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Muhammad Ali Tahir¹, Kashif Hussain², Asghar Abbas², Muhammad Umair Waqas², Nauman Zaheer Ghumman³, Muhammad Muneeb⁴, Muhammad Shoaib Shafqat¹, Sohaib Khan⁵, Ugochukwu, Iniobong Chukwuebuka Ikenna^{6,7}, Junaid Ali Khan², Sugiharto sugiharto⁸ and Muhammad Asif Raza^{2,8,9}

ABSTRACT

The Zika virus (ZIKV) has emerged as a serious threat to global health. To fully understand the virus's epidemiology, virology, dynamics of transmission, clinical symptoms, implications for public health, and preventive and control measures, extensive research and collaboration have been conducted. The virological investigation compares strains from Asia and Africa and highlights distinctive features present in the virus's genome to investigate the genetic variability of ZIKV lineages.

The chapter delves into the complex processes of Zika virus transmission, specifically highlighting the primary carriers—Aedes aegypti and Aedes albopictus mosquitoes. It elucidates not only the conventional vector-borne pathways but also non-vectoral modes like blood transfusion and sexual contact. It comprehensively details the diverse clinical manifestations of ZIKV infection, placing particular emphasis on the profound impact on expectant mothers and its link to neonatal Zika illness. Symptoms vary from mild, resembling dengue fever, to severe neurological complications, presenting a spectrum of health challenges.

The significance of ZIKV for public health is underlined, underscoring the critical requirement for effective preventive and control interventions. The chapter advocates for a comprehensive plan that includes mosquito control methods, vaccine development, and public awareness initiatives to lessen the spread of ZIKV. The paper also examines the challenges and potential solutions for managing and preventing ZIKV, including mechanical, chemical, and biological approaches to mosquito population reduction.

The final sections of the chapter delve into ongoing research and progress in treatment strategies for Zika virus (ZIKV), exploring potential treatments and their mechanisms of action. The abstract concludes by underscoring the critical importance of collaboration among academia, policymakers, and the global health community. This collaboration is essential to collectively address the multifaceted challenges posed by ZIKV and mitigate its adverse impact on public health.

Keywords: Zika Virus, Arboviral disease, Virology, Transmission dynamics, Clinical manifestation, public health implications, Prevention and control strategies

CITATION

Tahir MA, Hussain K, Abbas A, Waqas MU, Ghumman NZ, Muneeb M, Shafqat MS, Khan S, Ikenna UIC, Khan JA, Sugiharto S and Raza MA, 2023. Zika virus: an arboviral disease. In: Aguilar-Marcelino L, Zafar MA, Abbas RZ and Khan A (eds), Zoonosis, Unique Scientific Publishers, Faisalabad, Pakistan, Vol 3: 204-215. <u>https://doi.org/10.47278/book.zoon/2023.97</u>



¹Department of Pathobiology, Bahauddin Zakariya University, Multan

²Department of Pathobiology, MNS- University of Agriculture, Pakistan

³Department of Veterinary Medicine, University of Veterinary and Animal Sciences, Lahore

⁴Department of Pathology, University of Agriculture Faisalabad

⁵Livestock and Dairy Development Department, Punjab.

⁶Department of Veterinary Pathology and Microbiology, University of Nigeria, Nsukka.

⁷Dipartimento di Medicina Veterinaria, Universita degli Studi di Bari, Valenzano, Bari.

⁸Department of Animal Science, Faculty of Animal and Agricultural Sciences, Universitas Diponegoro, Semarang, Central Java Indonesia (50275)

⁹Xinjiang Agricultural Vocational Technical College, Changji, China

*Corresponding author: Kashif.hussain@mnsuam.edu.pk; Asghar.abbas@mnsuam.edu.pk

1. INTRODUCTION

After being discovered in 1947 in Uganda, the Zika virus (ZIKV) was initially restricted to equatorial Africa and Asia for 60 years, but it was first discovered outside this region in 2007 on Yap Island. From there, the virus spread to other Pacific Islands in 2013–2014, then to Latin America in 2015, and finally to North America in 2016. Its connection to fetal microcephaly caused made it a health emergency in 2016. (Ramos da Silva and Gao 2016; Song et al. 2017). The United States' Center for Disease Control and Prevention (CDC) has confirmed 4,944 and 36,367 cases of Zika Virus in USA. Infection with ZIKV has so far been documented in 66 countries. ZIKV, which has been identified as a neurotropic virus, has been connected to several diseases, primarily in countries that were exposed to it during the Federated States of Micronesia pandemic in 2007, which showed up as a variety of neurological problems. The most noticeable consequence of ZIKV infection that has been noticed is the abrupt increase in fetal microcephaly incidence in Brazil (Ramos da Silva and Gao 2016).

A Brazilian outbreak that was characterized by a rash-like skin eruption accompanied by pyrexia and a dramatic rise in the number of infants and fetuses with microcephaly at the end of 2015 made the Zika virus (ZIKV), which was first identified 70 years ago, a public health concern (Duffy et al. 2009; Teixeira et al. 2016). Since then, researchers from all over the world have been frantically trying to understand the pathogenesis of ZIKV infection. They are particularly interested in discerning the differences between the infection brought on by the first described strain of African MR766, which only caused a few mild symptoms. Additionally, they aim to compare it to the infection found in Asia in 2007 on Yap Island of the Federated States of Micronesia and later in French Polynesia in 2013, which resembles the infection in Brazil. Nearly every day, fresh scientific data about ZIKV is made public (Duffy et al. 2009; Bradley and Nagamine, 2017; Krause et al. 2017).

