WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.453
Volume 14, Issue 1, 1068-1085. Review Article ISSN 2277–7105

UNDERSTANDING THE EMERGENCE AND IMPACTS OF ZIKA VIRUS: PATHOGENESIS, TRANSMISSION, AND CLINICAL OUTCOMES

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Article Received on
18 November 2024,

Revised on 08 Dec. 2024,
Accepted on 28 Dec. 2024

DOI: 10.20959/wjpr20251-34939

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ABSTRACT

The Zika virus (ZIKV) is an emerging mosquito-borne flavivirus that has become a significant public health concern due to its rapid spread and severe implications, including congenital microcephaly and neurological disorders. Initially identified in Uganda in 1947, ZIKV remained relatively obscure until a major outbreak occurred on Yap Island in 2007, followed by a larger epidemic in French Polynesia in 2013-2014. The virus gained widespread attention in 2015 when it reached pandemic levels in the Americas, particularly in Brazil, where a significant increase in microcephaly cases was observed. ZIKV is primarily transmitted by Aedes mosquitoes but can also spread through sexual contact, blood transfusion, and from mother to foetus. The virus's ability to infect various tissues, including the brain, placenta, and reproductive organs, has been linked to severe developmental issues in foetuses, particularly microcephaly, and neurological complications such as Guillain-Barré syndrome in adults. Research into ZIKV's pathogenesis has revealed that the virus can evade the host immune system, leading to prolonged infections and contributing to its severe clinical outcomes. Ongoing studies aim to understand the molecular mechanisms underlying ZIKV infection, with the goal of developing effective diagnostics, vaccines, and treatments. Despite

advancements, the virus's rapid mutation and ability to adapt to different hosts continue to challenge public health efforts, underscoring the need for continued vigilance and research.

KEYWORDS: Zika Virus (ZIKV), Microcephaly, Epidemiology, Mosquito-borne diseases, Pathogenesis.

INTRODUCTION

Zika virus (ZIKV) is an emerging mosquito-borne virus that was first discovered in 1947 in Uganda, where it caused occasional human cases. In 2007, Yap Island experienced its first outbreak, with almost 75% of the population infected with ZIKV. In 2013 and 2014, a second epidemic was reported in French Polynesia and the Pacific Islands. However, it wasn't until 2015 that ZIKV transmission reached pandemic levels and reached the American continent. In May 2015, Brazil reported the first human case of ZIKV infection in the Americas.[1]

Subsequently, several countries reported an increase in the incidence of infection, which was followed by an unexpected decrease in Zika cases since 2017. Arthropods are the main means of transmission for the Zika virus (ZIKV) and other arboviruses, including the African swine fever virus, the Crimean-Congo hemorrhagic fever virus, the dengue virus (DENV), and the West Nile virus (WNV). Interestingly, all of these viruses have the ability to spread sexually, with ZIKV having the most research done on this front. Moreover, it has been established that ZIKV can spread by additional routes, such as blood transfusions, saliva, breast milk, and vertical mother-to-foetus transmission.[2]

With regard to ZIKV infection, it is noteworthy that case reports linked it to microcephaly, which prompted the World Health Organization to proclaim a Public Health Emergency of International Concern in February 2016.[1]

ZIKV BIOLOGY

Initially identified in 1947 from the serum of a febrile sentinel rhesus macaque (Macaca mulatta) in the Zika Forest area near Entebbe, Uganda, the Zika virus (ZIKV) is a flavivirus spread by mosquitoes. It was later discovered in Aedes africanus mosquitoes in the same area (Dick 1952; Dick et al. 1952). The virus is a member of the genus Flavivirus under the family Flaviviridae, which also includes other vector-borne viruses important to human health, including the West Nile virus (WNV), dengue virus (DENV), yellow fever virus (YFV), and Japanese encephalitis virus (JEV).[3]

