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Zika Virus (ZIKV) - An Uncommon Zoonotic Virus

Bishnu Parida*

Amity Institute of Biotechnology, Noida, India

***Corresponding author:** Bishnu Parida, Amity Institute of Biotechnology, Noida, India, Tel: +91-9971810677; E-mail: paridabishnu340@gmail.com

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Abstract

***Zika virus* (ZIKV) remained a comparatively incomprehensible animal virus to us so far. During a recent series of outbreaks with severe clinical complications, this virus came into the spotlight as a serious infective agent and raised worldwide public health concern. In this article, attempt was made to present the history and medical issues of ZIKV infection, recent outbreaks and also the emergence of ZIKV in different hemisphere. This article also focuses on recently reported complications of ZIKV infection together with Guillain-Barre syndrome and abnormality, potential interactions between ZIKV and break bone fever virus, and also the prospects for the event of antiviral agents and vaccines. Considering the recent outbreaks, it is important to increase the public awareness with more information related to the disease, symptoms, prevention and control.**

Keywords:* *Zika virus; Aedes aegypti; Microcephaly; Guillain-Barre syndrome; Neuropathology; Flavivirus; Viral epidemic; Epidemic; Health policy

Introduction

Zika virus is an arbovirus. It is a member of the Flaviviridae family, belongs to genus *Flavivirus* and Spondweni group which is responsible for infection in human population. *Zika virus* is a single stranded RNA virus with two major lineages: Asian and African.

This virus was first isolated in 1947 from a febrile rhesus macaque monkey in the Zika Forest of Uganda and later identified in *Aedes africanus* mosquitoes from the same forest. *Zika virus* transmission is observed between non-human primates (such as monkeys and apes) and mosquitoes, with humans as occasional accidental hosts. In areas outside African continent, however, humans have possibly become the principal hosts [1]. Phyletic analysis of a Netherlands Guiana *Zika virus* indicates that it belongs to the Asian genotype.

Most closely involving strain of Asian lineage caused epidemic in French Oceania in 2013, sharing 99.7% and 99.9% of ester and amino alkaloid acid identity, respectively. This finding agreed with the results obtained during the analysis of envelope sequences from Brazilian patients. A mutation within the Asian lineage could have allowed the virus to adapt to the human as critical non-human primate host.

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Until recently, *Zika virus* was having less importance compare to other *Flaviviruses*, because it wasn't thought to be of public health importance. Limited literature exists on the pathological process of the *Zika virus* to assist in understanding the clinical sickness spectrum and to focus on treatments.

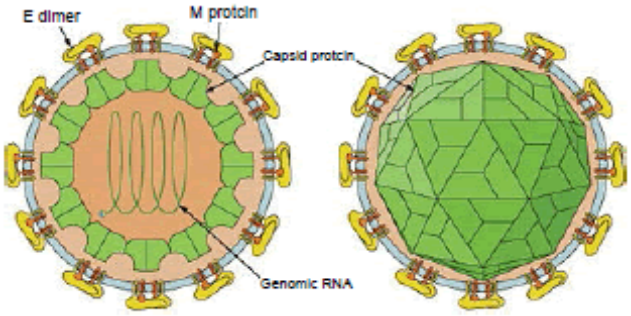

FIG 1. **Structure of the *Flaviviridae virus* (*Zika virus*)**.

Zika virus replicates promptly in skin immune cells and certain receptors are able to mediate the entry of the virus into cells. Studies on the skill of the virus to duplicate in somatic cell allowed to link with medical issues and specific disorders [2].

Epidemiology

Between the primary isolation of *Zika virus* in monkeys in 1947 till 2007, reports of human cases were rare. Unpredictable proof on the extent of human infection was primarily based on serological studies. In some cases, isolation of the virus from human source was also the reason. Infectious agent isolation urged a good distribution in Africa and South East Asia, though no epidemics were ascertained.

In 2007, Asian lineage strains caused epidemic in the island of Yap and the States of Micronesia. Calculable cases affected during this epidemic and resulting outbreaks up to now are most likely imprecise.

Moreover, reports from the laboratory testing are also not confirmation for all the cases, sometimes due to similarities in clinical investigation of *Zika virus* with alternative virus infections present throughout the tropics [3].

In Yap Island, 49 confirmed and 59 probable cases were known over a four month period. Estimation suggested that more than 73 people were infected over a period of three years in this island. A further episode of infection occurred by the closely connected Asian lineage strain in 2013 during which 294 cases were confirmed by RNA detection over a ten week period. Regionally, non-inheritable cases on Easter Island in 2014 marked the primary arrival of *Zika virus* within the Americas [4]. This was continued in 2015 by confirmation of cases in north east Brazil, where once more the *Zika virus* sequence linked to the Asian lineage was found.

