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Zika virus, a pathway to new challenges

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ABSTRACT

The current Zika outbreak is largest of its kind with 1.4 million cases in Brazil alone. World Health Organization declared the current outbreak as the public health emergency of international concerns. The major route of Zika virus transmission is mosquito bites. Sexual transmission and monkey bites are also observed in few cases. There is dire need to evaluate the other routes of transmission like blood transfusion, lactation and contact with body fluids. Zika virus is infecting infants, not only causing microcephaly but also creating number of complications resulting in bad outcomes of pregnancy. In Brazil alone, 4000 cases of microcephaly have observed during the current outbreak. The incidence of Guillain-Barre (GB) syndrome is also observed during the current Zika virus outbreak. GB syndrome is acute medical condition leading the patients to death due to weakness of respiratory muscles or can cause the life time disability. There is no anti-viral drug or vaccine available for Zika virus. Zika infection can be prevented by using mosquito repellents, mosquito nets, cooling rooms by air conditions and wearing full sleeves or permethrin-treated clothes. The current outbreak of Zika has not only affected the health care but also caused great economic loss. Estimated loss in Latin America and Caribbean is US\$3.5 billion. United Nation's sustainable development goal 3.d stresses the strengthening of early warning, risk reduction and management of national and global health risks. The world will keep on facing new challenges in the form of Ebola or Zika; there is strong need to prepare ourselves for any disease outbreak.

1. Introduction

On 1st February 2016, World Health Organization declared Zika virus (ZIKV) as public health emergency of international concerns [1]. Zika virus is an emerging mosquito-borne virus belonged to family Flaviviridae [2–5]. The virus has a great chance to spread to many countries outside Africa and Asia where its vectors are present [3]. Worldwide spread of this disease will not only impact the public health but it will also exert major burden on economic status of countries [4].

Zika virus got its name when it was first isolated in 1947 from rhesus monkeys of the Zika forests of Uganda. Its presence

in humans was reported in 1952 [3,6]. It is a single-stranded RNA virus comprising of 10800 nucleotides which encodes more than 3000 amino acids [6,7].

2. Transmission routes

2.1. Mosquito-borne route

Zika virus is a mosquito-borne virus [3,6]. It completes its zoonotic cycle between mosquitoes and nonhuman primates [5]. The first identified route of transmission of Zika virus was mosquito belonged to *Aedes aegypti* specie [7]. Later on presence of Zika virus was confirmed by PCR in ten species of genus *Aedes*, *Mansonia uniformis*, *Anopheles coustani*, and *Culex perfuscus* [8]. After entering the body of human, Zika virus replicates in dendritic cells and then spreads in the body through lymphatic channels and blood [7].

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2.2. Sexual transmission

Recently it is reported that the Zika virus is not only transmitted by blood but also by other body fluids. Sexual transmission of this disease came under discussion when one person during outbreak in French Polynesia came to seek medical advice after noticing blood in semen. Zika virus was isolated from his semen raising the possibility of sexual transmission of this infection [9]. Recently, France has confirmed first case of sexually transmitted Zika virus in a lady who has acquired the infection from her partner who recently visited Brazil [10]. CDC is recently investigating 14 possible sexually acquired Zika virus cases [11].

2.3. Animal bites

Transmission of Zika virus through animal's saliva during bite is also possible [12]. This route of transmission came under discussion when Zika virus was isolated from person's blood after monkey bite [12].

2.4. Rarer routes of transmission

Mosquito bites, sexual intercourse and animal bites are documented routes of Zika virus transmission [9,12]. There is dire need to evaluate the other possible route of Zika transmission like blood transfusion, lactation and contact with body fluids so that the spread of this virus through these invisible routes can be minimized.

3. Epidemiology and current situation

Human cases of Zika virus has been reported since 1951 [7]. The first large outbreak occurred in Yap Island [Federated state of Micronesi, Northwest of Indonesia] in 2007 [3,6]. The second outbreak occurred in French Polynesia in 2014 [3,6]. Many African and Asian countries such as Uganda, Tanzania, Egypt, India, Malaysia, the Philippines, Thailand, Vietnam, and Indonesia have reported Zika virus infected cases [7].

