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Review Article

Zika virus: A potential menace

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Abstract

Zika virus is gradually emerging and leading to an alarming concern all over the world in recent times. Zika virus is considered as positive strand single stranded RNA virus belonging to the genus Flavivirus in the Flaviviridae family. The non-segmented virus possesses an icosahedral shape with a virion of size ranging from 40-60nm in diameter where the genome size is of 11kb approximately. This arbovirus is a mosquito-borne virus which was first isolated from rhesus monkey in the ZIKA forest, Uganda in the year of 1947. In India the first reported case of ZIKA was noted in Bapunagar area, Ahmedabad District, Gujarat in 2017 and the biggest outbreak in India happened in 2018 which strikes two states that is Rajasthan, Madhya Pradesh. The infection gets transmitted to humans through several ways such as bites of infected mosquito vectors in the genus of *Aedes*, vertical transmission, from mother to infant while breastfeeding and transmission through interpersonal sexual contact and blood transfusion.

This study aims to comprehensively document the history of Zika virus outbreaks by assembling information from diverse sources including reputable websites and literature along with the transmission dynamics. This article involves a systematic search and collection of data on Zika outbreaks from World Health Organization, Integrated Disease Surveillance Programme, and European Centre for Disease Prevention and Control and several literatures from 2015 to till date. The article was reviewed to gather comprehensive data on the timeline, geographical spread, transmission dynamics, and symptoms associated with Zika virus outbreaks globally.

Keywords: Zika virus, Arbovirus, Flaviviridae, Zika epidemiology and outbreak, Congenital zika syndrome, Diagnosis and prevention of zika, Flavivirus.

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1. Introduction

Zika virus is an arbovirus that belongs to the genus Flavivirus in the family named as Flaviviridae.[1,2] Zika Virus is closely related to the other virus present in this group including yellow fever virus (YFV), West Nile virus (WNV), dengue virus (DENV), Chikungunya virus,[3,4] Murray Valley encephalitis virus (MVEV), Japanese encephalitis virus (JEV), and tick-borne encephalitis virus.[5,6] This virus, first isolated from rhesus monkey in Kampala Zika Forest, Uganda in 1947 possesses the potential to cause future public health emergency crisis. The report of the first isolation of ZIKV from human in Nigeria has been performed from a 10-year-old female in the year 1953.[7] As a result of genomic studies and phylogenetic analysis, two distinct lineages of ZIKV i.e. African and Asian, have been confirmed but the origin of both of them belongs to East Africa.[8] The non-segmented and enveloped virus owns nucleocapsid organized in icosahedral symmetry[9,10] consisting of a positive sense, single-stranded ribonucleic acid (RNA) genome of size about 11Kb.[11,12] It encodes a single polyprotein, comprised of 3423 amino acids, that results in the formation of three structural proteins such as C, prM/M and E and seven non-structural proteins such as NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS5 upon cleavage with the help of viral and host proteases.[5,13,14]

This mosquito borne arbovirus is transmitted via the mosquito species Aedes including *A. aegypti*, *A. albopictus*, *A. africanus*, *A. hensilli* and *A. polynesiensis*.[15] Furthermore, it also includes numerous other means like Sexual activity, mother to fetus transmission known as vertical transmission,[16] blood transfusion etc.[17,18] Zika virus is found in several body fluids like blood,[19] semen,[20] urine,[21] saliva, amniotic fluid, cerebrospinal fluid.[22-24] Though all these fluids can be used for detecting the presence of ZIKV, blood

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is generally preferred in diagnostic purposes for ZIKV through the methods such as either antibody-based serological methods or molecular diagnosis of viral RNA.[25,26] In comparison to blood, ZIKV RNA is detected in higher levels and longer periods of times in urine.[27] The manifestation of ZIKV in infected personnel involves mild fever temperature ranging from 37.8ºC to 38.5ºC, joint pain, headache, myalgia, conjunctivitis, retroorbital pain and cutaneous maculopapular rash[22] where most of the cases seems to be asymptomatic.[28]

Mother to fetus transmission of ZIKV retards the brain development of fetus and microcephaly in newborns resulting severe repercussions. Several other neurological and autoimmune complications like Guillian–Barré syndrome (GBS[29] and acute disseminated encephalomyelitis (ADEM) have also been reported. (American Academy of Neurology, 2016) As there are no vaccines available so far, more researches are required for the control as well as prevention of transmission of the disease. Zika virus possesses an important impact on the domain of public health. Therefore, it calls for sensitive, rapid but cost-effective diagnostic techniques. As a result of this, characteristics of ZIKV, transmission methods, clinical manifestations, diagnosis techniques, treatment, and preventive measures are emphasized in this review for future research purposes.