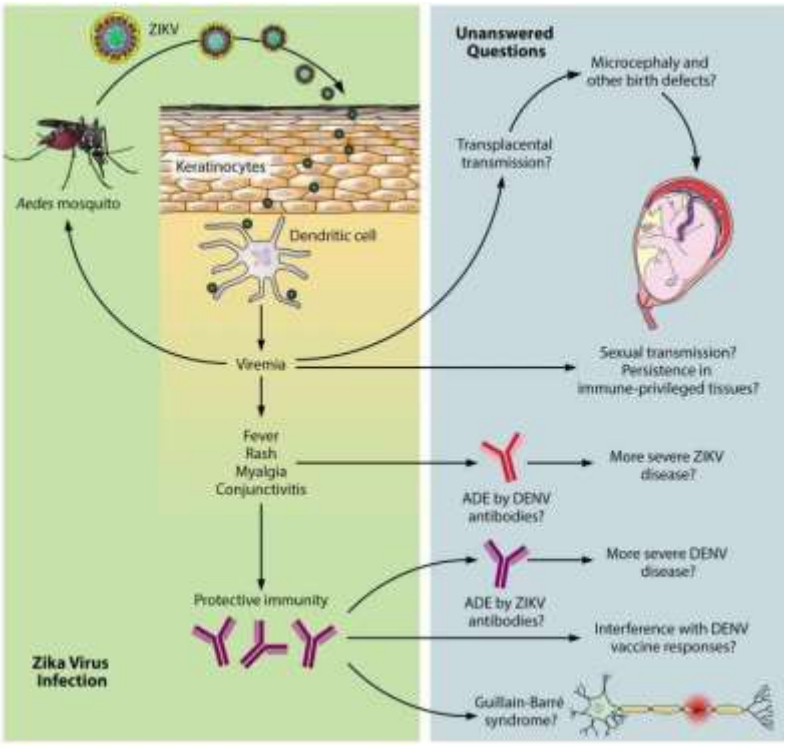

Fig. 1: Life Cycle of ZIKV.

METHODOLOGY

- **Culture and Inactivation of Viruses**

According to Moser and colleagues' description, the Zika virus (Brazilian isolate, ZIKVBR) produced in Vero E6 cells and titrated in Vero cells. Thermal treatment was used to inactivate the virus for one hour at 56 °C.[4]

- **Atomic Force Microscopy**

The AFM measurements were conducted with the same methods as Cardoso-Lima et al., wherein glass slides with a 13 mm diameter were coated with 10 µL of a solution containing viral particle suspensions. The slides were previously handled using poly-L- lysine 1% (Sigma, St. Louis, MO, USA) to promote ZIKV particle adhesion to glass slide surfaces (just for fluid measurements).[5]

This is achieved through the interaction of the negatively charged viral particles with the positively charged polymers in the poly-l- lysine. The slides were examined using Multimode 8 (Bruker, Santa Barbara, CA, USA), and the probes utilized in the peak force quantitative nano mechanics analysis were SNL (Bruker) with a nominal spring constant of 0.06 N/m and a radius of 2 nm radius in the peak force quantitative nano mechanics (QNM) mode configuration. The Gwydion 2.57 software was utilized to compute the structural properties

of the viral particles by using boundary grain detection to the 2 µm2 scan area topographic pictures. These areas provided statistical data on the diameter and height of 107 particles. With dried materials, the diameter measurements were carried out in an ambient environment.[6]

The measurements were conducted within 4 hours after the sample preparation, adhering to the Oropesa et al. protocol, hence the impact of these circumstances was not taken into account for the diameter measured. AFM measurement of dehydrated virus-like particles. Given that the radius is just around 3% of the particle's size, the impact of the tip radius is insignificant and was not taken into account.[7]

Nine distinct viral particles were used in the indentation trials, and each one underwent between thirty and seventy indentation cycles. Analysis of adhesion maps was done on six virus particles.[6]

The measurements for the indentation analysis were made using the QNM Ramp Mode in fluid, adhering to the same protocol as Cardoso-Lima et al. We used a tip velocity of 100 nm/s and a force setpoint of around 6 nN. With the use of software called Mountains SPIP8 and Nano scope Analysis, AFM data were examined and maps produced.[7]

EPIDEMIOLOGICAL STUDIES

- **Surveillance**
  - **Active surveillance:** Proactive case-finding through regular screening of populations, especially in high-risk areas.
  - **Passive surveillance:** Relies on healthcare providers to report suspected cases.
  - **Syndromic surveillance:** Monitors disease clusters based on symptoms rather than specific diagnoses.
- **Case-control studies:** Compare individuals with ZIKV infection (cases) to those without (controls) to identify risk factors.
- **Cohort studies:** Follow groups of people over time to assess the incidence of ZIKV infection and its outcomes.
- **Mathematical modelling:** Uses statistical and computational methods to simulate the spread of ZIKV, evaluate intervention strategies, and predict future outbreaks.