In Uganda's Zika Forest, ZIKV was initially discovered in a monkey in 1947 and an Aedes africanus in 1948 (Lanciotti et al. 2008). In the following years, the outbreak occurred in individuals across several regions of Africa as well as South and Southeast Asia (Wikan et al. 2017) Based on the area, Zika virus virus outbreaks from 2007 to 2015 had differential influences. Only modest symptoms such as a fever, headaches, and skin rashes were reported by the majority of Yap Island's inhabitants during an epidemic in 2007 (Khatri et al. 2018.) In 2013, the virus was transmitted to French Polynesia (Cao-Lormeau et al. 2016).

ZIKV was discovered for the first time in Brazil in 2015. The number of infants and fetuses with microcephaly had accelerated by the end of the year (Cardoso et al. 2015). Infections with Zika virus infection was deemed a Public Health Emergency of International Concern by the World Health Organization (WHO) in February 2016 (Heymann et al. 2016) and the United States Center for Disease



Control and Prevention (CDC) confirmed the link between ZIKV infection and microcephaly in April 2016 (Rasmussen et al. 2016).

2. VIROLOGY

This far, description of the ZIKV lineages from Asia and Africa have been published. The variants isolated from samples in Brazil between 2015 and 2016 were strikingly identical to the Asian strains as well as the French Polynesia strain (Giovanetti et al. 2016; Sheridan et al. 2018). A part of the Flavivirus genus and the Flavivirus family, ZIKV is an arbovirus which also includes the following viruses: Dengue virus (DENV-1 through DENV-4), West Nile virus (WNV), Japanese encephalitis virus (JEV), and Yellow fever virus (YFV) (Gubler and Musso 2016).

Single full gene encodes (ORF), less than 11 kb in size, makes up the ZIKV genomes. It comprises seven non-structural proteins, such as NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS5, in addition to various structural proteins, as well as the capsid, envelope glycoprotein (E), membrane (M), or premembrane (prM), are also present like other flaviviruses. Depending on its newly disclosed 3.8 structure, the E protein's amino acids near Asn154 show significant variation from those of other flaviviruses (Sirohi et al. 2016). This glycoprotein possesses a glycosylation site for ZIKV at Asn154, while DENV has two glycosylation sites at Asn67 and Asn153 that influence viral assemble, escape, and pathogenicity, correspondingly (Ruiz Jimenez et al. 2022).

ZIKV encompasses an Asn154-based glycosylation location that has been connected with neurotropism. Differences in the glycosylation sites may be accountable for alterations in the phenotypic expression, pathogenicity, viability, and virulence of different strains of ZIKV (Beasley et al. 2005). However, it's uncertain whenever the variations arose in the initial isolated strains —possibly pushed on by the rapid spread African strains lacking specific glycosylation regions. The Asian and African lineages of ZIKV differed in 59 amino acids, with 10% of these mutations appearing in the prM region, as per a comprehensive examination of the available isolates (Wang et al. 2016).

One of the NS proteins named NS1, which also features N-glycosylation sites, is essential for the proliferation and subsequent invasion of flaviviruses (Muller and Young 2013). There seem to be distinctive electrostatic prospects between ZIKV, DENV, and WNV that may be included in the ZIKV NS1 due to the structural changes that have been recently discovered. The discrepancies in pathogenicity between these viruses and other ZIKV strains may be elucidated by these data. Numerous isolates from Brazil exhibited an NS1 mutant region as compared to other Asian strains, albeit the technique used in this study seemed uncertain. Other distinctive aspect of the ZIKV structure is its resilience along a temperature range, from 4 to 40°C (Kostyuchenko et al. 2016).

3. TRANSMISSION

The most prevalent vectors of ZIKV infection in humans are *Aedes aegypti* and *Aedes albopictus* mosquitoes, which are the major means of transmission. The first cycle of transmission is only seen in non-human primates classified as sylvatic, while the second cycle of transmission is through the human-mosquito-human cycle (urban cycle) (Petersen et al. 2016). In Brazil, ZIKV has recently been found in marmosets and capuchin monkeys, the majority of whom are kept as pets (Favoretto et al. 2016).

Recently, further transmission paths have been identified. After the ZIKV epidemic in South America, autochthonous transmission that was not aided by a mosquito has been documented in Brazil and Colombia, including an HIV-positive individual (Calvet et al. 2016). It has also been reported that ZIKV may be sexually transmitted through vaginal, oral, and anal intercourse, and that the virus can be found in



saliva, urine, and semen samples (D'Ortenzio et al. 2016). In a case reported in Italy (Venturi et al. 2016), sexual transmission of the ZIKV from Thailand was documented. Brazil has documented blood transfusion transmission from an asymptomatic donor (Cunha et al. 2016).

4. CLINICAL SIGNS

The incubation period of the Zika virus is reported to be 3-12 days, and in about 80% of the cases, the infection is asymptomatic (loos et al. 2014). The asymptomatic patient poses a great threat and is considered a perilous source of virus transmission (Musso et al. 2014). Initially, for 2-7 days, the mild "dengue-like" symptoms are shown by the virus, followed by a wide range of symptoms. The more noticeable signs and symptoms are a slight fever, arthralgia, edema of the extremities, headaches, retro-orbital pain, and maculopapular rashes (Heang et al. 2012). Furthermore, the major clinical symptom that characterizes the Zika virus is the eruption of maculopapular rashes, observed in around 90% of patients. Although the rash remains for 2-14 days, the fever generally lessens within one or two days after the onset of the rash (Mallet et al. 2015).

