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Zika Virus: A Concise Viewpoint

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Abstract

In 2013, a sudden upsurge of ZIKA virus took place accompanied by concomitant malformations like microcephaly and Guillain–Barr´e Syndrome. A public health emergency was declared in 2016, with largest flare-up in human history. The virus has advanced in sizeable areas of Asia and Africa. It is spread mostly by the bite of an infected Aedes species mosquito (Ae. aegypti and Ae. albopictus). These mosquitoes are aggressive daytime biters. They can also bite at night. Zika can be passed from a pregnant woman to her fetus. Infection during pregnancy can cause certain birth defects. There is no vaccine or medicine for Zika Infection with Zika virus may be suspected based on symptoms and recent history of travel e.g. residence in or travel to an area with active Zika virus transmission. Considering the gravity of the situation, an overview about the virus has been written for the physicians.

Keywords: Epidemics, Prevention and control, Viruse, Zika Virus.

Introduction

Zika virus (ZIKV) is an Arbovirus which belongs to the family Flavi viridae and phylogenetically, it relates to Spondweni virus, originally found in sub-Saharan Africa, and Papua New Guinea. The name 'ZIKA' originates from Zika forest located near the Lake Victoria in Uganda**.** [1] In year 2013, an outbreak of ZIKV occurred in French Polynesia, which was accompanied by dengue epidemic and during this outbreak, for the first time malformations such as Guillain–Barr´e Syndrome (GBS) and microcephaly were reported in the patients. [2] In 2016, ZIKV wasreported in more than 28 countries with highest numbers of infections in Brazil. According to the recent estimates, total numbers of ZIKV cases during this outbreak may surpass 1.5 million. It was the largest outbreak recorded in human history and became a reason for public health emergency in Brazil. [3] On 1st February

2016, World Health Organization declared Zika virus (ZIKV) as public health emergency of international concerns. The virus has a great chance to spread in many countries outside Africa and Asia where its vectors are present. [4] Considering the graveness of the situation, following is a concise review for clinicians, to revamp their knowledge in the field.

Structure

It is a single-stranded RNA virus comprising of 10800 nucleotides which encodes more than 3000 amino acids. [5,6]

Transmission

Zika virus is a mosquito-borne virus. [7] Aedes aegypti (A. aegypti), is known as predominant vector for the transmission of both DENV [8] and ZIKV. Second important vector of ZIKV is Aedes albopictus. Currently, both mosquito species are persistent across wider Asian and American territories. [9] Other than mosquito-borne transmission, perinatal, sexual transmissions and animal bites virus were also reported. [10,11]

Pathogenesis

After entering the body of human, Zika virus replicates in dendritic cells and then spreads in the body through lymphatic channels and blood. [6]

Clinical Signs

Majority of the ZIKV infections remain asymptomatic and less than 20% of the infected individuals show symptoms which include but are not limited to fever, maculopapular rash, conjunctivitis and arthralgia. Hence, asymptomatic infections may remain unnoticed. Incubation period for the virus is suggested to be (3–12) d while the course of infection may extend up to (2–7) d, which is mostly self-limiting. However, persons exposed to secondary infections of dengue fever virus may experience severe form of the infection. [12-14]

Microcephaly: Mothers of infants with marked microcephaly have history of travelling to Zika virus infected areas during pregnancy. This transmission is proven after isolating virus from not only amniotic fluid of these mothers but also from cerebrospinal fluids of these babies. [15] One hypothesis has proposed that Zika virus infects primary progenitor cells of neurological system and prevents their growth. 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. [16]

Guillain Barre (GB) Syndrome: 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. [17]

Diagnosis

Like all the other viruses, diagnosis can be done by finding IgM and IgG antibodies against Zika virus by Elisa, viral RNA detection by PCR, urine and nasopharyngeal swab analysis. 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. [6]

However, the virus was identified (by virus genomic amplification) at the 11th day upon symptom onset in one patient from the epidemic on the island of Yap. [18, 19] The primary means of diagnosis is nucleic acid detection by RT-PCR targeting the non-structural protein 5 (NS-5) genomic regions. Standard RT-PCR and quantitative RT-PCR usually provide a rapid, specific and sensitive method for early detection of ZiV. The virus may also be detected by using molecular techniques in other body fluids like saliva and in urine. [20, 21] The presence of ZIKV epidemics in regions where dengue virus was previously

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in circulation may represent a diagnostic challenge. Even the use of a plaque reduction neutralization test (PRNT), also used in the epidemic on the island of Yap, is unable to differentiate possible cases of ZIKV infection in patients with previously acquired anti-dengue virus antibodies, even when the anti-ZIKV titres were higher than the heterologous (non-ZIKV). [19]

Further, it is a known fact that performing ELISA for Zika virus would be further challenging in countries like India due to endemicity of other flavi viruses like dengue, Japanese encephalitis and west nile viruses,

Prevention

A. **Mosquito bite**

During the first week of ZIKV infection, the infected patient should avoid further mosquito bite because the ZIKV can be found in the blood and pass from an infected person to a mosquito. Consequently, an infected mosquito can then spread the virus to another person. An infected female mosquito lays several hundred eggs on the wall of the water filled containers. Therefore, it is important to eliminate standing water in and outside of the home by emptying, washing and scrubbing thoroughly, and then tightly covering water storage containers (buckets, cisterns, rain barrels) once a week so that mosquitoes cannot get inside to lay eggs. [22]