Virological and Molecular Studies

- **Virus isolation:** Cultivating ZIKV in cell culture to obtain sufficient quantities for further study.
- **Molecular characterization:** Determining the genetic sequence of the virus to understand its evolution and relationship to other flaviviruses.
- **Real-time RT-PCR:** Detecting and quantifying ZIKV RNA in clinical specimens.
- **Droplet digital PCR:** Highly sensitive and precise method for quantifying viral load.
- **Next-generation sequencing:** Analyzing the complete genome of the virus to identify genetic variations and potential drug targets.

Serological Studies

- **Enzyme-linked immunosorbent assay (ELISA):** Detecting antibodies against ZIKV in blood samples.
- **Neutralization tests:** Measuring the ability of antibodies to prevent the virus from infecting cells.
- **Immunofluorescence assay (IFA):** Detecting ZIKV-specific antibodies in patient sera.

Clinical Studies

- **Case series and case reports:** Detailed descriptions of individual patients with ZIKV infection to identify clinical features and complications.
- **Cohort studies:** Following groups of people with ZIKV infection to assess long-term outcomes.
- **Clinical trials:** Testing the safety and efficacy of potential treatments or vaccines.

Vector Studies

- **Entomological surveys:** Studying the distribution and abundance of Aedes mosquitoes, the primary vectors of ZIKV.
- **Vector competence studies:** Determining the ability of mosquitoes to transmit the virus.
- **Larvicide and adulticide efficacy trials:** Evaluating the effectiveness of mosquito control measures.

Animal Models

- **Mouse models:** Developing genetically modified mice susceptible to ZIKV infection to study pathogenesis and evaluate potential treatments.

- **Non-human primate models:** Using primates to study ZIKV infection and its impact on foetal development.

Imaging Studies

- **Ultrasound:** Assessing foetal growth and development in pregnant women with ZIKV infection.
- **Magnetic resonance imaging (MRI):** Evaluating brain abnormalities in infants with microcephaly.

Other Methodologies

- **Geographic information systems (GIS):** Mapping the spatial distribution of ZIKV cases to identify risk areas.
- **Meta-analysis:** Combining the results of multiple studies to draw conclusions about the overall effect.
- **Systematic reviews:** Critically evaluating and summarizing the available evidence on a specific topic.

MICROCEPHALY ASSOCIATED WITH ZIKV

An infant with microcephaly, a rare disorder, is born with an unusually tiny head as a result of the radial glia population being reduced due to either cell death, cell cycle arrest, or early differentiation. Before contracting ZIKV, the possible reasons diseases (such as rubella, toxoplasmosis, or CMV), maternal malnourishment, drug misuse, genetic predispositions, or exposure to the environment during pregnancy were among the causes of microcephaly.[8]

Nonetheless, ZIKV infection was suggested as a potential cause of microcephaly due to the rise in instances of microcephaly and other birth problems recorded in northeast Brazil during the first ZIKV epidemic in South America in October 2015. In the northeast of Brazil, the microcephaly rate was 48 per 10,000 newborns at first. Though it hasn't happened in other Brazilian states (the southeast has 5.5–14.5 births per 10,000).[9]

Rate of microcephaly, respectively or in other nations where ZIKV has proliferated, the peak was 24 times greater than the mean microcephaly frequency. Data from pregnant women with ZIKV infection during pregnancy was recently gathered by the United States and its freely affiliated states, and it revealed that some live-born children had CZS.[10]

