



## EMERGING ZOOONOTIC DISEASES: ZIKA VIRUS AS A CASE STUDY .

Ogunmodede A.Funmilola  
Registrar, Dept of Internal medicine  
FMC Owo  
Ondo, Nigeria  
[bimpefunmilola@yahoo.com](mailto:bimpefunmilola@yahoo.com)  
07036306078

### ABSTRACT

Communicable diseases are major causes of pandemics in the world. Aetiology of recent outbreaks are diseases that appear hidden in wild primates and arboreal mosquitoes . Zika virus is an example of such. It was first discovered in Africa in 1947, was silent for some period of time only to re-appear in Asia 60 yrs later. It is now ravaging countries in South America. About 1.3 million cases were suspected in Brazil in december 2015. It is an RNA arthropod borne flavivirus transmitted by mosquitos of *Aedes aegypti* and *Aedes albopictus* groups in tropic and temperate regions respectively. It has affinity for neural cells which explains how it causes microcephaly in neonates and Guillain barre syndromes in adults. It is a self limiting infection which presents with fever, maculopapular rash and joints pain. It is diagnosed by identification of the virus in the serum or urine of the affected individual by reverse transcriptase PCR. Bedrest and supportive care are part of the management of this infection. Avoidance of travel to affected areas and aggressive mosquito control are methods of preventing the spread of the virus.

### Introduction

Zoonotic diseases are infectious disease of animals(vertebrates) that can naturally be transmitted to humans (Adetokunbo and Herbert,2003).The past few years have witnessed the outbreak of some zoonotic diseases such as Yellow fever, Ebola ,Lassa and Dengue fevers. These diseases

are notable for their ease of transmission and high fatality. Some of these zoonotic diseases are transmitted by Arboviruses (Anthony and David ,2016).Arboviruses is a term used to describe hundreds of predominantly RNA viruses that are transmitted by arthropods, notably mosquitoes and ticks . They are often maintained in complex cycles involving vertebrates such as mammals or birds and blood-feeding vectors. They are responsible for some clinically significant diseases like some mosquito-borne alphaviruses such as chikungunya and flaviviruses such as dengue and West Nile (Anthony and David,2016)

Viruses are the smallest infectious agents with diameter varying from 3 to 20nm. They contain only one kind of nucleic acid (RNA or DNA) as their genome. The nucleic acid contains information necessary for programming the infected host cells to synthesize virus specific macromolecules required for the production of viral progeny. The nucleic acid is encased in a protein shell which may be surrounded by a lipid containing membrane (Rajesh and Rattan,2008). Zika virus is an RNA flavivirus and it's the only flavivirus linked with teratogenic effect (O'Leary *et al.*,2006).It is a positive sense single stranded RNA virus . It has an envelope with icosahedral nucleocapsid (Knipe and Howley; 2007).

