



Emergence and Re-emergence of Zika Virus; History and Current Trend

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Authors' contributions

This work was carried out in collaboration among all authors. Author BAA designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors AAS and MMI managed the analyses of the study. Author AA managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Zika virus is an emerging and re-emerging disease of medical and public health importance. The World Health Organization has already declared the virus a new emerging disease to be managed. The virus was first discovered in Uganda in the year 1947, and the last major outbreak was in Brazil in 2015 and then witness again in India 2017-2018. *Aedes aegypti* is one of the mosquitoes responsible for transmitting the Zika virus, dengue virus, yellow fever virus and chikungunya virus as a primary vector in certain parts of the world. and other south and Central American countries that made it considered as a re-emerging virus. The infectious agent of Zika virus (*Aedes aegypti*) has been introduced to vulnerable populations through trade, travel and climate change. As earth's climate warms and habitats are altered the virus has spread to new geographic areas such that warm temperatures allow mosquitos and diseases spread. There is currently no vaccine, but its development is still ongoing. Public awareness about this silent monster virus must be propagated and proper management of the virus is necessary to avoid future occurrences.

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1. BACKGROUND

Zika virus is an emerging and re-emerging virus of medical and public health importance [1]. Zika virus disease is caused by the Zika virus (ZIKV; genus *Flavivirus* family *Flaviviridae*) that is spread through the bite of an infected *Aedes aegypti* mosquitoes. It is also classified as a virus belonging to the *Flaviviridae* family same to Dengue virus family and transmitted by the same type of mosquitos that causes, yellow fever, west Nile virus and dengue virus. The world health organization (WHO) has already declared Zika virus infection a new emerging disease to be managed [2]. At present this infection can be seen worldwide in many countries, the disease now has an explosive pandemic potential with outbreaks occurring in Africa, South East Asia, and Pacific. Symptoms may include fever, red eyes, joint pain, headache and a maculopapular rash, it has not caused any initial death throughout the initial infection.

There is a growing concern across the globe due to detection and isolation of this viral pathogen being associated with increasing incidence of microcephaly in newborn infected fetuses and Guillain-Barre syndrome in adults [3]. The virus that causes the disease was first discovered in Uganda in the year 1947 the virus remained obscure and confined to equatorial belt, then it gradually spread from Africa to Asia in 1951-1981 [4,3]. It is tough to diagnose Zika infection through supported clinical signs and symptoms alone [5]. There is presently no treatment for Zika virus, care is corroborative with treatment of pain, fever, and itchiness. No vaccines is available for virus, however authority warns that development of a vaccine might take years [6].

This article aimed to review emergence of Zika virus as an infectious disease through its related history and predisposes factors that made it a re-emerging disease of public health importance.

2. HISTORY AND ORIGIN OF ZIKA VIRUS

Zika virus was first discovered in East Africa in April 1947 from rhesus monkey in the Zika forest of Uganda [7], it was found by the Rockefeller Foundation during investigations on the ecology of yellow fever, in fact Zika virus is not a new virus it has been discovered and mentioned for more than 50 years. It is transmitted by mosquito

primarily female *Aedes aegypti*. The scientist researching yellow fever placed a rhesus macaque in a cage in the Zika forest (Hence Zika meaning 'overgrown' in the Luganda language), near the East Africa virus research institute Entebbe, Uganda. The monkey developed a fever, and researchers isolated from its serum a transmissible agent. First evidence of human infection was identified in Uganda and the United Republic of Tanzania in 1945 in a study demonstrating the presence of neutralizing antibodies to Zika virus in sera [8], it was also subsequently isolated from a human in Nigeria in 1954 [9]. Zika which remained obscure and confined to equatorial belt gradually spread from Africa to Asia in 1951 1981 [4]. More recent epidemic has occurred in Polynesia, Easter Island, the cook island, Yap Island and New Caledonia and India.

From its discovery until 2007, there were only 14 confirmed human cases of Zika virus infection from Africa and South East Asia [10,11]. Since 2007 there are series of outbreaks occurring in most part of the world, alerting for preparedness for the pandemic Zika emergence. Today cases have been reported from Indonesia, Spain and Europe.

The World Health Organization declared a Public Health Emergency of International Concern (PHEIC) on February 1, 2016. On January 22, 2016, CDC activated its Emergency Operations Center (EOC) to respond to outbreaks of Zika occurring in the Americas and increased reports of birth defects and Guillain-Barre syndrome in areas affected by Zika. Most recently is a related outbreak was reported in India in western city of Ahmedabad in January 2017, second outbreak in southern state of Tamid Nadu in July 2017 and Zika virus cases spike in India's Jaipur as peak tourist season in 2018.