Normally, the fever is low, but in Brazil, the incidence of severe pyrexia, around 39° C, has also been reported (Zanluca et al. 2015). Regarding the symptoms of the Musculo-skeletal system, the Zika virus causes muscle, joints, and low-grade back pain. The pain is usually observed in the knees, ankle joints, and hands for one week and normally reduces after a week (Cao-Lormeau et al. 2014). Frequently, non-purulent conjunctivitis has also been observed in many cases of Zika virus infection. Other symptoms include vomiting, nausea, dizziness, and retroorbital pain (Moghadam et al. 2016) Infants and Children are also susceptible to Zika virus infection, and similar signs are observed in them as in adults (Lebov et al. 2018).

Likewise, in adults, Children, and infants; it causes arthralgia, characterized by irritability, walking with a limp, or sometimes extreme pain while walking, thus reluctance to walk (Fleming-Dutra et al. 2016). In addition, several congenital infections are linked to the Zika virus. It affects pregnant women in any trimester and causes microcephaly in infants. In Brazil, it has been reported that there was a link between microcephaly and the Zika virus in newborns and even in dead infants (Melo et al. 2016). Children born with microcephaly caused by the Zika virus have been linked to muscle atrophy in many cases in Brazil (Ventura et al. 2016). Similarly, infection with this virus during pregnancy negatively impacts the fetus's outcomes. It causes placental inefficiency, in vitro growth restriction of the fetus, and injury to the central nervous system (Mayor 2016). Moreover, the Zika virus is also responsible for neurological problems, including meningoencephalitis and acute myelitis (Carteaux et al. 2016).

5. PUBLIC HEALTH IMPORTANCE OF ZIKA VIRUS

The Zika virus has emerged as a significant public health concern due to its potential adverse outcomes and rapid spread (Panchaud et al. 2016). Understanding its importance in public health is crucial for implementing effective prevention and control measures. Zika virus infection leads to various diseases and conditions in humans, causing significant health impacts and burden on healthcare systems (Noorbakhsh et al. 2019).

One of the primary concerns associated with Zika virus infection is its effect on pregnant women and their unborn babies. When a woman in pregnancy is infected with the Zika virus, it is transmitted to the fetus, leading to a condition known as congenital Zika syndrome (Chan et al. 2016). This syndrome is characterized by a range of severe neurological abnormalities, including microcephaly, where the baby's head size is significantly smaller than average, indicating improper brain development (Melo et al. 2016).



Additionally, congenital Zika syndrome results in other birth defects, such as eye abnormalities, hearing loss, impaired growth, joint and muscle problems. These conditions have long-term implications for affected infants and their families, requiring specialized care and support (Pomar et al. 2019).

Apart from congenital Zika syndrome, Zika virus infection also causes several diseases and conditions in non-pregnant individuals. Most infected individuals, approximately 80%, do not exhibit any symptoms and are asymptomatic (Paixao et al. 2018). However, those who do develop symptoms may experience mild to moderate flu-like symptoms such as fever, maculopapular rash, joint pain, muscle pain, asthenia, headache, conjunctivitis and peripheral edema at extremities These symptoms typically last for few days to a week and are generally self-limiting (Pomar et al. 2019).

In some rare cases, Zika virus infection leads to more severe complications. One of the notable complications is Guillain-Barré syndrome (GBS), a rare neurological disorder characterized by muscle weakness and potential paralysis. GBS occurs when the body's immune system mistakenly attacks the peripheral nervous system, leading to nerve damage and subsequent muscle weakness (Mier-y-Teran-Romero et al. 2018). Although the association between Zika virus infection and GBS is still being studied, evidence suggests a link between the two, highlighting the importance of monitoring and early detection of GBS cases during Zika outbreaks.

In addition to GBS, other potential complications of Zika virus infection include meningoencephalitis, an inflammation of the brain and meninges, and autoimmune manifestations These complications are relatively rare but underscore the need for further research to fully understand the spectrum of diseases associated with Zika virus infection (Schwartzmann et al. 2017).

The public health importance of the Zika virus lies in its potential to cause significant harm to individuals, particularly pregnant women and their unborn babies. The devastating consequences of congenital Zika syndrome highlight the urgency of prevention and control efforts to minimize the risk of transmission. Preventing Zika virus infection among pregnant women is crucial in reducing the incidence of congenital Zika syndrome and its associated disabilities (Rice et al. 2018).

Furthermore, Zika virus outbreaks also strain the healthcare systems, particularly in regions with limited resources. The need for specialized care and support for infants with congenital Zika syndrome places a significant burden on healthcare providers and facilities (Bailey and Ventura 2018). Investing in surveillance systems, research initiatives, and public health interventions is essential for effectively addressing the public health impact of Zika virus infection (Bailey and Ventura 2018).

6. PREVENTION & CONTROL

Preventing and controlling the spread of the Zika virus is of utmost importance to safeguard public health. There is a need for a comprehensive approach which encompasses various strategies aimed at reducing mosquito populations, implementing personal protective measures, and developing effective vaccines to prevent Zika Virus infection and spread. The viral infection can be haltered by using following strategies (Poland et al. 2018; Singh et al. 2018).