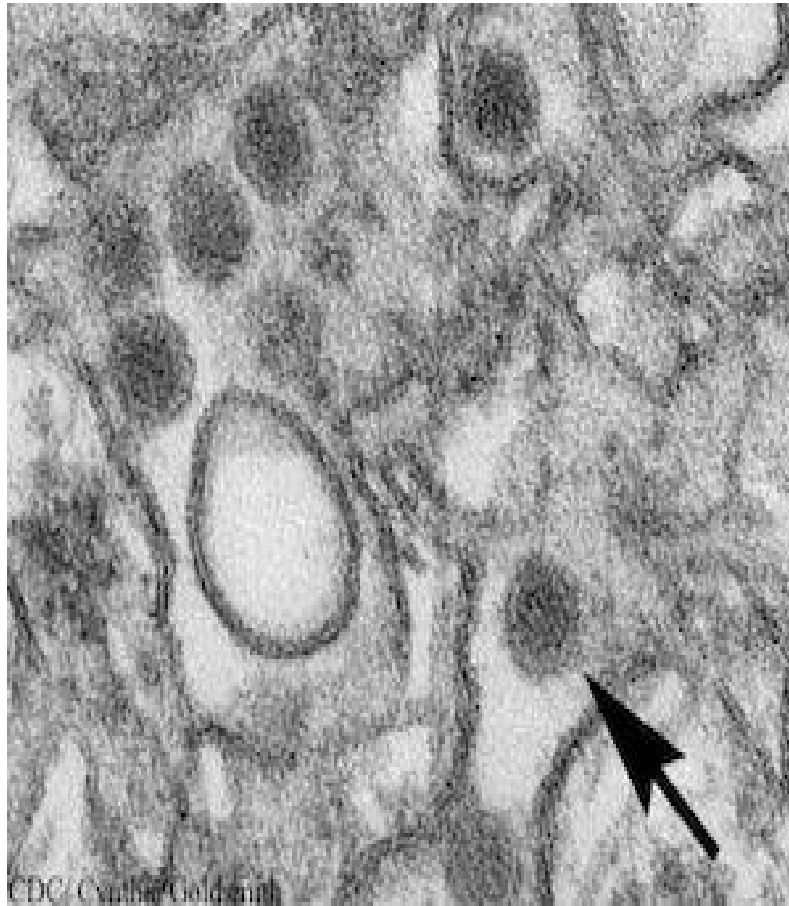


Fig 1: The microscopic view of zika virus under transmission electron microscope .  
(mag x150,000) Source: (CDC,2016)

Zika was incidentally discovered in Uganda in 1947 (Dick *et al.*,1952).Then it had just little evidence of mild human infection. There were few reporting on illnesses caused by zika virus in Africa and Asia (Pierson and Diamond,2014). Its sudden pandemic re-appearance in South America is disturbing with its appearance round the globe arriving not only in the Americas but also in the country of Cape Verde in West Africa, near its presumed ancient ancestral home (Anthony and David, 2016).

### **Timeline**

Zika virus was discovered in 1947 at Zika Forest in near Entebbe in Uganda (Simpson,1964).It was discovered accidentally during a mosquito and primate surveillance (Dick *et al.*,1952) . Antibodies in the serum was the evidence of human infection then in Africa and Asia. The virus

was isolated from humans in Uganda (Dick,1953), Nigeria (Mac Namara,1954) and Egypt (Smithburn *et al.*,1954). Five thousand people were infected in an outbreak that occurred (Duffy *et al.*,2009).

French Polynesia, New Caledonia, the Cook Islands and Easter Island reported some cases of zika virus infection between 2013 and 2014 (Cao-lormeau *et al.*,2014).

An exanthematous illness was identified in Brazil in march 2015 and had spread to Columbia in October of the same year (Campos *et al.*, 2015). 1.3million suspected caseswere reported by the Brazil Ministry of Health by the end of that year(MMWR,2016). The rapid spread of the virus and the large number (4,300) of microcephaly cases led the World Health Organisation (WHO) to declare Zika a Public Health Emergency of International Concern (Gulland,2016). The fatality rate is zero (CDC,2016).

### Mode of transmission

**A bite by mosquito of *Aedes species****A. aegypti* is well distributed in the tropical and subtropical regions while *A. albopictus* exist more in the temperate region. (Chouin *et al.*,2016).



Fig.3: Picture of *Aedes aegypti*, The vector of Zika virus.

Source:( Gathany, 2016)

**Blood transfusion with an infected blood.** Blood transfusion is a medical intervention in which blood and blood products are been infused from a donor to a recipient. Just like other viral illness like hepatitis and HIV which can be transmitted during blood transfusion ,zika virus can also be transmitted. Zika virus screening has been included in the screening tests done before transmission in areas affected by the present zika pandemic (Musso *et al.*, 2014).

**Sexual transmission** (oral, vagina and anal sex) zika virus can be transmitted by sexual contact (Venturi *et al.*, 2016). Many cases have been reported in sexual contact with someone with recent travel to areas affected.

**Vertical Transmission** (mother to child) uteroplacental circulation between a mother and fetus provides a means of transmitting zika virus to an unborn child. This is the cause of many complications of zika virus infection like miscarriages, chorioamnionitis and the most deadly of them which is microcephaly (Indura and Michael,2016).