2. Characteristics and Structure of Virus

Zika virus, one of the well-known enveloped viruses in recent time, contains non-segmented, positive sense, single-stranded ribonucleic acid (RNA) of a genome size ranging from 10kb to 11kb.[5] The diameter of the virion ranges from 50 to 60 nm. The nucleocapsid of this enveloped virus is of icosahedral symmetry and has the diameter of 25-30nm.[9,10] Two types of envelope protein named E and M are found in this virus. It possesses single open reading frame that has two untranslated regions (UTR) at both 3′ and 5′ ends.[30] A polyprotein is formed upon translation of the RNA that codes for 3 structural proteins named capsid (C), membrane (M) and envelope (E) and 7 nonstructural proteins i.e. NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS5. Capsid (C) and Membrane (M) are generated from its precursor premembrane (prM). The structural proteins contribute to the formation of virus particle whereas the nonstructural ones are engaged in replication, packaging of the genome and most importantly to subvert the host pathways.[5]

Some states of Zika Virus could be captured by cryo-electron microscopy (cryo-EM) that defines two states of this virus; Mature and immature states.

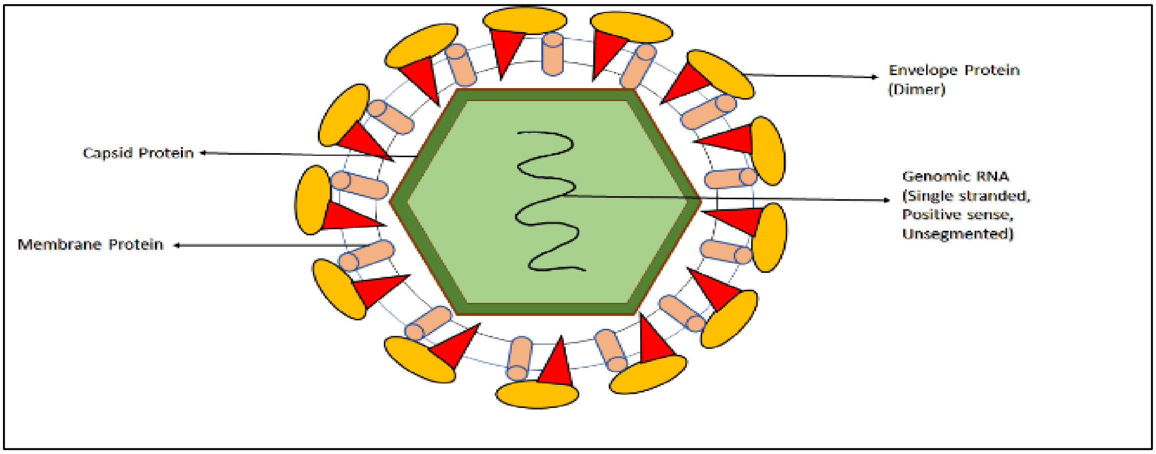

Figure 1: Structure of Zika Virus (ZIKV)

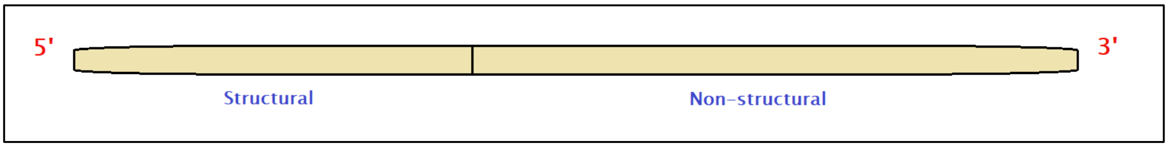

Figure 2: Zika virus genome

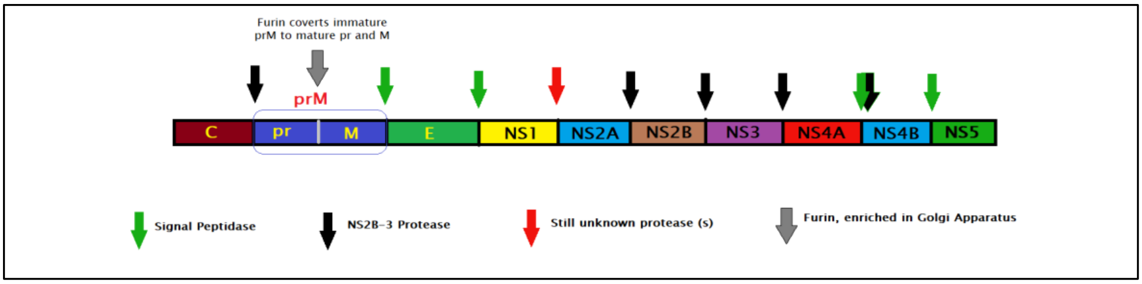

Figure 3: Structure of the genome of the Zika Virus (ZIKV)