World Health Organization has reported presence of Zika virus in 40 countries from 2007 to February 2016. Out of these 40 countries, 33 have Zika virus transmission in the year 2015 [1]. The recent Zika outbreak is largest of its kind with 1.4 million cases in Brazil alone. Whereas the second leading number of 20000 cases are reported from Colombia and Cape Verde [1].

4. Clinical features

The symptoms and signs of patients who are affected by Zika virus are similar to dengue virus and other viral diseases [3]. The patient presents with fever, body aches, joint pains, fatigue, malaise and conjunctivitis. Maculopapular rash can also occur with it like other viral illnesses [2,4]. Total duration of illness can lasts up to 5–7 days [6].

Almost all cases reported yet have shown mild symptoms [4] but some neurological and autoimmune complications are also reported in some patients. But these patients were having concomitant dengue virus infection. So whether Zika virus alone or dual infection by these viruses are responsible for these complications this needs further evaluation and studies [3].

During Zika virus outbreaks many cases of Guillain-Barre (GB) syndrome are also reported [2]. Many viruses are thought to

be playing their role as causative agents for GB syndrome but whether Zika virus is also causative agent or not, this needs further documentation [2].

5. Neurological complications

The incidence of Guillain-Barre syndrome during the current Zika virus outbreak alerted the medical community. It is considered that the Zika virus is causing GB syndrome which is acute medical condition leading the patient towards death due to respiratory muscles involvement or can left the patient with life time residual disability [2]. The point to consider at this stage is the involvement of many viruses as causative agents for GB syndrome but whether Zika virus alone or in conjunction with other viruses is causative agent or not, needs further confirmation [2].

The most under debate topic of Zika virus which has become alarming signal for the global health authorities is its proven association with microcephaly [13]. Mothers of infants with marked microcephaly have history of travelling to Zika virus infected areas during pregnancy. They acquire this infection during their travel and then this virus gets transmitted to foetus and resulting in microcephaly. This transmission is proven after isolating virus from not only amniotic fluid of these mothers but also from cerebrospinal fluids of these babies [13]. But how it is causing microcephaly in infants? One hypothesis has proposed that Zika virus infects primary progenitor cells of neurological system and prevents their growth.

In Brazil alone 4000 cases of microcephaly have been suspected due to Zika virus [14]. In America, presence of Zika virus is confirmed by Centre of Disease Control in 9 pregnant females who visited virus infected areas during their pregnancy [15]. One of them gave birth to microcephalic child, two ended in miscarriages and two underwent medical termination of their pregnancy after finding microcephalic infants [16].

World Health Organization has released its statement in late February that the Zika virus is infecting infants and is causing not only microcephaly but also a number of complications resulting in bad outcomes of pregnancy like placental insufficiency, early abortions, foetus mental and body growth retardation [11].

This is the reason that CDC has developed guidelines to take care of pregnant females during Zika virus outbreaks [17]. Recently CDC has forbidden the pregnant females to travel to areas where Zika virus is largely reported particularly Brazil which is endemic for Zika virus [16]. Philippines ministry urged their females to delay their pregnancy so that chances of microcephaly can be minimized [18].

Zika virus has proven transmission from mother to infants during pregnancy; there are also chances of Zika transmission to new borne infants from infected mother by lactation. This route of transmission is not studied yet and it is not under debate. We are purposing that the transmission through lactation should be considered, so that the Zika virus transmission to new born will become minimum.

6. Management

6.1. Diagnosis

Like all the other viruses, diagnosis can be done by finding IgM and IgG antibodies against Zika virus by Elisa [7], viral RNA detection by PCR, urine and nasopharyngeal swab

analysis [19]. First samples should be taken as early as possible after the onset of symptoms and these tests can be repeated after 2 weeks if needed [7].