### **Pathogenesis**

Zika virus is neurotropic which means it is basically attracted to neural cells (Bell *et al.*,1971). Zika virus infects human neural progenitor cells leading to decreased growth and cell death (Nathalie *et al.*,2016). This explains the microcephaly in infants of mothers with Zika virus and meningoencephalitis in adult with zika virus A rise in the incidence of Guillain–Barré syndrome ( an immune-mediated flaccid paralysis often triggered by infection) was first reported in 2013 during a Zika outbreak in French Polynesia(Nathalie *et al.*,2016). An increase in the incidence of microcephaly (a clinical sign that can be caused by underdevelopment of the fetal brain) was first reported in northeastern Brazil in 2015, after Zika virus transmission had been confirmed there (Oliverameloet *al.*,2016).The reports of excess cases of Guillain–Barré syndrome and microcephaly led the World Health Organization (WHO) to declare a Public Health Emergency of International Concern on February 1, 2016, and to recommend accelerated research into possible causal links between Zika virus and neurologic disorders (Gulland, 2016).

**Signs and symptoms.:** usually mild. It's self limiting just like other viral infections like measles, chicken pox. Symptoms last for several days to week and may not warrant hospital visit. They include:

Fever (a temperature greater than 37.5°C)

Maculopapular rash (a rash on the skin that is 0.5cm raised and coloured) which is pruritic (Brasil *et al.*,2016).

Conjunctivitis (red, inflamed eyes).

Joint pain which is generalized (Musso *et al.*,2014). It could be mistaken for other febrile illnesses like malaria.

Pregnant women may have miscarriage. (Annemiek *et al.*,2016)

Fetus of infected pregnant women may have microcephaly . Microcephaly is defined as head circumference that is less than 2 standard deviation from normal (William *et al.*, 2009). In September 2015, researchers reported a substantial increase in the number of cases of neonatal microcephaly among women giving birth in northeastern Brazil (Oliveramelo *et al.*,2016). A subsequent increase was reported in southeast Brazil (MMWR,2016). ZIKV has been isolated from the amniotic fluid of women who are pregnant with infants who have confirmed microcephaly ( Calvet *et al.*, 2016) and from the brain of a fetus with central nervous system (CNS) abnormalities (Jernej *et al.*,2016 ).

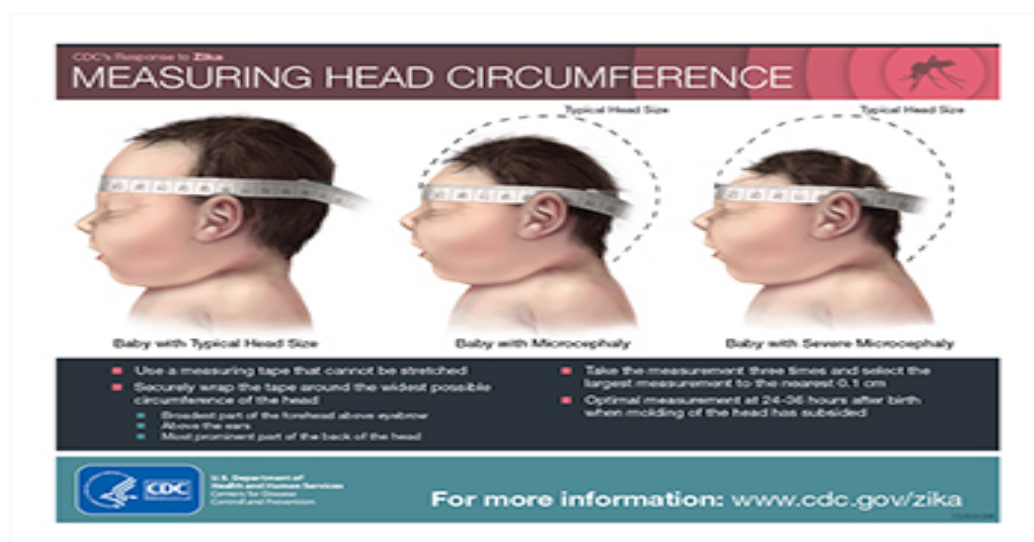


Fig.5: Picture showing how to measure head circumference.