6.1. MOSQUITO CONTROL STRATEGIES

Mosquito control strategies play a crucial role in preventing the transmission and spread of the Zika virus. *Aedes* mosquitoes, particularly *Aedes aegypti* and *Aedes albopictus*, are the primary vectors responsible for transmitting the virus to humans (Gasperi et al. 2012). These mosquitoes are highly adaptive, capable of breeding in small water containers, and have a preference for biting humans. By implementing effective mosquito control measures, we can significantly reduce the population of these vectors and minimize the



risk of Zika virus transmission (Von Seidlein et al. 2017). There are various strategies to control mosquitos transferring this virus. These strategies encompass various methods aimed at controlling mosquito populations, preventing their breeding, and protecting communities from the mosquitoes (Hajra et al. 2016). Effective mosquito control requires the implementation of mechanical, chemical, and biological measures (Araújo et al. 2015). Following are the ways, which could be adopted to curb the mosquito spread of disease.

6.1.1. MECHANICAL CONTROL OF MOSQUITOS

Mechanical control measures are long-standing and cost-effective techniques widely employed in various countries for mosquito population control. These methods involve the removal of objects that collect stagnant water, as they serve as breeding grounds for mosquitoes. Ensuring proper cleanliness of streets, maintenance of buildings and housing units, and promoting personal and community hygiene are integral aspects of this approach. Encouraging the use of mosquito nets on windows and employing mosquito-proof water storage options are also effective strategies. Ovitraps, which are low-cost and require minimal upkeep, can be utilized to reduce mosquito populations (Barrera et al. 2014). It is crucial to raise public awareness about identifying and eliminating potential mosquito breeding sites within residential areas. By adopting a hygienic lifestyle and actively preventing mosquito bites and breeding sites, the risk of mosquito-borne diseases such as Zika virus can be significantly reduced (Bancroft et al. 2022).

6.1.2. CHEMICAL CONTROL OF MOSQUITO

Chemical control measures are employed to combat mosquitoes, primarily targeting their nervous system. The chemicals like Pyrethroids, organochlorides, and organophosphorus compounds are commonly used (Van Den Berg et al. 2012). However, the use of Imidacloprid, thiacloprid, and thiamethoxam demonstrate good efficacy against mosquito larvae and adults. The fogging with insecticides is utilized outdoors to kill the insects, but it can lead to resistance development in mosquitoes (Maciel-de-Freitas et al. 2014). Likewise, the use of chemicals also poses other challenges, including resistance development, bioaccumulation, and negative impacts on non-target organisms like other arthropods, birds and mammals in the environment. However, prioritizing a comprehensive analysis of the benefits and costs is essential before implementing widespread insecticide use (Uragayala et al. 2014). Moreover, there are certain repellents which proved efficacious against in mosquito control studies, such as N,N-Diethyl-meta-toluamide (DEET) and p-menthane-3,8-diol, offer protection against mosquito bites and also proved safe for pregnant women (Kline and Schutze 2016). Additionaly, the Insect growth regulators (IGRs), such as methoprene and pyriproxyfen, also provide effective and environmentally safe larvicidal options (Khan 2021). IGRs like pyriproxyfen have shown promise in autodissemination strategies against Zika virus vectors (Unlu et al. 2017). Ensuring judicious use of appropriate chemicals can effectively control mosquito populations and mitigate the spread of diseases like Zika virus (World Health Organization 2016).

6.1.3. BIOLOGICAL CONTROL OF MOSQUITO

Biological control measures have been explored as an alternative to chemical methods for controlling mosquito populations and preventing the spread of the Zika virus (Niang et al. 2018). Several biological approaches have shown efficacy in combating mosquitoes on a large scale. One method involves the use of bacteria, such as *Bacillus thuringiensis* subsp. *israelensis* (Bti) and *Bacillus sphaericus* (Bs), which



produce toxins that specifically target mosquito larvae (Singh et al. 2018). These bacteria have been commercialized as insecticides and are widely used in many countries. Another strategy involves the use of the intracellular bacteria *Wolbachia*, which can reduce mosquito lifespan and vector competence for the Zika virus. *Wolbachia*-infected mosquitoes have been released in certain areas to control mosquito populations (Lees et al. 2015). Fungi like *Metarhizium anisopliae* and *Beauveria bassiana* can also be employed as biocontrol agents against mosquitoes. These fungi infect and kill mosquitoes, and their spores can be sprayed to control mosquito populations (Tiago et al. 2014). Moreover, mosquitoes can also be controlled using other species of mosquitoes that prey on them, such as *Toxorhynchites splendens*, which feeds on mosquito larvae (Benelli et al. 2016). Additionally, copepods like *Mesocyclops* and *Macrocyclops* have also been used as mosquito biocontrol measures by preying on mosquito larvae (Singh et al. 2018). Finally, certain plant-derived products have been tested for their effectiveness against mosquitoes, including the use of plant extracts and essential oils with larvicidal and repellent properties These biological control measures provide environmental-friendly alternatives to chemical pesticides for controlling mosquitoes and reducing the transmission of the Zika virus (Souza et al. 2011).

6.2. VACCINAL CONTROL OF ZIKA VIRUS INFECTION

Preventing the transmission of Zika virus (ZIKV) requires controlling the vector population and implementing individual-level preventive measures like vaccines or strategies that interfere with non-vectoral transmission. Although there is currently no commercial ZIKV vaccine available, ongoing research shows promising developments in vaccine development (Wang et al. 2022).