Table 1: Details of structural and non-structural proteins present in Zika Virus (ZIKV)

Name		**Size (amino acids)**	**Function**	**References**
Structural Proteins	Capsid Protein	122	(a) Synthesize viral nucleocapsid; (b) Acts as RNA chaperone;	31
	Envelope Protein	178	(a) targets host cell receptors (b) Induces virus entry into the host cell (c) contributes to stabilization (d) Viral capsid formation.	13
	prM	500	(a)forms capsid and membrane protein	5
Non-structural Proteins	NS1	384	(a) emission, virulence and replication of virus (b) slowdown of complement system (c) provocates immune responses	32
	NS2A	26	(a) Binds to the 3’ untranslated region of RNA for replication (b) Viral transcription and assembly (c) generation of viral particles from cell (d) dominates the antiviral interferon of the host response	33
	NS2B	130	(a) association and complexes of virus replication on the endoplasmic reticular membrane (b) forms the serine protease complex with NS3 (c) polyprotein cleavage	34
	NS3	617	(a) unwinds the structured templates (b) process polyprotein of virus	35
	NS4A	127	(a) Acts as determinant factors for pathogenesis	36
	NS4B	252	(a) forms viral replication complex (b) localization of NS3 protein in membranes	37
	NS5	902	(a) cellular factors recognition (b) stabilization (c) translation process (d) RNA packaging	38

3. History of Zika Out-Break

In 1947 during the study of yellow fever from a Rhesus Monkey a new virus was isolated called zika virus as per the name of the forest Zika forest of Uganda.[1] In 1953, zika virus was first isolated from humans in Nigeria, Tanzania & Uganda[7,39] and from Uganda Zika Virus infection in human was firstly reported.[40] In 1966, Malaysia reported the presence of zika virus in *Aedes* mosquito in their country[41] and during the periods of 1950-1980 mild zika virus infection cases were reported from Asian countries like Pakistan, Indonesia, Thailand and Philippes.[41-45] The first outbreak of Zika virus disease was reported from Yap Island of Federated States of Micronesia in the year 2007 and it was the first reported case from outside of Africa And Asia. Serum samples of patients with clinical symptoms were collected and the presence of zika virus disease was confirmed by either the presence of zika virus RNA or specific antibody response to zika virus in the reported from the 9 municipalities of Yap Island but no cases of hospitalization or death due to zika virus infection were not reported. As *Aedes hensilli* is considered the main species of transmission, this outbreak was designated as the first largest outbreak as previously only 14 human zika virus infection was documented.[28,40,44,46-48] During October, 2013, and April, 2014, French Polynesia was flighted with the Zika Virus infection disease where nearly about 28000 cases were reported as this was the biggest outbreak of that time (represented around 11·5% of the Polynesian population.)[49] Guillain-Barré syndrome was simultaneously increasing during the increase of Zika virus infection suggesting a possible association with the Zika Virus infection. 41 patients with Guillain-Barré syndrome were reported of having Anti zika virus IgM or IgG out of 42 patients that reported Guillain-Barré syndrome at that period all of them have neutralizing antibody against Zika.[50] In March, 2014, 49 confirm zika virus infection was reported from Cook Island and near about 630 patients were suffering from the mosquito-borne disease.[51] In 2014, another zika surge was reported from Easter Island, South Pacific where 89 patients' samples were collected during the periods of January to May. The common symptoms within the first five days are fever with maculopapular erythematous rash and additional one of the symptoms like conjunctival hyperemia, arthralgia, and myalgia. Out of 89 serum samples, 51 samples were found positive for zika virus by RTPCR of which 42 are adult patients (age > 16 years) and the rest 9 are Children (age < 16 years) and 33 patients are female and 9 are male.[52] A Total number of 1385 zika Laboratory cases have been reported from New Caledonia in the year 2014 where the first case was imported from French Polynesia in November 2013. Out of 1385 zika confirmed cases, 35 cases are imported cases which includes 32 cases from French Polynesia, 2 cases from Vanuatu and 1 from the Cook Islands. In February 2014, New Caledonia Health Authority declared it was an Zika Virus outbreak situation.[53]

