ZIKA VIRUS: A CHALLENGE TO FETO-MATERNAL HEALTH CARE

Gimba, R.[1], and Mohammed, T.[2]
[1]Department of Medical Laboratory Science University of Maiduguri
[2]WHO Polio Laboratory, University of Maiduguri Teaching Hospital
Corresponding author: Gimba Rukaiya, rugilisa@gmail.com

ABSTRACT

Background: The wide spread of Zika virus (ZIKV) is a public concern because of possibility of mother to child transmission and risk of birth defects. Zika has caused a devastating impact around the globe with severe sequelae in the general population. Although zika is self-limiting infection associated with miscarriages and neonatal deaths. However recent report suggested it can be potentially associated with Guillan-Barre and microcephaly syndrome.

Aim: The epidemiological evidence indicating the possibility of an association between ZIKV infection and the occurrence of microcephaly in fetuses of affected mothers is a sufficiently alarming challenge that requires an urgent joint effort from all areas of healthcare directly or indirectly linked to the diagnosis and care of pregnant women and newborn.

Methodology: The diagnosis of Zika virus is established via real-time reverse-transcription polymerase chain reaction (rRT-PCR) testing for Zika viral RNA or serology.

Result: Between October 2015 and march 2016 a total of 6776 cases of microcephaly and central nervous system malformation were reported by brazil including 208 death, investigation have been concluded for 2485 cases and 944 in 21 out of 27 states were confirmed with microcephaly and CNS suggestive of congenital infection. This contrast with the period from 2001 to 2014,when an average of 163 microcephaly cases was recorded nationwide

Conclusion: There is no specific treatment for Zika virus infection, currently vector control seem to be the most effective available preventive measure against ZIKV spread.

Key words: Zika Virus, Feto- maternal Health, mirocephaly.

INTRODUCTION

Zika virus (ZIKV) is a member of the virus family flaviviridae and genus flavivirus (Malone *et al., 2016*), zika virus is an enveloped positive single stranded RNA virus belonging to group IV Spondweni, (Knipe *et al*.,2007).It was initially identified in Uganda in 1947 in a rhesus monkey used as a sentinel during sylvatic yellow fever surveillance in the Zika forest in Uganda ([Dick *et al*.,1952). It is spread by a daytime active *Aedes* mosquito, such as *Aedes aegypti* and its name came from the zika forest of Uganda, where the virus was first isolated. Zika virus is related to the dangue, yellow fever, Japanese encephalitis and West Nile virus. Before 2007, ZIKV was reported as causing only sporadic human infections in tropical Africa and in some areas in Southeast Asia, since 2007, several outbreaks have been documented across the Pacific Islands showing the viral circulation outside its previously known geographic region (knipe *et al*,2007). Autochthonous transmission of ZIKV in South America was reported in early 2015 (Campus, 2015; Zanluca, 2015). However, in 2007 the first large outbreak occurred on the island of Yap, in Micronesia, resulting in a drastic change in the outlook on the ZIKV infection and a growing interest for this newcomer to the world of arboviruses. Until recently, the clinical manifestations of ZIKV infection ranged from asymptomatic infections to mild, self-limited febrile illness, similar to that of a mild dengue-

like syndrome, characterized by fever, headache, muscle and joint pains, as well as a characteristic maculopapular rash reminiscent to measles. Moreover, the disease occurred mainly within a narrow equatorial belt from Africa to Asia (A.Enfissi et al,2016). However, an association with neurological complications such as Guillain-Barre Syndrome and congenital microcephaly has been suspected (Oehler *et al.*, 2014 ; Oliveira *et al*.,2016), in particular following spreading of the virus in the Americas where the vectors are present given the rapid worldwide spread of ZIKV and the current pandemic in Latin America and the Caribbean.