The common ways of protection include protecting oneself from mosquito bites by using mosquito repellents, mosquito nets, and cooling rooms by using air conditions, covering body with full sleeves and pants and using permethrin-treated clothes. Vector can be controlled by preventing water pooling and spraying on larval breeding places. [15]

B. **Travelers**

Travelers visiting countries where the ZIKV virus is active should use individual protective measures to avoid mosquito bites. There is evidence that the ZIKV can be sexually transmitted from a man to his sexual partners. Therefore, men who reside in or have traveled to an area of active ZIKV transmission should abstain from sexual activity, or consistently and correctly use condoms when having sex within 2 weeks after he returns, and postpone giving blood for at least 28 days to prevent ZIKV transmission. [23] Due to potential risks of ZIKV infection by sexual transmission in women of reproductive age (15-44 years), the CDC has recommended that healthcare providers should discuss and provide counseling about reproductive screening, testing and pregnancy planning in those women residing in areas with ongoing ZIKV infection. [24]

C. **Pregnant Women**

The Centers for Disease Control and Prevention (CDC) has recommended that women who are pregnant or plan to become pregnant in the near term consider delaying travel to areas with active Zika virus. Pregnant women residing in or traveling to areas of active ZIKV transmission should take steps to prevent ZIKV infection through prevention of mosquito bites, including use of insect repellant. For those pregnant women who have recently travelled to Zika-infected areas, they should consult with their healthcare provider even if they don't feel any symptoms of the disease**.** [23]

D. WHO called for health authorities to collaborate with the transport sector to ensure disinfection of aircraft from affected areas. [22]

Vaccine Development

Vaccines for various flavi viruses have been produced during the past years, some of them being already in the market, such as those for YFV or WNV. [25, 26] These vaccines have been produced using different strategies, inactivated or live-attenuated viruses, recombinant proteins or peptides expressed in different heterologous systems, recombinant subviral particles, chimeric

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backbone viruses, or naked cDNA. [27] Thus, it seems reasonable to think that similar strategies can be applied to ZIKV. Indian Bharat Biotech International company reported that it has two ZIKV vaccine candidates that will be entering pre-clinical trials in animal and commenced in late February 2016. [28]

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. [29]

Treatment

There are no specific antiviral vaccines or drugs and treatment is symptomatic. Analgesics and antipyretic agents must be carefully used, in order to prevent any adverse effects including hepatopathy, allergy and nephropathy. The use of aspirin should be avoided in order to prevent the induction of bleeding disorders in patients with dengue misdiagnosed with ZIKV infection due to an inconclusive clinical diagnosis and to an unreliable serological analysis.

The severe pruritus that follows the rash has been described by patients as an intense discomfort. The approach to pruritic rash may start with the recommendation that patients should avoid hot baths, the excessive use of soap and use adequate skin moisturizers. When these are not successful, cold baths and the use of refreshing lotions with calamine or menthol is recommended. The pathogenesis of skin manifestations is still unclear and thus the use of older antihistamine agents may benefit the patient due to the sedative action rather than to some direct action on the cause of pruritus. [30, 31]

Topical corticosteroids should be avoided as their efficacy on this symptom is unknown. GBS should be conventionally approached. Diagnosis is established when the patient presents with progressive weakness affecting two or more limbs, are flexia and clinical progression in up to four weeks. Cerebrospinal fluid (CSF) analysis may show protein increase and low cellularity (albuminocytologic dissociation). Patients with suspected GBS should be monitored in intensive care units due to the risk of progression to respiratory muscle paralysis. GBS therapeutic options include plasmapheresis or hyperimmune IVIG (hyperimmune immunoglobulin): both reduce time to recovery despite being expensive therapies. [32]

Curb the Disease Extension

Vector control measures based on the use of insecticide agents are difficult due to (i) financial constraints, (ii) logistic issues, (iii) strict regulations regarding the use of insecticide agents and/or (iv) spreading of resistances in vector population, removal of larval breeding sites has a crucial role in the control of this vector. Individual protection measures should also be encouraged, involving the use of insect repellents and window and door screens to keep insects outside. The detection and study of suspected cases, aimed to prevent transmission in more problematic regions should be the priority in health surveillance. Those with an active disease or that recently presented with it are unable to donate blood. [6] Although no ZIKV-related deaths occurred until now, health professionals should be aware and trained in order to differentiate ZIKV disease from other diseases that simultaneously circulate, namely dengue. [33] Attention to travellers returning from regions with ZIKV transmission should be a priority in ZIKV-free regions. Early recognition may contribute to take measures aimed to

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prevent disease spreading, considering the spread of *Ae. albopictus* in temperate regions. [34]

Considerations for Health Professional

The rapid spread of ZIKV in Brazil and the Americas, with the suspected neonatal malformations associated, is being cause for alarm and the mass media. Even the 2016 Olympic Games in Rio were questioned. Practitioners should consider following points.

E. Detailed history of each patient should be taken with special emphasis on records of travel tales, sexual intercourse and pregnancy.
F. Regular monitoring of signs and symptoms for initiation, progression and duration of disease development should be done.
G. Prompt differentiation from other viral fevers, especially dengue is important.
H. Susceptible cases should be sent for special investigations.
I. Prompt instructions, motivation and reinforcement should be given unvaryingly.

Conclusion

Though the presence of Zika virus has not been widely reported in India, the association of this virus infection with microcephaly and other neurological symptoms warrants preparedness for this dangerous virus in our country. Knowledge on the virus pathogenicity and precise guidelines on preventive measures helps the practitioners to handle such cases with less ambiguity.

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