There is presently no report of Zika outbreak in Nigeria, but there is risk of ongoing Zika virus transmission in the country. The vector is widely distributed in the country and is also responsible for other flavivirus diseases such as dengue and yellow fever occurrence. However, in a research conducted by Fagbami in 4 different communities in Oyo state: the neutralizing test done showed that 40% of Nigerians had Zika virus neutralizing antibody, 50% of the Zika virus immune persons had neutralizing antibody to Zika alone or to Zika and one other flavivirus [12].

Table 1. Showing outbreaks in chronological

	Date	Country/Event
1	1947	First Zika virus discovered in Zika forest Uganda. [11]
2	1954	The virus was isolated from a young girl in Eastern Nigeria [9]
3	1958	Two further Zika virus strains are isolated from <i>Aedes africanus</i> mosquito caught in the Zika forest Uganda.
4	1960s-1980s	Zika is now being detected in mosquitos and sentinel rhesus monkeys used for field research studies in a narrow band of countries that stretch across equatorial Africa [4].
5	1969-1983	The known geographical distribution of Zika expands to equatorial Asia, including India, Indonesia, Malaysia and Pakistan, where the virus is detected in mosquitos [11].
6	2007	Zika spreads from Africa and Asia to cause the first large outbreaks in humans on the Pacific island Yap, in the Federated States of Micronesia [10].
7	2008	US scientist conducting field work in Senegal fell ill with Zika infection upon his return home to Colorado and infects his wife in what is probably the first documented case of sexual transmission of an infection usually transmitted by insects.
8	2012	Researchers publish findings on the characterization of Zika virus strains collected in Cambodia, Malaysia, Nigeria, Senegal, Thailand and Uganda, and construct phylogenetic trees to assess the relationships. Two geographically distinct lineages of the virus, African and Asian are identified [13].
9	2013-2014	The virus causes outbreaks in four other groups of Pacific islands: French Polynesia, Ester Island, the Cook Island, and New Caledonia. The results of retrospective investigation are reported to WHO on 24 November 2015 and 27 January 2016. These reports indicate a possible association between Zika virus infection and congenital malformations and severe neurological and autoimmune complications. An increase in the incidence of Zika infection towards the 2013 was followed by a rise in the incidence of Guillain-Barre syndrome.
10	2015-2016	Zika is spreading from Brazil to whole of South America.
11	2017-2018	Zika virus outbreak in western city of Ahmedabad in January 2017, second outbreak in southern state of Tamid Nadu in July 2017 and Zika virus cases spike in India's Jaipur as peak tourist season in 2018.

2.1 Outbreaks in Chronology

The outbreaks of Zika virus varies with different years and showed some significant characteristics in different countries. This outbreak was depicted in chronological order in Table 1.

2.2 Epidemiology of Zika Virus Infection

At first, Zika virus epidemiology was limited to Africa. The well-known pioneer report was from Nigeria. Fagbami studied sero-epidemiology in Oyo State, Nigeria in 1950s and revealed a high prevalence of antibodies to Zika and three other flaviviruses used. The percentage of positive sera were as follows: Zika (31%), yellow fever

(50%), West Nile (46%), and Wesselsbron (59%). Fagbami also mentioned that the percentage of neutralizing antibodies to other flavivirus in Zika virus immune sera was 81% to dengue type1, 58% to yellow fever, 7% to Wesselsbron, 6% West Nile and 3% to Uganda [12]. After the pioneer report from Nigeria, there was some sporadic reports on epidemiology of Zika virus worldwide. Since the first identification in Uganda in the year 1947, few human cases were reported until 2007 when a Zika outbreak occurred in Yap, even though Zika virus activity had been reported in Africa and in Asia through virologic surveillance and entomological studies [14]. Zika virus had been framed to infect humans from the results of serologic surveys in Africa nation and Africa country. A serosurvey of 84 folks of all ages showed fifty had antibodies,

with all higher than 40 years of age being immune. It was not until 1954 that the victorious isolation of Zika virus from a person was printed [9]. This came as part of a 1954 irruption investigation of jaundice suspected to be black vomit, it was discovered within the blood of a ten-year-old Nigerian female with low grade fever, headache and proof of protozoan infection, however no jaundice [15]. From its discovery till 2007, there have been solely 14 confirmed human cases of Zika viral infection from Africa and Southeast Asia [16]. The virus had been seen in several tropical countries and it is now be seen returning travelers to non-tropical areas. However, the big concern is the recent epidemics in South America and report on neonatal problem in neonate born to infected mother leads to the present urgent concern on the public health threat of Zika virus at present [17].