Source: CDC;2016

## Diagnosis

Diagnosis a bit difficult with signs and symptoms, history of recent travel to areas majorly affected maybe helpful. It can be identified by:

Reverse transcriptase PCR in acutely ill patients (Peterson *et al.*,2016 b) . The detection of viral nucleic acid in the serum provides a definitive diagnosis . Serum sample can be used within 1-3days of onset of symptoms (Musso *et al.*,2015). Urine sample can be used within 3-5 days of onset of symptoms (Gourinat *et al.*,2015) .

Aminocentesis can be done in pregnant women to check its presence in the amniotic fluid of fetus of infected mothers. In-situ hybridization with the use of ZIKV-specific probes can reveal that placental amniotic epithelium is positive or not for ZIKV RNA ( Annemiek *et al.*, 2016).

Placental tissue in abortus of women who are suspected to have zika virus infection could be examined by doing histopathological and immunohistochemical investigation with the use of CD45 and CD3 antibodies to detect increased inflammatory-cell infiltration (Annemiek *et al.*,2016).

Ultrasonography done in pregnant women may reveal microcephaly (small head circumference) due to the destruction of different parts of the brain(Jernej *et al.*,2016).

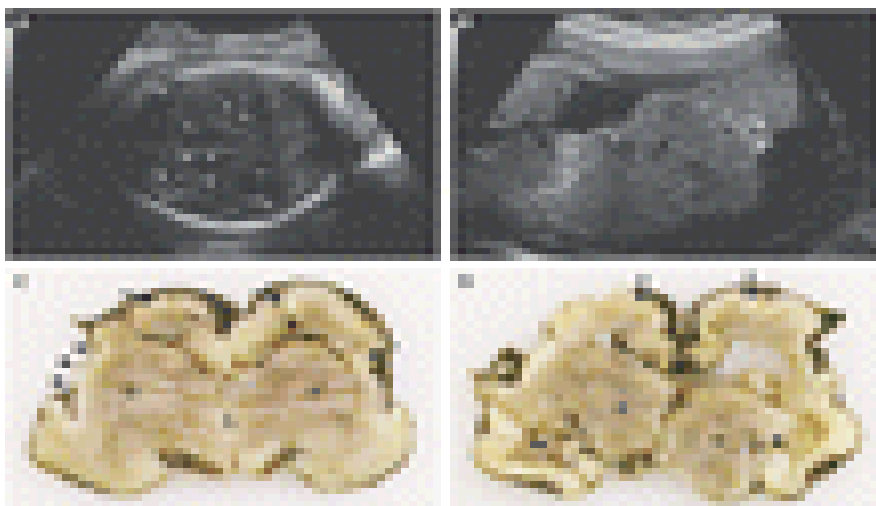


Fig 6: Prenatal ultrasonographic images and photographs of coronal slices of brain in fetal microcephaly. Source: Jernej *et al.*,(2016)

## **Management**

Bed rest and supportive care (Anthony and David,2016).

Pregnant women who travel to affected areas should be tested after 2-12 weeks of their return from such areas.

Fetus of pregnant women should be monitored by ultrasound every 3 -4 weeks to monitor their anatomy and growth (CDC,2016).

Preconceptional counselling should be done for couples living in such areas and should be advised to delay pregnancy for some time. This is to reduce the chances of infecting a fetus with zika virus in- utero (Petersen *et al.*,2016).

A pharmaceutical company expressed the possible development of a vaccine by the end of 2016. Research is however ongoing towards its development. The primary goal of this review is to develop medical measures which should include diagnostics, therapeutics, and vaccines (Anthony,2017). Challenges specific to the development of a zika vaccine include the lack of adequate animal models, uncertainties in the epidemiology which affect clinical trial site selection, the likelihood that the vaccine will need to induce sterilizing immunity to prevent congenital Zika syndrome (CZS).

