

A CASE STUDY: ANALYSIS OF ZIKA VIRUS

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ABSTRACT

ZIKV is one of the rising pathogens in the different geographical regions of the world. More than 84 countries have recently acknowledged the zika virus outbreak. From 2016 to 2019, there were 81,852 confirmed cases of infected patients. Zika virus (ZIKV) is a Flaviviridae family member that has been related to dengue (DENV) and Chikungunya (CHIKV). The genome and virion structure of the Zika virus are both complexes. Virion endocytosis, which facilitates entry into the host cell, is part of its reproductive cycle in the host cell. The infection spreads easily from infected mosquitoes, from a pregnant woman to her fetus, through sexual contact, blood transfusion, and laboratory exposure. In humans, the virus has been linked to foetal microcephaly. There are currently no vaccines available for treatment, but common drugs are recommended for symptom relief. The cross reactivity of the antibodies with other flaviviruses, which leads to antibody-dependent intensification of infection, may make developing an effective vaccine against Zika virus difficult.

KEYWORDS: ZIKA virus, spread, replication, microcephaly, analysis, infection.

INTRODUCTION

Zika virus (ZIKV) is an RNA virus that is transferred by mosquitos and linked to yellow fever, dengue fever and West Nile virus. It first appeared in East Africa in the early twentieth century, then moved to Southeast Asia. The virus is known after the Ugandan Woodland where it was discovered in 1947 in a rhesus monkey.^[1] The Zika virus is spread through a mosquito bite from an infected Aedes species. It poses a major threat to women who are pregnant. The Zika virus has also been linked to an elevated risk of Guillain-Barre syndrome and many other congenital neurological disorders.^[2] It causes acute febrile sickness, arthralgia, fever, myalgia, rash, headache, and conjunctivitis and is clinically similar to dengue fever.^[3,4] The identification of the viral genome by RT-PCR genomic amplification and viral isolation confirms the diagnosis of Zika virus infection.^[1] The Zika virus is a single-stranded RNA virus that belongs to the Flaviviridae family. The infectious Zika virus has been found in human blood as early as the day of commencement of sickness, but the virus's nucleic acid has only been proven 11 days later.^[5]

Headaches, low-grade fever, conjunctivitis, and a maculopapular skin rash on the face or trunk that may spread. The most prevalent symptoms of Zika virus infection are myalgia and arthralgias.^[4,6,7,8] In many cases, hydrocephalus, agyria, and multifocal dystrophic calcifications in the sub cortical white matter and cortex,

as well as mild focal inflammation and cortical displacement, have been observed, as have hydrocephalus, agyria, and multifocal dystrophic calcifications in the subcortical white matter and cortex.^[9]

The Centers for Disease Control and Prevention has provided some recommendations for treating Zika virus symptoms, including getting plenty of rest, increasing fluid intake to avoid dehydration, fever and pain relievers, and avoiding aspirin and non-steroidal anti-inflammatory drugs.^[12] People must wear long-sleeved shirts and pants and use doors and windows with intact screens, as well as EPA-registered insect repellants and permethrin-treated clothes, to protect themselves from the Zika virus.^[10] To avoid infection, remove water reservoirs and containers because stagnant water serves as a breeding ground for the Aedes mosquito, which is a Zika virus carrier, and Spraying insecticides on mosquito habitats is an effective technique for preventing Zika.^[11,12] Human-to-human transmission can occur through sex and transfusion of infected blood products as well as from mother to child during or after pregnancy.^[6,13] No approved medical countermeasures exist to prevent or treat ZIKV infection, but several vaccine candidates are under evaluation in pre-clinical through phase 2 studies.^[14,15] We focus our discussion mainly on virion structure, a protein responsible for replication of host cell attachment, symptoms and

analysis of several people infected with the disease and their treatments.