Children diagnosed with ZIKV infection who are born with congenital microcephaly have well- characterized early childhood development. Evaluation of these children's growth and development between birth and 26 months revealed feeding issues, sleep issues, severe motor deterioration, cerebral palsy, abnormalities of vision and hearing, and seizures, indicating that the virus causes severe neurological impairments during foetal development and in the first two years of infected individuals' lives. Larger research is yet required to fully comprehend the neurological and cognitive ramifications. While there is a strong correlation between ZIKV infection and a higher risk of microcephaly in expectant mothers, the exact mechanisms by which the virus causes microcephaly remain unclear.[11]

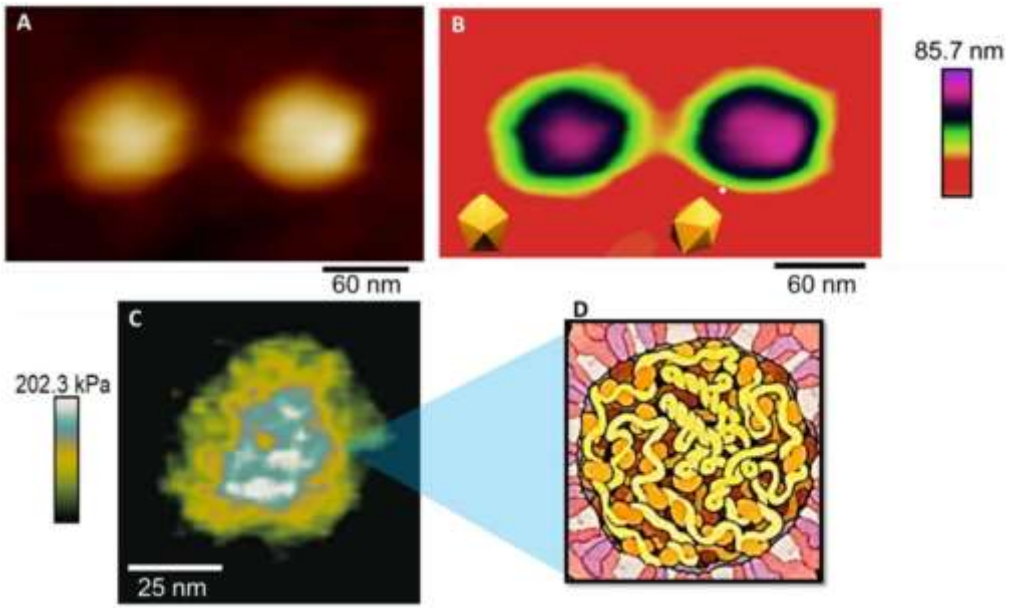

Fig. 2: Molecular Analysis of ZIKV.

A) Heightmap of two ZIKV particles;
B) The same particles with a different height scale contrast, evidencing the icosahedral type of the adsorption pattern.
C) Young Modulus map showing internal structure arrangement.
D) Pictographic representation of the internal assembly of the ZIKV.

MODES OF TRANSMISSION

1. Vector-borne transmission.

ZIKV is a virus that is spread by mosquitoes. Although ZIKV has been isolated from a wide variety of Aedes mosquito species, only a small portion of them (Ae. aegypti, Ae. albopictus, Ae. hensilii, and Ae. polynesiensis) are capable of transmitting the virus.[12]

The insect Aedes aegypti is believed to be the main vector responsible for spreading ZIKV during the ongoing outbreak in Latin America and the Caribbean; this is probably because the mosquito is anthropophilic and abundant in urban areas. Although the main species of ZIKV has not been identified, monkeys are thought to act as reservoir hosts for the virus.[13]

It's uncertain if ZIKV will spread primarily through urban transmission cycles or if it will become endemic in New World monkeys and create a sylvatic transmission cycle in Latin America similar to that observed with YFV. In spite of the fact that there have been widespread ZIKV outbreaks on the Micronesian island of Yap, there are no nonhuman primates living there. There is presently no proof that nonhuman primates and animals other than humans act as amplifying hosts for ZIKV, implying a transmission method akin to DENV, YFV, and CHIKV. ZIKV epidemics are mostly caused by mosquito-borne transmission, however there have also been reports of alternative mechanisms of transmission.[12]

