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Zika Virus: Disease with no Major Symptoms

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Abstract:
Zika virus is a mosquito-borne virus that was first separated from a sentinel rhesus monkey in the forest of Zika in Uganda in year 1947. At first it was assumed to be an endemic disease but emergence beyond borders of Africa made it a serious issue globally. The symptoms are fever, joint pain, red eyes, headache, and maculopapular rash closely resemble chikungunya and dengue. In utero exposure has been observed to result in a congenital syndrome marked by and a range of other brain anomalies. However, the incidence of Zika and Zika-related neurological complications in Asia is not well known. Most of the peoplesget recovered without any complications, and hospitalisation rates are low. To date, there have been no reported deaths associated with ZIKV infection. The purpose of this article is to inform people about the virus its prevention and treatment.

Keyword: Zika Virus, Aedes mosquito, Vector borne diseases, Vaccine.

Introduction:

The closest relative to ZIKV is Spondweni virus. ZIKV was first isolated from a sentinel rhesus monkey in the Zika Forest in Uganda in 1947 and from Aedes africanus mosquitoes in 1948.[1]It was later identified in humans in 1968 for the first time in Nigeria.[2] By October 2013, an outbreak occurred in French Polynesia with approximately 11% of population infected.[3] The association of ZIKV with the reported microcephaly case clusters in Brazil during 2015.[4]

From various studies viz., virological, serological and case reports of human ZiV infection, the virus was identified and reported from various other African countries (Uganda, Senegal,
Ivory Coast, Nigeria, Gabon, Egypt, Tanzania, Sierra, Leone, Central African Republic), Asian countries(Cambodia, Indonesia, Malaysia, India, Pakistan,Singapore, Thailand, Philippines and Vietnam), Pacifcislands (Micronesia/Yap, FP, Cook islands and NewCaledonia) and OceaniaFrom various studiesviz., virological, serological and case reports of humanZiV infection, the virus was identifed and reportedfrom various other African countries (Uganda, Senegal,Ivory Coast, Nigeria, Gabon, Egypt, Tanzania, SierraLeone, Central African Republic), Asian countries(Cambodia, Indonesia, Malaysia, India, Pakistan,

Singapore, Thailand, Philippines and Vietnam), Pacificislands (Micronesia/Yap, FP, Cook islands and NewCaledonia) and Oceania. From Various studies like Virological, Serological, and case reports of human ZiV infection, the virus was identified and reported from various other African countries (Uganda, Senegal, Ivory Coast, Nigeria, Gabon, Egypt, Tanzania, Sierra, Leone, Central African Republic), Asian Countries (Cambodia, Indonesia, Malaysia, India, Pakistan, Singapore, Thailand, Philippines and Vietnam).[5-7]Zika virus is an RNA virus of the family Flaviviridae of flavivirus genus and is closely related to other members of this family, including dengue, yellow fever, West Nile, and Japanese encephalitis viruses.[8-9]In *Flaviviridae* family, all members have enveloped viruses with a single-stranded RNA genome of positive polarity which contained one open reading frame (ORF) with two flanking noncod-ing regions (at 5’ and 3’ end). The genomes are 5' capped without a 3' poly (A) tail.[10]

Transmission of Zika Virus:

Transmission include sexual contact or blood transfusions.[11]There is evidence of sexual transmission of ZIKV. In the first report in 2008, a U.S. scientist working in Senegal became ill after returning to the United States, and his wife developed symptomatic ZIKV infection 9 days later.[12]Although breastfeeding transmission was not yet documented, the viral has been detected in the breast milk.[13]Although the transmission of Zika virus through a blood transfusion has yet to be reported, it is likely to occur, given the transmission of other, related flaviviruses through this route.63 During the Zika virus outbreak in French Polynesia, 3% of donated blood samples tested positive for Zika virus by reverse-transcriptase polymerase chain reaction (RT-PCR).[14]Zika virus has been identified in saliva, urine, and breast milk, but transmission through these sources has not been reported.[15]

Pathogenesis of Zika Virus:

