

Zika Virus: Yet Another Emerging Threat to Nepal

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ABSTRACT

Zika virus (ZIKV) is a flavivirus with single stranded RNA related to yellow fever, dengue, West Nile, and Japanese encephalitis viruses and is transmitted by Aedes mosquitoes primarily by Aedes aegypti which is widely distributed in Nepal. ZIKV was first identified incidentally in Rhesus monkey in Uganda in 1947 and human infection in 1952; and by now outbreaks of ZIKV disease have been recorded in Africa, the Americas, Asia and the Pacific. The World Health Organization (WHO) has recently declared the ZIKV an international public health emergency. The aim of this paper is to briefly summarize origin, signs, symptoms, transmission, diagnosis, preventions and management of ZIKV and possible threat to Nepal in light of endemicity of other arbovirus infections and common mosquito vector species in Nepal.

Keywords: Aedes aegypti; aedes albopictus; zika virus; microcephaly; birth defect; nepal.

INTRODUCTION

Nepal is endemic for at least four vector-borne viral diseases (VBVDs). These varieties of arboviruses are Japanese encephalitis (JEV), dengue (DENV), chikungunya (CHIKV) and West Nile fever (WNV) transmitted by vector mosquitoes of the genus Aedes and Culex.¹⁻¹¹ Of the four arboviruses, JEV was first reported in 1978,¹² DENV in 2004⁸ and WNV in 2006,¹³ and CHIKV in 2013.¹ Now, the warning comes in light of the possible arrival of important mosquito-borne Zika virus (ZIKV) which can cause birth defects like fetal microcephaly and calcification or severe illness like Guillain-Barre Syndrome (acute immune-mediated demyelinating polyneuropathy).

ZIKV belongs to the genus flavivirus, family flaviviridae, and is closely related to other flaviviruses of public health relevance including DENV, yellow fever, WNV and JEV.^{14, 15} It is an emerging mosquito-borne virus transmitted by Aedes mosquitoes in the subgenus Stegomyia primarily Aedes aegypti¹⁶ and possibly, Ae. albopictus. Transmission of ZIKV by artificially fed Ae. aegypti mosquitoes to mice and a monkey in a laboratory was reported in 1956.¹⁷ Arboviruses are often maintained in complex biological cycles involving a primary

vertebrate host such as mammals or birds and blood feeding vectors. Until recently, only a few arboviruses had caused clinically significant human diseases, including mosquito-borne alphaviruses such as CHIKV and flaviviruses such as DENV, yellow fever, JEV and WNV. A widespread epidemic of ZIKV infection was reported in 2015 in South and Central America and the Caribbean with a major concern of apparent increased incidence of microcephaly in fetuses born to mothers infected with ZIKV.¹⁸ Following this pandemic, the World Health Organization (WHO) has recently declared the ZIKV an international public health emergency. Therefore, the aim of this paper is to briefly summarize origin, signs, symptoms, transmission, diagnosis, preventions and treatment of ZIKV and possible threat to Nepal in light of endemicity of other arboviral infections and common mosquito vector species in Nepal.

ORIGIN AND EPIDEMIOLOGY

ZIKV was first identified incidentally in the Zika forest, Uganda in 1947 in a rhesus monkey in the course of mosquito and primate (mammals in tropical forest) surveillance.¹⁹ It was subsequently identified in humans

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in 1952 in Uganda and the United Republic of Tanzania.¹⁶ Outbreaks have been seen since then elsewhere in Sub-Saharan Africa, arriving in South-East Asia at latest by mid-20th-century in humans.²⁰ In the 21st century, it spread across the Pacific Islands reaching South America around 2014 and spread rapidly northwards reaching Brazil in May 2015 via the infected traveler and in Mexico in November 2015.²⁰ To date, outbreaks of ZIKV have been recorded in Africa, the Americas, Asia and the Pacific.¹⁶

SIGNS, SYMPTOMS, DIAGNOSIS AND MANAGEMENT OF ZIKA VIRUS CASES

The ZIKV is from the same family as and is similar to dengue and chikungunya. The incubation period of ZIKV disease is not clear, but is likely to be a few days to a week. About 1 in 5 people infected with ZIKV become ill (i.e., develop Zika) and symptoms which include acute fever, maculopapular rashes, arthralgia and conjunctivitis; some may have myalgia and headache which is similar to dengue or other viral illness. These symptoms are usually mild and last for 2-7 days. ZIKV must be confirmed by laboratory test since the fact that only 20% will be symptomatic and may not be serious. The real worry is what the ZIKV seems to be doing to pregnant women. As reported in Brazil it causes severe birth defect such as microcephaly and calcification. The other worry is causing Gullain-Barre Syndrome (progressive ascending weakness of lower limbs) in patients infected with this virus.¹⁶