2. Blood-bornetransmission.

A ZIKV viraemic donor might possibly contaminate the blood supply, much like in the case of other blood-borne viruses. Although ZIKV transmission through donated blood transfusions has not yet been reported, instances have been recorded in Brazil. Many regions, such as the US, Canada, and Europe, already have an adequate supply of blood. Once a screening test is developed, the same strategy might be used to identify ZIKV. Plans are in place in a number of nations to either screen the blood supply for ZIKV or to postpone blood donation from individuals who have visited nations where ZIKV is circulating.[14]

3. Sexual transmission

ZIKV has been shown to be sexually transmitted, and semen has been shown to contain ZIKV RNA. All documented cases of ZIKV that have been transmitted sexually males that are afflicted have infected their female companions.[15]

Even after viremia had cleared (undetectable ZIKV RNA in serum), infectious ZIKV was found in semen even in cases where hematospermia was present, supporting the idea that bloodborne transmission is unlikely. Furthermore, not all instances of sexually transmitted ZIKV infection have shown hematospermia, despite the fact that this is a typical presentation of other sexually transmitted illnesses. reports of infectious ZIKV in urine and ZIKV discovery in recent times.[16]

4. Maternal Transmission

Breast milk has been found to contain ZIKV RNA. Mothers with ZIKV infection may be able to transfer the virus to their nursing infants, since this mode of transmission has been reported for other flaviviruses as well. Mothers with ZIKV infection are still advised to nurse their children, however it is unknown if infectious ZIKV is present in breast milk or how long it could last in comparison to an acute illness. There have been reports of ZIKV being transmitted to infants in French Polynesia, however it is unclear if this was due to in utero, breast milk, or blood-borne transmission following delivery.[17]

Since the emergence of ZIKV in Brazil has coincided with a concerning rise in microcephaly cases—the northeastern states have reported ~4,000 cases over about 4 months, a more than 20-fold increase from previous years, the issue of in utero transmission has become more urgent. A congenital condition known as microcephaly causes the embryonic brain to grow inadequately. Microcephaly is not universally defined; criteria vary from a newborn's head circumference measuring 32 cm to 33 cm to being 2 to 3 standard deviations below the gestational age mean.[18]

PATHOGENESIS OF ZIKV

Despite the lack of current research on ZIKV pathogenesis to explain the putative microcephaly seen in Brazil, studies conducted 40 and 60 years ago on mice may have shown that ZIKV has a tropism for brain cells in some situations. After an intracerebral inoculation with the serum of a feverish sentinel rhesus macaque, the brain of a 5- to 6-week-old Swiss mouse was used by George Dick and colleagues in 1947 to isolate the initial ZIKV strain (MR 766).[19]

Subsequently, the same group demonstrated that intracerebral injection of mice of varying ages with passaged ZIKV strains resulted in indications of central nervous system (CNS) illness, such as motor weakness and paralysis. When administered intraperitoneally, animals younger than 7 days of age were susceptible to a fatal ZIKV infection, but mature mice showed decreased susceptibility. The disease's pathological signs and symptoms were limited to the CNS tissues in mice.[20]

In addition, a pathological examination of a human foetus infected with ZIKV in utero revealed evidence of neural damage. Diffuse astrogliosis and microglia activation were seen in this instance, along with damage to the spinal cord and brain stem as well as Wallerian

degeneration of the descending corticospinal tracts. No other tissue, such as the kidney, lung, spleen, or liver, sustained a substantial ZIKV infection outside of the central nervous system. In contrast, even after intracerebral vaccination, rhesus monkeys, cotton rats, guinea pigs, and rabbits did not have CNS illness. Infection of human keratinocytes, dermal fibroblasts, and skin biopsy specimens was shown in more recent experiments employing a ZIKV isolate from French Polynesia. This is consistent with the skin being the first site of ZIKV replication following mosquito bites.[21]

Zika virus (ZIKV) is a significant public health threat, with its ability to rapidly mutate and cross species barriers, making it a formidable and constantly evolving pathogen. The virus's pathogenesis has been extensively studied, and it is believed that its ability to manipulate the host's immune system plays a critical role in its ability to cause a range of severe diseases, including microcephaly, Guillain-Barré syndrome, and other neurological disorders.[20]

