

“An Outlook on Zika Virus”

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ABSTRACT

Zika virus (ZIKV) is an ordinary mosquito-borne flavivirus, its vast proportions and deleterious consequences in imitation of humans drew the interest on each the clinical and lay community. ZIKV infection manifests as much a self-limited febrile sign associated along with rash, conjunctivitis, and arthralgias. Although the most emblematical fact concerning that epidemic used to be the association over ZIKV infection all through being pregnant along a dreadful increase of congenital microcephaly cases, vile medical manifestations had been also attributed in imitation of infection via that virus, such as much possible associations along auditory alterations, both in acquired and congenital infections. Here, I present the origin story of ZIKV, transmission, pathogenicity, clinical manifestations, diagnosis, possible treatment and drug developmental strategies.

Keywords: Zika virus; Hearing loss, Microcephaly, Pregnancy, Guillain-Barre syndrome

I. INTRODUCTION

Zika virus is a part of the household Flaviviridae, which also includes dengue, West Nile, yellow fever, or Japanese encephalitis viruses. ZIKV was once preceding isolated in 1947 in a Rhesus macaque monkey in the Zika forest over Uganda.^[1] The virus used to be as a result remotefrom *Aedes africanus* mosquitoes in the same forest the consonant year.^[2]

ZIKV used to be first stated in human beings between 1952 beside Uganda and the United Republic of Tanzania. Later, ZIKV occurrence used to be stated of 2007 from the Yap Island. ZIKV re-emerged as much fundamental outbreak of the year 2013 from French Polynesia followed by means of second outbreak within the 12 months 2015 from Brazil.^[3] In February 2016, the World Health Organization declared ZIKV infection a Public Health Emergency concerning International Concern. India pronounced the forward Zika action of 2017. Subsequently, 157 laboratory-confirmed

cases regarding ZIKV consisting of 63 with young girls had been pronounced from Rajasthan, India of 2018.^[4]

ZIKV is recognised in imitation of reason extreme fetal microcephaly and adult GBS.^[5] During the 2015 fall within Brazil, the chance on microcephaly surged together with a 20-fold make bigger within the variety concerning instances observed. Later research risen up to expectation pregnant women infected with ZIKV do dispose the virus to the fetus, causing fetal loss, microcephaly then other significant brain defects of new-borns. Similarly, neurological affections had been additionally acknowledged within incomplete infected adults developing GBS.^[6]

Microcephaly is a neurodevelopmental disease which gives so a much smaller head size in the fetus and new born. The condition primarily arises out of inadequate neural stem cell proliferation, impaired neurogenesis, or the death concerning neural stem cells or neurons, which results in a reduced cerebral cortex. Microcephaly does appear as an end result over a traditional genetic disorder, infection, drug abuse then a wide variety of other reasons. In ZIKV infection, microcephaly is believed in conformity with appear in particular as a consequence over dying of neural cause cells as a consequence on direct viral contamination over this cells, though lousy cells in the developing brain along with glial cells make contributions in imitation of the overall pathology.^[2]

GBS is one of the major neurologic manifestations over arboviruses, specifically ZIKV infection.^[7] GBS is a clinical diagnosis, with progressive weakness and are flexia evolving over less than 4 weeks. GBS is believed to keep appropriate in conformity with an autoimmune assault on peripheral nerves, taking place between previously healthy patients barring proof of ignoble autoimmune diseases. GBS, including an yearly occurrence on 1–2 per 100,000, is the close frequent reason of neuromuscular paralysis into the western world.^[8]

Guillain-Barre Syndrome is one of the main neurologic manifestations of arboviruses, especially Zika Virus Infection



During the 2015 ZVI epidemic swiping thru the Americas, not many instances of ZVI with severe, potentially life-threatening thrombocytopenia were reported.^[9]

Transmission: ZIKV is transmitted in conformity with human beings with the aid of an arthropod vector, particularly mosquitoes from the *Aedes* genus. Some transmission at once through sexual contact has been reported. Infectious virus is able stay detected among semen and vaginal secretions, alongside with other body fluids. Therefore, ZIKV has the uncommon potential among arboviruses to persist, within at least a constrained manner, so a sexually transmitted infection.^[6] Following transmission through the mosquito bite, Zika virus be able infect various different cell types including skin keratinocytes, dermal fibroblasts and DCs. Different cell surface receptors have been proposed to treat Zika infection over permissive cells; such as DC-SIGN, AXL and Tyro3 molecules. Following cell entry, Zika virus induces strong interferon responses in contaminated cells.^[10] In humans, ZIKV antagonizes the kind 1IFN response, within part thru its NS5 protein, who promotes proteasomal degradation of STAT2 a transcription factor that is activated downstream over signaling with the aid of the Ifnar1.^[11]