Virus Structure and Genome organization

The African prototype ZIKV strain (MR 766) had its entire genome sequenced for the first time in 2007, and epidemic ZIKV strains are now being sequenced at a breakneck pace.^[16] The symmetry of the proteins on the surface is icosahedra-like.^[17] Zika virus is a single-stranded positive-sense RNA virus belonging to the Flaviviridae family with roughly 11 000 bases, a 100 nt 5' untranslated region (UTR), a single open reading frame of 10 kb, and a 420 nt 3' UTR.¹⁷ The open reading frame encodes a single polyprotein, which is eventually processed into three structural proteins, capsid protein (C), pre membrane/membrane protein (prM), and envelope protein (E), as well as seven non-structural proteins (NS1, NS2A, NS2B, NS3, NS4A, 2K, NS4B, and NS5).^[16,18] The E protein is responsible for the majority of the virion's surface and is involved in features of replication such as host cell attachment and membrane fusion. The structural proteins are responsible for viral particle formation and pathogenicity.^[17] Non-structural proteins and untranslated regions (UTRs) play an important function in viral replication (3). According to this evolutionary tree, ZIKV has two major lineages: African and Asian. Between 2013 and 2017, an outbreak of the Asian-lineage ZIKV was documented in the South Pacific islands, South America, and Asia.^[19]

Reproductive cycle of zika virus

As viruses are ultimate cellular parasites that rely on the host metabolism for every step of their life cycle in a host cell, manipulating host processes as an alternative to suppressing virus reproduction and spread presents an opportunity.^[20] When Zika virus particles have entered the human body, they must multiply and produce additional viruses by entering specific cells. Because a Zika virus particle's outer envelope contains specialised proteins that connect with receptor proteins on human cells, cell entry is conceivable. The viral proteins "trick" the cells into taking up the viral particle when they attach to cell receptors. The virus's RNA genome is released into the cytoplasm, the cell's fluid-filled major compartment, inside the cell. There, enzymes in the cell "read" (transcribe) the RNA molecule to produce a lengthy protein that is then cut up into several smaller proteins. Some of these proteins, such as capsid and envelope proteins, are structural components required for the formation of new viral particles. The RNA genome is copied and processed by other viral proteins. At the

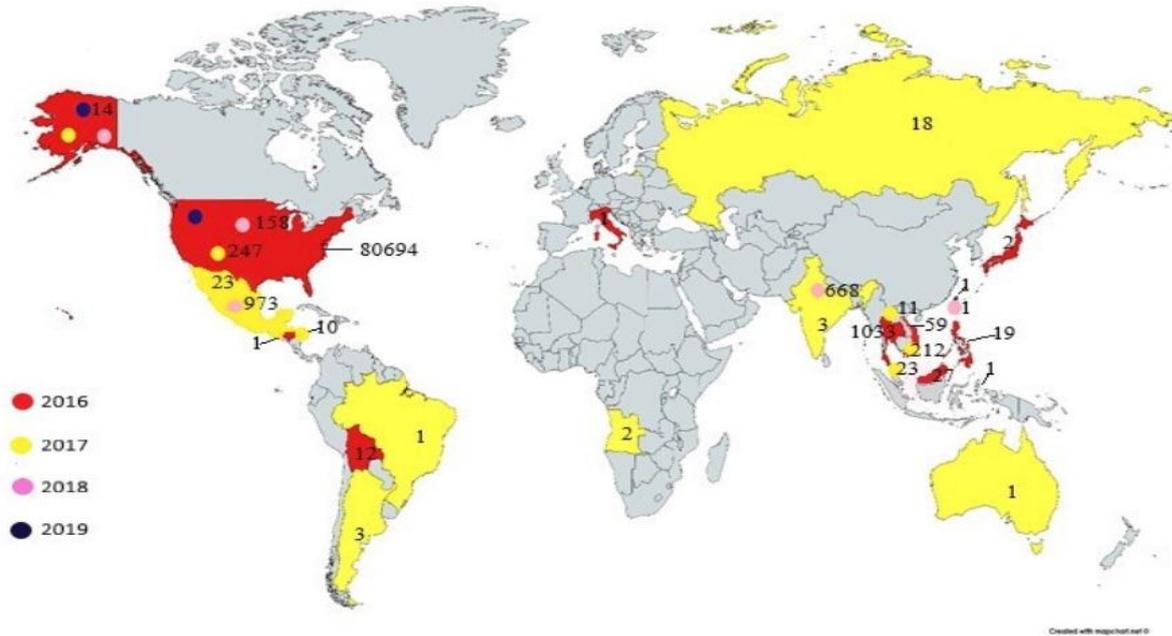
surface of the endoplasmic reticulum, a membrane compartment that is part of the cell's export system, viral proteins and copies of the RNA genome assemble. New viral particles break out into the ER's interior, carrying with them a small patch of the ER membrane. The viral envelope will be formed from this "stolen" membrane. The particles subsequently pass through the Golgi apparatus, where they are further processed before being released at the cell surface. Viral particles that have been released can infect other cells, perpetuating the infection cycle.^[17]

