CHRONICLE OF ZIKV

Zika virus (ZIKV) is a 70 years back begun story to which still scientists are searching for an end. It was identified in Uganda and stretched over Africa, America, Asia, and the Pacific. It emerged as primary health concern infecting millions of people manifesting neurological complications and congenital malformations. This piece of writing provides an insight into the origin, transmittance, symptoms, complications and congenital malformations. This review focuses on the historical background, structure, phylogeny, transmission, symptoms, diagnosis, prevention, and treatment of ZIKV along with strategies planned for control and monitoring of ZIKV.

BACKGROUND

Zika virus (ZIKV) is a mosquito-borne virus which startled the world with its tremendous outbreaks in Africa, America, Asia, and Pacific region. Although the symptoms are mild such as fever and headache, its complications are severe in newborn: Guillain-Barre Syndrome and congenital Zika syndrome including microcephaly. Its ability to transmit through vector and non-vector means especially vertical transmission made it a potential threat. The World Health Organization with the support of other organizations implemented several programs to eradicate the spread of the virus. Development of a vaccine for ZIKV is still under clinical trials. An anti-hepatitis C drug was repurposed for treating infected persons especially pregnant women to limit vertical transmission of ZIKV. This review focuses on the historical background, structure, phylogeny, transmission, symptoms, diagnosis, prevention, and treatment of ZIKV along with strategies planned for control and monitoring of ZIKV.

ABSTRACT

Zika virus (ZIKV) is a mosquito-borne virus which started the world with its tremendous outbreaks in Africa, America, Asia, and Pacific region. Although the symptoms are mild such as fever and headache, its complications are severe in newborn: Guillain-Barre Syndrome and congenital Zika syndrome including microcephaly. Its ability to transmit through vector and non-vector means especially vertical transmission made it a potential threat. The World Health Organization with the support of other organizations implemented several programs to eradicate the spread of the virus. Development of a vaccine for ZIKV is still under clinical trials. An anti-hepatitis C drug was repurposed for treating infected persons especially pregnant women to limit vertical transmission of ZIKV. This review focuses on the historical background, structure, phylogeny, transmission, symptoms, diagnosis, prevention, and treatment of ZIKV along with strategies planned for control and monitoring of ZIKV.

Keywords: Zika virus, Structure, Phylogeny, Guillain-Barre syndrome, Congenital Zika syndrome, Microcephaly, Zika strategic response plan, Zika vaccine, Sofosbuvir, India.

© 2018 The Authors. Published by Innovare Academic Sciences Pvt Ltd. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/) DOI: http://dx.doi.org/10.22159/ajpcr.2018.v11i7.25377

BACKGROUND

Zika virus (ZIKV) is a 70 years back begun story to which still scientists are searching for an end. It was identified in Uganda and stretched over Africa, America, Asia, and the Pacific. It emerged as primary health concern infecting millions of people manifesting neurological complications and congenital malformations. This piece of writing provides an insight into the origin, transmittance, symptoms, complications and congenital malformations. This review focuses on the historical background, structure, phylogeny, transmission, symptoms, diagnosis, prevention, and treatment of ZIKV along with strategies planned for control and monitoring of ZIKV.

ABSTRACT

Zika virus (ZIKV) is a mosquito-borne virus which startled the world with its tremendous outbreaks in Africa, America, Asia, and Pacific region. Although the symptoms are mild such as fever and headache, its complications are severe in newborn: Guillain-Barre Syndrome and congenital Zika syndrome including microcephaly. Its ability to transmit through vector and non-vector means especially vertical transmission made it a potential threat. The World Health Organization with the support of other organizations implemented several programs to eradicate the spread of the virus. Development of a vaccine for ZIKV is still under clinical trials. An anti-hepatitis C drug was repurposed for treating infected persons especially pregnant women to limit vertical transmission of ZIKV. This review focuses on the historical background, structure, phylogeny, transmission, symptoms, diagnosis, prevention, and treatment of ZIKV along with strategies planned for control and monitoring of ZIKV.

