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REVIEW ARTICLE

Global scenario of Zika virus transmission and prevention: recent updates

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ABSTRACT

Zika virus is considered an emerging infectious disease with the potential to spread to new areas where the *Aedes* mosquito vector is present. Since the start of Zika epidemic this year, till date there are more than 44 countries with active Zika virus transmission. The virus can also be transmitted by substances of human origin from donors after clinical recovery from Zika virus disease due to possible prolonged viraemia or a persistence of the virus in semen after viraemia has cleared. Zika virus infection has been associated with neurological anomalies especially Guillain-Barré syndrome which has symptoms like weakness of the arms and legs that is usually the same on both sides of the body. Recently after careful review of the existing evidence the scientists at CDC concluded that Zika virus causes Microcephaly a condition in which the size of baby's brain and head is smaller than the normally expected. Apart from that there may be other severe brain defects in the new born baby. Till date there are no FDA approved vaccines or treatments for Zika at this time and recently FDA approved the Focus Diagnostics, Inc.'s Zika Virus RNA Qualitative Real-Time TR-PCR test for detection in emergencies. The World Health Organization has forecast that the smaller Caribbean economies would be losing anywhere from 1 to 2 percent of their GDP to the Zika virus in the coming months. The World Bank estimates figures that Zika has already cost the region a total of \$3.5 billion USD or approximately 0.06 percent of the GDP of the Latin American and the Caribbean region. For planning more effective disease control and prevention activities for Zika fever there is great need for a functional and intensified Public Health Surveillance system Preparedness for the prevention and control of Zika virus infection will require capacities and capabilities for early detection, response and communication.

KEY WORDS: *Zika virus, Public health emergency, Guillain-Barre Syndrome, Microcephaly, autochthonous transmission, vector control, Prevention*

Introduction

Zika virus is a member of the Flaviviridae family and is transmitted to humans by mosquitoes. It is related to other pathogenic vector borne flaviviruses including dengue, West-Nile and Japanese encephalitis viruses but produces a comparatively mild disease in humans. Since 2007 Zika virus has caused several outbreaks in the Pacific, and since 2015 it further spread in the Americas. These were the first documented transmissions outside of its traditional endemic areas in Africa and Asia. Zika virus is considered an emerging infectious disease with the potential to spread to

new areas where the *Aedes* mosquito vector is present. The ability of Zika virus which is recently confirmed to cross the placenta of pregnant women and affect the fetus makes it very unique from other arboviruses (Cancian, 2016). The highly suspected association between microcephaly and the rapid increase in Zika cases during the current outbreak has contributed to the virus' notoriety and is one of the key reasons behind ongoing global containment efforts (Sikka *et al.*, 2016).

Locations affected and under threat

Zika virus transmission was documented in 66 countries and

territories from 1 Jan 2007 to April 2016. Since the start of Zika epidemic this year, till date there are more than 44 countries with active Zika virus transmission. These are 36 countries and territories in the Americas, 7 Pacific Islands and Cape Verde in Africa (CDC Atlanta, USA) (Figure 1). On February 1, 2016, WHO has declared Zika virus as Public Health Emergency of International Concern (PHEIC). The most common symptoms of Zika include fever, rash, joint pains, conjunctivitis. The illness is mild and symptoms lasts for few days to a week after being bitten by an infected mosquito and many people don't realize that. It is estimated that four out of five people with Zika infection have no symptoms at all (Zika virus updates from FDA). WHO has warned that a warming weather throughout Europe could mean an increased chance of spreading the virus in the region as the two species of Aedes mosquito which transmit the virus will begin to circulate in the community. Apart from the local transmission the likelihood of sexual transmission could lead to an increase in number of Zika related complications. France, Italy and Portugal are among the eight countries that have reported transmission through sexual contact.