As per the epidemic history, *Zika virus* is new within the Americas and the population had no evidence of showing immunity to this virus. Quick spread of the disease and enormous variety of cases reflects the similar situation as the Chikungunya infection occurred within the Americas in 2013.

Common public infected with Zika initially ignored the infection due to regular and overlapping symptoms with other general diseases, thus, there was issue with proper reporting of the exact number of cases too. Estimates were also influenced due to the standards used for definition of a suspected case and assumptions created regarding the proportion of subclinical infections.

Brazilian authorities estimated that around 1.5 million cases of Zika viral infection have occurred since the eruption begun [3,5]. Reports were suggesting that in Colombia due to transmission in October 2015, there might be over 25,000 suspected cases.

Zika Virus Transmission

The main transmission route of the *Zika virus* is via the Aedes mosquitoes, a similar vector that transmits Dengue fever or Chikungunya. When infected insect bite, symptoms typically seem following time period of 3 to 12 days. The virus is transmitted from human to human by the bites of infected female Aedes mosquitoes, primarily by the Asian tiger mosquito.

During the primary week of infection, *Zika virus* is often found in the blood passed from an infected person to a different dipterous insect through dipterous insect bites. Infected dipterous insect will then pass the virus to others. To prevent the further spread of the virus through these mosquito bites, avoiding insect bites is the feasible option [6-8]. But as we know, this is not possible always. Many a times, a person may receive the infection from an infected mosquito unknowingly too.

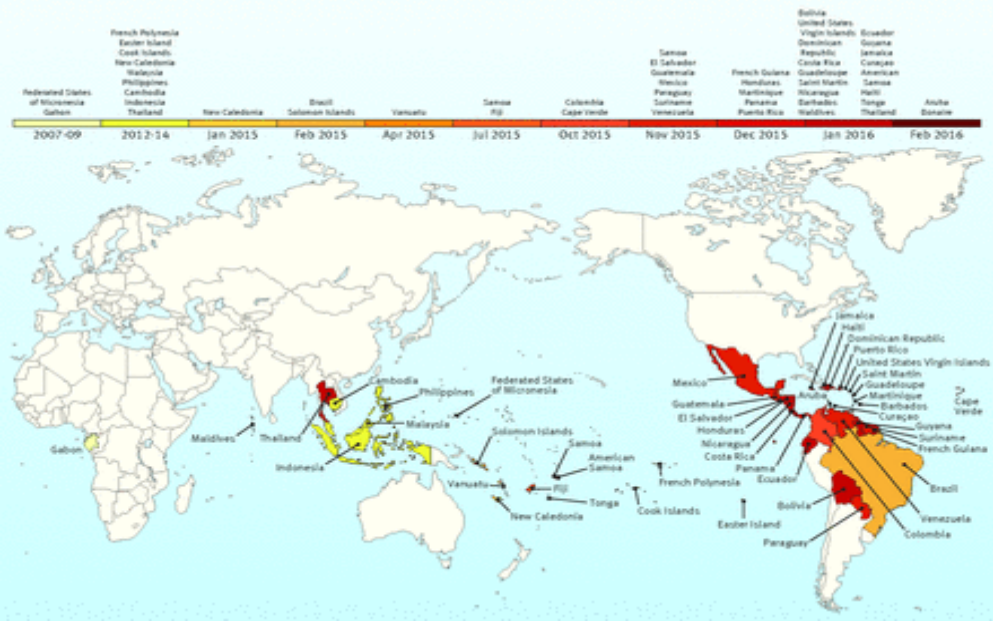

FIG 2. **Epidemiology of *Zika virus* shows the areas with confirmed locally acquired cases in the past nine months.**

Mosquito-Borne Transmission

In Africa, *Zika virus* exists in an exceedingly sylvatic transmission cycle involving non-human primates and forest-dwelling species of genus *Aedes* mosquitoes. In urban and residential district environments, *Zika virus* is transmitted in a human-mosquito-human transmission cycle. Two species within the stegomyia taxonomic category of genus *Aedes*, *i.e.*, *A. aegypti* and, to a lesser extent, *A. albopictus* have been reported with nearly all well-known *Zika* outbreaks. Though two other species, *A. hensilli* and *A.polynesiensis*, were thought to be vectors within the Yap and French Polynesia outbreaks. *A. aegypti* and *A. albopictus* are the sole well-known species within the Americas.