Keywords: Zika virus, Structure, Phylogeny, Guillain-Barre syndrome, Congenital Zika syndrome, Microcephaly, Zika strategic response plan, Zika vaccine, Sofosbuvir, India.

© 2018 The Authors. Published by Innovare Academic Sciences Pvt Ltd. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/) DOI: http://dx.doi.org/10.22159/ajpcr.2018.v11i7.25377

ZIKV is a member of Flaviviridae family transmitted by mosquitoes so alternatively referred as flavivirus and arbovirus. It shares the same family of human pathogens such as dengue virus, West Nile virus, and yellow fever virus. As all flaviviruses, ZIKV consists of a membrane surrounding the capsid with viral ribonucleic acid (RNA) genome. About 180 copies of both envelope (E) glycoprotein and the membrane (M) protein inserted into lipid membrane constitute the icosahedral capsid. Major viral proteins of ZIKV are structurally and functionally similar to other flaviviruses except at asn154 glycosylation site which may serve as an attachment point to host cells. From structural elucidation, researches suggested E glycoprotein as a possible target of drugs for therapy [12,13]. Although phylogenetic studies revealed a common lineage of American and Asian strains, researches identified a set of amino acid residues that are uncommon between the strains and also from ancient African strains. This might be due to recombination which provided an increase in pathogenicity and transmission efficiency of ZIKV [13].

TRANSMISSION

Vector transmission

As specified earlier during a study by Dick et al, several varieties of mosquitoes, namely, A. africanus, Aedes furcifer, A. furcifer, Aedes japonicus, and Aedes albopictus have been reported to be associated with the transmission of ZIKV. In the United States, the primary mosquito vector for ZIKV is Aedes aegypti, which is highly prevalent in the southern states. In addition, several other mosquito species such as Aedes albopictus and Culex quinquefasciatus have been identified as potential vectors in certain regions. Human-to-human transmission via blood transfusion or sexual contact has also been reported in some cases.

ACQUIRED IMMUNITY

The acquired immunity in ZIKV infection is incompletely understood due to the lack of prior exposure to the virus. Research studies have suggested that the acquired immunity against ZIKV is not long-lasting, and reinfection can occur in some cases. The role of long-term immunity and the development of protective immunity against ZIKV remain areas of active research.

REFERENCES

1. WHO. (2018). Zika virus. World Health Organization. Retrieved from https://www.who.int/mediacentre/factsheets/zika/en/
2. WHO. (2018). Zika virus: FACTSHEET. World Health Organization. Retrieved from https://www.who.int/mediacentre/factsheets/zika/en/
3. WHO. (2018). Zika virus: Northern Hemisphere. World Health Organization. Retrieved from https://www.who.int/mediacentre/factsheets/zika/en/
4. WHO. (2018). Zika virus: Southern Hemisphere. World Health Organization. Retrieved from https://www.who.int/mediacentre/factsheets/zika/en/
5. WHO. (2018). Zika virus: Central America and Caribbean region. World Health Organization. Retrieved from https://www.who.int/mediacentre/factsheets/zika/en/
6. WHO. (2018). Zika virus: Oriental region. World Health Organization. Retrieved from https://www.who.int/mediacentre/factsheets/zika/en/
7. WHO. (2018). Zika virus: Western Pacific region. World Health Organization. Retrieved from https://www.who.int/mediacentre/factsheets/zika/en/
8. WHO. (2018). Zika virus: African region. World Health Organization. Retrieved from https://www.who.int/mediacentre/factsheets/zika/en/
SIGNS AND SYMPTOMS

Symptoms of ZIKV often coincide with others and virus infections especially dengue virus. Often the symptoms of ZIKV are left unnoticed due to their mildness. Symptoms start with mild headache followed by maculopapular rash on face, neck, upper arms and palms, fever, conjugate, joint pain, and malaise. These symptoms typically last for 7 days [25].

COMPLICATIONS

Although the symptoms of ZIKV appears to be mild and less attention needed, often ZIKV infection leads to severe complications which could be life-threatening.