Analysis

The Zika virus spread has devastating consequences all around the world, causing dramatic population decline.^[21] More than 84 countries have recently acknowledged the Zika virus outbreak. Illness with the Zika virus usually causes no symptoms, although the infection can range from mild to severe, with complications. Zika may cause abortion, congenital defects such as microcephaly, and Guillain-Barre syndrome.^[22]

The investigation of yellow fever led to the detection of a new virus, the Zika virus, in the Ugandan woodlands in 1947. Zika mosquitoes bite at all hours of the day and night. It was initially discovered in monkeys in 1947. It was discovered in humans in 1952. The Zika virus was transmitted to equatorial Asia between 1969 and 1983, including India, Pakistan, Malaysia, and Indonesia. In 2007, the first Zika virus epidemic was reported on the island of Yap (Federated States of Micronesia). Then, in 2013, it was discovered in French Polynesia. Then, in 2015-16, there were Zika epidemics in Brazil, as well as 31 other countries in the Americas.^[23,24] After a big outbreak of Zika in Brazil, a new infection, Guillain Barre syndrome (GBS), was discovered in July 2015, which is a neurological disorder characterised by nerve cell abnormalities. Many incidences of foetal autopsy and foetal imaging were also documented between 2013 and 2015. The following data pertains to the calendar years 2016 through 2019. These include Zika virus infection reports provided by Epi Watch, an open-source surveillance system.

From 2016 to 2019, there were 81,852 confirmed cases of infected patients, with 609 (2017), 1800 (2018), and 15 (2019) cases detected (Fig.1). In addition, a large number of Zika cases were reported in Thailand (1044), Mexico (996), and India (671).^[21]



	2016	2017	2018	2019
Total number of reported zika cases	81,852	609	1,800	15

Fig. 1: World confirmed cases of zika virus 2016-2019, WHO.^[25]

Figure. 2 depict the number of infected pregnant women. The cases of microcephaly were discovered in 2016 and 2017. In 2017, there were 67 cases of microcephaly reported. Guillain-Barre syndrome, a rare neurological illness, was identified in seven cases in 2016.^[26]

Brazil was the country most impacted by the outbreak, reporting the highest number of cases in the globe. Rio de Janeiro alone reported 71000 cases of possible Zika infection in 2016. In 2017, however, there was a significant decline in cases, with only 2210 cases

reported. In 2018, there were 2952 microcephaly cases reported in Brazil. The information below depicts a virus infection in transmission mode.^[27] There were 1695 incidents of travel-related illness reported. 277 and 15 were also locally transmitted and sexually transmitted. The mode of transmission confirmed 35 deaths in all. In 2017, 25 babies died as a result of abortion during pregnancy. The zika virus has now been discovered in Kerala, India. Kerala reported 41 confirmed cases in July 2021.