In Asia, a sylvatic transmission cycle has not been well known. Many dipterous insect species, stegomyia and diceromyia which are subgenera of genus *Aedes*, together with *A. africanus*, *A. luteocephalus*, *A. furcifer*, and *A. taylori* are possibly acting as endemic vectors in Africa and Asia.

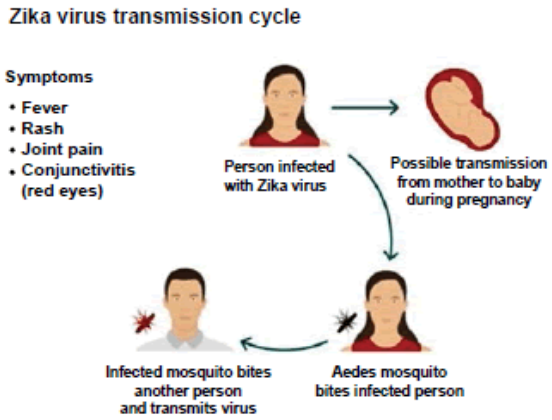

FIG 3**. Zika Virus Transmission Cycle.**

Despite the association of *A.aegypti* and *A.albopictus* with outbreaks, each were found to possess unexpectedly low but similar vectorial capacity for the Asian genotype of the *Zika virus* strains. However, *A. aegyptiis* thought to possess high vectorial capacity as this species usually bites multiple humans in an exceedingly single feed, has nearly invisible bite, and lives in close association with human habitation [9,10].

Both *A.aegypti* and *A.albopictus* bite primarily throughout the daytime and are cosmopolitan in nature throughout the tropical climatic zone. *A. albopictus* resides in temperate areas than *A.aegypti*. Therefore, these vectors extend the potential of the outbreaks in different geographical locations. *A. aegypti* is endemic throughout the U.S. Virgin Islands and in present in Hawaii too.

Zika virus was reportedly associated with other species too, such as *A. unilineatus*, *Anopheles coustani*, and *Mansonia uniformis.* However, studies have indicated that these species have low potential for transmission of the virus. It is notable that *Zika virus* is being transmitted by majorly *Aedes sp.* and can have drastic health effect other than viral fever too including microcephaly [11].

Non Mosquito Transmission

Substantial proof currently indicates that *Zika virus* can get transmitted from the mother to child during pregnancy. Evidence of such transmission has been found in more than one cases *where* the virus particle was found within the bodily fluid of mothers whose foetuses had cerebral abnormalities detected by sonography [11]. Infectious agents were found within the brain tissue and placentas of foetus that were later born with nanocephaly and died shortly after the birth. Furthermore, in certain cases miscarriages were reported where viral infection may be indirectly responsible. The frequency and risk factors for transmission are unknown yet.

Two cases of peripartum transmission of *Zika virus* are reported for mother–infant pairs. In these incidents, Zika virus polymer was detected in each child; one infant had light rash and ill health along with blood disorder, whereas the other child was clinically fine [12].

Sexual transmission to partners of returning male travellers who acquired *Zika virus* infection abroad has been reported. So far, other than the evidence of sexual transmission of Zika virus, no detail information is available. Replicative infectious agent particles related to Zika, usually in high copy numbers, were found in sperm cell, and infectious agent polymer has been detected up to sixty two days after the onset of symptoms [13,14].

Although, the transmission of *Zika virus* through an insertion have not been reported so far. There is a single report of *Zika virus* transmission occurrence by a monkey bite in Republic of Indonesia, which requires further literature support to establish such kind of transmission. Mosquito-borne transmission is the most dominant transmission mode for this deadly virus till now. Transmission through breast milk has not been documented, though the breast milk of a lady was found with Zika virus infection where on the day of delivery she contained infective Zika infectious agent particles with considerably high titre [15-18].

Virology

Zika virus originated in East Africa and unfolds to geographical region and so to Asia, leading to distinct lineages (Nigerian Cluster, MR766 Cluster, and therefore the Asian genotype) [19].

FIG 4. **Microscopic view of *Zika virus* strains.**

Likewise, other Flavivirus family members, Zika also follows almost similar mechanism of action where inoculation of the human host through mosquito vectors follows cellular entry of the virus particle through the skin cells via the support of specific receptors. Thus, the virus particle moves through blood stream to the lymph glands for further fulfilling of its life cycle. Several studies reported in detail regarding the pathogenesis of Zika virus [20-22].