2.2.1 Outbreak alertness In America 2015 - 2016

Since April 2015 a large progress happening of Zika virus had begun in Brazil which has unfold to a lot of South, Central America and the Caribbean. The Pan America Health Organization and WHO issue epidemiology alert asking PAHO Member states to report observed increases of congenital microcephaly and other central nervous system malformations under the International Health Regulations [18]. In Jan 2016, the agency issued a pair of travel alert for folks traveling to regions and sure countries where Zika virus transmission was in progress and instructed that women that are pregnant ought to talk to their physicians before traveling. Government or health agencies of the UK, Ireland, New Zealand, Canada, and the international organization presently issued similar travel warning. In Colombia, Minister of Health and Social Protection Alejandro Gaviria Uribe counseled avoiding physiological state for eight months, whereas the countries in South America, Central American, and Jamaica have issued similar warning. As at January 2016, the authorities in American state Janeiro Rio city metropolis urban center de Janerio. Brazil declared plans to stop the unfold of Zika virus throughout the 2016 Summer Olympic Games therein town. In between Oct 2015 and 2016, Brazilian health authorities reportable 500 abnormal cases, some with a sever sort and a few having died [19]. The worst affected region of Brazil is its poorest, consisting of the three Northeastern States Paraiba, Pernambuco and Bahia. As of Gregorian calendar 2016, fifty-two

travel associated Zika virus illness cases with no domestically non-inheritable vector borne cases had been reportable from the United States of America to the agency. Although there have been nine native cases from United States of America territories [20]. The continued public health emergency in Brazil presents the biggest affected population to this point and a singular chance to scrupulously study the potential link between Zika virus and abnormal condition is ongoing [21].

3. EMERGING AND RE-Emerging OF ZIKA VIRUS DISEASE

Zika virus is an emerging and re-emerging disease due to its transmission to humans via the bite of an infected mosquito (zoonosis). The geographic range of the virus is rapidly increasing, when first discovered in Uganda in 1947 the virus remained obscure and confined to equatorial belt, then it gradually spread from Africa to Asia in 1951-1981 [4,3], which makes it an emerging disease. From its discovery until 2007 there were only 14 confirmed human cases of Zika virus infection from Africa and South East Asia [10,11]. Then the virus declined dramatically up until 2015, when a large progress of Zika virus began to unfold in Brazil and other south and Central American countries that made it considered as a re-emerging virus.

The infectious agent of Zika virus (*Aedes aegypti*) has further been introduced to vulnerable populations through trade, travel and climate change. As earth's climate warms and habitats are altered, the virus has spread to new geographic areas such that warm temperatures allow mosquitos and diseases, they transmit to expand their range into regions where they previously have not been found. The distribution of the vector is now the most extensive ever recorded across all continents including North America and even European from Africa. Zika virus vector can spread readily from person to person and cause disease through its bite, which is what makes it an emerging virus. And the virus can also re-emerge in the future due to this same global distribution of the vector *Aedes aegypti* (Fig. 1). New population of mosquitos capable of carrying Zika virus are been found such as in new capitol hill neighborhood of Washington D.C, and there is a potential of other *Aedes species* likely to play role in transmission of the vector e.g. *A. africanus*, *A. hensilli* due to their ability to thrive in wider range of water filled breeding sites [22].

Absence of specific treatments for Zika virus due to lack of comparative study caused the main eruption in 2015 and made the virus to survive over time because the disease was not well controlled in the past. Also, the interaction between human population and our environment has changed, especially in the last century which has triggered the re-emergence of the virus. Factors that have contributed to these changes are population growth, migration from rural areas to cities, international air travel, poverty, wars and destructive ecological changes.

3.1 Factors Influencing the Re-Emerging of Zika Virus

Directly or indirectly the weather conditions are important in the infectious disease's occurrence. For Zika virus occurrence, scientists suggest various driving factors:

- Rising temperature (abnormal warming) leads to increased incidence of mosquito-borne infections [23]. For instance, an El Nino phenomena that happened in the Pacific Ocean brought heavy rain resulting in a good opportunity for mosquitos' reproduction and multiplication site.
- Regarding the vector distribution there might be slight increase in the range of *Aedes aegypti* (Fig. 1), moving northward in the northern and southward hemisphere comparing to its distribution in the past. The movement of mosquito is related directly with the re-emergence of Zika virus infection, provided an infected case is present [24].

