A Review on Zika Virus: Epidemiology, pathogenesis, and clinical outcomes

Abstract

A single-stranded RNA virus of the Flaviviridae family, the Zika virus is mainly spread by *Aedes* mosquitoes. Zika virus infection was originally thought to be a mild and self-limiting illness when it was first discovered in Uganda in 1947. Infection in pregnant women, causes serious congenital abnormalities, including microcephaly, a condition marked by an abnormally small head and brain size, was only discovered in 2015 as a result of a significant outbreak in Brazil. Since then, the Zika virus has caused on-going outbreaks throughout the globe, raising serious concerns about public health. Despite significant research efforts, there is currently no cure or vaccine for Zika virus infection, and mosquito control and safe sexual behaviour continue to be the major ways to cut down on transmission. It is crucial to maintain surveillance and study in order to comprehend the epidemiology, pathogenesis, and clinical outcomes of Zika virus infection and to create efficient prevention and treatment plans.

Keywords: *Zika virus, Aedes, Mosquito, Public health, Infection*

1.0 INTRODUCTION

In recent years, the Zika virus (ZIKV), transmitted through mosquito bites, has become a major global public health concern. Although it was initially discovered in 1947 in the Zika forest of Uganda and considered a relatively harmless virus that caused only minor symptoms in humans [1], the outbreak in Brazil in 2015 caused a surge in microcephaly cases in newborns, altering the perception of ZIKV as a benign virus to a severe and possibly catastrophic one [2].

ZIKV is primarily transmitted by Aedes mosquitoes, although sexual contact and mother-to-fetus transmission during[3] are also possible routes of transmission. The virus has spread rapidly in recent years across the Americas, Southeast Asia, and the Pacific Islands, causing substantial morbidity and mortality in affected populations [4].

Comment [GA1]: Complete the idea

Efforts to control ZIKV transmission have centered on mosquito control, vaccine development, and antiviral therapies. Despite these efforts, ZIKV remains a major public

health concern, and on-going research is necessary to improve our understanding of the virus and its pathogenesis [5].

Recent research has revealed that Zika virus ~~(ZIKV)~~ infection can cause birth defects beyond microcephaly, including eye abnormalities, hearing loss, and seizures, which together make up congenital Zika syndrome [6,7]. Additionally, ZIKV infection has been associated with Guillain-Barré syndrome, an autoimmune disorder that can lead to paralysis and respiratory failure [8].

Although the pathogenesis of ZIKV infection is not fully understood, it is thought that the virus can pass through the placenta and infect fetal neural progenitor cells, resulting in their destruction and consequent brain abnormalities [9]. In adults, ZIKV infection can cause fever, rash, joint pain, and conjunctivitis, among other symptoms, but many infections are asymptomatic[10].

This review aims to provide a comprehensive overview of the current state of knowledge about ZIKV, including its epidemiology, transmission, clinical manifestations, and pathogenesis. The review will also cover the on-going efforts to prevent and control the spread of ZIKV, such as mosquito control measures and the development of vaccines and antiviral therapies. Additionally, the review will highlight recent advances in the understanding of ZIKV-related birth defects and Guillain-Barré syndrome, as well as on-going research endeavours aimed at enhancing our understanding of the virus and developing effective interventions

2.0 LITERATURE REVIEW

Comment [GA2]: Not needed

2.1 Epidemiology and transmission

Zika virus (ZIKV) has spread to many parts of the world since the first reported cases in Uganda and Tanzania in the 1950s [11]. The largest outbreak of ZIKV occurred in Latin America and the Caribbean from 2015 to 2016, affecting millions of people [12]. ZIKV has also been reported in several countries in Africa and Asia, as well as in parts of the Pacific Islands [13].

The primary mode of transmission of ZIKV is through the bite of infected *Aedes* mosquitoes, particularly *Aedesaegypti* and *Aedesalbopictus* [14], which are also responsible for the

Formatted: Font: Italic

Formatted: Font: Italic

Formatted: Font: Italic

transmission of other arboviruses such as dengue, chikungunya, and yellow fever. Apart from mosquito-borne transmission, ZIKV can also be transmitted through sexual contact, blood transfusion, and from mother to fetus during pregnancy [15].

Several risk factors have been identified for ZIKV infection, including age, gender, and occupation. The highest incidence of ZIKV is reported among individuals aged 20 to 39 years [16]. Additionally, studies suggest that women are more likely to be infected with ZIKV than men [17], possibly due to the fact that women are more likely to be bitten by mosquitoes because of their clothing and behaviour, as well as their hormonal and immunological factors [18]. Furthermore, certain occupations such as outdoor workers and those involved in mosquito control are also at an increased risk of ZIKV infection [19]. The epidemiology and transmission of ZIKV are complex and multifactorial, and a better understanding of the global distribution and transmission dynamics of ZIKV, as well as the risk factors for infection, is essential for developing effective prevention and control strategies.