Various vaccine platforms are being explored worldwide to develop an effective ZIKV vaccine. Over 40 vaccine candidates are under preclinical study, with 7 in phase I trials and one in phase 2b trial (Veljkovic and Paessler 2016). Researchers have found that antibodies generated against the hemagglutinin subunit 1 (HA1/H1) protein of influenza virus pdmH1N1 can neutralize ZIKV, suggesting the possibility of using the seasonal influenza vaccine to prevent ZIKV spread (Veljkovic and Paessler 2016).

Different types of ZIKV vaccines are being developed. Inactivated vaccines, created by killing the pathogenic organism and administering it with an adjuvant, are effective but require repeated immunizations. Inactivated ZIKV vaccines are currently in phase I clinical trials, showing promising protection in monkeys and mice (Sumathy et al. 2017). Moreover, the live attenuated ZIKV vaccines, created by weakening the virus through genetic or chemical manipulation, can modulate both arms of the immune system and provide protection with fewer doses. Studies with live attenuated vaccines have shown protection in mice, including pregnant mice and male mice protecting against testicular damage caused by ZIKV (Shan et al. 2017). DNA-based vaccines are also being developed, using the DNA of ZIKVA proteins, and are currently in clinical trials. These vaccines have shown safety and efficacy in initial studies (Morabito and Graham 2017). However, extensive research is underway to develop an effective ZIKV vaccine. Although commercial availability is yet to be achieved, the advancements made in various vaccine platforms offer hope for the future (Wang et al. 2022).

6.3. OTHER PREVENTIVE STRATEGIES

There are certain other preventing strategies for the control of Zika virus (ZIKV) keeping in mind the nonvector borne routes of transmission. Among which public awareness plays a vital role in eliminating breeding spaces for vector larvae through basic cleanliness measures. Sexual transmission of ZIKV necessitates safe sexual practices and refraining from intercourse for six months after the onset of

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symptoms in male partners or diagnosis. Safe sex should be practiced in high-risk areas, and couples planning to conceive after visiting endemic regions should wait for at least 28 days (Musso et al. 2015).

Moreover, to minimize the incidence of ZIKV-associated microcephaly, parental care and the use of contraceptives should be promoted in ZIKV-endemic countries (Sharma and Lal 2017). Although ZIKV has been detected in semen and saliva, the advantages of breastfeeding outweigh the possible transmission risk, and infected mothers are advised to continue breastfeeding. Blood transfusion can also transmit ZIKV, if preventive measures are not taken. Various methods such as pasteurization, solvent/detergent treatment, and filtration can effectively reduce viral load in plasma-derived medicinal products (Blümel et al. 2017).

Additionally, the hygienic practices should be followed by health workers to minimize the spread of ZIKV within hospitals. In the initial week following ZIKV infection, avoiding mosquito bites and using bed nets are recommended. Travelers to endemic areas should be educated about the use of mosquito repellents and nets. Pregnant women are advised to avoid visiting such areas, and if they have already traveled, they should receive proper medical supervision (Lin et al. 2017).

Surveillance and monitoring should be done at entry points to prevent the introduction of ZIKV from endemic countries. Mosquito control programs combined with surveillance studies have shown effectiveness in preventing ZIKV cases Addressing vulnerable societies and considering climate change's influence on vector density are crucial in policymaking at the government level. Advance planning, infrastructure development, and collective efforts from both the government and the public are necessary for efficient prevention and control of ZIKV infection (Marano et al. 2016).

7. TREATMENT STRATEGIES

Preventing mosquito breeding is the primary strategy for controlling the Zika virus infection. Moreover, it is preferable to use palliative care to treat Zika virus infection, which includes rest and hydration intake. Although there is no drug of choice against the Zika virus, some drug classes, including paracetamol or Acetaminophen, can be used to treat fever and headache (Da Silva et al. 2018). However, salicylates are prohibited in children to prevent the development of Reye's syndrome. Besides, Acetaminophen, there are risks of hemorrhage complications associated with using another non-steroidal anti-inflammatory (NSAID) drugs, so they should not be used (Atif et al. 2016). Various molecules interfere with the life cycle of the Zika virus and can be used to treat the infection. Niclosamide and cyclin-dependent kinase inhibitors have significantly inhibited the Zika virus infection. These compounds have been found to stop viral replication, and when used with Emricasan, they show a synergistic effect (Xu et al. 2016).

Additionally, Chloroquine is another drug with FDA approval and can be used to treat Zika virus infection, particularly in pregnant women. It serves as a useful protective measure against the microcephaly caused by the Zika virus by blocking the initial phases of viral replication (Li et al. 2017). Similarly, another drug used to treat Zika virus infection is sofosbuvir. This drug has been seen to lower the concentration of the Zika virus in the blood, brain, and kidney because it prevents the Zika virus from replicating (Bullard-Feibelman et al. 2017). In the same way, Azithromycin, an antibiotic from the macrolide class, can also be used to treat an infection caused by the Zika virus because it effectively prevents viral replication. In particular, it is safe to treat pregnant women with the Zika virus infection (Retallack et al. 2016). Likewise, azithromycin and, sofosbuvir, Merimepodib also stop viral replication and have been shown to have strong antiviral effects against Zika virus infection (Tong et al. 2018).