The viral genome of ZIKV is composed of a single-stranded RNA molecule, 10,794 nucleotides in length, with a lipid envelope containing three structural proteins: capsid, pre-membrane, and envelope. The virus is thought to start its infection by invading the host cells, typically mononuclear cells such as macrophages and dendritic cells, leading to a systemic infection and the production of viral particles that can be transmitted through both vertical and horizontal routes.[22]

The pathogenesis of ZIKV involves a complex interplay between the virus and the host's immune system. The virus has the ability to evade the host's immune defences, leading to a prolonged and undetected infection, which can increase the risk of reproductive complications and neurological disorders. This manipulation of the host's immune system can result in a range of immunological responses, including pro-inflammatory and anti-inflammatory reactions, further contributing to the diverse clinical manifestations observed in ZIKV infections.[23]

Understanding the intricate molecular mechanisms underlying ZIKV's pathogenesis and its interaction with the human host is crucial for the development of effective diagnostic tests, vaccines, and treatments. Ongoing research aims to elucidate the complex network of interactions between ZIKV and the host, with the ultimate goal of combating this significant public health threat.[24]

The rapid mutation and adaptive capabilities of ZIKV, which allow it to infect different mosquito species and hosts, present a formidable challenge for public health control measures and vaccine development. Researchers are working tirelessly to stay ahead of this constantly evolving pathogen, leveraging their knowledge of ZIKV's epidemiology, pathogenesis, and immunology to devise innovative strategies to combat this emerging infectious disease, transmission dynamics.[25]

VIRAL ENTRY AND REPLICATION

- **Viral attachment:** ZIKV enters cells through receptor-mediated endocytosis. The viral envelope protein interacts with specific receptors on the host cell surface.
- **Uncoating:** Once inside the cell, the viral envelope is removed, releasing the viral genetic material (RNA).
- **Replication:** The viral RNA is translated into viral proteins, which then replicate the viral genome.

IMMUNERESPONSE

- **Initial immune response:** The body's immune system responds to ZIKV infection, but the exact nature of this response is still under investigation.
- **Immunopathology:** In some cases, the immune response itself may contribute to tissue damage.
- **Viral persistence:** ZIKV can persist in certain tissues, such as the placenta and testes, leading to long-term consequences.

IMPACTONTHEDEVELOPINGFETUS

- **Placental infection:** ZIKV can infect the placenta, leading to impaired placental function and reduced foetal growth.
- **Foetal brain damage:** The virus can directly infect foetal brain cells, causing microcephaly (abnormally small head) and other neurological abnormalities.
- **Other foetal complications:** ZIKV infection during pregnancy has been associated with other birth defects, including eye problems, hearing loss, and joint contractures.

Neurological Complicationsin Adults

- **Guillain-Barré syndrome:** A neurological disorder that can cause muscle weakness and paralysis.

- **Other neurological manifestations:** Although less common, ZIKV has been linked to encephalitis, meningitis, and other neurological complications in adults.

Key Factors in ZIKV Pathogenesis

- **Viral factors:** The specific strain of ZIKV and its genetic makeup can influence disease severity.
- **Host factors:** Individual genetic susceptibility, immune status, and pregnancy status can affect the outcome of infection.
- **Environmental factors:** Factors like mosquito density and climate can impact the spread of the virus.

CLINICAL FEATURES OF ZIKV

In the past, human ZIKV infection has resulted in a varied clinical presentation that ranges from no symptoms at all to an influenza-like viral disease that first resembled illnesses brought on by other pandemic arboviruses, such as DENV and CHIKV. Hospitalization is uncommon, however 20% of infected people with ZIKV go on to have a fever that is clinically noticeable. Usually appearing 3–7 days after mosquito inoculation, signs and symptoms of ZIKV infection include fever that spikes suddenly, headache, arthralgia, myalgia, conjunctivitis, vomiting, lethargy, and/or maculopapular rash.[26]

For a long time, ZIKV infection was thought to be self-limiting with no long-term effects. However, during the more recent ZIKV outbreaks in the South Pacific and Latin America, more serious complications have emerged. This could be because the higher infection rate has made it easier to detect and report rare outcomes, though other factors may also play a role in the increased pathogenesis of ZIKV. ZIKV infection has been linked to thrombocytopenia and hematospermia, but it has not been documented to induce the plasma leakage and bleeding seen with severe DENV disease. There are no documented fatal ZIKV cases in otherwise healthy individuals. In individuals with comorbidities, such as sickle cell disease, ZIKV- associated mortality has been documented; moreover, congenital ZIKV infection and post-ZIKV Guillain- Barré syndrome (GBS) can be lethal.[27]