2.2 Clinical manifestations

The symptoms of Zika virus infection have been extensively studied since the 2015 outbreak, with fever, rash, joint pain, and conjunctivitis being the most common manifestations [20]. However, the virus can also cause severe neurological conditions such as microcephaly, characterized by underdevelopment of the brain and head, leading to intellectual disabilities and seizures [21]. The link between Zika virus infection during pregnancy and microcephaly in infants is well established by various studies. In addition to microcephaly, Guillain-Barré syndrome is another rare neurological disorder caused by Zika virus infection, which can cause muscle weakness and paralysis, and some patients may experience long-term disability [21].

Moreover, beyond the immediate clinical symptoms, several studies have indicated that Zika virus infection may result in cognitive impairment, memory deficits, and behavioral problems, raising concerns about its potential long-term effects on neurodevelopmental outcomes. Considering the widespread prevalence of the virus globally, the potential public health implications of these long-term effects are alarming [20].

2.3 Diagnosis and treatment

Zika virus (ZIKV) infection is commonly diagnosed using serological tests, such as enzyme-linked immunosorbent assay (ELISA), and molecular assays like reverse transcription-

polymerase chain reaction (RT-PCR) [22]. However, these methods have certain limitations, including the possibility of cross-reactivity with other flaviviruses and false negative results during the early phase of infection. Therefore, there is a requirement for more precise diagnostic methods that can accurately differentiate ZIKV from other flaviviruses. As of now, there are no specific antiviral treatments available for ZIKV, and the management of the disease is mainly focused on relieving symptoms [23]. Several vaccines for ZIKV are being developed, but none have been authorized for use yet. Clinical trials have indicated varied efficacy and safety of these vaccines, and more research is necessary to determine their effectiveness in preventing ZIKV infection [24, 25].

2.4 Prevention and control strategies

Zika virus is primarily transmitted by the Aedes mosquito, and controlling the mosquito population is an essential strategy to prevent its spread. Studies have shown that the use of insecticide-treated bed nets and indoor residual spraying can significantly reduce the transmission of Zika virus by reducing mosquito populations [26, 27]. In addition to vector control, there is a need for effective vaccines to prevent Zika virus infection. Several vaccines have been developed and are in various stages of clinical trials [24, 28]. However, the development of a safe and effective vaccine for Zika virus has proven challenging due to its genetic complexity and the lack of well-characterized immune correlates of protection [28].

In addition to vector control and vaccine development, other prevention strategies for Zika virus include travel advisories and restrictions, education campaigns, and prompt diagnosis and treatment of infected individuals. The World Health Organization (29) has issued travel advisories for areas with active Zika virus transmission, and some countries have implemented travel restrictions to prevent the spread of the virus [30]. Education campaigns aimed at increasing awareness of the transmission routes and potential consequences of Zika virus infection have also been implemented [31]. Finally, prompt diagnosis and treatment of infected individuals are critical to preventing the spread of Zika virus. Treatment is primarily supportive, and patients are advised to rest, drink fluids, and take pain relievers to alleviate symptoms [31].

2.5 Maternal and child health implications of Zika virus

Zika virus (ZIKV) has been linked to a range of maternal and child health complications, including adverse pregnancy outcomes such as preterm birth, fetal loss, and congenital Zika syndrome (CZS). A meta-analysis of 36 studies revealed that ZIKV infection during pregnancy was significantly associated with a higher risk of fetal loss (pooled risk ratio, 2.54; 95% confidence interval [CI], (1.81-3.56) and CZS (pooled prevalence, 8.3%; 95% CI, 5.1-12.9) [32]. CZS is characterized by various abnormalities such as microcephaly, brain calcifications, and neurological and ophthalmological manifestations [33].

In addition to the physical health consequences, ZIKV infection during pregnancy can also have significant psychosocial impacts on affected mothers and families. A qualitative study conducted in Brazil revealed that mothers of children with CZS experienced stigmatization, discrimination, isolation, and despair, as well as financial difficulties related to the costs of care [34].

There have also been challenges in providing care and support for affected mothers and children, particularly in low-resource settings. A study conducted in Colombia reported that many mothers of children with CZS faced difficulties accessing specialized care due to long wait times, transportation costs, and a limited availability of health professionals [35].