In addition, the D2 and D3 dopamine receptor agonist bromocriptine can be utilized to treat Zika virus infection. It binds to the Zika virus NS2B-NS3 protease's active site and prevents the action of that enzyme (Chan et al. 2017). Apart from modern medicine, homeopathy and ayurveda can also be used to treat

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infection caused by this virus because these preparations have shown effective results in treating the Japanese encephalitis virus, which belongs to a similar genus as the Zika virus (Bandyopadhyay et al. 2010). Herbal plants have therapeutic potential due to secondary metabolites, i.e., alkaloids which have antimicrobial properties and hence the part of prescriptions in many countries (Perumal Samy 2010). Considering the therapeutic potential of homeopathic medicine, the Eupatorium perfoliatum can be used to treat the infection of this virus because this drug can treat the symptoms experienced by patients with Zika virus infection. In addition to homeopathic medicine, Ayurvedic herbs, including *Tinospora cordifolia*, can also treat the infection that occurs due to Zika Virus (Saxena et al. 2016).

8. CONCLUSION

The Zika virus is a mosquito-borne viral infection that gained global attention due to its association with severe birth defects, particularly microcephaly. The virus can be transmitted through mosquito bites, sexual contact, blood transfusions, and from mother to child during pregnancy. Following the outbreak in the Americas in 2015 and 2016, significant efforts were made to understand and control the virus. These efforts included the development of diagnostic tests, mosquito control strategies, and potential vaccines.

REFERENCES

- Araújo HR et al., 2015. Aedes aegypti control strategies in Brazil: incorporation of new technologies to overcome the persistence of dengue epidemics. Insects 6: 576–594.
- Atif M et al., 2016. Zika virus disease: a current review of the literature. Infection 44: 695-705.
- Bailey Jr DB and Ventura LO, 2018. The likely impact of congenital Zika syndrome on families: considerations for family supports and services. Pediatrics 141: 180-187.
- Bancroft D et al., 2022. Vector control strategies in Brazil: a qualitative investigation into community knowledge, attitudes and perceptions following the 2015–2016 Zika virus epidemic. BMJ Open 12(1): e050991.

Bandyopadhyay B et al., 2010. Decreased intensity of Japanese encephalitis virus infection in chick chorioallantoic membrane under influence of ultradiluted Belladonna extract. American Journal of Infectious Diseases 6: 24-28.

- Barrera R et al., 2014. Uso de la ovitrampa letal para hembras grávidas de los CDC para controlary prevenir los brotes de Aedes aegypti (Diptera: Culicidae). Journal of Medical Entomology 51: 145-54.
- Beasley DW et al., 2005. Envelope protein glycosylation status influences mouse neuroinvasion phenotype of genetic lineage 1 West Nile virus strains. Journal of Virology 79: 8339-8347.
- Benelli G et al., 2016. Ethnopharmacology in the fight against Plasmodium parasites and brain disorders: in memoriam of Philippe Rasoanaivo. Journal of Ethnopharmacology 193: 726-728.
- Blümel J et al., 2017. Inactivation and removal of Zika virus during manufacture of plasma-derived medicinal products. Transfusion 57: 790-796.
- Bradley MP and Nagamine CM, 2017. Animal Models of Zika Virus. Comparative Medicine 67(3):242-252
- Bullard-Feibelman et al., 2017. The FDA-approved drug sofosbuvir inhibits Zika virus infection. Antiviral Research 137: 134-140.
- Calvet GA et al., 2016. First detection of autochthonous Zika virus transmission in a HIV-infected patient in Rio de Janeiro, Brazil. Journal of Clinical Virology 74: 1-3.
- Cao-Lormeau VM et al., 2014. Zika virus, French Polynesia, South Pacific, 2013. Emerging Infectious Diseases 20: 1085-1086.
- Cao-Lormeau VM et al., 2016. Guillain-Barré Syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study. The Lancet 387: 1531-1539.
- Cardoso CW et al., 2015. Outbreak of exanthematous illness associated with Zika, chikungunya, and dengue viruses, Salvador, Brazil. Emerging Infectious Diseases 21: 2274.
- Carteaux G et al., 2016. Zika virus is associated with meningoencephalitis. New England Journal of Medicine 374: 1595-1596.