6.2. Treatment

As Zika virus is causing mild illnesses so these cases have been managed conservatively. No anti-viral treatment is available [17].

6.3. Vaccination

No vaccine is available for prevention of this disease but nearly 15 research groups in Europe are trying to develop vaccine against Zika virus [20]. Christ Church Clinical Studies Trust is also looking forward to develop oral vaccine against Zika virus [21].

7. Prevention

There is no specific treatment available for Zika virus, the best strategy is to block viral transmission [3,7]. The common ways of protection include protecting oneself from mosquito bites by using mosquito repellents, mosquito nets, cooling rooms by using air conditions, covering body with full sleeves and pants and using permethrin-treated clothes [13]. Vector can be controlled by preventing water pooling and spraying on larval breeding places. The emergence of permethrin resistant strains has urged the need of other alternative routes of controlling vectors.

8. Development of virus resistant mosquito strains

Development of virus resistant mosquito strains by using genetic engineering techniques is also under consideration. One method involves the growing of male mosquitoes in control environment with diet containing tetracycline and then these male will mate with wild females resulting in off springs who are not surviving in their adulthood [14]. The other method is the use of endosymbiotic bacteria introduced in vectors and these vectors will prevent the replication of viruses in their bodies.

9. Challenging situation

Zika virus has posed a great challenging situation not only for health and public sectors but also for economic sectors of different countries. The breakout has not only increase the expenditure on health system but has also shaken the economy by reducing travelling and tourism to Zika affected countries [15].

Brazil is going to host the Olympics 2016. Large number of participants, tourists, travellers and residents from all over the world will attend the event [16]. Will such mega gathering not aid in further transmission of this disease to other countries when Brazil is already considered endemic for Zika? If Olympics will fail to gather mass crowding, what will be its impact on Brazil who is already facing a great economical loss due to its expenditure on health systems and reduction in tourism and travelling?

10. Funding

According to World Bank, Brazil has lost US\$300 million or 0.01% of its GDP by Zika virus outbreak. Estimated loss in

Latin America and Caribbean countries by Zika virus is about US\$3.5 billion [15]. World bank has announced the immediately release of US\$150 million for Zika affected countries [17]. White House releases its statement regarding need of more funding of about US\$1.8 billion. These funds will be used to develop methods for effective vector control, providing effective diagnostic tests and development of effective vaccine and drugs for Zika virus [18].

United Nation's sustainable development goal 3.d stresses the strengthening of early warning, risk reduction and management of national and global health risks. The world will keep on facing new challenges in the form of Ebola or Zika; there is strong need to prepare ourselves for any disease outbreak.

Conflict interest statement

We declare that we have no conflict of interest.