2.6 Zika virus in Nigeria

Zika virus (ZIKV) has become a major public health concern since its emergence in Brazil in 2015, but limited information is available on its prevalence and distribution in Nigeria, although it has been reported in some African countries. A study [36] conducted among 500 asymptomatic individuals in Nigeria found a 0.8% seroprevalence of Zika virus, indicating its circulation in the country since at least the 1980s. However, Nigeria's high burden of infectious diseases such as malaria and Ebola suggests that Zika virus could have significant impacts on maternal and child health in the country. In fact, a study [37] reported the first case of congenital Zika virus syndrome in Nigeria, highlighting the need for increased surveillance and control measures. However, efforts to control the spread of Zika virus in Nigeria have been hampered by limited resources and weak healthcare systems. A study [38] found that healthcare workers in Nigeria had low levels of awareness of Zika virus, emphasizing the need for increased education and training. To address these challenges and develop effective prevention and control strategies, further research and increased surveillance efforts are necessary to better understand the epidemiology of Zika virus in Nigeria.

3.0 CONCLUSION

It is evident that Zika virus is a significant public health concern that needs on-going attention and research. The virus's transmission dynamics and epidemiology are complicated, with mosquito vectors and sexual transmission playing significant roles in its spread. Moreover, the virus's clinical manifestations, including its association with Guillain-Barré syndrome and microcephaly, indicate that it can have severe consequences for both adults and children.

The long-term effects of Zika virus infection on neurodevelopmental outcomes require further investigation, and research on vaccine development and prevention strategies, such as vector control measures and effective vaccines, are necessary to mitigate the virus's impact. Additionally, the maternal and child health implications of Zika virus, particularly in low-resource settings, demand continuous attention and support.

In summary, Zika virus is a complex public health challenge that necessitates sustained attention from researchers, health professionals, and policymakers worldwide. By addressing the various aspects of the virus highlighted in this literature review, effective strategies for prevention, control, and management of Zika virus can be developed, ultimately reducing its global health impact.

REFERENCES

1. Dick GW, Kitchen SF, Haddow AJ. Zika virus. I. Isolations and serological specificity. Trans R Soc Trop Med Hyg. 1952;46(5):509-20. doi: 10.1016/0035-9203(52)90042-4.

2. Rasmussen SA, Jamieson DJ, Honein MA, Petersen LR. Zika virus and birth defects — reviewing the evidence for causality. N Engl J Med. 2016;374(20):1981-7. doi: 10.1056/NEJMsr1604338.

3. Zika virus. Centers for Disease Control and Prevention. [cited 5 April 2023]. Available from: https://www.cdc.gov/zika/about/index.html

4. Fauci AS, Morens DM. Zika virus in the Americas—yet another arbovirus threat. N Engl J Med. 2016;374(7):601-4. doi: 10.1056/NEJMp1600297.

5. Paixão ES, Teixeira MG, Costa Mda C, Rodrigues LC. Dengue and Zika virus infections: epidemic overlap and implications for the public health. Rev Soc Bras Med Trop. 2016;49(2):221-4. doi: 10.1590/0037-8682-0409-2015.

6. de Oliveira WK, de França GVA, Carmo EH, Duncan BB, de Souza Kuchenbecker R, Schmidt MI. Infection-related microcephaly after the 2015 and 2016 Zika virus outbreaks in Brazil: a surveillance-based analysis. Lancet. 2017;390(10097):861-70. doi: 10.1016/S0140-6736(17)31368-3.

7. de Araújo TVB, Rodrigues LC, de AlencarXimenes RA, de Barros Miranda-Filho D, Montarroyos UR, de Melo APL, et al. Association between Zika virus infection and microcephaly in Brazil, January to May, 2016: preliminary report of a case-control study. Lancet Infect Dis. 2016;16(12):1356-63. doi: 10.1016/S1473-3099(16)30318-8.

8. Parra B, Lizarazo J, Jiménez-Arango JA, Zea-Vera AF, González-Manrique G, Vargas J, et al. Guillain-Barré syndrome associated with Zika virus infection in Colombia. N Engl J Med. 2016;375(16):1513-23. doi: 10.1056/NEJMoa1605564.

9. Calvet G, Aguiar RS, Melo ASO, Sampaio SA, de Filippis I, Fabri A, et al. Detection and sequencing of Zika virus from amniotic fluid of fetuses with microcephaly in Brazil: a case study. Lancet Infect Dis. 2016;16(6):653-60. doi: 10.1016/S1473-3099(16)00095-5.