3.1. Zika outbreaks in the Americas

In 2015, zika virus autonomous transmission was reported from the state of Rio Grande do Norte, Brazil where "dengue-like syndrome" appeared as a public health concern at that time. 21 acute phase patient samples were collected and tested by The Molecular Virology Laboratory of Carlos Chagas Institute, Oswaldo Cruz Institute, state of Paraná, Brazil for dengue and chikungunya but all came negative. After checking with the Zika Virus RTPCR of the samples, 8 samples came positive for the zika virus, and rest came negative due to might be low viremia. Phylogenetic analysis of the 364 base pair size the amplicon of envelope protein coding gene of zika virus shows it linked to the Asian lineage of zika virus.[54]

Table 2: Following table contains the data available since 2015 to 2023 regarding the Zika virus cases in Americas[75]

Year	Area or countries	Cases
2015	Brazil	Total cases 56159 (confirmed cases:17825)
	Colombia	Total cases 16763 (confirmed cases:1697)
	El Salvator	Total cases 4597 (confirmed cases:9202)
	Suriname	Total cases 509 (confirmed cases:110)
	Martinique	Total cases 332 (confirmed cases: 00)
	Guatemala	Total cases 292 (confirmed cases:68)
	Mexico	Total cases 23 (confirmed cases:23)
2016	Brazil	Total cases 2,73,904 cases (confirmed cases:1,28,793)
	Colombia	Total cases 91,711 cases (confirmed cases:8017)
	Venezuela	Total cases 61691 cases (confirmed cases:00)
	Martinique	Total cases37665 cases (confirmed cases:00)
	Puerto Rico	Total cases 37,478 cases (confirmed cases:37478)
	Guadeloupe	Total cases 32,278 cases (confirmed cases:28)
	Honduras	Total cases 31468 cases (confirmed cases:260)
	French Guiana	Total cases 10,790 cases (confirmed cases: 48)
	Mexico	Total cases 8508 cases (confirmed cases: 8508)
	El Salvador	Total cases 7873 cases (confirmed cases: 03)
	Costa Rica	Total cases 7,556 cases (confirmed cases: 7533)
	Jamaica	Total cases 6,974 cases (confirmed cases: 186)
	Curacco	Total cases 5,966 cases (confirmed cases: 1880)
	Dominican Republic	Total cases 5,575 cases (confirmed cases: 336)
	Guatemala	Total cases 4062 cases (confirmed cases: 882)
	Panama	Total cases 3893 cases (confirmed cases: 756)
	Haiti	Total cases 3,065 cases (confirmed cases: 00)
	Suriname	Total cases 3,031 cases (confirmed cases:622)
	Ecuador	Total cases 2,902 cases (confirmed cases: 874)
	Saint Martin	Total cases 1,780 cases (confirmed cases: 200)
	Peru	Total cases 1,669 cases (confirmed cases: 778)