Table 1: Transmission mode of the virus.^[25]

Zika cases	2016	2017	2018	2019
Locally-transmitted cases	267	10	0	0
Travel-associated cases	1470	207	30	15
Reported zika-associated deaths	6	25	4	0
Sexually-transmitted cases	14	1	0	0

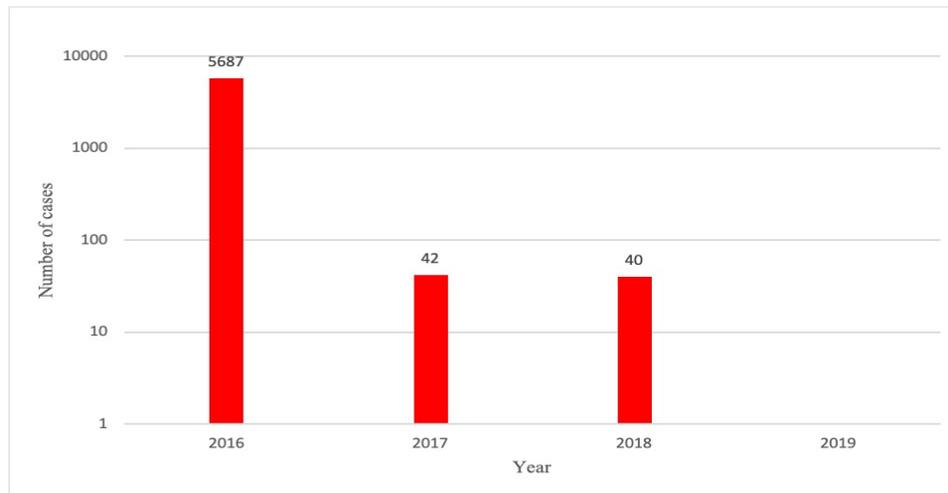


Fig. 2: Depicts the number of infected pregnant women.^[25]

Case report

In early December 2013, during the ZIKV outbreak, a 44-year-old man in Tahiti had symptoms of ZIKV infection: asthenia, low-grade fever (temperature from 37.5°C to 38°C) and arthralgia. Symptoms lasted 3 days. Eight weeks later, he described the second episode of symptoms compatible with ZIKV infection: temperature from 37.5°C to 38°C, headache on days 1–3, and wrist arthralgia on days 5–7. Because the patient refused therapy, no biological samples were taken during the first two episodes of illness. The patient healed completely from the second incident, but he noticed evidence of hematospermia two weeks later and sought therapy. The patient was referred to our laboratory at the Institute Louis Malardé in Papeete, Tahiti, for ZIKV infection diagnostic testing since he had had symptoms of ZIKV infection a few weeks prior. There were no indicators of urinary tract infection, prostates, urethritis, or cystitis on the medical questionnaire, and the patient stated that he had no recent personal contact with those who had acute ZIKV infection. We took blood and sperm samples. Hematospermia was established by direct and macroscopic investigations of the sperm. We extracted RNA from 200 liters of blood and 500 liters of sperm and urine using the NucliSENS easyMAG system (bioMérieux, Marcy l'Etoile, France); both were eluted with 50 litres of elution buffer. For amplification, we used 5 litres of harvested RNA. We used real-time reverse transcription PCR (rRT-PCR) to evaluate blood and sperm RNA extracts, as described, employing two ZIKV-specific primers/probe amplification combinations.^[28] The RT-PCR results for ZIKV were positive in semen but negative in blood, and this was verified by sequencing of the genomic location 858–1138, which encompasses ZIKV's prM/E protein-coding regions. The sequence generated (GenBank accession number KM014700) was identical to those reported at the start of the ZIKV outbreak.^[1] We took a urine sample three days later, followed by a second set of blood and sperm samples. Both direct and macroscopic investigations detected no evidence of blood in the sperm and urine from the second collection. ZIKV RNA was

