

# **Review Article**

## **EMERGENCE AND RE-EMERGENCE OF ZIKA VIRUS; HISTORY AND CURRENT TREND**

### **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. *Aedes aegypti* is a small mosquito 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.

**KEYWORDS:** Zika virus; Emergence; *Aedes aegypti*; Vaccine; History

### **1.BACKGROUND REVIEW**

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 classified as a new dengue –like virus, transmitted by the same type of mosquitos that causes, yellow fever, west Nile virus and dengue virus. The world health organization 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 but the Bureau of Public Health Laboratories recommends serum sample collection within the first 7 days of illness and urine sample collected within the first 21 days of illness other samples that may be tested using PCR if available [5].

There is presently no treatment for Zika virus, care is corroborative with treatment of pain, fever, and itchiness. And, no vaccines, but development may be a priority of the United States of America National Institutes of Health (NH), however officers warn 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.

### **2.0 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 recently epidemic have occurred in Polynesia, Easter Island, the Cook Island, Yap Island and New Caledonia.

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.

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].

## 2.1 OUTBREAKS IN CHRONOLOGY

**1947:** First Zika virus discovered in Zika forest Uganda. [11]

**1954:** The virus was isolated from a young girl in Eastern Nigeria [9].

**1958:** Two further Zika virus strains are isolated from *Aedes africanus* mosquito caught in the Zika forest Uganda.

**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].

**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].

**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].

**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.

**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].

**2013-2014:** The virus causes outbreaks in four other groups of Pacific islands: French Polynesia, Easter 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.

**2015-2016:** Zika is spreading from Brazil to whole of South America.

## **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, Micronesia, even though Zika virus activity had been reported in Africa and in Asia through virologic surveillance and entomological studies [14]. Until present the virus can be seen in several tropical countries and it can also be seen in returning travelers to non-tropical areas. However, the big concern is the recent epidemics in South America. The 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 [15].

### **2.2.1 Virus isolation in monkeys and mosquitoes 1947**

The virus was initially isolated in April 1947 from rhesus monkey, old world monkey that had been in the Zika Forest of Uganda, close to Lake Victoria, by the scientist of infectious disease analysis Institute. A second isolation from the two-winged insects. Once the monkey developed a fever, researchers isolated from its blood serum “filterable transmissible agent” that was named Zika virus in 1948 [7].

### **2.2.2 First evidence of human infection 1954**

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. Blood was injected into the brain of laboratory mice, followed by up to 15 mice passages, the virus from mouse brains was then tested in neutralization tests mistreatment rhesus sere specifically resistance to Zika virus. In distinction no virus was isolated from the blood of 2 infected adults with fever, jaundice, cough, diffuse joint pains symptoms in one and fever, headache, pain behind the eyes and within the joints in another. Infection was proven by an increase in Zika virus specific bodily fluid antibodies [16]. A 1952 analysis study conducted in Republic of India had shown a significant number of Indians tested for Zika had exhibited associate immunologic response to the virus, suggesting it had long been widespread among human population. [7].

### **2.2.3 Spread in equatorial Africa and to Asia, 1951-1981**

From 1951 through 1981, proof of human infection with Zika virus was reported from different African countries, like the Central Africa Republic, Egypt, Gabon, Sierra Leone, Tanzania, and Uganda moreover as in components of Asia together with Asia country, Indonesia, Malaysia, Philippines, Thailand, and Vietman [4]. From its discovery till 2007, there have been solely 14 confirmed human cases of Zika viral infection from Africa and Southeast Asia [17].

### **2.2.4 Micronesia 2007**

In April 2007, the primary eruption outside Africa occurred on the island of Yap within the Federate States of Micronesia, characterized by rash, pinkeye, and hurting that was at the start thought to be break bone fever, chikungunya, or Ross stream disease. Serum samples from patients within the acute section of health problem contained RNA of Zika virus. There have been 49 confirmed cases, 59 unofficial cases, no hospitalization and no deaths [10].

### 2.2.5 America 2015:(Current outbreak)

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 and 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 Puerto Racketeer Influenced and corrupt Organization Act and the United States of America Island [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 [21].



Fig 1: Pictorial representation of countries with cases of Zika virus [21].

### 3.0 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 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*. 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 cause the main eruption in 2015 and made the virus to survive over time and 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 2), moving northward in the northern hemisphere and southward in the southern 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].