Guillain-Barre syndrome

It can be categorized as an autoimmune disorder as this body's immune system attacks part of the peripheral nervous system and damages the myelin sheath. This syndrome can affect nerves allied to muscle movement, pain, temperature, and touch. It is a rare condition commonly seen in males of all ages. Symptoms comprise tingling sensation and weakness initiating in legs and spread to arms and face leading to paralysis in some cases. About 20–30% of patients with affected chest muscles showed difficulty in breathing which can be life-threatening. 3–5% of patients die due to paralysis of muscles concerned with important systems. In many of the situations, patients showed complete recovery, even though weakness remains as a part of them. Guillain-Barre syndrome is generally headed by a bacterial or viral infection, vaccine administration, or surgery [26]. This statement can be correlated to the increased cases of Guillain-Barre syndrome during the outbreak of ZIKV in Brazil and other countries. ZIKV infection served as triggering agent for Guillain-Barre syndrome. Diagnosis is through monitoring symptoms and neurological testing including decreased or loss of deep-tendon reflexes. There is no known cure, but treatment can recover symptoms and cut down its duration [26].

Different types of Guillain-Barre syndrome attribute different types of immunity attacks. Main types include acute inflammatory demyelinating polyradiculoneuropathy (AIDP), Miller Fisher syndrome, acute motor axonal neuropathy, and acute motor – sensory axonal neuropathy. In AIDP variant the demyelination is done by white blood cells (T lymphocytes and macrophages) where in case of axonal variants it is mediated by IgG antibodies and complement against the cell membrane covering axon [27].

As a part of neurovirus emergence in the Americas study, all the patients diagnosed with Guillain-Barre syndrome from January to March 2016 underwent clinical and neurological evaluation. This study suggested that temporal profile of neurological symptoms related to ZIKV caused Guillain-Barre syndrome is not the same as a syndrome associated with other infections. The syndrome is observed to be parainfectious rather than postinfectious which can be possibly accounted as: ZIKV triggers an immune molecular mimicry against nervous system antigens leading to immune dysfunction and Guillain-Barre syndrome. Furthermore, there is a prolonged period of viruria which even endure after viral syndrome suggesting the use of RT-PCR urine test as a valuable diagnostic tool for ZIKV infection in Guillain-Barre syndrome patients. The study also found a potential relationship between ZIKV associated Guillain-Barre syndrome and previous exposure of the patient to dengue virus. 86% of patients with Guillain-Barre syndrome had evidence of antibodies against dengue virus indicating prior exposure to dengue virus, and ZIKV has been a secondary flavivirus infection. Most of the patients in the study had AIDP form of Guillain-Barre syndrome the reason for which is yet to be revealed [28].

Microcephaly

Microcephaly is a birth defect where the size of baby’s head is smaller than anticipated. In gestation period, the head size depends on brain development which is yet to be revealed [28].

ZIKV increased the incidence of microcephaly in babies born to infected mothers in various regions which called the need for a study on microcephaly in ZIKV-infected pregnant women. Mlakar et al. through his study reported intratruernal transmission of virus causing severely
affected central nervous system (CNS) and growth retardation. Virus damaged the placenta which was confirmed through calcification of placenta and low placental-fetal weight ratio. ZIKV is primarily found to be neurotropic in nature, which is also reported in other flaviviruses. Remains of replication complexes are diagnosed in the damaged endoplasmic reticulum of nerve tissues indicating fetal brain as the site of replication of ZIKV. The viral copies are several times higher in fetal brain than reported in adult infected serum but similar to the infected semen samples [30].

In 2017 research revealed the underlying relationship between the ZIKV infection and microcephaly in newborns. Cerebral cortex formation involves neuron formation through direct and indirect methods. In direct method, neurons born from the symmetric division of apical progenitors (APs), while in indirect method APs convert to intermediate progenitors (IPs) which divide to form neurons. A balance exists between direct and indirect neurogenesis regulated by unfolded protein response (UPR). Disruption of this balance leads to microcephaly in humans. ZIKV is vertically transmitted to fetal cortical region targeting APs, but it did not induce apoptosis instead it interrupted the conversion of APs to IPs, hence leading to decreased neuronal output in the infected developing cortex. Any interference with codon translation induced endoplasmic reticulum stress and the UPR which the reason for the hindrance of APs conversion to IPs. UPR is mediated by three pathways, inhibition of these pathways could prevent the chance of microcephaly in newborns of infected women by inhibiting the UPR induced apoptosis [31].