found in the semen and urine samples, but not in the blood sample, according to RT-PCR. We used an RNA synthetic transcript standard that encompasses the region targeted by the two primers/probe sets to quantify ZIKV RNA burdens. The first and second semen samples had RNA loads of 2.9 10⁷ copies/mL and 1.1 10⁷ copies/mL, respectively, and the urine sample had a load of 3.8 10³ copies/mL. We cultivated sperm and urine in the same way that we cultured the dengue virus from urine.^[29] Briefly, Vero cells were inoculated with 200 μ l of each sample diluted in 200 μ l of 1 % foetal calf serum (FCS) minimum essential medium (MEM) and cultured for 1 h at 37°C; the inoculum was then withdrawn and replaced with 1 mL of culture medium. A negative control (200 μ l of 1% FCS-MEM) and positive control (5 μ l of ZIKV-positive serum diluted in 200 μ l of 1% FCS-MEM) were also infected. The cells were then cultured for 6 days at 37°C in 5% CO₂. ZIKV was discovered in the culture fluids using rRT-PCR, as previously described. In the two sperm samples, replicative ZIKV particles were discovered, but none in the urine sample. This observation doesn't rule out the likelihood of ZIKV particles in the urine. There were no titered positive samples.

Diagnosis

The detection of viral nucleic acid by RT-PCR and the detection of IgM antibodies by the IgM-capture enzyme-linked immunosorbent assay (MAC-ELISA) are the pillars of the routine diagnosis of Zika virus infection.^[30,31] In a pregnant woman whose foetus had indications of congenital infection, viral RNA was discovered in her serum approximately 10 weeks after infection.^[32] As a result, RT-PCR testing of blood samples obtained within the first week of clinical illness and MAC-ELISA testing of samples not tested by RT-PCR or found to be negative by RT-PCR is anticipated to have the highest diagnostic yield.^[33] A recent Zika virus infection could result in a positive MAC-ELISA test for dengue fever. The plaque reduction neutralisation test (PRNT), the most specific test for distinguishing antibodies from closely similar viruses, can be performed

to assist verify MAC-ELISA results.^[34] Another large study comparing RT-PCR results in serum and saliva samples found that saliva had higher sensitivity than serum, even though some patients' samples were positive in serum but not saliva, and saliva testing did not extend the duration of viral nucleic acid detectability after the onset of illness.^[35] When ultrasonography was conducted at 29 weeks of pregnancy, calcifications in the placenta and foetal brain were discovered. Microcephaly is defined as a head circumference smaller than the 2.5th centile for gestational age, and USS is a sensitive screening test for microcephaly in combination with other intracranial abnormalities such as ventriculomegaly and calcification.^[36] However, throughout the viremic period, molecular testing is required.^[31]

Prevention

The main goals of mosquito prevention and control are to avoid mosquito bites, reduce sexual transmission, and control the mosquito vector. Avoiding unnecessary travel to areas where Zika virus transmission is ongoing, avoiding unprotected sexual contact with partners who are at risk for Zika virus infection, and using mosquito repellent,^[4] permethrin treatment for clothing,^[1] bed nets.^[37,38] Window screens and air conditioning are all potentially effective methods of prevention that are focused on reducing infections among pregnant women.^[39] During dengue outbreaks, per domestic pesticide spraying is widely used, although there is no evidence that it is effective as a single control intervention.^[40] Indoor mosquito-killing sprays with active ingredients Imidacloprid and Cyfluthrin, which is available on the market, should be used to kill mosquitoes. Pregnancy should be avoided in high-risk ZIKV-infected areas until the virus is completely eradicated, or extra caution should be taken because Microcephaly is linked to ZIKV infection.^[41]