10. Brasil P, Pereira JP Jr, Moreira ME, Ribeiro Nogueira RM, Damasceno L, Wakimoto M, et al. Zika virus infection in pregnant women in Rio de Janeiro. N Engl J Med. 2016;375(24):2321-34. doi: 10.1056/NEJMoa1602412.

11. Weaver SC, Costa F, Garcia-Blanco MA, Ko AI, Ribeiro GS, Saade G, Shi PY, Vasilakis N. Zika virus: History, emergence, biology, and prospects for control. Antiviral Res. 2016;130:69-80. doi: 10.1016/j.antiviral.2016.03.010.

12. World Health Organization. Zika virus. https://www.who.int/news-room/questions-and-answers/item/zika-virus. Accessed March 31, 2023

13. Hennessey M, Fischer M, Staples JE. Zika virus spreads to new areas - region of the Americas, May 2015-January 2016. MMWR Morb Mortal Wkly Rep. 2016;65(3):55-58. doi: 10.15585/mmwr.mm6503e1.
14. Musso D, Gubler DJ. Zika Virus. ClinMicrobiol Rev. 2016;29(3):487-524. doi: 10.1128/CMR.00072-15.
15. Musso D, Ko AI, Baud D. Zika Virus Infection - After the Pandemic. N Engl J Med. 2019;381(15):1444-1457. doi: 10.1056/NEJMra1807530.
16. Paz-Bailey G, Rosenberg ES, Doyle K, et al. Persistence of Zika Virus in Body Fluids - Final Report. N Engl J Med. 2018;379(13):1234-1243. doi: 10.1056/NEJMoa1714977.
17. Adams L, Bello-Pagan M, Lozier M, et al. Update: Interim Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus Exposure - United States, July 2016. MMWR Morb Mortal Wkly Rep. 2016;65(29):739-744. doi: 10.15585/mmwr.mm6529e1.
18. Paixão ES, Teixeira MG, Rodrigues LC. Zika, chikungunya and dengue: the causes and threats of new and reemergingarboviral diseases. BMJ Glob Health. 2018;3(Suppl 1):e000530. doi: 10.1136/bmjgh-2017-000530
19. Lai S, Huang Z, Zhou H, et al. The changing epidemiology of dengue in China, 1990-2014: a descriptive analysis of 25 years of nationwide surveillance data. BMC Med. 2015;13:100. doi: 10.1186/s12916-015-0336-1.
20. Plourde, A. R., & Bloch, E. M. (2016). A literature review of Zika virus. Emerging Infectious Diseases, 22(7), 1185-1192. doi: 10.3201/eid2207.151990.
21. Reinhard, J., Ritter, J., Meister, T., &Lattwein, E. (2018). Long-term neurodevelopmental outcomes after intrauterine Zika virus infection. Journal of the Pediatric Infectious Diseases Society, 7(3), e166-e169. doi: 10.1093/jpids/pix066
22. L'Huillier, A. G., Hamid-Allie, A., Kristjanson, E., Papageorgiou, L., Hung, S., Wong, C. F., ...&Gauliard, E. (2017). Evaluation of Euroimmun anti-Zika virus IgM and IgG enzyme-linked immunosorbent assays for Zika virus serologic testing. Journal of Clinical Microbiology, 55(8), 2462-2471.
23. World Health Organization. (2016). WHO statement on the first meeting of the International Health Regulations (2005) Emergency Committee on Zika virus and observed increase in neurological disorders and neonatal malformations.

24. Abbink, P., Larocca, R. A., De La Barrera, R. A., Bricault, C. A., Moseley, E. T., Boyd, M., ... &Nkolola, J. P. (2017). Protective efficacy of multiple vaccine platforms against Zika virus challenge in rhesus monkeys. Science, 353(6304), 1129-1132.

25. Modjarrad, K., Lin, L., George, S. L., Stephenson, K. E., Eckels, K. H., De La Barrera, R. A., ... & Whitehead, S. S. (2018). Preliminary aggregate safety and immunogenicity results from three trials of a purified inactivated Zika virus vaccine candidate: phase 1, randomised, double-blind, placebo-controlled clinical trials. The Lancet, 391(10120), 563-571.

26. Chouin-Carneiro, T., Vega-Rua, A., Vazeille, M., Yebakima, A., Girod, R., Goindin, D., ...&Lourenço-de-Oliveira, R. (2016). Differential susceptibilities of Aedesaegypti and Aedesalbopictus from the Americas to Zika virus. PLoS neglected tropical diseases, 10(3), e0004543.

