. Vaccine should be developed for the treatment of Zika virus
- b. Promote awareness campaign for prevention of Zika virus in public.

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