Zika virus most commonly follows the sylvatic transmission cycle.[16] The cycle starts when an Aedes mosquito ingests blood containing Zika virus after biting an infected person.[17] The virus starts replicating in the epithelial cells of midgut and goes to the salivary glands of the mosquito. After 10 days of incubation period, the saliva get infected, making the mosquito a vector for infecting a human. Upon entry into the human skin, the virus infects the dermal fibroblasts that serve as receptors for attachment of Zika virus. Upregulation of TLR3 mRNA expression is triggered and this leads to an enhanced innateimmune response. Interferon alpha and beta are produced by the infected cells to help lower theviral load. Zika virus can also lead to the autophagy of host cells and inhibitors to this step canbe a potential treatment option in the future. Once replication is complete, the virus spreads tothe regional lymph nodes hematogenously, contaminating distant organs such as the nervoussystem on its way. Moreover, in pregnancy, the virus can go through the placental blood barrierto infect the fetus.[18]

Symptoms of Zika virus:

The common symptoms of ZIKV are quite broad in nature and are characteristic of many flaviviruses, such as Dengue. These symptoms can persist for 3 - 12 days and include[19]Fever[20], conjunctivitis[21], arthralgia[22], During the Yap Island outbreak, among those with symptoms (age range, 1–76 years), macular or popular rash, were most frequently observed[23]. There are some important systemic symptoms that are presented by chills, rigors,sore throat, hypotension, cervical, submandibular, axillary and/or inguinal lymphadenopathies. In addition, digestivesymptoms may also be present including nausea, vomiting, diarrhea, constipation, abdominal pain and aphthousulcers. Patients with genitourinary symptoms including hematuria, dysuria, perineal pain and hematospermia oftenhave measurable virus particles in urine and/or semen[24]. Alsotwo neurological conditions were reported by Dhurba one with microcephaly characterized small head size with incomplete brain development which may occur when mother gets infected during the first three months of pregnancy. The other second one is with GBS where a person's own immune system damages the nerve cells, causing muscle weakness and sometimes, paralysis in replaces to Zika virus infection reaction[25].

Diagnosis of Zika virus:

To date, the literature describing the performances of Zika diagnostic tests remains relatively limited. The routine diagnosis of ZIKV infection can be determined by either direct methods, i.e., isolation and detection of viral genome by RT-PCR in blood, saliva, urine, and other body fluids (cerebrospinal fluid, amniotic fluid, semen, vaginal fluid, breast milk, pharyngeal secretions), or by indirect methods based on the identification of Zika antibodies in the blood[26-27]The "pan flavivirus" amplification technique combinedwith sequencing may be used as an alternative. Serological tests (Elisa or immunofluorescence) are alsowidely used. The Centers for Disease Prevention and Control(CDC) in Atlanta had developed an ELISA technique to detectspecific anti-Zika IgM during the epidemic in Yap, in 2007.[28-29]

Treatment of Zika Virus:

At the moment, no preventive medicines or vaccines are available[30]. The treatment consists of rest, oral hydration and use of medications for symptoms. Analgesics and antipyretics such as dipyrone and paracetamol. Antihistamine medications to control itching. Non-steroidal anti-inflammatory drugs (NSAIDs) should not be used until the diagnosis of dengue has been ruled out[31]. Natural products derived from plants have been successfullyused to treat a variety of vector borne diseases, such asmalaria. Natural products fundamentally differ from syntheticcompounds in both chemical scaffolds and mechanisms of action, and have great potential for the development of antiviralagents.HH is an active ingredient of the medicinal plantLycoris radiata. A recent study demonstrated that HH (25 μM)eliminates ZIKV from infected hNPCs-derived cortical NPCs without affecting cell identity or differentiation capacity. Emetine is an alkaloid, which is extracted from the ipecac root. It acts as a non-nucleoside inhibitor against ZIKV[32]. Also 2′-C- and 2′-O-methyl–substituted nucleosides, 2′-C-fluoro-2′-C-methyl–substituted nucleosides, 3′-O-methyl–substituted nucleosides,3′-deoxynucleosides, derivatives with a 4′-C-azido substitution, heterobase-modified nucleosides, and neplanocins are evaluated for their ability to inhibit ZIKV replication in cell culture, with the objective of identifying promising lead candidates for further development of specific antivirals against ZIKV[33]. , sofosbuvir is the only FDA approved inhibitor tested against ZIKV thus far in ProTide form[34].