Neurological issues were associated with ZIKV infection during the 2013–2014 epidemic in French Polynesia due to a rise in GBS incidence, a postinfection autoimmune neuropathy that can cause weakness, paralysis, and even death. According to a case-control analysis of the epidemic, there were 0.24 instances of GBS for every 1,000 ZIKV infections, suggesting that

GBS patients had a higher likelihood of having prior ZIKV infection than controls. Compared to patients with GBS from other etiologies, individuals with post-ZIKV GBS exhibited atypically low levels of anti- ganglioside antibodies, indicating that ZIKV may cause GBS by mechanisms distinct from those of other causes.[26]

Brazil, El Salvador, Colombia, and Venezuela have also reported cases of a diffuse demyelinating disease comparable with GBS that are temporally related with ZIKV infection. To fully comprehend the connection between ZIKV infection and GBS, especially the pathophysiological processes involved, more research is required.[28]

There are a few potential explanations:

1. Immunopathology brought on by the virus's antigen mimicking a host protein.
2. Virus sequence alterations that lead to increased peripheral nerve system tropism.
3. A connection to previous or ongoing immunological responses to DENV.

The most alarming development is the significant rise in infant microcephaly cases in northeastern Brazil, which is linked to pregnant women's ZIKV infection. Several suspected intrauterine ZIKV infections ledto extensive cerebral calcifications in various brain areas of foetuses in utero or newborn babies. In addition, a recent investigation on a microcephalic foetus that recovered following an elective termination at 32 weeks of gestation found several calcifications in the frontal, parietal, and occipital lobes of the cerebral cortex, both cortically and subcortically. A foetus with microcephaly was found to have hydrops fetalis and hydranencephaly, which were followed by foetal death.[27]

SYMPTOMS OF ZIKA VIRUS

Zika symptoms usually last several days to a week and clear up on their own, and hospitalization is rare. The best way to prevent Zika is to avoid mosquito bites if you are in an affected area. You can also try these steps to prevent mosquitoes:

- Empty, turn over, or remove anything that holds water, like buckets, toys, and vases
- Get rid of old tires or drill holes in the bottom of tire swings
- Clear clogged rain gutters
- Treat rain barrels for mosquitoes
- Seal openings
- Patch torn screens
- Repair leaky faucets

- Empty bird baths or change the water weekly
- Empty wading pools when not in use

DIAGNOSIS OF ZIKV INFECTION

It is difficult to differentiate ZIKV from other viral infections clinically since it creates a vague influenza- like illness without pathognomonic characteristics. This is particularly valid given that ZIKV cocirculates and uses the same mosquito vectors as DENV and CHIKV, both of which cause fever, rash, arthralgia, and myalgia as its typical symptoms. Recent investigations have described coinfection of various arboviruses, such as ZIKV and DENV, in addition to cocirculation.[28]

The gold standard for diagnosing ZIKV is a laboratory-based diagnosis because clinical diagnosis might be difficult. The most accurate diagnostic method available today, aside from direct viral isolation, which can be challenging outside of highly specialized laboratories, is an assay based on reverse transcription- PCR (RT-PCR) that finds ZIKV RNA and able to differentiate between ZIKV and other viral illnesses, such as DENV and CHIKV. Serum RT-PCR tests are highly specific, but their sensitivity rates are poor because ZIKV viremia in people only lasts for a period of three to five days. Samples of saliva and urine may be more useful than serum for RT-PCR diagnosis of ZIKV infection because viral RNA may be found in these bodily fluids at higher loads and for longer periods of time.[16]