In a "pure" Zika epidemic situation, a diagnosis can be made reliably on clinical grounds i.e., with the persons with the history of recent travel to an area within 2 weeks where ZIKV is known to present. ZIKV diagnosis can only be confirmed by laboratory testing for the presence of ZIKV RNA in the blood or other body fluids, such as urine or saliva. Unfortunately, the fact that dengue and chikungunya fever, which result in similar clinical manifestations, have both been epidemic in Nepal confounds clinical diagnosis. Specific tests for dengue and chikungunya are not widely available, and commercial tests for Zika have not yet been developed. Moreover, gene-detection tests such as the polymerase-chain reaction (PCR) assay can reliably distinguish the three viruses, but such facility is also not yet widely available indicating problem in differential diagnosis until five days after the symptoms. Serological assay can be performed after 5 days of symptoms in serum samples for ZIKV specific IgM Antibodies by ELISA or Immunofluorescence assay. Since serum in acute phase is presumptive in the first samples, it is recommended to have second sample be taken after 1-2 weeks to demonstrate the seroconversion. The tests that can

be done during pregnancy are maternal serum or plasma, amniotic fluid after 15 weeks, histopathology or immunostaining of placenta or cord, cord blood, frozen placenta or cord tissue and fetal ultrasound examination. For the positive Zika virus test in serum or amniotic fluid, serial ultrasound for fetal anomaly and growth monitoring every 3-4 weeks is of help. Neonatal screening by testing and measuring head circumference after 24 hours of birth will help to identify the cases. Although any cases of ZIKV are not reported yet in Nepal, ZIKV test can be performed in National Public Health Laboratory, Teku, Kathmandu, Nepal.

There is neither vaccine against ZIKV nor specific medicine to treat Zika infections. Hence, symptomatic treatments such as taking plenty of drink/fluids to prevent dehydration, take medicine such as acetaminophen to relieve fever and pain and rest for few days is recommended. Aspirin and other non-steroidal anti-inflammatory drugs should be avoided unless dengue is excluded.

THREAT OF ZIKA VIRUS TRANSMISSION IN NEPAL

The ZIKV is transmitted by the bite of an infected *Ae. aegypti* mainly and potentially *Ae. albopictus* mosquitoes, the same species that transmit CHIKV and DENV. Elevated temperatures induced by global climate change (within a temperature envelope) can expand the geographic vector range, decrease the extrinsic incubation period of the pathogen, and increase the female mosquito biting rate and can put tropical highland and temperate regions at potential risk of VBVDs such as DENV and ZIKV.²¹⁻²³

The CHIKV, DENV, JEV and WNV are widely circulating in Nepal.¹⁻¹¹ *Ae. aegypti* has expanded its range globally throughout the tropical, subtropical, and parts of the temperate world, through global trade and shipping activities.²⁴ On the other hand, *Ae. albopictus*, like *Ae. aegypti*, has expanded globally throughout the tropical, subtropical, and temperate world, primarily through international trade in used tires.²⁵ The spread of these arboviruses may precede by the expansion of their vectors. In Nepal, both of these vector species of ZIKV mainly, *Ae. aegypti* and potentially, *Ae. albopictus* are widely expanding its geographical range at least upto 2000 m above mean sea level (msl).^{5, 27-31} *Ae. aegypti* has high vectorial capacity for above mentioned diseases and *Ae. albopictus* is able to persist in more temperate climates powered by adaptability in a range of temperature including cooler temperatures and also has expanded its ecological habitat range. Further, it is complicated by same breeding habitat

sharing by both species coupled with availability in close proximity to people and spreading to new geographic locations. Keeping all in mind, establishment of vector population, conducive climatic condition for survival of vector and replication of virus and introduction of any viremic travelers/tourists visiting or returning to the country with established populations of vector species *Ae. aegypti* and/or *Ae. albopictus* mosquitoes could initiate local ZIKV transmission in Nepal.

PREVENTIVE MEASURES

There is no any preventive medication till date and the only strategy will be the mosquito prevention. This can be done by removing and modifying breeding sites such as stagnant water and dark confined places like discarded tyres, tanks, barrels, containers etc. Other measures will be using larvicidals, insect repellent like DEET, picaridin and IR3535 that are safe in pregnancy; using permethrin treated clothing and wearing long-sleeved shirts and pants; using physical barriers such as window screens, closed doors and windows; and if needed, additional personal protection, such as sleeping under mosquito nets during the day.¹⁶ For this massive public awareness is needed. Public awareness efforts focusing on elimination of larval habitats are extremely important to empty, clean or cover containers regularly that can store water, such as buckets, drums, pots etc. Other mosquito breeding sites should be cleaned or removed including flower pots, used tyres and roof gutters. Communities must support the efforts of the local government to reduce the density of mosquitoes in their locality. Hence, with no vaccine or antiviral therapy available, possible interventions include vector control and avoidance of mosquito-man contact.

CONCLUSIONS

The ZIKV is rapidly expanding its range across the world creating pandemic situation where conducive climatic conditions exist, vector presence and viremic travelers have introduced. Following this pandemic situation, WHO has recently declared the ZIKV an international public health emergency. As the risk of ZIKV transmission appears to be high in Nepal due to established vector populations, conducive climatic condition and international movement of people which introduced viremic travelers, it is a high time to enhance surveillance of ZIKV and potential complications before onset of monsoon season in Nepal. The mosquito prevention strategies, fetal and neonatal screening and monitoring, and spreading overall awareness programs are the necessary means to address the situation at local level. In the globalized world, in the context of weakest

health surveillance, Zika can easily cross the border and poses constant danger especially in country like Nepal. For this, national capacity in risk communication needs to be enhanced to help countries like Nepal to meet commitments under the International Health Regulations.

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