- Chan et al., 2016. Zika fever and congenital Zika syndrome: an unexpected emerging arboviral disease. Journal of Infection 725: 507-524.
- Chan JFW et al., 2017. Novel antiviral activity and mechanism of bromocriptine as a Zika virus NS2B-NS3 protease inhibitor. Antiviral Research 141: 29-37.
- Cunha MS et al., 2016. First complete genome sequence of Zika virus (Flaviviridae, Flavivirus) from an autochthonous transmission in Brazil. Genome Announcements 4: 16.
- D'ortenzio E et al., 2016. Evidence of sexual transmission of Zika virus. New England Journal of Medicine 374: 2195-2198.
- Da Silva S et al., 2018. A review of the ongoing research on zika virus treatment. Viruses 10: 1-18.
- Duffy MR et al., 2009. Zika virus outbreak on Yap Island, federated states of Micronesia. New England Journal of Medicine 360: 2536-2543.
- Favoretto S et al., 2016. First detection of Zika virus in neotropical primates in Brazil: a possible new reservoir. BioRxiv 10: 049395.
- Fleming-Dutra KE et al., 2016. Update: interim guidelines for health care providers caring for infants and children with possible Zika virus infection—United States, February 2016. Morbidity and Mortality Weekly Report 65: 182-187.
- Gasperi G et al., 2012. A new threat looming over the Mediterranean basin: emergence of viral diseases transmitted by Aedes albopictus mosquitoes.
- Giovanetti M et al., 2016. Zika virus complete genome from Salvador, Bahia, Brazil. Infection, Genetics and Evolution 41: 142-145.
- Gubler J and Musso D, 2016. Zika virus. Clinical Microbiology Reviews 29: 487-524.
- Hajra A et al., 2016. Zika virus: a global threat to humanity: a comprehensive review and current developments. North American Journal of Medical Sciences 83: 123.
- Heang V et al., 2012. Zika virus infection, Cambodia, 2010. Emerging Infectious Diseases 18: 349-351.
- Heymann DL et al., 2016. Zika virus and microcephaly: why is this situation a PHEIC? The Lancet 387: 719-721.
- loos S et al., 2014. Current Zika virus epidemiology and recent epidemics. Medecine et Maladies Infectiousness 44: 302-307.
- Khan HA, 2021. Post treatment temperature influences toxicity of insect growth regulators in Musca domestica. Parasitology Research 120(2): 435-41.
- Khatri et al., 2018. Zika virus (ZIKV) disease: past, present and future. Journal of Drug Delivery and Therapeutics 8(6): 320-327.
- Kline MW and Schutze GE, 2016. What pediatricians and other clinicians should know about Zika virus. JAMA Pediatrics 1704: 309-310.
- Kostyuchenko VA et al., 2016. Structure of the thermally stable Zika virus. Nature 533: 425-428.
- Krause KK et al. 2017. Understanding the Pathogenesis of Zika Virus Infection Using Animal Models. Immune Network 17(5): 287-297.
- Lanciotti et al., 2008 "Genetic and serologic properties of Zika virus associated with an epidemic, Yap State, Micronesia, 2007." Emerging Infectious Diseases 14(8): 1232.
- Lebov JF et al., 2018. Evidence of neurological sequelae in children with acquired Zika virus infection. Pediatric Neurology 85: 16-20.
- Lees RS et al., 2015. Back to the future: the sterile insect technique against mosquito disease vectors. Current Opinion in Insect Science 10: 156-162.
- Li C et al., 2017. Chloroquine, an FDA-approved drug, prevents Zika virus infection and its associated congenital microcephaly in mice. E Bio Medicine 24: 189-194.
- Lin HZ et al., 2017. A review of Zika virus infections in pregnancy and implications for antenatal care in Singapore. Singapore medical journal.
- Maciel-de-Freitas R et al., 2014. Undesirable consequences of insecticide resistance following Aedes aegypti control activities due to a dengue outbreak. PloS one 93: 92424.
- Mallet HP et al., 2015. Bilan de l'epidemie a virus Zika en Polynesie Francaise, 2013–2014. Bulletin d'information sanitaires, épidémiologiques et Statistiques 2015: 20-21.



- Marano G et al., 2016. Zika virus and the never-ending story of emerging pathogens and transfusion medicine. Blood Transfusion 142: 95.
- Mayor S, 2016. Data indicate that Zika infection in pregnancy is linked to a range of fetal abnormalities. British Medical Journal 2016: 352.
- Melo AO et al., 2016. Zika virus intrauterine infection causes fetal brain abnormality and microcephaly: the tip of the iceberg? Ultrasound in obstetrics & gynecology: the official journal of the International Society of Ultrasound in Obstetrics and Gynecology 4: 6-7.
- Mier-y-Teran-Romero L et al., 2018. Guillain–Barré syndrome risk among individuals infected with Zika virus: a multicountry assessment. BMC Medicine 16: 1-8.
- Moghadam et al., 2016. Zika virus: A review of literature. Asian Pacific Journal of Tropical Biomedicine 6(12): 989-994.
- Morabito KM and Graham BS, 2017. Zika virus vaccine development. The Journal of Infectious Diseases 216: 957-963.
- Muller DA Young PR, 2013. The flavivirus NS1 protein: molecular and structural biology, immunology, role in pathogenesis and application as a diagnostic biomarker. Antiviral Research 98: 192-208.
- Musso D et al., 2014. The rapid spread of the emerging Zika virus in the Pacific area. Clinical Microbiology and Infection 20: 595-596.
- Musso D et al., 2015. Potential sexual transmission of Zika virus. Emerging Infectious Diseases 212: 359.
- Niang EH et al., 2018. Biological control of mosquito-borne diseases: the potential of Wolbachia-based interventions in an IVM framework. Journal of Tropical Medicine 2018.
- Noorbakhsh et al., 2019. Zika virus infection, basic and clinical aspects: A review article. Iranian Journal of Public Health 481: 20.
- Paixao et al., 2018. Asymptomatic prenatal Zika virus infection and congenital Zika syndrome. Open Forum Infectious Diseases 5: 4.
- Panchaud A et al., 2016. Emerging role of Zika virus in adverse fetal and neonatal outcomes. Clinical Microbiology Reviews 293: 659-694.
- Perumal Samy R, 2010. Therapeutic potential of plants as anti-microbials for drug discovery. Evidence-based complementary and alternative medicine.
- Petersen LR et al., 2016. Zika virus. New England Journal of Medicine 374: 1552-1563.
- Poland GA et al., 2018. Development of vaccines against Zika virus. The Lancet Infectious Diseases 18: e211–19
- Pomar L et al., 2019. Zika virus during pregnancy: From maternal exposure to congenital Zika virus syndrome. Prenatal Diagnosis 396: 420-430.
- Ramos DA Silva S and Gao SJ, 2016. Zika virus: an update on epidemiology, pathology, molecular biology, and animal model. Journal of Medical Virology 88: 1291-1296.
- Rasmussen SA et al., 2016. Zika virus and birth defects—reviewing the evidence for causality. New England Journal of Medicine 374: 1981-1987.
- Retallack H et al., 2016. Zika virus cell tropism in the developing human brain and inhibition by azithromycin. Proceedings of the National Academy of Sciences 113: 14408-14413.
- Rice ME et al., 2018. Vital signs: Zika-associated birth defects and neurodevelopmental abnormalities possibly associated with congenital Zika virus infection—US territories and freely associated states. Morbidity and Mortality Weekly Report 67(31): 858.
- Ruiz Jimenez et al., 2022. The effect of mutations in the envelope protein of Zika virus on cellular tropism. PhD Dissertation, University of Nottingham.
- Saxena SK et al., 2016. Zika virus outbreak: an overview of the experimental therapeutics and treatment. Virus Disease 27: 111-115.
- Schwartzmann PV et al., 2017. Zika virus meningoencephalitis in an immunocompromised patient. Mayo Clinic Proceedings 923: 460-466.
- Shan C et al., 2017. A live-attenuated Zika virus vaccine candidate induces sterilizing immunity in mouse models. Nature Medicine.
- Sharma A and Lal SK, 2017. Zika virus: transmission, detection, control, and prevention. Frontiers in Microbiology 8: 110.