Report suggested that human skin fibroblasts, keratinocytes, and immature dendritic cells allow entry of *Zika virus*. Several entry and adhesion factors (e.g., AXL receptor tyrosine kinase) facilitate infection, and cellular autophagy, needed for flaviviral replication, enhances *Zika virus* replication in skin fibroblasts [19]. Followed by cellular entry, replication of *flaviviruses* generally occurs in the vesicles of endoplasmic reticulum. Zika antigens were also discovered in the nucleus of infected cells too, suggesting possible additional replication site which was never recorded for other viruses of the same family. Additional investigation is required for confirming such information [23-26].

The present similarity information counsel that any immunizing agent product developed against any strain of *Zika virus* ought to be protecting against all strains. The terrible nature of the shut connection among the *flaviviruses* is chargeable for the challenges in developing diagnostic algorithms for determining common characteristic among these viruses.

Diagnosis

The main step of the routine diagnosis of *Zika virus* infection are the detection of viral nucleic acid by RT-PCR and the detection of IgM antibodies by IgM-capture enzyme-linked immuno-sorbent assay (MAC-ELISA). The detection of infective agent molecule in blood serum provides a definitive diagnosis. But, in most instances pathology is transient, and identification by RT-PCR has been most self-made at intervals of one week. RNA of the infectious agent was found in the blood serum of patients and pregnant woman which might have infected the foetus.

Due to low level of pathogenic agent in the circulation, isolation gets hampered sometimes. Onset and response by the immunoglobulins are detectable through MAC-ELISA, but most of the times remains undetected due to common symptoms with other diseases, lower level of pathogenic agent expression and delay in onset of symptoms [27,28]. Thus, RT-PCR testing of blood serum samples obtained at intervals the primary week of clinical health problem and MAC-ELISA testing of samples that aren't tested by RT-PCR or that area unit found to be negative by RT-PCR area unit possible to provide the best diagnostic yield.

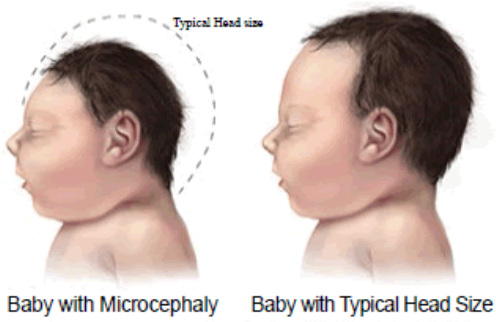

FIG 5. **Clear difference in average head size shown in microcephaly affected baby with normal head size baby unaffected.**

However, this test is labour-intensive and expensive, involves handling of live virus, takes up to every week to perform, needs standardized reagents that always don't seem to be accessible, and isn't wide performed [19-20]. In settings wherever PRNT isn't accessible or the degree of testing makes PRNT impractical, specimens that measure found positive by *Zika virus* MAC-ELISA and negative by infectious disease MAC-ELISA is also understood as a presumptive recent Zika viral infection. However, the diagnostic accuracy of this approach has not been established. Even the PRNT sometimes cannot faithfully establish identification of the Zika virus presence in patients due to "original antigenic sin" event [29,30]. This is often significantly problematic in areas during which infectious disease is endemic, wherever quite ninetieth of the population might have had previous exposure to infectious disease virus and infectious disease and *Zika viruses* is also co-circulating. So far, definitive identification of Zika viral infection is established by RT-PCR in general [31]. Although microcephaly and different fetal abnormalities is also detected as early as eighteen to twenty weeks of gestation, they're usually not detected in later physiological state. Moreover, to notice microcephaly, we have to rely on clinical and technical factors, and imaging isn't a sensitive means that of detecting microcephaly [32,33].

Treatment, Prevention and Control

Similar to the other mosquito-borne *flaviviruses*, treatment for uncomplicated Zika viral infection focuses on symptoms. No *Zika virus* vaccine exists till now. So, interference and management measures focus on avoiding dipterous insect bites, reducing sexual transmission, and dominant the dipterous insect vector [34,35].

FIG 6. **Prevention practices for *Zika virus* [35].**

Infections among pregnant women can be avoided through reduction in travelling, dodging unprotected sexual contact with zika patients, applying mosquito repellent regularly, maintaining regular hygienic condition at home and outside etc. Elimination of the mosquito vectors such as *A. aegypti* through proper management measure is the only effective preventive measure to be considered in all over the world.