**Congenital ZIKA syndrome**

Congenital ZIKA syndrome includes all birth defects caused by Zika viral infection before birth and is mainly featured by severe microcephaly (earlier discussed), reduced brain tissue including subcortical calcifications, macular scarring and focal pigmentary retinal mottling, arthrogryposis multiplex congenital (curving of joints), and hypertonia (restricted body movements due to CNS damage). The syndrome is also associated with hydrocephalus, redundant scalp skin, tremors, seizures, and irritability [32]. Ophthalmological studies on neonates born with ZIKV infection revealed severe eye abnormalities such as optic nerve hypoplasia, congenital glaucoma, microphthalmia, cataracts, lens subluxation, and intracranial calcifications [33].

**DIAGNOSIS**

Asymptomatic nature of ZIKV-infected subjects and its potential to transmit through blood transfusion, sexual contact, and congenital transmission elicited the urgency for the development of the diagnostic method. As no licensed laboratory test for biological quantification of ZIKV is available but as a necessity to control the outbreak is present, FDA has issued emergency use authorization for several diagnostic tools on February 26, 2016, such as Trioplex real-time RT-PCR assay, Zika-MAC ELISA, and real-time Zika test [34].

Multiple assays are to be performed to diagnose the ZIKV infection due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followed by rise due to temporal nature of virus in an infected person. Viral RNA can be detected in infected person in earlier days of infection followe...
of help to the needed without duplication and deficits. Immediate priority of funding is given to preventing and managing the medical complications, expanding health system’s competence, sexual and reproductive health risk and integrated vector management.

To achieve the objectives five strategies are employed: Detection, prevention, care and support, research, and coordination. Detection concentrates on integrated surveillance systems to provide up to date information, to guide response. Prevention - prevent adverse outcomes of ZIKV by integrated vector management, risk communication, and community engagement. Care and support involve strengthening of health and social systems at different levels to offer services and support to affected. Research includes interventions to prevent, detect, and control ZIKV infection and manage its complications. It also encloses research on Aedes mosquito control tool, vaccines, and diagnostic tests. Coordination involves establishment and maintenance of adequate, transparent coordination for accurate response to ZIka infection [10].

First quarterly report on Zika strategic response plan was released enclosing the latest information on different strategies of the plan. These updates are for guidance, coordination, and collaboration among the WHO and its partners to support countries [30].

VACCINE DEVELOPMENT

Vaccination is the ideal remedy for ZIKV infection. WHO along with UNICEF developed ZIKV vaccine target product profile for use in an emergency scenario in July 2016. About 30 organizations, including 8 public sector institutions are engaged in vaccine development. Two DNA vaccines (by GeneOne Life Sciences Inc and National Institute of Allergy and Infectious Diseases [NIAID] in the United States) reached Phase I trials while many other candidates are about to move to Phase I trials [38,39].

Synthetic DNA vaccine that targets the ZIKV premembrane and envelope proteins are prepared by GeneOne life sciences and are delivered through CELLECTRA-3P electroporation device. The vaccine reached Phase I on producing cellular and humoral immune responses along with the production of neutralizing antibodies, in mice and nonhuman primates. In the Phase I, open-label clinical trial, it elicited anti-ZIKV immune responses, achieving a clarity for Phase I. However, studies on further safety and efficacy are yet to be performed [40].