	Table 2 continued….	
	Bolivia	Total cases 1,294 cases (confirmed cases: 186)
	Dominica	Total cases 1,233 cases (confirmed cases: 79)
	Trinidad & Tobago	Total cases 722 cases (confirmed cases: 722)
	Barbados	Total cases 688 cases (confirmed cases: 144)
	Nicaragua	Total cases 608 cases (confirmed cases: 608)
	Grenada	Total cases 447 cases (confirmed cases: 113)
	Cuba	Total cases : 245 cases (confirmed cases: : 245)
	Unite States of America	Total cases : 224 cases (confirmed cases: : 224)
2017	Brazil	Total cases 31754 (confirmed cases:9202)
	Peru	Total cases 5361 (confirmed cases:513)
	Mexico	Total cases 3260 (confirmed cases:3260)
	Costa Rica	Total cases 2414 (confirmed cases:2414)
	Ecuador	Total cases 2331 (confirmed cases:2134)
	Panama	Total cases 1891 (confirmed cases:243)
	Bolivia	Total cases 1736 (confirmed cases:628)
	Belize	Total cases 1132 (confirmed cases:187)
	Aruba	Total cases 706 (confirmed cases:617)
	Guatemala	Total cases 703 (confirmed cases:164)
	Argentina	Total cases 684 (confirmed cases:250)
2018	Brazil	Total cases 19020 (confirmed cases:1379)
	Panamma	Total cases 2752 (confirmed cases:83)
	Guatemala	Total cases 2300 (confirmed cases:106)
	Bolivia	Total cases 1736 (confirmed cases:486)
	Mexico	Total cases 877 (confirmed cases:877)
	Colombia	Total cases 857 (confirmed cases:607)
2019	Brazil	Total cases 30500 (confirmed cases:4257)
	Peru	Total cases 2500 (confirmed cases:2292)
	Colombia	Total cases 429 (confirmed cases:12)
	Mexico	Total cases 138 (confirmed cases:138)
	Cuba	Total cases 131 (confirmed cases:131)
2020	Brazil	Total cases 18941 (confirmed cases:2644)
	Mexico	Total cases 20 confirmed cases:20)
	Bolivia	Total cases 728 (confirmed cases:16)
	Peru	Total cases 119 (confirmed cases:14)
2021	Brazil	Total cases 17496 (confirmed cases:3617)
	Mexico	Total cases 35(confirmed cases:35)
	Peru	Total cases 28 (confirmed cases:06)
	Bolivia	Total cases 125 (confirmed cases:04)
	Guatemala	Total cases 2500 (confirmed cases:03)
2022	Brazil	Total cases 34176 (confirmed cases:3238)
	Mexico	Total cases 12 (confirmed cases:12)
	Peru	Total cases 20 (confirmed cases:09)
	Bolivia	Total cases 190 (confirmed cases:04)
	Guatemala	Total cases 1815 (confirmed cases: 02)
	Belize	Total cases 2508 (confirmed cases: 00)
	Paraguay	Total cases 1094 (confirmed cases: 00)
	Bolivia	Total cases 190 (confirmed cases: 04)
	El Salvator	Total cases 171 (confirmed cases: 00)
2023	Brazil	Total case : 33863 (confirmed case: 3599)
	Bolivia	Total case : 870 (confirmed case: 07)
	Belize	Total case : 281 (confirmed case: 00)
	Guatemala	Total case : 112 (confirmed case: 00)

	Table 2 continued….	
	Colombia	Total case : 116 (confirmed case: 00)
	El Salvator	Total case : 106 (confirmed case: 00)
	Puerto Rico	Total case : 46 (confirmed case: 00)
	Peru	Total case : 25 (confirmed case: 01)
	Panama	Total case : 50 (confirmed case: 50)
	Mexico	Total case : 29 (confirmed case: 29)

Table 3: The following table contains the data available since 2015 to 2021 regarding the Zika virus cases in Europe[76]

Country	**2021**	**2020**	**2019**	**2018**	**2017**	**2016**	**2015**
United Kingdom	0	1	6	2	14	194	3
Sweden	0	3	0	0	16	34	1
Spain	4	0	24	9	44	301	10
Slovenia	0	0	0	0	0	7	0
Slovakia	0	0	0	0	0	3	0
Romania	0	0	0	0	0	3	0
Portugal	0	1	0	0	1	18	0
Poland	0	0	0	0	0	0	0
Norway	0	0	2	0	4	8	0
Netherlands	0	0	0	3	6	98	11
Malta	0	0	1	0	0	2	0
Luxembourg	1	0	0	0	1	2	0
Lithuania	0	0	0	0	0	0	0
Liechtenstein	0	0	0	0	0	0	0
Latvia	0	0	0	0	0	0	0
Italy	0	4	4	2	25	101	0
Ireland	0	2	0	0	4	15	1
Iceland	0	0	0	0	0	0	0
Hungary	0	0	1	1	0	2	0
Greece	0	0	0	2	1	2	0
Germany	2	6	11	18	69	0	0
France	0	3	16	10	28	1141	0
Finland	0	1	2	0	2	6	1
Estonia	0	0	0	0	0	0	0
Denmark	0	0	2	0	6	8	0
Czech Republic	0	1	1	2	4	13	0
Cyprus	0	0	0	0	0	0	0
Croatia	0	0	0	0	0	0	0
Bulgaria	0	0	0	0	0	0	0
Belgium	0	0	1	2	42	120	1
Austria	0	1	0	0	8	41	1
Total cases	**7**	**23**	**71**	**51**	**275**	**2119**	**29**