Unfortunately, keeping vigilance on the mosquito breeding sites, regular application of larvicides and pesticides is not easy always [36-38]. Constant effort is required to pursue clean surroundings free of mosquito vectors. All these vector control measures are old and have their own limitations as well. Everything depends on the authority controlling the indoor and outdoor environment of a neighbourhood and geographical locations. Sometimes, these simple measures provide excellent outcome to save a particular community area through spraying such chemicals [39-40].

Future Prospects

The connection of expressed symptoms and incidence of Zika infection worldwide is tough to measure. Laboratory diagnosis isn't accessible everywhere whenever required. Nevertheless, given the traditionally high incidence of break bone fever within the region and therefore the recent expertise with the *chikungunya virus* within the Americas, many *Zika virus* infections ought to be expected because the virus continues to unfold [41-42]. Brazil remained the bellwether for the worldwide infection. Therefore the Caribbean, substantial numbers of infants with microcephaly and different adverse physiological condition outcomes may be known within the forthcoming months. The potential burden of ill health from Guillain–Barré syndrome is difficult to assess, given the difficulties with medical science diagnosing in areas wherever dengue fever is endemic and also the scarceness of printed knowledge on current incidence.

The underlying reasons for the emergence of *Zika virus* within the past decade are unknown.Recent world can increase with the incidence and unfold of dandy fever, chikungunya and presently *Zika virus* all with *A. aegypti* as a result of the first vector counsel common underlying mechanisms for his or her emergence, appreciate economic process and urbanization [43]. The semi-permanent outlook with connection this *Zika virus* happening inside dry land is unsure. Whether or not associated where the virus becomes endemic and whether or not a pestilence transmission cycle will develop somewhere inside dry land are matters of conjecture, but they are of tidy importance for the semi-permanent development and property of counter measures, appreciate a *Zika virus* immunogen [44-46]. What's clear is that they have to be compelled to speedily and consistently address known analysis gaps. These embody an entire understanding of the frequency and full spectrum of clinical outcomes ensuing from craniate Zika viral infection and of the environmental factors that influence emergence, likewise because the development of discriminating diagnostic tools for *flaviviruses*, animal models for craniate organic process effects because of virus infection, new vector management product and methods, effective medical specialty, and vaccines to guard humans against the illness.

Conclusion

Diseases have been always a major concern to us. Several diseases including viral [47-50], bacterial [51-55], parasitic [56-63], nematodes [64-66], life style oriented [67] and other types always challenged our dream of having a healthy and better life. But infection such as Zika virus claims more attention due to its enormous infectivity and causing mass fear.

Zika virus has been declared a public health emergency. As approximately, 1.3 million persons are affected in Brazil alone and twenty countries or territories have rumoured native transmission of the virus throughout 2016.

Thanks to the benefit of aviation and international trade, any unfold into regions wherever the virus isn't endemic is probably going, and transmission is probable in locations with competent two-winged insects vectors. A robust, many-sided response could be a foot that involves public health authorities, government agencies, the medical science trade, medical practitioners, and researchers.

However, uncertainty remains regarding aspects of the virus's vectors, medical science, and biological process. As a result of the epidemic unfolds, evaluating incoming data critically goes to be necessary to separate reality from speculation. Foremost, identification remains suboptimal. However, though not distinctive to *Zika virus*, laboratory infrastructure and testing capability is lacking in resource-constrained settings wherever *Zika virus* is most prevailing. *Zika virus's* association with drugs disorders, any as potential neuropath physiological mechanisms, is being actively investigated.

Viral infection has been a cause of concern all over the world recently. After 2000 it has been observed apart from Flaviviridae group, influenza, Ebola were responsible for multiple epidemics. Excellent scientific studies have been conducted in the recent times [47-49] on these viruses to understand these viruses in details and attempts are on-going to find a possible solution to prevent future epidemics.

Continued medical science study, combined with analysis involving animal models, can provide hyperbolic insight that may spur novel hindrance methods. If confirmed, insights into the property of infection relative to physiological condition outcomes can guide policy. At intervals the interim, new cases of Zika infection ought to be monitored for complications, significantly in babies born to mothers residing in *Zika virus* affected areas. The results of *Zika virus* in varied vulnerable clinical subsets, as will co-infection by co-circulating viruses.

Zika virus has the propensity to infect very large numbers of persons with severe consequences and the epidemic has serious medical, ethical, and economic ramifications. Continued vigilance is secure, at the side of a conjunct effort toward up for our understanding, management and hindrance of this rising organism.

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