3rd International Conference on Influenza and Zoonotic Diseases August 21-22, 2017 Birmingham, UK- A review of the evidence linking Zika virus to the developmental abnormalities that lead to microcephaly in view of recent cases of birth defects in Africa

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Abstract

Statement of the problem: The World Health Organization (WHO) in May 2016 confirmed an outbreak of the Zika virus on the African island chain of Cape Verde, linking it to cases of the brain disease, microcephaly. This finding is of concern because Zika was first discovered in East Africa in 1947 with no known link to brain or birth disorders until the WHO reported findings. The question, therefore, is: if the Zika virus has been in Africa for 70 years, why wasn't any association to microcephaly detected before the recent WHO findings? This paper reviews the evidence linking Zika to microcephaly in view of recent cases of birth defects, with the aim of providing vital clues as to why there was no documented case of such birth defects in Africa, where the Zika virus originated. Review methodology: The literature for this review was gathered through internet searches, including the websites of the European Centre for Disease Prevention and Control (ECDC), the United States Centre for Disease Control and Prevention (CDC), the World Health Organization (WHO) and Public Health England (PHE). Findings: Materials from these sources were reviewed on the link between the Zika virus and microcephaly in relation to the recent cases of birth defects in Africa. Two possible explanations emerged from the review. The first explanation suggests that the phenomenon called herd immunity may have taken place in Africa. The Zika virus cannot infect the same person twice because it reaches a stage where there are too few people left to be infected for transmission to be sustained. The second explanation suggests that microcephaly linked to birth defects is caused by other conditions, especially exposure to chemical spraying. In conclusion: The findings of this review opens up the debate on the connection between the Zika virus and the birth defect attributed to mosquito-borne microcephaly, given that there is no documented case of birth defect in Africa 70 years after the discovery of the Zika virus. Large-scale research is recommended on the Zika virus and pregnancy for better understanding of the ecology and epidemiology of the virus.

Zika virus (ZIKV), a mosquito-borne virus in the family Flaviviridae and genus Flavivirus, is mainly transmitted by many Aedes mosquitoes. Besides, ZIKV can also be transmitted by placenta, transfusion, transplantation, sexual activity, etc.. It was first isolated from a rhesus monkey in 1947, and it was not until 1952 that was first identified in humans. In recent decades, outbreaks of ZIKV have occurred in areas ranging from Yap Island, Micronesia, in 2007 to French Polynesia in 2013 and South America in 2015. As of 13 October 2016, 73 countries and territories have reported evidence of mosquito-borne ZIKV transmission since 2007, mainly distributed in Africa, America, Asia and the Pacific regions. Furthermore, there were some countries had reported travel-associated transmission ZIKV cases, which gained increasing international attention.

ZIKV infection often causes mild symptoms, such as fever, skin rashes, headache, conjunctivitis, and muscle and joint pain, which usually last for two to seven days. Interestingly, increasing evidence has indicated a possible causal link between ZIKV infection and adverse pregnancy outcomes, especially microcephaly. Microcephaly is a neonatal malformation defined as a head size much smaller compared with the normal size for the infant's age and sex. The etiology of microcephaly is complex and appears to be affected by multiple factors, including both genetic and environmental contributions, such as exposure to toxic chemicals, radiation, genetic abnormalities, severe malnutrition during fetal life, certain metabolic disorders, or infection in the womb such as toxoplasmosis, rubella, herpes, syphilis, cytomegalovirus and HIV, etc. However, West Nile virus is the only flavivirus previously reported to be associated with encephalitis resulting in fetal brain damage . This review aims to summarize possible evidence of the causal link between ZIKV infection and microcephaly.

ZIKV Outbreak and the Subsequent Increase in Microcephaly Cases

In April 2015, a ZIKV outbreak began in Brazil. The subsequent September, dramatic increases in the number of microcephaly cases were identified in Pernambuco State. Then, the Brazil Ministry of Health released a report declaring an unusual increase in cases of microcephaly in Pernambuco and suggesting an association with ZIKV infection. On 30 November 2015, a microcephaly incidence 20 times greater than that observed in previous years was reported in Brazil. On 1 February 2016, the Emergency Committee of the WHO declared that the recent cluster

of microcephaly cases and other neurological disorders constituted a Public Health Emergency of International Concern (PHEIC). As of 22 June 2016, 12 countries and territories have reported cases of microcephaly and other central nervous system malformations potentially associated with ZIKV infection.

Management, Prevention and Suggestions

No specific antiviral treatment or vaccine is currently available for ZIKV infections; therefore, ZIKV infection treatment generally consists of supportive care, including rest, fluids, and use of analgesics and antipyretics. For pregnant women, the most important way to avoid congenital ZIKV infection is to prevent maternal infection; this can be accomplished by either avoiding areas where ZIKV transmission is ongoing or avoiding mosquito bites. The Centers for Disease Control and Prevention (CDC) recommends all pregnant women consider postponing travel to areas of ongoing ZIKV transmission if possible and avoid unprotected sex with a partner who has recently traveled to a ZIKV endemic area. Serial ultrasounds should be considered to monitor fetal anatomy and growth every three to four weeks in pregnant woman with laboratory evidence of ZIKV. Serological tests and RT-PCR assays are recommended in infants whose mothers have had a risk of ZIKV exposure during pregnancy. Further scientific studies are necessary for the prevention and control of ZIKV-related adverse outcomes. The development of vaccines and antiviral pharmaceuticals that are suitable for use in pregnant women and fetuses should be taken in the first place on the basis of existing research. The development of rapid, scalable diagnostic tests is also needed because the current RT-PCR assay detects viral RNA and is therefore only effective for detection during the period of viremia, which may be relatively short. In addition, current serologic assays have considerable cross-reactivity with other pathogens such as Dengue virus which might be endemic in the same areas and cause symptoms similar to those of the ZIKV. Besides, more evidence between ZIKV infection and microcephaly should be provided by case-control studies, animal model development, and other relative studies.

In conclusion, there is increasing evidence suggesting that there is a causal link between ZIKV and microcephaly, especially ZIKV infection occurred in the first trimester of pregnancy. However, the mechanism by which ZIKV infection cause microcephaly needs more deep-in research.

Note: This work is partially presented at 3rd International Conference on Influenza and Zoonotic Diseases A review of the evidence linking Zika virus to the developmental abnormalities that lead to microcephaly in view of recent cases of birth defects in Africa on August 21-22, 2017.