THERAPY BY REPURPOSING APPROVED DRUG

While the world is busy in designing immunization strategies through vaccine development, some researches concentrated on the screening of FDA approved drugs to repurpose for ZIKV. Need to cure infected persons and avoid vertical transmission in already infected pregnant women (in whom prevention is no longer an option) insisted the search for a drug to cure Zika infection. Sofosbuvir (SOF), a RNA dependent RNA polymerase inhibitor was a FDA approved a drug to treat and cure hepatitis C infections. SOF intracellularly converts into its triphosphate and inhibits RNA polymerase of hepatitis C virus (HCV). RNA polymerase of ZIKV and HCV is similar in their active sites. Due to the phylogenetic and structural similarity of HCV and ZIKV, SOF are tested for possible action on ZIKV. SOF tested on infected neural progenitor cells, and three-dimensional neurospheres prevented cell death by ZIKV infection. In vivo testing on immunodeficient mouse models also showed promising results. Efficacy of SOF in blocking vertical transmission in ZIKV permissive SJL strain21 was tested. Decrease in serum concentration of ZIKV was reported in pregnant SJL strain21 along with blocking of vertical transmission [41].

ZIKA IN INDIA

On September 30, 2017, Indian Council of Medical Research (ICMR) has released ZIKV update revealing the preparedness and response. ICMR has conducted three training programs for 25 laboratories to diagnose ZIKV. Human surveillance network for ZIKV was established to screen the human serum/blood and urine samples of suspected persons, patients with dengue and chikungunya and pregnant women. About 45,820 samples are tested through this surveillance till the date of which three different individuals found to be positive for ZIKV. (1) 34-year-old female developed low-grade fever 1 week after delivering healthy baby and tested negative for dengue, chikungunya fever but positive for ZIKV. (2) 22-year-old pregnant female in 37 weeks of pregnancy was tested positive and (3) 64-year-old male with febrile illness of 8 days duration tested negative for dengue fever and positive for ZIKV. (4) 27-year-old male with acute febrile illness for 3 days was tested positive for ZIKV in urine, but blood was negative. Further confirmation by PCR showed 98% sequence similarity with ZIKV Asian lineage. Since July 2016, three ICMR institutes initiated vector surveillance in different parts of India and tested 25,960 pools of mosquitoes by RT-PCR technique, but no sign of ZIKV was reported.

The reproductive and child health division of ministry of health and family Welfare has initiated programs on newborn birth defect screening and stillbirth surveillance, under Rashtriya Bal Swasthya Karyakram. It focuses on reporting 8 externally visible birth defects including microcephaly. ICMR and Monash University has signed MoA on February 2017 regarding strategies for vector control in India [42]. Several such programs are being successfully implemented by Indian government agencies in collaboration with the WHO.

CONCLUSION

Due to high complications and multiple modes of transmission of ZIKV, there is a necessity for improving knowledge on ZIKV among the health-care professionals and the general public to regulate the spread of infection. Government of all countries along with the WHO and several other organizations are implementing programs to effectively eradicate ZIKV infection. Programs on assessing awareness among people are also necessary for effective functioning of Zika strategies [43]. Approval of vaccine can keep an end to the story of ZIKV.

AUTHOR’S CONTRIBUTIONS

Authors equally contributed to articles collection and framing of manuscript. Each author has reviewed and revised the article for efficient presentation of viewpoint.

CONFLICTS OF INTEREST

The authors declared that they have no conflicts of interest.

REFERENCES

1. Dick GW, Kitchen SF, Haddow AJ. Zika virus. I. Isolations and emergency scenario in Nigeria. Trans R Soc Trop Med Hyg. 1954;48:139-45.
2. Smithburn KC. Neutralizing antibodies against certain recently isolated viruses in the sara of human beings residing in East Africa. J Immunol 1952;69:223-34.
3. Macnamara FN. Zika virus: A report on three cases of human infection during an epidemic of jaundice in Nigeria. Trans R Soc Trop Med Hyg 1954;48:139-45.
4. Kindhauser MK, Allen T, Frank V, Santhana R, Dye C. Zika: The origin and spread of a mosquito-borne virus. Bull World Health Organ 2016. DOI: org/10.2471/BLT.16.171082.
5. Fay BD, Kobylianski KC, Foy JL, Bliéthy BJ, Rosa AT, Haddow AD, et al. Probable non-vector-borne transmission of zika virus, Colorado, USA. Emerg Infect Dis 2011;17:880-2.
6. Besnard M, Lastère S, Teissier A, Cao-Lormeau VM, Musso D. Evidence of perinatal transmission of Zika virus, French polynesia. Euro Surveill 2014;19 pii:pii20751.
7. Musso D, Nhan T, Robin E, Roche C, Bierlaire D, Zisou K, et al. Potential for zika virus transmission through blood transfusion demonstrated during an outbreak in French polynesia, november 2013 to february 2014. Euro Surveill 2014;19 pii:pii20761.
8. FDA. Revised Recommendations for Reducing the Risk of Zika Virus Transmission by Blood and Blood Components. Maryland, US. August 2016. Available from: https://www.fda.gov/downloads/biologicsbloodvaccines/guidancecomplianceregulatoryinformation/guidances/blood/ucm518213.
9. WHO. Prevention of Sexual Transmission of Zika Virus. Interim
Guidance Update. Geneva. 6 September 2016. WHO/ZIKV/MOC/16.1
Rev. 3. Available from: http://www.who.int/csr/resources/publications/
Zika/sexual-transmission-prevention/en.