EPIDEMIOLOGY

The first description of ZIKV occurred in 1947 when it was isolated in Rhesus monkeys used as sentinels for yellow fever. This discovery occurred in the Zika forest in southern Uganda, hence the name of the virus (WHO, 2015). The description of the first infection in humans occurred in Nigeria in 1954 (F.N. &Macnamara1954), and its dispersion within the African continent can be considered slow. Until 2007, documented reports indicated that the number of people affected by this viral infection did not exceed 50 in sporadic occurrences in Africa and in some countries of Southeast Asia. After this apparent decrease in its dispersion, the first epidemic of ZIKV was observed in 2007 on the Pacific island of Yap in the Federated States of Micronesia in the Pacific Ocean.(Imperato, 2016),during the outbreak forty nine ZIKV infected cases were confirmed, while serological evidence of infection was obtained from 73% older than 3years(Faye et al,2014). In 2013, there were other epidemic outbreaks in French Polynesia and Easter Island before it finally reached Brazil between 2013 and 2014.(Geraldo *et al*.,2016) The epidemiological evidence indicating the possibility of an association between ZIKV infection and the occurrence of microcephaly in fetuses of affected mothers is a sufficiently alarming challenge that requires an urgent diagnosis and care of pregnant women and newborn affected by this infection.(Geraldo *et al*.,2016) After the first evidence of human infection in 1952,(Fagbami,1979) sporadic cases and serological evidence of Zika were reported in surveys and case reports, showing that Zika was active in several countries in Africa and Asia(Pellissier,1954) before spreading to the Pacific region and more recently to the Americas. In 1954, a serological surveillance in French Equatorial Africa showed only 0.5% was positive for Zika antibodies (Pellissier, 1954). In Nigeria (1971–1975), 38% of the individuals had neutralizing antibodies to Zika in sera,(Fagbami,1979) and this disease was serologically confirmed in 3.1% of febrile patients in a hospital in Java, It was higher among women and the mean age was 36years. (Duffy *et al*.,2009). The Nigeria Centre for Disease Control, NCDC, has released a risk assessment of Zika virus infection for Nigeria, in the document, entitled "Public Health Risk Assessment of Zika Virus in Nigeria and Interim Recommendations", the NCDC notes that the current epidemiology of Zika in Nigeria has not been well documented or understood due to paucity of recent data. The document which contains a risk assessment of Zika virus infection for Nigeria, and recommendations to healthcare workers and the general public on how to protect themselves from the virus, observes that the virus shares a similar vector; the *Aedes Steogmyia* mosquitoes, also responsible for other flavivirus infections recorded in Nigeria such as yellow fever and dengue. Stating its intention to carry out a nationwide surveillance to understand and monitor the epidemiology of Zika virus in Nigeria for appropriate interventions to be put in place, the NCDC says that the environmental and human behavioural risk factors in areas with reported Zika outbreaks are similar to those found in Nigeria and would thus favour the circulation of Zika. According to the document:

"Possible cross-reaction with other endemic flavivirus like yellow fever and dengue; genetic host factors protecting against infection or disease; low vector competence and transmission efficiency; lack of diagnostic testing; and the absence of systematic surveillance are potential limitations to detect on-going transmission of Zika in Nigeria." (NCDC, 2016). Nigeria has a previous Zika virus transmission but there is no current evidence of an ongoing Zika virus outbreak. (https,2020).

Table 1: Comparison of Zika virus outbreak in Yab, French Polynesia, and Brazil.

	Island (pacific)	**French Polynesia(pacific)**	**Brazil(Americas)**
Population	7500	270000	206000000
Confirmed Cases	49	340	697
Estimated infection (% of population)	5005(75%)	30000(11.5%)	220213(0.1%)
New Epidemiological Finding	1st reported out break;1st detection outside Asia and Africa	Non- vector borne transmission possible (materno-fetal,sexual transfusion)	1st detection in the Americas; microcephaly association
Clinical Finding	Rash, fever, arthralgia and conjunctivitis.	GBS, CNS, and malformation	GBS,CNS and malformation
CNS malformation Cases	0	17	2653
Main challenge	Identification of zika Virus	High incidence of GBS	High incidence of microcephaly

Transmission

Viral transmission occurs during the blood feeding of *Aedes* mosquitoes, some cases of non-vector-borne infection have also been reported, referred to as perinatal transmission (Besnard *et al*.,2014), with mother and baby presenting the same clinical signs of the disease, transmission by blood transfusion has not yet been demonstrated although a potential risk cannot be excluded (Musso *et al.,2013).* The viral genome has been detected in saliva (Musso *et al*., 2015) and urine (Gourinat *et al*., 2015). Zika can be transmitted through sex, as a sexually transmitted case was reported in the U.S.A (Foy *et al*., 2011) and the presence of ZIKV was demonstrated in the semen of an infected patient in French Polynesia (Musso *et al.,* 2015) these findings nevertheless support the hypothesis that sexual relations potentially transmit ZIKV, followings a zoonotic transmission from mosquito to non-human primate/monkey and then to humans following the bite of an infected mosquito.(Musso & Gubler 2016)

Sign and Symptoms

Most people with Zika virus infection are asymptomatic. (Duffy *et al.,2009*) symptom when present range from mild to severe symptoms, features most often observed include maculopapular rash, fever, arthralgia, and non-purulent conjunctivitis; symptoms typically last several days to 1 week (Hannesaey *et al*., 2016). The incubation period for Zika virus in humans is unknown but is believed to be similar to that of other flaviviruses, in the range of 3 to 14 days. (Rudolph *et al*.,2014). All age groups are at risk for Zika virus infection.