References

- [1] World Health Organization. *WHO statement on the first meeting of International Health Regulations [2005] [IHR 2005] Emergency Committee on Zika virus and observed increase in neurological disorders and neonatal malformations.* [Online] Available from: <http://who.int/mediacentre/news/statements/2016/1st-emergency-committee-zika/en/> [Accessed on 28 February 2016].
- [2] Cardoso CW, Paploski ADI, Kikuti M, Rodrigues MS, Silva MMO, Campos GS, et al. Outbreak of exanthematous illness associated with Zika, Chikungunya, and Dengue viruses, Salvador, Brazil. *Emerg Infect Dis* 2015; **21**: 2274-2276.
- [3] Ios S, Mallet HP, Leparac GI, Gauthier V, Cardoso T, Herida M. Current Zika virus epidemiology and recent epidemics. *Med Mal Infect* 2014; **44**: 302-307.
- [4] Balm MN, Lee CK, Lee HK, Chiu L, Koay ES, Tang JW. A diagnostic polymerase chain reaction assay for Zika virus. *J Med Virol* 2012; **84**: 1501-1505.
- [5] Diallo D, Sall AA, Diagne CT, Faye O, Faye O, Ba Y, et al. Zika virus emergence in mosquitoes in southeastern Senegal, 2011. *PLoS One* 2014; **9**: e109442.
- [6] Gubio SC, Antonio CB, Silvia IS. Zika virus outbreak, Bahia. *Braz Emerg Infect Dis* 2015; **21**: 1885-1886.
- [7] Hayes EB. Zika virus outside Africa. *Emerg Infect Dis* 2009; **15**: 1347-1350.
- [8] Ayres CF. Identification of Zika virus vectors and implications for control. *Lancet Infect Dis* 2016; **16**: 278-279.
- [9] Musso D, Roche C, Robin E, Nhan T, Teissier A, Cao-Lormeau VM. Potential sexual transmission of Zika virus. *Emerg Infect Dis* 2015; **21**: 552.
- [10] Elgot J. France records first sexually transmitted case of Zika in Europe. *The guardian* 2016. [Online] Available from: <http://www.theguardian.com/world/2016/feb/27/zika-france-records-first-sexually-transmitted-case-europe> [Accessed on 28 February 2016].
- [11] Duhaime-Ross A. Zika linked to more birth defects than just microcephaly. *The verge*, 2016. [Online] Available from: <http://www.theverge.com/2016/3/8/11181088/zika-birth-defects-fetal-death-growth-retardation-who> [Accessed on 9 March 2016].
- [12] Leung GH, Baird RW, Druce J, Anstey NM. Zika virus infection in Australia following a monkey bite in Indonesia. *Southeast Asian J Trop Med Public Health* 2015; **46**: 460-464.
- [13] Schuler-Faccini L, Ribeiro EM, Feitosa IM, Horovitz DD, Cavalcanti DP, Pessoa A, et al. Possible association between Zika virus infection and microcephaly – Brazil, 2015. *MMWR Morb Mortal Wkly Rep* 2016; **65**: 59-62.
- [14] Yakob L, Walker T. Zika virus outbreak in the Americas: the need for novel mosquito control methods. *Lancet Infect Dis* 2016; **4**: e148-e149.
- [15] Tozzi J. 9 pregnant American tourists confirmed with Zika virus. *Bloomberg: Skift* 2016. [Online] Available from: <https://skift.com/>

- 2016/02/27/9-pregnant-american-tourists-confirmed-with-zika-virus/ [Accessed on 28th February 2016].
- [16] Palmer KM. CDC sees birth defects in pregnant US travelers with Zika weird; 2016. [Online] Available from: <http://www.wired.com/2016/02/cdc-sees-birth-defects-pregnant-us-travelers-zika/> [Accessed on 28 February 2016].
- [17] Petersen EE, Staples JE, Meaney-Delman D, Fischer M, Ellington SR, Callaghan WM, et al. Interim guidelines for pregnant women during a Zika virus outbreak – United States, 2016. *Morb Mortal Wkly Rep* 2016; **65**: 30-33.
- [18] Reuters. Zika scare prompts Philippines to advise women to postpone pregnancy. Reuters; 2016. [Online] Available from: <http://news.trust.org/item/20160215124828-ax52g/> [Accessed on 28 February 2016].
- [19] Fonseca K, Meatherall B, Zarra D, Drebot M, MacDonald J, Pabbaraju K, et al. First case of Zika virus infection in a returning Canadian traveler. *Am J Trop Med Hyg* 2014; **91**: 1035-1038.
- [20] Maurice J. WHO reveals its shopping list for weapons against Zika. *Lancet Infect Dis* 2016. [Online] Available from: [http://thelancet.com/pdfs/journals/lancet/PIIS0140-6736\(16\)00390-1.pdf](http://thelancet.com/pdfs/journals/lancet/PIIS0140-6736(16)00390-1.pdf) [Accessed on 28th February 2016]
- [21] Stewart A. Vaccine for Zika virus may be trialled in Christchurch, as New Zealand cases climb. *Health* 2016. [Online] Available from: <http://www.stuff.co.nz/national/health/77183359/vaccine-for-zika-virus-may-be-trialled-in-christchurch-as-new-zealand-cases-climb> [Accessed on 28 February 2016]