Studies on ZIKV-infected human major fibroblasts hold proven intensive up regulation of interferon-beta transcripts 24 to 48 h after infection. A milder rejoinder has been observed for interferon-alpha. Up regulation over intracellular 'PRRs' involved in sensing non-self-nucleic acids appears according to be a crucial section of the preliminary immune response to the virus. Studies on ZIKV-infected fibroblasts bear produced intensive induction of RIG-I and MDA-5 transcripts. Both of these molecules are successful of initiating a signaling method consonant the detection on intra-cytoplasmic viral RNA molecules. Innate immune responses are observed

by means of adaptive immune activities which include the activation on T cells; ZIKV-infected DCs migrate in conformity with provincial lymph nodes the place they develop T cell proliferation, differentiation and cytokine production.

Productive infection about dermal fibroblasts and dendritic cells together with insufficient limit of infection through innate and adaptive immune mechanisms normally leads to ZIKV viremia, which underlies the non-specific medical symptoms who may last because a not much days. In a pregnant woman, maternal viremia may conduct according to fetal viremia. It is not properly known what the virus is transmitted after flourishing nervous system accordant the establishment on fetal viremia. While in circulation, ZIKV do infect fetal monocytes and these monocytes be able carry the infection in accordance with the flourishing nervous system. Studies over fetal brain tissue derived from ZIKV - infected mothers whichever have undergone aborted foetus hold proven viral particles of neural cells, indicating that the virus do proliferate inward neural cells of a growing brain. While inside the CNS, ZIKV can exert direct neurovirulence, comparable to other Flaviviruses. There is also evidence that ZIKV would possibly reason indirect neurovirulence through the activation on immune mechanisms including microglial activation and macrophage infiltration. Indeed, in adults ZIKV might keep an etiological component for ADEM, an immune-mediated disorder on the CNS, which takes place subsequent to sorts on viral and non-viral infections.^[10] It is necessary according to word that asymptomatic pregnant women perform nevertheless vertically transfer Zika virus after their neonates.^[1]

Pathogenicity ZIKV shows large tropism within human cells, present process replication then giant outgiving after cell entry through endocytosis. ZIKV preferentially aims neural stem cells and progenitor cells. In pregnancy, Hofbauer

macrophages and other immune cells concerning the placenta up to expectation normally adore as like a maternal-fetal barrier provide a mechanism for the virus to infect fetal cells. Zika virus has an incubation period of 3 to 14 days.^[1]

Clinical manifestations in ZIKV disorder consists of rash, fever, conjunctivitis, muscle or joint pain, headache, transverse myelitis, meningo-encephalitis, ADEM.^[3] Most contaminated persons are asymptomatic and show slight signs certain as fever, rash, or myalgias lasting on to 1 week. [1] ZIKV reveals that a numerous tropism, infiltrating several immunologically privileged areas within the body. These consist of the descent and female reproductive organs, adult and fetal CNS, PNS, urinary tract, and the structural or neurologic portions of the eye. The almost devastating issues about ZIKV happen throughout infection on the placenta then vertical transmission after the increasing fetus, propulsion after adverse being pregnant effects such as regular abortion or fetal brain abnormalities. Approximately 30% regarding congenitally infected fetuses exhibit neurologic (e.g., seizures, hypertonicity, and hyperreflexia) or morphologic abnormalities (e.g., microcephaly and brain calcifications).^[12] Congenital Zika symptom is notably a constellation of CNS abnormalities. In particular, fetal brain disruption adjunct outcomes between microcephaly and cortical atrophy, intracranial calcifications, ignoble neural then immediate abnormalities, then growth restriction. In infants, this manifests along developmental delay, visible and listening to impairment, seizures, and movement and behavioural disorders.^[11]

Evidence regarding causality among ZIKV infection and fetal abnormalities include evidence on infection in the course of pregnancy, a specific or uncommon phenotype of central nervous system abnormalities within infected fetuses then new-borns, or identification regarding the virus of the brain tissue on affected fetuses and neonates.^[13]

Thirteen studies were conducted, as protected 1275 children whichever are prenatally uncovered in conformity with Zika virus. In 852 on the cases an objective hearing comparison used to be observed the usage of either OAEs or ABR. 709 young people have been tested with ABR and seventy nine had a failed outcome. 143 kids have been examined with OAEs while over these, 30 had a failed outcome. Altered OAEs ranged from 8.7% to 30.2%, whilst altered ABR ranged beyond 0% after 19.9%. The initial pattern consists of 428 kids including microcephaly, whilst 5 on the research contain microcephaly to the inclusion criteria.^[14]