- Travelling effect is another factor influencing the re-emerging of Zika virus. Due to globalization effect, travelling to infected areas due to various activities, contributes to the acquiring of the infection easily. Factors such as; war, poverty, an investment activity, as the global people movement increase, the infectious agents will easily travel across the globe [25].

4. HOW TO DETECT ZIKA VIRUS

Bureau of Public Health Laboratories recommends that serum sample collection should be within the first 7 days of illness (2 ml serum/red or trigger top tube) AND/OR urine sample collected \leq 21 days of illness (10 ml collected in a sterile container). Other samples that may be tested using PCR if available are CSF amniotic fluid, birth cord and tissues [5].

Diagnostic testing of flavivirus infections also include an acute-phase serum sample collection as early as possible after onset of illness and a second sample collected 2 to 3 weeks after the first onset [27] Reverse-transcriptase PCR can also be used to detect Zika virus within 1st week of onset of illness (in blood and serum) to 2 weeks after (in urine) because immunoglobulin (IgM) and neutralizing antibodies typically develop toward the end of the first week of illness, hence an ELISA has been developed at the Arboviral Diagnostic and Reference Laboratory of the center for Disease Control and Prevention (Atlanta, USA) to detect IgM to ZIKV [27].



Fig. 1. Pictorial representation of *Aedes aegypti* [26]

4.1 Screening in Pregnancy

The authority recommends screening of pregnant ladies even though they do not have symptoms of infection. Pregnant ladies that have travelled to affected areas must be tested between 2 and 12 weeks when they arrive from the travel, also native health department must contact and help ladies living in affected areas. The authority also recommends testing at the primary antepartum visit with a doctor however, within the mid-second trimester, although this might be adjusted by the native health resources. Additional testing can also be done if there are any signs of Zika virus maladies with positive check result for the infection. The foetus must be monitored by ultrasound each 3 to 4 weeks to observe their anatomy and growth [28].

4.2 The Mechanism of Microcephaly and Infant Testing

Epidemiological studies show that in utero fetal infection with the Zika virus (ZIKV) may lead to microcephaly (Fig 2), an irreversible congenital malformation of the brain characterized by an incomplete development of the cerebral cortex [20]. ZIKV infection of cortical progenitors (stem cells for cortical neurons) controlling neurogenesis triggers a stress in the endoplasmic reticulum where some of the cellular proteins and lipids are synthesized in the embryonic brain, inducing signals in response to incorrect protein con-formation which is referred to as unfolded protein response. When it reaches the brain, Zika virus infects neuronal stem cells, which will generate fewer neurons, and by inducing chronic stress in the endoplasmic reticulum, it promotes apoptosis, i.e. the early death of these neuronal cells. These two combined mechanisms explain why the cerebral cortex of infected fetuses becomes

deficient in neurons and is therefore smaller in size [29].

Infants with suspected congenital Zika virus disease, CDC recommends testing with both serologic and molecular assays such as RT-PCR, IgM ELISA and plaque reduction neutralization test. Newborns with a mother who is potentially exposed and who have positive blood test, microcephaly or intracranial calcifications (Fig. 2) should have further testing including a thorough physical investigation for neurological abnormalities, dimorphic features, splenomegaly, hepatomegaly, and rash or other skin lesions done. Other recommended tests are cranial ultrasound, hearing evaluation, and eye examination. Testing must be done for abnormalities encountered as well as for other congenital infections such as syphilis, toxoplasmosis, rubella, cytomegalovirus infection, lymphocytic choriomeningitis virus infection, and herpes simplex virus [30].

4.3 Treatment

There is presently no specific treatment for Zika infection. Care is corroborative with treatment of pain, fever, and itchiness. Some authorities have counseled against victimization pain pill and different NSAIDs as these are related to harm syndrome once used for different flavivirus. In addition, pain pill use is mostly avoided in kids. Zika virus had seen comparatively very little studied till the main eruption in 2015 and no specific antiviral treatments were accessible. The advice to pregnant women is to avoid any risk of infection at any points possible, as once infected there is very little that be done as regards treatment [31]. Vitro study found that Zika virus could be sensitive to antiviral treatment that is often used against different infectious agent, but these results haven't been tested in animals or humans [32].