The current state of research indicates that accurate diagnostic tests for Zika virus infection are necessary to differentiate it from other flavivirus infections, identify pregnant women who may be at risk of developing complications from the virus, and ensure the safety of transfusion and transplantation in areas where the virus is actively being spread by mosquitoes. Currently, diagnostic tests for viral RNA can often detect Zika virus during the acute phase of infection and up to 14 days after the onset of symptoms. Antibody-based tests can also detect prior Zika infection; however, these tests may also detect or cross-react with antibodies against other flaviviruses, particularly dengue virus.[24]

TREATMENT OF ZIKV VIRUS

There is no specific treatment or vaccine for Zika virus infection, but symptoms can be treated. If you have symptoms like fever, rash, or joint pain, you should:

- Rest
- Drink fluids to avoid dehydration

- Take over-the-counter medicine like acetaminophen (Tylenol) to reduce pain and fever

PREVENTIONS ON ZIKV VIRUS

- **Avoid being bitten by mosquitoes**

Wear long sleeves and pants, sleep in air-conditioned or screened-in rooms, and apply an EPA- registered insect repellent according to the directions on the package. Although female mosquitoes can bite at other hours, they are most active between dawn and dusk. In order to keep mosquitoes out of your home, you may also remove standing water and water sources, close windows, or use window screens.[19]

- **Prevent sexual transmission**

Avoid having intercourse with somebody who could be contaminated, or use condoms appropriately. For at least three months, biological men should use condoms, and for at least two months, biological females should use condoms or refrain from having intercourse.[29]

Additionally, you should stay away from touching blood, vaginal fluid, and semen from individuals who may be contaminated. This covers visitors who return from Zika-affected regions up to three months after leaving or becoming ill. In addition, sharing needles is another way that the infection can spread.[30]

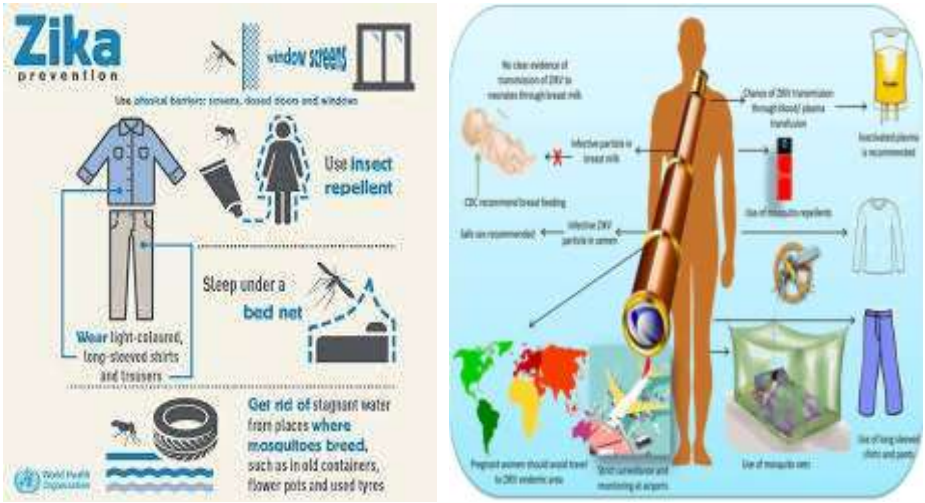

Fig. 3: Preventive Measures for ZIKV.

CONCLUSION

Zika virus (ZIKV) is a rapidly evolving pathogen that poses a significant public health threat due to its ability to mutate, cross species barriers, and spread through various transmission modes. The virus, primarily transmitted by Aedes mosquitoes, has been linked to severe

neurological conditions, including microcephaly in newborns and Guillain-Barré syndrome in adults. The global spread of ZIKV, particularly in the Americas since 2015, highlighted the need for enhanced surveillance, research, and intervention strategies.

ZIKV's pathogenesis is complex, involving interactions between the virus and the host's immune system, which can lead to a range of clinical manifestations from mild symptoms to severe complications. The virus's ability to persist in certain tissues, such as the placenta and testes, further complicates its control and treatment. Research into the molecular mechanisms of ZIKV infection is critical for developing effective vaccines, treatments, and public health strategies.

Despite significant progress in understanding ZIKV, challenges remain, particularly in addressing the long-term impacts of infection and preventing future outbreaks. Continued research and innovation are essential to combat this evolving virus and mitigate its impact on global health.

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