- Sheridan MA et al., 2018. African and Asian strains of Zika virus differ in their ability to infect and lyse primitive human placental trophoblast. PloS one 13(7): e0200086. https://doi.org/10.1371/journal.pone.0200086
- Singh RK et al., 2018. Prevention and control strategies to counter Zika virus, a special focus on intervention approaches against vector mosquitoes current updates. Frontiers in Microbiology 9: 87.
- Singh Raj K et al., 2018. Prevention and control strategies to counter Zika virus, a special focus on intervention approaches against vector mosquitoes—current updates. Frontiers in Microbiology 9(2018): 87.

Sirohi D et al., 2016. The 3.8 Å resolution cryo-EM structure of Zika virus. Science 352: 467-470.

- Song BH et al., 2017. Zika virus: History, epidemiology, transmission, and clinical presentation. Journal of Neuroimmunology 308: 50-64.
- Souza TM et al., 2011. Toxicity of Brazilian plant seed extracts to two strains of Aedes aegypti (Diptera: Culicidae) and nontarget animals. Journal of Medical Entomology 484: 846-851.
- Sumathy K et al., 2017. Protective efficacy of Zika vaccine in AG129 mouse model. Scientific Reports 71: 46375.
- Teixeira MG et al., 2016. The Epidemic of Zika Virus-Related Microcephaly in Brazil: Detection, Control, Etiology, and Future Scenarios. American Journal of Public Health 106(4): 601-5.
- Tiago PV et al., 2014. Controle biológico de insetos utilizando Metarhizium anisopliae: aspectos morfológicos, moleculares e ecológicos. Ciência Rural 444: 645-651.
- Tong X et al., 2018. Merimepodib, an IMPDH inhibitor, suppresses replication of Zika virus and other emerging viral pathogens. Antiviral Research 149: 34-40.
- Unlu I et al., 2017. Effectiveness of autodissemination stations containing pyriproxyfen in reducing immature Aedes albopictus populations. Parasites and Vectors 101: 1-10.
- Uragayala S et al., 2015. Adulticidal & larvicidal efficacy of three neonicotinoids against insecticide susceptible & resistant mosquito strains. The Indian Journal of Medical Research 142: 64.
- Van Den Berg H et al., 2012. Global trends in the use of insecticides to control vector-borne diseases. Environmental Health Perspectives 1204: 577-582.
- Veljkovic V and Paessler S, 2016. Possible repurposing of seasonal influenza vaccine for prevention of Zika virus infection.
- Ventura CV et al., 2016. Zika virus in Brazil and macular atrophy in a child with microcephaly. The Lancet 387: 228.
- Venturi G et al., 2016. An autochthonous case of Zika due to possible sexual transmission, Florence, Italy, 2014. Eurosurveillance 21: 30148.
- Von Seidlein L et al., 2017. Novel vector control approaches: the future for prevention of Zika virus transmission? PLoS Medicine 141: 1002219.
- Wang L et al., 2016. From mosquitos to humans: genetic evolution of Zika virus. Cell Host and Microbe 19: 561-565. Wang Y et al., 2022. Current Advances in Zika Vaccine Development. Vaccines 10(11): 1816.
- Wikan et al., 2017. Zika virus from a Southeast Asian perspective. Asian Pacific Journal of Tropical Medicine 10(1): 1-5.
- World Health Organization, 2016. Zika strategic response plan, revised for July 2016-December 2017.
- Xu M et al., 2016. Identification of small-molecule inhibitors of Zika virus infection and induced neural cell death via a drug repurposing screen. Nature Medicine 22: 1101-1107.
- Zanluca C et al., 2015. First report of autochthonous transmission of Zika virus in Brazil. Memórias do Instituto Oswaldo Cruz 110: 569-572