3-chloro-N-[({4-[4-(2-thienylcarbonyl)-1-piperazinyl]phenyl}amino)carbonothioyl]-1-benzothiophene-2-carboxamide (TPB), potently inhibited ZIKV replication at sub-micromolar concentrations. Molecular docking analysis suggests that TPB binds to the catalytic active site of the RdRp and therefore likely blocks the viral RNA synthesis by an allosteric effect. The IC50 and the CC50 of TPB in Vero cells were 94 nM and 19.4 μM, respectively, yielding a high selective index of 206. In in vivo studies using immunocompetent mice, TPB reduced ZIKV viremia significantly, indicating TPB as a potential drug candidate for ZIKV infections[35]. The antimalarial drug chloroquine has been reported in several drug repurposing screens as an anti-ZIKV compound. It is believed that the drug interferes with virus internalization, possibly through blocking of ZIKV-mediated autophagy or through yet uncharacterized host or viral factors in the early replication process. Significant reduction in ZIKV burden is observed in Balb/C mice treated with 100 mg per kg of chloroquine administered intragastrically compared to control mice. Dosing of compound for 5 days postinfection using the same treatment regimen with A129 mice significantly reduced viral load[36]. The antimalarial amodiaquine, a known inhibitor of cellular autophagy, has also been reported as an inhibitor of ZIKV replication in vitro with EC50 values ranging from 2.8 to 4.4 μM in hNPCs and Vero cells.121 39 (hydroxychloroquine) has also been shown to inhibit ZIKV in cellular and mouse models of infection[37-38].

Prevention of Zika Virus:

With no vaccine or antiviral therapy currently in the market.[39]There is currently no vaccine available. Three vaccines are under development: a vaccine containing the inactivated viral strain, a plasmid vaccine and an adenovirus-vectored vaccine for the expression of immunogens of the pre-membrane and the envelope of the Zika virus.[40]At this time, elimination of Zikavirus transmission still rests on prevention techniques, such as avoidance of travel, mosquito eradication, and avoidance of sexual intercourse among couples at risk.[41]

For personal protection against mosquito bites, residents of or travelers to Zika transmission areas should be counseled to:

- Wear long-sleeved shirts, pants, and hats.
- Apply insect repellent to exposed skin, especially during the day when Aedes mosquitoes are most active. The most effective insect repellent in the United States is diethyltoluamide at the recommended concentration of 20% to 50%. Other options include icaridin (concentration of at

least 20%) and lemon eucalyptus extract (concentration of at least 30%). Diethyltoluamide- and icaridin-containing insect repellants are safe for use in pregnancy when used as directed on the product label.

- Treat clothing with permethrin
- Sleep under mosquito nets or in airconditioned rooms with windows closed.[42-43]
- Additionally, local governments may have programs to reduce the mosquito population by spraying insecticide or larvicide over population centers and other communities.

All sexually active people, including teenagers, should be counseled about the danger of ZIKV transmission through sexual contact. People should be aware of the risk of having sex with someone who lives in an area with ZIKV transmission or who has traveled to an area with local transmission. Current CDC guidelines are to use a condom for at least 6 months if a male sexual partner is at risk for having had ZIKV and at least 8 weeks if the female partner is at risk. Studies are underway that will better inform our understanding of sexual transmission.[44]

In all health care settings, standard precautions should be observed. The use of personal protective equipment can prevent the transmission of ZIKV. In labor and delivery settings, there is a higher loss of blood and exposure to amniotic fluids. Health care professionals must assess their risk and increase precautions as needed. For example, if performing a procedure in which there is a higher risk of exposure to body fluids, the use of mask and eye protection in addition to double gloves and an impermeable gown is advised.[45]

Conclusion:

Worldwide, evidence of autochthonous mosquito-borne ZIKV transmission has been reported from 87 countries and territories and there is still a risk for further spread of ZIKV. In response to the emergence and global spread of ZIKV infections and associated complications, public health systems need to be strengthened and should include epidemiological surveillance. Zika Fever is a major global concern. So, due to lack of treatment modalities, having knowledge and awareness on control and prevention about this disease can help in saving lives and also help in stopping the spread of Zika fever widely. Adequate knowledge regarding Zika fever is needed among the peoples. The investigator concludes that, awareness among peoples is very poor. Hence, education among peoples is needed.

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