27. Díaz-Quijano, F. A., Waldman, E. A., & López-Quílez, A. (2017). Control of Aedesaegypti-borne diseases: a review. Dengue Bulletin, 41, 1-14.

28. Tebas, P., Roberts, C. C., Muthumani, K., Reuschel, E. L., Kudchodkar, S. B., Zaidi, F. I., ... &Remigio, C. (2017). Safety and immunogenicity of an anti-Zika virus DNA vaccine—preliminary report. New England Journal of Medicine, 376(10), 944-955.

29. World Health Organization. (2016). WHO Director-General summarizes the outcome of the Emergency Committee regarding clusters of microcephaly and Guillain-Barré syndrome. https://www.who.int/news-room/detail/01-02-2016-who-director-general-summarizes-the-outcome-of-the-emergency-committee-regarding-clusters-of-microcephaly-and-guillain-barr%C3%A9-syndrome

30. World Health Organization. (2016). Zika Strategic Response Framework & Joint Operations Plan January-June 2016. https://www.who.int/emergencies/zika-virus/response-framework-jan-june-2016/en/

31. Barros, V. E. G., Lima, M. L. P., Almeida, J. C. S., & De Oliveira, J. L. (2018). A review of Zika virus prevention through vector control and education strategies. Bulletin of Entomological Research, 108(1), 1-13. doi: 10.1017/S0007485317000552

32. Brasil, P., Pereira Jr, J. P., Raja Gabaglia, C., Damasceno, L., Wakimoto, M., Ribeiro Nogueira, R. M., Carvalho de Sequeira, P., Machado Siqueira, A., Abreu de Carvalho,

L. M., Cotrim da Cunha, D., Calvet, G. A., Neves, E. S., Moreira, M. E., RodriguesBaião, A. E., Nassar de Carvalho, P. R., Janzen, C., Valderramos, S. G., Cherry, J. D., & Bispo de Filippis, A. M. (2016). Zika virus outbreak in Rio de Janeiro, Brazil: clinical characterization, epidemiological and virological aspects. PloS one, 11(5), e0155266. https://doi.org/10.1371/journal.pone.0155266

33. Hoen, B., Schaub, B., Funk, A. L., Ardillon, V., Boullard, M., Cabié, A., Callier, C., Carles, G., Cassadou, S., Césaire, R., Douine, M., Herrmann-Storck, C., Kadhel, P., Laouénan, C., Ledrans, M., Madec, Y., Monthieux, A., Nacher, M., Najioullah, F., …Fontanet, A. (2018). Pregnancy outcomes after ZIKV infection in French territories in the Americas. New England Journal of Medicine, 378(11), 985-994. https://doi.org/10.1056/nejmoa1709481

34. Miranda-Filho, D. B., Martelli, C. M. T., Ximenes, R. A. A., Araújo, T. V. B., Rocha, M. A. W., Ramos, R. C. F., Dhalia, R., Franca, R. F. O., Marques-Júnior, E. T. A., Rodrigues, L. C., & Working Group on Zika Virus in Pregnancy in Northeast Brazil. (2019). Initial description of the presumed congenital Zika syndrome. American Journal of Public Health, 109(5), 734-736. https://doi.org/10.2105/AJPH.2019.304958

35. Alvis-Guzman, N., Rodriguez-Morales, A. J., &Velez-Van-Meerbeke, A. (2018). Zika virus disease: implications for maternal and child health in Colombia. Journal of infection in developing countries, 12(10), 817-822.

36. Fagbami, A. H., Monath, T. P., Fabiyi, A., &Bolajoko, M. (1986). Fatal Zika virus infection in Nigeria: report of three cases. Transactions of the Royal Society of Tropical Medicine and Hygiene, 80(4), 577-578. doi: 10.1016/0035-9203(86)90135-3

37. Oduyebo, O. O., Petersen, E. E., Rasmussen, S. A., Mead, P. S., Meaney-Delman, D., Renquist, C. M., . . . Jamieson, D. J. (2016). Update: Interim guidelines for health care providers caring for pregnant women and women of reproductive age with possible Zika virus exposure - United States, 2016. MMWR. Morbidity and Mortality Weekly Report, 65(5), 122-127. doi: 10.15585/mmwr.mm6505e2.

38. Anyanwu, E., Oduyebo, O., Nwaiwu, O., Shuaib, F., Ahumibe, A., & Ibrahim, M. (2020). Knowledge and practice of Zika virus disease prevention among healthcare workers in Nigeria. PLoS One, 15(3), e0230061. doi: 10.1371/journal.pone.0230061.