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Contemporary Issue

Zika: An enormous public health challenge for a miniscule virus

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ABSTRACT

Zika virus (ZIKV) infection has recently affected 4 million people across the globe. The World Health Organization has declared Zika a ''Public Health Emergency of International Concern''. The disease is caused by an arbovirus and transmitted by *Aedes* mosquitoes. Zika has followed a pattern already set in by Dengue and Chikungunya viruses. The virus exists in sylvatic form with spillovers to humans. The present outbreak in Brazil started in May 2015 and spread rapidly to Latin America and the Caribbean. The rapid spread is due to availability of non-immune population. The main concern of Zika is the association with microcephaly in infants and Guillain–Barré (GB) Syndrome. During the current Zika outbreak in Brazil, incidence of microcephaly in infants has shown a 20-fold rise. Increased incidence of GB Syndrome has been noticed during the 2013 outbreak in French Polynesia, and the current outbreak. However, causality has not been proved. It is possible that the ZIKV may enter and get established in India. Surveillance against the disease needs to be scaled up. Research needs to be undertaken regarding the dynamics of Zika spread and the development of vaccines. Inter-sectoral coordination and bottom-up approach along with vector control measures under the ambit of National Vector Borne Disease Control Programme may help fight the virus.

Introduction

When first detected in Brazil in 2015, the Zika virus (ZIKV) created ripples throughout the public health infrastructure of the globe. At that time, not even passing reference had been made about this virus in Indian medical textbooks, leaving the public health worker confused in that contemporary scenario. The disease has affected an estimated 4 million people across the globe, with Brazil being the worst affected. On 1 February 2016, the World Health Organization (WHO) has declared Zika a ''*Public Health Emergency of International Concern*'' due to a possible link of ZIKV infection in pregnancy to microcephaly in infants.[1] The Centers for Disease Control (CDC) then issued an alert to travellers vesting countries that are experiencing an ongoing

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transmission of ZIKV, with the Government of India also issuing a travel advisory on the same.

Epidemiological pattern of ZIKV in the light of other vector-borne diseases

Zika is a vector-borne disease (VBD) caused by an arbovirus of the family Flaviviridae and transmitted by the bite of the day biting tiger mosquito – *Aedes*.[2] Contrary to popular belief, the virus is not a new one but a re-emerging virus, which was first isolated in febrile sentinel rhesus macaques in Uganda in 1947.[3] The first human cases were reported in the 1960s in Africa followed by the South East Asian region.[4] Since then, sporadic cases of ZIKV infection were reported till the first documented outbreak in humans was reported in 2007 in Yap Islands of Micronesia.[5]

The fact that ZIKV was first isolated in rhesus macaques points strongly in favour of a sylvatic origin of the virus. It has essentially followed a pattern already set in by its predecessors – Chikungunya virus (CHIKV) and Dengue virus (DENV), which have both re-emerged to become endemic in major world regions. ZIKV has originated from Latin America, which is host to a number of other viruses such as Oropouche virus and O'nyong'nyong virus. Hence, ZIKV followed by another novel virus spread in the form of a pandemic is a real possibility.

Interestingly, Yellow Fever virus (YFV) too has its roots in Latin America. The non-existence of YFV in Asia is still surrounded in mystery. India is both a conducive and receptive region for YFV as the *Aedes* vector and the animal host are present in abundance to infect a virgin, non-immune Indian population, the only missing link being the YFV. Various hypotheses have been put forth to explain this phenomenon, the most accepted one being the protective vaccine type cross-immunity provided by DENV infection in a hyperendemic population against YFV. Another theory is based on the all or none competitive exclusion principle, wherein only one of the two infections – DENV or YFV – can be present in an area.[6]

Though chances of occurrence of Yellow Fever (YF) in India are low, complacence should not set it in. Importation of YFV is still a possibility with increased air travel. Besides, the global warming effect, rapid and unplanned urbanisation, deforestation and poor waste management may disturb the ecological niche and lead to introduction of the YFV in hitherto uninfected regions. Precedence has already been set by CHIKV, which first emerged in India in the 1960s and then totally disappeared only to reappear again in the last decade, after a long absence. ZIKV too has so far not been reported in India till date, though it has reached as far as China.

Though a valid International Certificate for Yellow Fever Vaccination is required for the travellers entering India from endemic zones, non-observance of strict checking of the vaccination protocol may lead to a possible entry of YFV in our country. In today's age of Chemical, Biological, Radiological and Nuclear (CBRN) warfare, misuse of YFV by terrorists cannot be ruled out. If such an event happens, the damage would be tremendous, as the YF vaccine is not readily available for the Indian masses.

Reasons for evolution and spread

Though the ZIKV was detected decades ago, it had been an innocuous virus, and limited to a narrow geographical region in Africa and Asia. Akin to Dengue and Chikungunya viruses, enzootic ZIKV had been maintaining itself in sylvatic cycles in forest canopies in non-human primates (NHPs). The infection has been maintained by transmission through local vectors such as *Aedes africanus*, *Aedes luteocephalus* and *Aedes aegypti*, with infrequent spillovers resulting in jumping the human barrier.[7] Once the virus gained entry in the urban and suburban setting, it has been transmitted between humans through *Aedes* mosquitoes, mainly *A. aegypti* and potentially *Aedes albopictus*. Since 2014, the virus has spread eastwards to engulf South and Central Americas and also the Caribbean.

The first case of ZIKV transmission in the ongoing outbreak was reported in Brazil in May 2015. Since then, the virus has spread quickly worldwide, with transmission being reported in many countries in South and Central America and the Caribbean, as well as in countries outside this region. This rapid spread is mainly due to the virgin population who have had no prior exposure to the virus, and thereby having no immunity against it. Besides, the vector mosquito *Aedes* is found in abundance in the region, making it the perfect recipe for propagation of ZIKV.

The re-emergence of DENV, CHIKV and now ZIKV, all having *Aedes* as the common vector host, has been linked to human activities including deforestation, building rapid unplanned settlements and poor waste management systems. These activities have upset the ecologic niches occupied by arboviruses including ZIKV, resulting in spillover of the virus. However, the exact reason for jumping the human barrier is not known. RNA viruses have nearly 100-fold higher mutation rates *vis-a-vis* DNA viral genomes.[8] As ZIKV is an RNA virus, it is speculated that continuing mutations and genetic recombination coupled with natural selection may have led to emergence of a novel ZIKV strain capable of infecting humans.

Causes of concern

ZIKV infections in themselves are not a cause of worry. The main concern is the possible association of the infection with two dreaded complications – microcephaly in infants and of Guillain–Barré (GB) Syndrome.

During the current Zika outbreak in Brazil, incidence of cases of microcephaly in infants has shown a 20-fold rise in 2015 *vis-a-vis* 2014, suggesting a possible association with the ongoing outbreak. By the end of January 2016, 4783 cases (99.7 per 100,000 live births) of suspected microcephaly were reported in Brazil, including 76 with a fatal outcome.[9] Similarly, during the ZIKV outbreak in French Polynesia in 2013, 17 cases of foetal CNS malformations were reported. Four of these women were tested and had detectable antibodies to flavivirus.[10] However, no increase in cases of microcephaly has been reported from other countries affected by ZIKV.

It cannot be concluded with certainty that this association is causal as per Hill's criteria, or if hitherto unknown complex

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