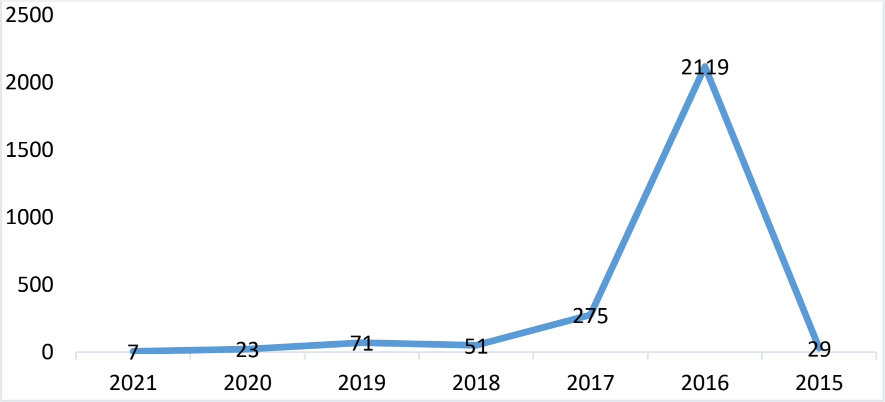

Figure 4: 2015 to 2021 regarding the Zika virus cases in Europe (Based on the ECDC Data)[76]

3.2. Zika out-breaks in Europe

As the abundance of zika virus vector i.e. *Aedes aegypti* is not widely available in Europe, the assessment of the spreading of the zika virus was moderate to low although in Madeira Island (Portugal) and the north-eastern Black Sea Coast had reported the presence of *Aedes aegypti.* Aedes *albopictus* has been considered as the potential vector for zika virus transmission as it is present primarily in Mediterranean Basin. (European Centre for Disease Prevention and Control)

3.3. Zika out-break in India

Virus Research centre, Pune (now it is famous as the National Institute of Virology, Pune) tested samples from the Bharuch district of Gujrat in 1954 in which 16.8 percent of the sample was found Zika Antibody Positive. As the virus belongs to the family of Flaviviridae, the similar virus-like dengue and Chikungunya are also the member of this family, therefore it was quite difficult to confirm the presence of Zika virus in India at that time by only serology testing as this antibody was too much cross-reactive to others members of this Flaviviridae family also[55] Like several other countries, India faced its first Zika outbreak in 2017 in Bapunagar area, Ahmedabad District, Gujarat. Three patients were tested Zika positive by reverse transcriptase real-time Polymerase Chain Reaction (RTPCR) in which one was detected positive after giving birth of her healthy child, the second one was a 37-week pregnant lady during the surveillances at Antenatal clinic (ANC) and the third one was detected during Acute Febrile Illness (AFI) surveillances.[77,78] In 2017 a 27 years old man was reported Zika positive from from krishnagiri district of Tamil Nadu. 2018, the biggest outbreak of Zika was happened in India, strikes two states i.e. Rajasthan, Madhya Pradesh.[2] In Jaipur district of Rajasthan, a 85 years of an old woman was tested positive for Zika virus (without having any travel history in last one months) by RTPCR at VRDL, SMS medical College, Jaipur which was further confirmed by NIV Pune. Door to Door Surveillances was carried out from then epicentre to 3 km radius and 2043 samples was collected during this field collection process and which 153 samples was found to Zika Virus positive and 6 samples was also found positive from the normal routine Zika surveillances, which ultimately concludes that total 159 patients samples was found positive in which 64 are pregnant in Rajasthan.[2,56] Complete genome sequencing by using Next Generation Sequencing (NGS) and Phylogenetic analysis shows that the Zika virus infection out break at Jaipur city was caused by Asian Lineage of Zika virus.[57] 130 Zika positive by RT-PCR cases was reported from multiple district of Madhya Pradesh [which includes Bhopal (50), Vidhisha (50), Sehore (21), Sagar (02), Hoshangabad (02), Raisen (01), Narsinghpur (01)] by testing of 486 blood samples at AIIMS Bhopal and reported 2 deaths (which includes a male person at the age of 18 years with Zika, dengue and JE co-infection and another 23 years female with Zika positive and multiorgan failure.)[79] The next and most recent case reported in India was in the year 2021 when the world is facing the deadliest second wave of the COVID-19 pandemic situation. In the middle of the year, 2021(specifically on the 20th week) 65 Zika Virus RT-qPCR positive cases were reported from Kerala States. From Thiruvananthapuram, 19 samples (tested SARS CoV-2 negative) were collected from healthcare professionals with various symptoms like rashes, fever, headache, arthralgia, sore throat, rhinitis, etc and sent to the National Institute of Virology, Pune and after carrying out various virological delectation 03 of them are tested positive for Epstein-Barr virus (EBV) infection. A 24 years pregnant woman with typical infection symptoms tested positive for Zika virus by triplex RT-qPCR from Thiruvananthapuram and the presence of Zika Virus infection in Thiruvananthapuram triggers NIV to recheck the previously collected 19 samples with Zika virus. Surprisingly from these 19 samples, 13 samples tested positive for zika viral RNA and 10 samples were positive for anti-Zika IgM. The previously detected three EBV-positive samples were found to be coinfected with the Zika virus. The Next Generation Sequencing Data of Zika positives sample shows nucleotides similarities with the Zika strains of Rajasthan.[58] In 2022, two cases of Zika virus infection cases were found in India, first one in the November month from Kerala state, Kollam district where the patient with the symptoms of headache, cough, was detected zika virus RT-PCR positive and the second cases was also in November month from Karnataka state, Raichur district, where the patients had symptoms like fever, vomiting, loose stool &