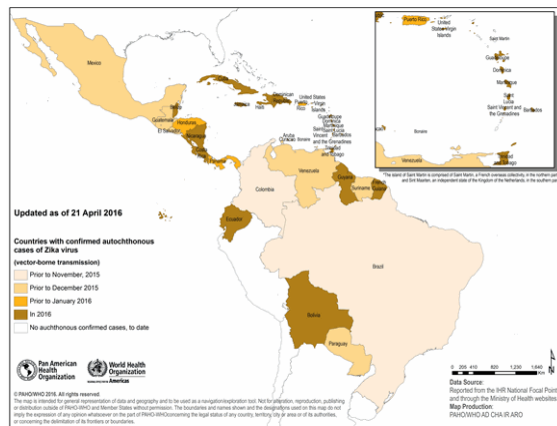


Figure 1: Countries and Territories in the Americas with the confirmed cases of Zika virus (as of 21 April, 2016) source: PAHO/WHO

Transmission via substances of human origin

People with asymptomatic infections and those who are viraemic in the incubation period of Zika disease could potentially donate contaminated substances of human origin without their infections being recognised at the time of donation. The virus can also be transmitted by substances of human origin from donors after clinical recovery from Zika virus disease due to possible prolonged viraemia or a persistence of the virus in semen after viraemia has cleared.

Zika virus RNA has been detected in blood, urine, saliva, seminal fluid and breast milk as shown in Table 1. Data on the survival of Zika virus in processed and stored substances of human origin are lacking. There are no documented transmissions of the virus via saliva, urine or breastfeeding. Cases of Zika virus transmission through donated cells, tissues and organs have not been reported, but this possibility cannot be excluded due to the confirmed presence of the virus in human blood and bodily fluids.

Guillain- Barre Syndrome

The recent Zika virus infection (Zika) epidemic in Brazil has been associated with neurological anomalies, including an increase in the number of cases of microcephaly and, more recently, Guillain-Barré syndrome (GBS) (Lucey and Gostin, 2016; Fauci and Morens, 2016) . The correlation between Zika and GBS was first reported in 2013 in French Polynesia (Oehler *et al.*, 2014). GBS symptoms include weakness of the arms and legs that is usually the same on both sides of the body. In some cases, the muscles of the face that control eye movement or swallowing may also become weak. In the most serious cases, this muscle weakness can affect breathing, and people sometimes need a breathing tube to help them breathe. These symptoms can last a few weeks or several months. Although most people fully recover from GBS, some people have permanent damage, and in 1 out of 20 cases people have died.

Pregnant Women and Birth defects

The fetus can be infected in womb from the pregnant mother and recently after careful review of the existing evidence the scientists at CDC concluded that Zika virus causes Microcephaly a condition in which the size of baby's brain and head is smaller than the normally expected. Apart from that there may be other severe brain defects in the new born baby. This implies that the woman who is infected with Zika during pregnancy has an increased risk of having baby with these problems and not all women who have Zika virus infection during pregnancy will have babies with problems since some infected women have delivered babies that appear to be healthy.

Updates of Medical Products

There are no FDA approved vaccines or treatments in

advanced developed for Zika at this time. Recently the Focus Diagnostics, Inc.'s Zika Virus RNA Qualitative Real-Time TR-PCR test to detect Zika virus is authorized for emergency use by the FDA and this is the first commercial test to detect Zika virus (Zika virus updates from FDA). The test is more useful for people who have symptoms of Zika virus infection, who live or travelled to an area with ongoing Zika virus transmission.

Impact on Economy in Americas & the Caribbean

Not unlike any health threats, the preparedness for Zika is necessary for an effective response from international agencies, governments, private businesses and individuals. The international community especially in the region of Americas (South, Central, North and the Caribbean) is grappling with containing Zika and its threats to human life in parallel with beginning to understand this mosquito-borne virus. Zika has located itself on the International and Caribbean agenda, like a thief in the night and at a time when the region is also grappling with major economic challenges. The Caribbean's public health response must therefore be prioritized with the same lenses that are analyzing matters of competitiveness, productivity and job creation. When health threats affect the attractiveness for doing business in a country, government and the private sector must also grapple with matters of preparedness to safeguard the health of their business.