Children with congenital ZIKV symptom may also have speech, language, or hearing issues such as hearing loss, dysphagia, alteration into the tongue frenulum, then delays in Neuro-psychomotor and speech development.^[15] In latest years, the ZIKV has arisen from a omitted flavivirus in accordance with a health-threatening pathogen that motives epidemic outbreaks. In collection in accordance with vaccination development, the discovery of precise antiviral agents has been pursued intensely. The ZIKV protease NS2B-NS3 catalyses the technology about the viral precursor poly-protein as like a quintessential steps during viral replication.^[16]

Diagnosis: The grasp of the molecular mechanism concerning ZIKV pathogenesis is very important in imitation of advance potential diagnostic and therapeutic interventions for ZIKV infected patients.^[3] ZIKV infection is usually detected through serum and urine RT PCR nucleic acid molecular screening and/or serologic IgM ELISA screening. Molecular trying out ought to lie rendered within 2 weeks about onset of symptoms, while serologic testing can stand precisely old up to 12 weeks after indication onset.^[1]

Possible Treatments and Drug Development Strategies

Currently, in that place are no specific medicine and licensed vaccines accessible for ZIKV infection, and in addition lookup is required in imitation of perceive host cell proteins involved in the virus's life cycle. Viruses are recognised in conformity with usage host cell membrane skeletal proteins, certain namely actin and spectrin, in conformity with perfect cell entry, transportation, and release. Here, based totally about immunoprecipitation, the Axl and ZIKV envelope (E) protein have been proven to have interaction together with the cell membrane skeleton protein 4.1R. Furthermore, deletion of 4.1R significantly reduced virus concentration and protein consistency.^[5]

A generally used strategy for antiviral remedy development entails focused on particular prone levels of the pathogen's life cycle in order to disrupt its creation within cells, efficaciously defending cells and theirs neighbours from viral spreading.

The inhibitors over the viral NS2B-NS3 protease have proven a proper brawny for the therapeutic development. By screening upon 2,800 selected and investigational drugs, identified temoporfin, niclosamide, and nitazoxanideas like

inhibitors of the ZIKV protease. These ternary compounds blocked the productive interactions on the viral NS2B co-factor along the NS3 protease area and inhibited the NS2B-NS3 protease endeavour with nanomolar potency. Temoporfin, a clinically elected drug, tested the just stated effect with the aid of defending NPCs and placental cells, and decreasing viremia or mortality in mice. More recently, research show that viperin (virus inhibitory protein, endoplasmic reticulum-associated, interferon-inducible, additionally acknowledged as like RSAD2) limited ZIKV and tick-borne encephalitis virus duplicate with the aid of focused on NS3 for proteasomal degradation. Viperin was once found in conformity with interact and co-localize with ZIKV NS2A, NS2B, and NS3. Interestingly, viperin disclosure reduced the NS3 protein level post-infection and the stability over the ignoble interacting viral proteins, however only between the availability on NS3. Although viperin interacted along NS3 beyond numerous mosquito-borne flaviviruses like; ZIKV, Japanese encephalitis virus, and yellow fever virus, solely ZIKV was sensitive in imitation of the antiviral effect concerning viperin. However, the in vivo working efficiency of viperin has now not yet been investigated.^[17]

II. CONCLUSION

The data summary into this article offers short facts in relation to ZIKV. ZIKV infection used to be a “newly emerging” infectious disease, along with the dynamic in imitation of purpose significant health issues in populace. Unlike the ignoble “newly emerging” infections which can lead to extreme morbidity and mortality in infected adults or paediatric hosts, Zika infection now didn’t get massive risk to infected adults and its consequences are extra due in accordance with the potent to purpose fetal abnormalities, occurred as the contamination takes place during pregnancy. The consequences concerning ZIKV bear already evolved an era over children together with microcephaly whoever will not at all lead an everyday life. Thus, improved cognizance over the medical community collectively improvements in vector control and disorder surveillance structures are of utmost importance for controlling potential Zika virus-related threats in underdeveloped or developing countries.

CONFLICT OF INTEREST STATEMENT: We declare that we have no conflict of interest.

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ABBREVIATIONS: Zika virus (ZIKV), Acute Disseminated Encephalomyelitis (ADEM), Guillain-Barre syndrome (GBS), dendritic cells (DCs), Type I interferon (Ifnar1), Pattern recognition receptors (PRRs)

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