Treatment

Individuals with ZIKV infection should drink enough water, get plenty of rest, and treat pain and fever with liquid treatments. They should seek counseling and therapy consideration if their symptoms worsen. Until far, there have been no specific drugs or vaccines available to treat even ZIKV infections. Only symptomatic drugs, such as paracetamol to reduce pain and fever associated with this infection, should be considered. Homoeopathy is a viable therapeutic option for ZIKV infection since it is effective in the treatment of the Japanese encephalitis virus, which belongs to the same genus as the ZIKA virus.^[42] Belladonna is a flowering plant that grows in North Africa, Western Asia, and Europe. The majority of alkaloidal content in *Atropa belladonna* is found in mature fruit and green leaves. It has been used to cure a variety of human problems since ancient times, including menstrual disorders, headaches, peptic ulcers, inflammation, and histaminic response.^[43] *Eupatorium* is a naturally occurring pharmaceutical homoeopathic chemical that is effective against the symptoms of ZIKV disease and can

be used as a ZIKV infection preventative treatment.^[44] The homoeopathic medications *Eupatorium perfoliatum*, *Rhus tox*, and *Atropa belladonna* may be used to treat ZIKV infection. These pharmaceutical medicines are effective against ZIKV illness symptoms.^[4] *Tinospora cordifolia* is a herb that has been used as a potential immunomodulator and effective natural therapy for viral sickness of any kind for many years. It strengthens the immune system and makes the body more resistant to illnesses. These herbs enhance macrophage phagocytic capacities.^[45] Because the astringent properties of these ayurvedic plants effectively treat intestinal sickness, urinary tract infections, dengue fever, and swine influenza, they may also be effective against ZIKV.^[46]

DISCUSSION

This data analyses the zika virus outbreak globally using EpiWatch data. This data shows us the zika virus outbreak from 2016 to 2019 and 2021. The greatest cases of zika were recorded in 2016. The peak decline substantially in 2017-19. Zika virus affects not only the population but also other factors including adults, pregnant women, and infants with mild to severe symptoms consisting of rash on the skin, fever, muscle cramps, conjunctivitis, birth defects, and muscle paralysis. The major problem is the pregnant women are at high risk of zika infection disease such as microcephaly.^[47,48]

Zika virus has also been recorded as a vector-borne disease and it can be also defects with other routes such as sexually, bloodborne transmission, travel-related cases have also been recorded by EpiWatch.^[49,50] There is a higher number of travel-related cases in 2016 and 2017. The study shows 96% of cases of zika infection who had a history of traveling to prone areas. Also, this highlights the importance of travel advisories, by appropriate information and precautionary approaches for pregnant women and sexually. Also, the Centre for disease control and prevention (CDC) has reported cases that are due to travelling and tourism during peaks and such kind of warning should be given to affected countries for prevention.

Also, zika related deaths have been reported in severe cases like Guillain Barre syndrome (GBS) in patients like adults and older age and some infants who had cause microcephaly disease.^[51] Also, the studies have shown cases such as fetal deaths and birth defects and severe neurological disorders causing deadly paralysis. Zika is a classic TORCH (Toxoplasma, other, Rubella, Cytomegalovirus, and Herpes) infection that reaches the embryonic brain during pregnancy, according to various research.^[52] Furthermore, the CDC warned that the re-emergence of two major zika virus lineages, Asian and African, may contribute to illness transmission and dissemination in many nations.^[53,10] Climate change favours the transmission of zika infection during rainy and wet seasons showing the seasonal surge and increasing number of infections in the United States,

India, Mexico, Singapore, Thailand, Vietnam. The upsurge of infection was founded during the tropical and subtropical regions.^[54,55]

WHO provided a global review of zika infection across six regions- African, Region of America, South-East Asia, Western Pacific. WHO publishes a cumulative situation summary. This it is very difficult to analyse the cases. Brazil followed by African Region with cases of microcephaly in Africa, West Pacific, south-east Asia were recorded highest number of cases provided by WHO.

CONCLUSION

Zika virus needs to be monitored closely in countries that are experiencing outbreaks, so they can provide accurate information. The virus is known to cause mild symptoms when infected. Microcephaly is the only major disease caused by the zika virus. Several other measures have been taken for proper control of mosquitoes such as tire traps, genetically altering of mosquitoes, and the billboard of trapping mosquitoes. This study provides a global analysis of zika out over time about epidemiology.

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