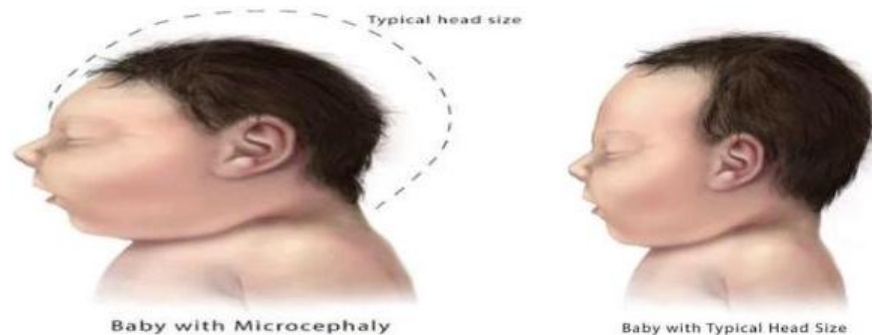


Fig. 2. Pictorial representation of a child with microcephaly [20]

4.4 Prevention and Control Strategies

The virus been spread by mosquitos, makes mosquito avoidance an important element to disease control. The US centers for Disease Control (CDC) recommends that individuals:

1. Cover exposed skin by wearing long-sleeved shirts and long pant
2. Use an insect repellent containing DEET, picaridin, oil of lemon eucalyptus or IR3535.
3. Always follow product directions and reapply as directed in point (2) above.
4. If you are also using sunscreen, apply sunscreen first, let it dry, and then apply insect repellent.
5. Follow package directions when applying repellent on children. Avoid applying repellent to their hands, eyes or mouth.
6. Stay and sleep in well air-conditioned rooms or well-ventilated room with netted windows as the case may apply.
7. Use a bed net if the area where you are sleeping is exposed to the outdoors.
8. Abstinence from indiscriminate sexual intercourse.

The center for Disease Control and Prevention additionally recommends ways for dominant mosquitos, like eliminating standing water, repairing septic tanks and victimization screens on doors and windows [33].

4.5 Actions Taken by PAHO/WHO Regarding Zika Fever

The Pan American Health Organization (PAHO) disseminates information on public health events of international concern by publishing alerts, interactive maps, and reports. The epidemiology alerts provide information on international public health events that have been confirmed with the Member States, along with the recommendations of the Pan American Health Organization. In areas where potential vectors are present, vigilance should be enhanced to detect imported cases of ZIKV, and laboratory capacity to confirm suspected ZIKV infections should be strengthened. Public awareness about this silent monster virus should be propagated, which would otherwise lead to the substitution of a deformed human population [34].

4.6 Vaccine Development

There is presently no vaccine/immunogen for Zika virus. Development may be a priority of the USA National Institute of Health (NIH), however officials warn that development of immunogen might take years [35]. Effective vaccines exist for many flavivirus, vaccines for black vomit virus, Japanese redness, and tick-borne redness were introduced within the 30s whereas the immunogen for dengue solely became obtainable to be used within the mid-2010s. Work has begun within the USA towards developing immunogen for the Zika virus, consistent with Anthony Fauci, director of the National Institute of hypersensitivity reaction and infectious Disease. The researchers at the immunogen center have intensive expertise from operating with vaccines for alternative viruses like West Nile virus, chikungunya virus, and dengue [5].

5. CONCLUSION

In conclusion Zika virus is fast spreading and causing panic across continents over the globe. The infection appears to have changed in character while expanding its geographical range of inhibition. The change is from an endemic mosquito borne infection causing mild illness across equatorial Africa and Asia, to an infection causing robust outbreaks linked with neurological disorder including Guillain-Barre syndrome and microcephaly. Zika virus should be properly cocktailed through various ways possible in order to avert its reoccurrence in the future. Also, the use of mathematical model in the control of Zika virus epidemic, reported in different literature can help to alert and enhanced the reduction of the number of zika infectives.

6. RECOMMENDATION

1. In areas where potential vectors are present, vigilance should be enhanced to detect imported cases of ZIKV and laboratories should be able to confirm suspected ZIKV infection especially in pregnant women.
2. More research should be done at the international level to determine the link between Zika virus and fetal damage.
3. Public awareness about this silent monster virus should also be propagated, which would otherwise lead to the substitution of a deformed human population.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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