Pathogenesis

Arthropod-mediated transmission of arbovirus is initiated when a blood-feeding female injects the virus into the human skin. (Briant *et al*.,2014).

Like many other members of the flavivirus family, ZIKV is transmitted following the bite of *Aedes* mosquitoes. Different cells types, such as epidermal keratinocytes, dendritic cells or neurons are known to be a target of flaviviruses. Given the knowledge on the entry route of flaviviruses, potential target cells for infection with ZIKV have been investigated. Recently, it was reported that various cells in the human skin compartment are able to support ZIKV replication (Hamel *et al*., 2015). Following infection with ZIKV, viral replication was observed in fibroblasts, keratinocytes and immature dendritic cells (iDCs), in a time dependent manner, with a substantial percentage of infected cells as early as 24h post infection, whereas all cells were able to produce infectious virions. The interaction between the E glycoprotein of the viral particle and cell surface receptors allows the entry of the flaviviruses into the target cells. However, despite many investigations, the key cellular receptors remain relatively unknown and their importance in viral entry have yet to be clearly established. (Rodolphe *et al*.,2016). Viral particle is lodged into the lymph node and this stimulate immune response by mobilizing macrophages and neutrophils , the viral particle is moved into the blood stream causing vireamia, were it infect several tissue like the brain, spinal cord, liver, spleen, joint, and Muscle cells. It replicate in the cytoplasm causing tissue damage and therefore patient present with clinical sign and symptoms.

Diagnosis

Diagnosis of this infection can be confirmed *via* laboratory testing for the presence of viral RNA in body fluids such as serum, saliva, and urine (Musso *et al.*, 2015). There are specific tests used to confirm the presence of ZIKV, RT-PCR has been used to detect the virus in serum. ZIKV has also been detected in urine using RT-PCR method 10 days after infection, a period longer than that of blood. Specific tests such as immunoglobulin enzyme linked immunosorbent assay (Ig-ELISA) are carried out to detect the presence of arbovirus antibodies like immunoglobulin-M and -G (Ig-M/G). Plaque reduction neutralization test (PRNT) is more specific for differentiation of flavivirus that are closely related, and can be carried out in addition to Ig-ELISA test. ZIKV has been shown to persist in semen for 55 - 65 days from first onset of symptoms, RT-PCR method has been used to confirm the presence of the virus in semen. Tests are also carried out on pregnant women exposed to ZIKV on the safety or otherwise of their fetuses, as a result of strong evidences associated with Zika virus infection and birth defects. Prenatal ultrasonography is carried out to evaluate microcephaly in fetuses from exposed or infected mothers. ZIKV was also detected in fetal brain using RT-PCR test [Abdullahi *et al*., 2017].

Guillan Barre and Microcephaly

GBS is an autoimmune disorder characterized by damage to peripheral nerves resulting in life threatening muscle weakness in the extremities and upper body, and as the disease progress it fatally affect the respiratory muscle.

Microcephaly is a cephalic disorder with cerebral artropy and ventriculomegaly, extensive intracranial calcifications, simplified gyral patterns dysgenesis of the corpus callosum, and cerebellear hypoplasia.(Costa F *et al.*, 2016)

Treatment and Prevention

There is no specific treatment for Zika virus infection, Management consist of having plenty of rest, and taking enough fluid, treat pain and fever with common medicine, if symptoms worsen medical care and advice should be seek. Prevention include, vector control by using mosquito repellent, wearing long sleeves and long pants, and staying indoors as feasible. Individuals with Zika virus infection may reduce spread of infection to others by following the same precautions to avoid mosquito bites during the first week of illness (the likely window of viremia).

Young children together with pregnant women can sleep under mosquito nets when sleeping during the day or early evening, mosquito breed should be eliminated by covering water storage container, removing standing water in flower pot (Plourde & Bloch, 2016).

CONCLUSION

Zika virus is still an ongoing challenge but has generally been at low level throughout 2018 to the present which require intense action, zika virus affect population including adult, pregnant women and infant with mild to moderate symptoms consisting of fever, muscle cramps conjunctivitis, birth defect and muscle paralysis, pregnant women are at risk of zika infection and its complications such as microcephally. There is no vaccine or effective treatment for the virus. In addition the co-circulation of ZIKV with other medically important arboviruses, such as Dengue and Chikungunya virus, constitutes an additional challenge which complicates the comprehension of this disease, and a thorough understanding of the molecular interactions that ZIKV establishes with the host cell during infection is also necessary to determine the targets for antiviral treatment.

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