## **Ethical issues associated with zika virus infection**

So many ethical issues have risen as a result of the ongoing zika virus outbreak. People have had to choose between their personal philosophies , belief system and having babies with congenital defects. Amongst other issues are the increase in the number of women procuring abortion in some of the regions affected by zika outbreak. Aiken *et al.*,(2016) documented that since some Latin American countries issued warnings to pregnant women about complications associated with Zika virus infection, requests for abortion through WoW (Women on Web) which is a nonprofit organization that provides access to abortion medications (mifepristone and



misoprostol) through online telemedicine (outside the formal health care setting) in these countries where safe abortion is not universally available increased significantly.

Latin Americans which are mostly catholics have had to encourage the use of contraceptives which is quite unusual. Pope Francis said that avoiding pregnancy is not an absolute evil (McElwee, 2016). He understood the use of contraceptives in preventing the spread of the zika virus as a "permitted case."

Pregnant women that have had zika virus infection had to personally request for the termination of their pregnancy because the clinical presentation raised suspicion of fetal viral infection. The National and hospital ethics committees have had to approve the medical termination of the pregnancies subject to the parents decision whenever a fetus is been given a poor prognosis for neonatal health because of severe brain disease and microcephaly (Jernej *et al.*,2016).

There were several debates on change in venue of the 2016 Olympic games because of the zika virus outbreak. It eventually held and contestants especially females had to choose between contesting and getting infected with the virus and its consequences on their unborn children.

## **Prevention**

A travel alert was raised by CDC . Areas affected are best avoided.

Reducing sexual transmission by avoiding unprotected sexual contact with partners who are at risk for zika virus infection (Petersen *et al.*, 2016).

Other methods of prevention are aggressive mosquito control which include:

The use of mosquito repellants, permethrin treatment of clothing (Banks *et al.*,2014)

House screens, Air conditioning (Brunkard *et al.*,2007)

Removal of yards , household debris (Heintzeet *et al.*,2007) .

Removal of Containers that provide mosquito breeding sites (Barrera *et al.*,2008).

Use of Sun screens, protective wear, mosquito repellants and insecticides (Barrera *et al.*,2008).

## **Complications of zika virus**

Microcephaly which is a major complication of Zika virus infection. It is defined as a head circumference that measures more than two standard deviations below the mean for age and sex. It results from failure of brain growth. The growth of the brain is usually influenced during pregnancy, labour and the first 2-3 yrs of life. Microcephaly is a major cause of mental retardation, seizure disorder and developmental delay (William *etal.*,2009).

Guillain-Barre syndrome (GBS) an uncommon sickness of the nervous system in which a person's immune system damages its own nerves causing muscle weakness and at times paralysis(WHO,2016). Though there are other causes of GBS, It is strongly associated with Zika virus and there has been an increase in the number of people with GBS in several Countries that have experienced Zika outbreak(WHO,2016). Symptoms of GBS include weakness of the arm and legs and in severe cases it can affect muscles that control breathing. The symptoms of GBS can last a few weeks or several months. Some people recover fully from GBS while others have permanent damage.

## Conclusion

Zika virus spread is associated with human activity. It has been discovered that Zika virus like every other arbovirus have continually evolved and adapted within ecologic niches that are constantly been perturbed by human, Zika virus is teratogenic and pandemic in nature and can be transmitted easily by mosquito *Aedes aegypti* and *A. albopictus* bite in an endemic region, sexual contact with an infected person and blood transfusion from and infected individual. The socio economic and psychologic burden of managing an infant that was infected with the virus from the mother while in the womb and the eventual growth into an adult with microcephaly is disturbing. All hands should be on deck in areas of integrated research work by the Ecologist, Policy makers, Medical Scientist and Entomologist on how to find a lasting solution to the imbalance in the eco system which has been linked to the sudden awakening of these "slumbering" infections.

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