10. WHO. Zika Strategic Response Plan for July 2016–December 2017.
Geneva. June 2016. Available from: http://apps.who.int/iris/bitstream/10665/246091/1/WHO-ZIKV-SRF-16.3-eng.
pdf?ua=1&ua=1&ua=1&ua=1.

11. Bushak L. A Brief History of Zika Virus, from its Discovery in the
Zika Forest to the Global Outbreak Today. Medical Daily. 8 April 2016.
Available from: http://www.medicaldaily.com/zika-virus-outbreak-
history-381132.

12. Sirohi D, Chen Z, Sun L, Klose T, Pierson TC, Rossmann MG, et al. The
3.3Å resolution cryo-EM structure of zika virus. Science (New York,
NY) 2016;352(6284):467-9. Available from: https://www.cdc.gov/pregnancy/Zika/testing-follow-
up/Zika-syndrome-birth-defects.html.

13. Ye Q, Liu ZY, Han JF, Jiang T, Li XF, Qin CF. Genomic characterization
and phylogenetic analysis of Zika virus circulating in the Americas.
Infect Genet Evol 2016;43:43-9.

14. Boorman JP, Porterfield JS. A simple technique for infection of
mosquitoes with viruses; transmission of Zika virus. Trans R Soc Trop
Med Hyg 1956;50:338-42.

15. Marchette NJ, Garcia R, Rudnick A. Isolation of Zika virus from Aedes
aegypti mosquitoes in Malaysia. Am J Trop Med Hyg 1969;18:411-5.

16. Olson JG, Ksiazek TG, Triwibowo S. Zika virus, a cause of fever in
central Java, Indonesia. Trans R Soc Trop Med Hyg 1981;75:389-93.

17. Song BH, Lee YM. Zika virus: History, epidemiology, transmission,
and clinical presentation. J Neuroimmunol 2016;298:50-64.

18. Kuehnert MJ, Basavaraju SV, Moseley RR, Pate LL, Galel SA,
Williamson PC, et al. Screening of blood donations for Zika virus
infection-Puerto Rico. Morb Mortal Wkly Rep 2016;24:65:627-8.

19. Barjas-Castro ML, Angerami RN, Cunha MS, Suzaki A, Nogueira JS,
Rocco IM, et al. Possible transference-transmitted Zika virus in Brazil.
Translfection 2016;56:1684-8.

20. Deckard DT, Chung WM, Brooks JT, Smith JC, Woldai S, Hennessey M.
Male-to-male sexual transmission of Zika virus–texas. MMWR
Morb Mortal Wkly Rep 2016;65:372-4.

21. Davidson A, Slavinski S, Komoto K, Rakeman J, Weiss D. Suspected
male-to-female sexual transmission of Zika virus-New York City, 2016.
MMWR Morb Mortal Wkly Rep 2016;65:24:65:627-8.

22. Barzon L, Pacenti M, Franchin E, Lavezzo E, Trevisan M, Sgarabotta D,
et al. Infection dynamics in a traveller with persistent shedding of Zika
virus RNA in semen for six months after returning from Haiti To Italy,
January 2016. Euro Surveill 2016;21:pii30316.