headache. Both blood & Urine samples were collected and found RT-PCR positive for Zika Viruses by RCVRDL, NIV Pune.[80-82] As the cases are already being reported from various part of India, proper surveillance as well as timely detection is utmost necessary.

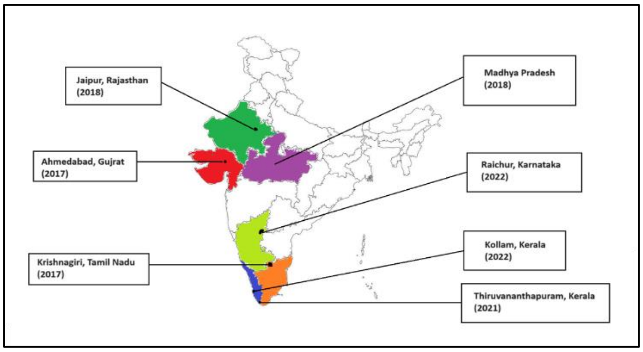

Figure 5: Indian Scenario of Zika Virus (ZIKV)

4. Symptoms

Zika infected patients face several types of symptoms within the 3-11 days after having the mosquito bite. But the viral RNA is detected in serum after Symptoms including fever, abdominal pain, anorexia, dizziness, conjunctivitis, malaise, diarrhoea and constipation, starts with very mild headache. It further causes maculopapular rash on different body parts such as face, neck, palms, upper arms, sole and trunks etc.[59] Apart from this, myalgia, edema, vomiting and retro-orbital pain are manifested in lesser frequency.[48] Different skin cells of human i.e., epidermal keratinocytes, dermal fibroblasts and immature dendritic cells demonstrates susceptibility towards the Zika Infection in vivo and ex vivo.[9] Different organs including kidney, bladder and spleen are also infected by this virus. It demonstrates the ability to also infect lymph, nodes, the hemolymphatic system, gastrointestinal part, integument, genitourinary, cardiopulmonary system, spinal cord, and cerebrospinal fluid.[60] The reproductive systems of male and female are also affected by the presence of this virus. testes, prostate and seminal vesicles[22,61] in male reproductive system and vagina, uterus in female reproductive system[62] are infected.[12]

5. Transmission

The spread of this virus follows several cycles such as enzootic cycle, epidemic cycle.

5.1. Vector borne Transmission

Zika virus used to be known as an arthropod-borne virus where Aedes species mosquitoes mostly play the role of the primary vector. Zika Virus has been isolated from different species of aedes mosquito i.e. *Aedes aegypti*, *Aedes albopictus*, *Aedes africanus*, *Aedes hensilli*.[63,64] In addition, Zika Virus has been found to be detected in a domestic mosquito named *Culex quinquefasciatus*.[16,65] There are mainly three cycles present for the transmission of this virus with the aid of mosquito. The jungle or sylvatic cycle causes the spread of Zika virus between non-human primates through mosquito in sylvatic habitat where mosquito transmit the virus from monkeys to other monkeys or humans visiting or working in the forest. Intermediate or savannah cycles are seen in Africa that involves transmission of Zika Virus from mosquitoes to humans living or working in jungle border areas. In this scenario, Transmission of virus happens monkey to human or from human to human by the presence of mosquitoes. The urban cycle leads to the spread of the virus between humans and mosquitoes. Zika Virus is thought to be brought to the urban region by viremic human, already infected in savannah or jungle area.