The Caribbean's preparedness for Zika and similar emerging disease threats must also be gauged in economic terms as the region strives to augment its efforts in the areas of

prevention detection and response. Of immediate concern are clusters of business which rely on the interaction of the consumption of their products and services *in loco* and especially where the interplay between person and the environment is integral to the experience. Tourism is among these businesses and within the industry ecotourism businesses. The World Health Organization has forecast that the smaller Caribbean economies would be losing anywhere from 1 to 2 percent of their GDP to the Zika virus in the coming months (Pandey, 2016). Pandey (2016) at the Indian Council of World Affairs shares a viewpoint and provides some insights on preliminary economic costs coming out from The World Bank.

The World Bank estimates figures that Zika has already cost the region a total of \$3.5 billion USD or approximately 0.06 percent of the GDP of the Latin American and the Caribbean region. This figure is projected to climb further as we seek improvements to current practices for prevention, detection and response. International funding bodies are pooling resources to direct activities in priority areas.

Prevention and Control

Surveillance:

For planning more effective disease control and prevention activities for Zika fever there is great need for a functional and intensified Public Health Surveillance system that can be based on the same system for Dengue and Chikungunya fever. As per the recommendations of PAHO/WHO (Epidemiological Alert, PAHO/WHO 7 May 2015), the surveillance for Zika fever should be focused to

Table 1. Risk of Zika virus transmission via substances of human origin

Sample origin	Time of detection (days)		Viral RNA load	Isolation of replicative particles	References
	Before the onset of symptoms	After the onset of symptoms			
Blood	2-3	11	up to 8.1 x 10 ⁶ copies/mL	+	Musso <i>et al.</i> , 2014
Urine	-	10-22	0.7–220 x 10 ⁶ copies/mL	+	Barzon <i>et al.</i> , 2016, Gourinat <i>et al.</i> , 2015, Rozé <i>et al.</i> , 2016
Saliva	-	2 to 29	3 x 10 ⁶ copies/mL	+	Barzon <i>et al.</i> , 2016, Musso <i>et al.</i> , 2016, Maria <i>et al.</i> , 2016
Seminal Fluid	-	21 to 62	up to 108.6 x 10 ⁶ copies/mL	+	Musso <i>et al.</i> , 2015, Hearn <i>et al.</i> , 2014, Atkinson <i>et al.</i> , 2016, Mansuy <i>et al.</i> , 2016
Breast Milk	-	3 to 8 after delivery	up to 2.1 x 10 ⁶ copies/mL	+	Besnard <i>et al.</i> , 2014, Dupont-Rouzeyrol <i>et al.</i> , 2016

- i. Determine if the virus is autochthonous or has been introduced to an area
- ii. Monitor the Zika virus in case if its introduced and
- iii. Monitor the disease process once it has been established.
- iv. Monitor for neurological and autoimmune complications

Considering the broad distribution of Aedes mosquito in the Americas and the high mobility of people in and outside of this region in this globalized world it poses a great risk for the spread of Zika virus with in the Americas.

The recommendations for the public health authorities in countries without autochthonous transmission of Zika virus:

1. Test for Zika virus from patients presenting with fever and arthralgia or fever and arthritis with no known etiology where malaria, dengue and chikungunya are ruled out.
2. Health authorities but be on high alert for the clusters of rash febrile syndrome of unknown etiology where dengue, chikungunya, measles, rubella and parvovirus B 19 have been ruled out
3. Early detection will help to identify the viral strains in circulation and also enhances proper response

of the outbreak.

In countries with autochthonous transmission of Zika virus, they are recommended:

1. To monitor the trend and geographical spread of virus to track the introduction to new areas.
2. To monitor the impact on public health and assess the clinical severity
3. To monitor potential neurological and autoimmune complications
4. To identify the risk factors those are associated with the Zika virus infection and if possible identify the virus lineages. The preventive measures are described below in Table 2.