23. Ye Q, Liu ZY, Han JF, Jiang T, Li XF, Qin CF. Genomic characterization
and phylogenetic analysis of Zika virus circulating in the Americas.
Infect Genet Evol 2016;43:43-9.

24. Ognian J, Beaton ML, Somsel P, Stobierski MG, Stoltman G,
Downes K, et al. Possible West Nile virus transmission to an infant
through breast-feeding-Michigan. MMWR Morb Mortal Wkly Rep
2002;51:877-8.

25. Lanciotti RS, Kosoy OL, Laven JJ, Velez JO, Lambert AJ, Johnson AJ,
et al. Genetic and serologic properties of Zika virus associated with an
epidemic, yape state, Micronesia, 2007. Emerg Infect Dis 2008;14:1232-9.

26. WHO. Guillain–Barré Syndrome, Fact Sheet Geneva. October 2016.
Available from: http://www.who.int/mediacentre/factsheets/guillain-
barre-syndrome/en/.

27. Van Doorn PA, Ruts L, Jacobs BC. Clinical features, pathogenesis, and
treatment of guillain–barré syndrome. Lancet Neurol 2016;7:939-50.

28. Abdullahi HS, Umar SH. An overview of recombinant vaccine
technology, adjuvants and vaccine delivery methods. Int J Pharm Pharm
Sci 2016;8:19-24. Available from: https://www.innovareacademics.in/
journals/index.php/ijpps/article/view/14311/7769.39.

29. Beckham JD. Zika virus is associated with microcephaly and eye
anomalies in neonates. Neurol Rev 2016;24:13.

30. Chaitanya and Anusha
Available from: http://www.medicaldaily.com/zika-virus-outbreak-
history-381132.

31. Gladwyn-Ng I, Cordón-Barris LF, Aliano C, Crepée C, Coudert T,
Morelli G. Stress-induced unfolded protein response contributes to
Zika virus-associated microcephaly. Nat Neurosci 2018;21:63-71.

32. Mlakar J, Korya M, Tul N, Popovic M, Prijatelj MP, Rocco IM。
Maderozo virus–birth defects. Georgia, United States. November 2017.
Available from: https://www.cdc.gov/pregnancy/Zika/testing-follow-
up/Zika-syndrome-birth-defects.html.

33. Beckham JD. Zika virus is associated with microcephaly and eye
anomalies in neonates. Neurol Rev 2016;24:13.

34. U.S. Department of Health and Human Services. Food and Drug
Administration. Emergency Use Authorizations, Maryland 2016.
Available from: https://www.fda.gov/MedicalDevices/Safety/
EmergencySituations/ucm161496.htm#Zika.34.

35. Centers for Disease Control and Prevention. Guidance for US Laboratories
Testing for Zika Virus Infection. Georgia, United States. July 24, 2017.
Available from: https://www.cdc.gov/Zika/laboratories/lab-guidance.html.

36. WHO. Information for Travellers Visiting Zika Affected Countries.
Geneva. April 2017. Available from: http://www.who.int/csr/disease/
Zika/information-for-travelers/en/.

37. WHO. Promising New Tools to fight Aedes mosquitoes. Bull World
Health Organ 2016;94,562-3. Available from: http://www.who.int/whrn
bulletin/volumes/94/8/16-020816.pdf.

38. WHO. Zika Strategic Response Plan Quarterly Update. Geneva.
October 2016. Available from: http://www.who.int/emergencies/Zika-
virus/response/en/.

39. Abdullahi HS, Umar SH. An overview of recombinant vaccine
technology, adjuvants and vaccine delivery methods. Int J Pharm Pharm
Sci 2016;8:19-24. Available from: https://www.innovareacademics.in/
journals/index.php/ijpps/article/view/14311/7769.39.

40. Tebas P, Roberts CC, Muthumani K, Reuschel EL. Safety and
immunogenicity of an anti-zika virus DNA vaccine—preliminary
report. N Engl J Med 2017. DOI: 10.1056/NEJMoa1708120.

41. Mlakar J, Korya M, Tul N, Popovic M, Prijatelj MP, Mraz J. Zika virus
associated with microcephaly. N Engl J Med 2016;375:1513-23.28.