**Fig 2: Pictorial representation of *Aedes aegypti*. [26].**

#### **4.0 HOW TO DETECT ZIKA VIRUS**

Sample collection: Bureau of Public Health Laboratories recommends serum sample collection within the first 7 days of illness (2ml 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, CSF amniotic fluid, birth cord and tissues [5].

Suggestions were made that diagnostic testing of flavivirus infections should include an acute-phase serum sample collected as early as possible after onset of illness and a second sample collected 2 to 3 weeks after the first [27] The virus was isolated from urine and semen of experimentally infected animals, and viremia developed in female boars that were artificially inseminated with the infectious semen [11].

Reverse-transcriptase PCR can be used to detect the Zika virus for 1 week (in blood and serum) to 2 weeks (in urine) of the illness. IgM and neutralizing antibodies typically develop toward the end of the first week of illness, cross-reaction with related flavivirus e.g. dengue and yellow fever virus) is common and may be difficult to discern. Plaque-reduction neutralization antibodies and discriminate between cross-reacting antibodies in primary flavivirus infection. An ELISA has been developed at the Arboviral Diagnostic and Reference Laboratory of the center for Disease Control and Prevention (Atlanta, USA) to detect immunoglobulin (Ig) M to ZIKV.

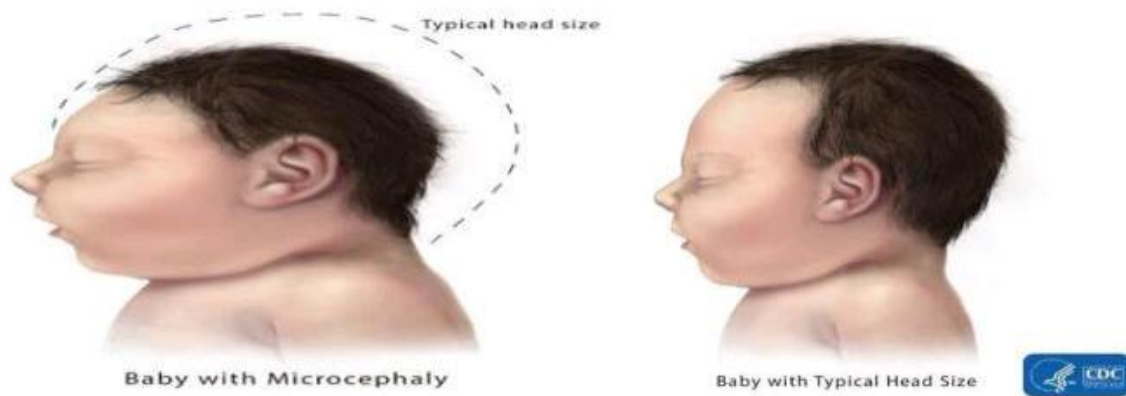
##### **4.1.1 Screening in pregnancy**

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

##### **4.1.2 Infant testing**

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 3) should have further testing including a thorough physical investigation for neurological abnormalities, dimorphic features, splenomegaly, hepatomegaly, and rash or other skin lesions should be done. Other recommended tests are cranial ultrasound, hearing evaluation, and eye examination. Testing should 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 [29].





**Fig 3: Pictorial representation of a child with microcephaly [20].**

## **4.2 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 [30]. 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 [31].

## **4.3 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.
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.
7. Use a bed net if the area where you are sleeping is exposed to the outdoors.
8. Abstinance 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 [32].

## **4.4 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 [33].

#### **4.5 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 [34]. Effective vaccines exist for many flaviviruses, vaccines for yellow fever virus, Japanese encephalitis, and tick-borne encephalitis 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 Health, National Center for Infectious Diseases. The researchers at the immunogen center have intensive expertise from operating with vaccines for alternative viruses like West Nile virus, chikungunya virus, and dengue.

Nikos Vasilakis of the Biodefense and Emerging Infectious Disease foresaw that it should take 2 years to develop an immunogen, however ten to twelve years could also be required before a good Zika virus immunogen is approved by regulators for public use.

An Indian company in India Biotech International, rumored in early February 2016 that it was acting on vaccines for the Zika virus. The corporation is functioning on 2 approaches to vaccine; of "Recombinant" involving biotechnology and "inactivated" where the virus is incapable of reproducing itself, it will still trigger a response.

#### **5.0 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.

#### **5.1 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.

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