Blood transfusions may potentially contribute to the spread of the disease as reported earlier in French Polynesia. The health authorities must ensure proper screening of blood from the donors to stop the chain of transmission. Many cases of sexual transmission of Zika virus are documented in different countries and as per latest updates, Canada has reported its first case transmitted due to sexual contact recently. If the threat of sexual transmission becomes substantial then contact tracing should be considered as done for other sexually transmitted infections.

Table 2: Preventive Recommendations (Adapted from PAHO/WHO guidelines on prevention of Zika virus transmission)

Strategy	Actions
Reduction of Mosquito density	1. Strengthen environmental management
	2. Ensure no vector breeding sites in common areas like parks, schools etc. to prevent vector propagation
	3. Organize mass sanitation campaigns to sensitize the public about cleanliness
	4. By applying risk stratification, identify the places like schools, hospitals, transport terminals and ensure mosquitoes are removed with a radius of 400 m around these places.
	5. In areas with virus, use adulticide treatment by spraying to interrupt transmission
	6. Ensure proper monitoring during integrated actions for vector control (larval control and adulticide treatment)
Interruption of human-vector contact/ Personal prevention measures	Individual Protection
	1. Rest under bed nets treated with or without insecticides
	2. Appropriate clothing to cover the extremities and exposed areas of skin
	3. Use repellents containing DEET, IR3535, Icaridin can be applied to exposed skin or clothing as per the instructions on the product label
	Household Protection
	1. Use wire-mesh screens on doors and windows
	2. At least once a week, empty, clean, turn over or dispose the containers that can hold water such as buckets, flower pots, tires inside and outside of dwellings to eliminate the mosquito breeding sites.

Patient isolation:

A Zika virus infected person should avoid being bitten by Aedes mosquitoes during the first week of illness. It is advised to stay under the bed-net and the treating health care workers should also protect from mosquito bites by appropriate measures. Pregnant women living or traveling to areas of Zika virus transmission: It is recommended to avoid the travel to these regions and if they travel they should avoid the mosquito bites by using bed-nets, appropriate

dressing and pregnant women traveling to those areas should follow the same advice as all travellers

Travellers:

The health authorities should alert the citizens heading to any country with documented spread and circulation of virus and advise them regarding the protective measures as listed below in Table 3.

Table 3: Travel Recommendations (Adapted from PAHO/WHO guidelines on prevention of Zika virus transmission)

Traveller status	Recommendations
Prior to Departure	<ol style="list-style-type: none"> Travelers heading to a country with circulation of virus are advised to protect themselves from mosquito bites Use mosquito repellents, appropriate full sleeve clothing to minimize skin exposure Use insecticides or bed-nets (treated with or without insecticide) Sensitize and inform the travelers about the signs and symptoms of Zika/Dengue/ Chikungunya virus in order to identify it promptly and to consult the physician as early as possible during their trip
While visiting places with Zika virus Transmission	<ol style="list-style-type: none"> Avoid mosquito-infested areas Protect from mosquito bites by appropriate measures by using repellents and appropriate clothing to reduce skin exposure Avoid the mosquito bites especially during day time as Aedes bites mostly at night time Use of bed-nets and/or insecticide Seek professional care in case there are symptoms of Zika/ dengue/ chikungunya
Upon return	<ol style="list-style-type: none"> Contact the health care provider in case if they suspect they have Zika. Dengue/ chikungunya after returning home.

Conclusions

Preparedness for the prevention and control of Zika virus infection will require capacities and capabilities for early detection, response and communication. Early detection mechanisms should ensure rapid notification of human cases, surveillance of Aedes mosquito species that transmit Zika virus and laboratory diagnosis capacity. The response mechanisms should cover organisational and planning mechanisms aimed at the prevention and control of mosquito-borne diseases, inter-sectoral and cross-disciplinary collaboration with all relevant partners, case management and safety of substances of human origin.

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