5.2. Sexual transmissions

Zika Virus could also be transmitted by the sexual activity. The initial report of sexual transmission has been documented in the year of 2008.[18,20] According to the several researches, Zika Virus and RNA of this virus has been detected in the semen of ZIKA infected males.[16] Though the sexual transmission of this virus is noted to be from male to female, male to male[66] and also female to male,[67] the cases from male to female have been reported with highest transmission frequency.[6,20,66-69]

5.3. Vertical transmission

The transmission of zika virus from mothers to fetuses during pregnancy comes under vertical transmission. The presence of zika virus in fetal brain, amniotic fluid[70] and in the serum of babies implies the proof of transmission from mothers to fetuses.[71,72] While placenta acts as a physical barrier in order to prevent the transplacental transmission, it fails to exhibit its potential in case of ZIKV. According to the research, placenta and fetus are prone to ZIKV infection. This transmission hampers the brain development of fetus causing neurological damages, further resulting in the microcephaly and scenarios like miscarriages.[2] Zika virus is able to cause microcephaly where the presence of IgM specific to this virus has been detected in the neonates. The presence of viral RNA has been confirmed in the amniotic fluid of a pregnant woman where the fetus of the pregnant woman has been diagnosed with microcephaly.[73] In addition, the viral RNA and even the antigens of the virus have been detected in several tissues such as placental tissue from miscarriages and fetal brain tissues from fetus and infants.

5.4. Urine and saliva transmissions

Zika Virus is not only present in semen, but it is also present in other body fluids such as Urine[21] and Saliva. It has been reported that *Aedes aegypti* and *Aedes albopictus* become susceptible to this viral infection at the time they breed on the contaminated urine or in the environment, infected with this virus.[74] mosquito.[16]

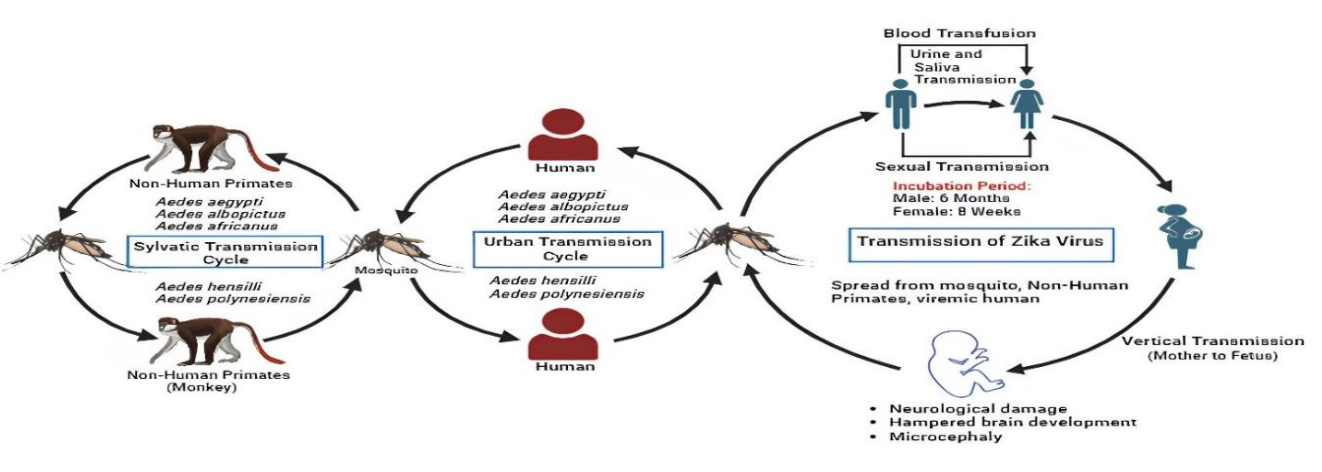

Figure 6: Various method of Zika transmission

5.5. Blood transfusion

Zika virus is found in blood as well. The transmission of ZIKV through blood via blood donation[19] reported the ZIKV transmission by blood transfusion in Brazil. As most of the infected patients are asymptomatic, those asymptomatic but infected patients render the spread of ZIKV further making the infection control system difficult to handle.[16,18]

6. Conclusion

The emerging cases of ZIKV across the world is drawing epidemiological importance and alarming attention recently. There is high possibility of occurrence of public health concerning scenario in near future. In addition to that, continuous surveillance programme is required in order to reduce the chances of transmission and outbreaks. Sequencing the genome of the detected virus along with the testing should be executed for the sake of checking the presence of protein level mutation. Routine pregnancy screening test must be implemented in all zika prone areas and countries, following the system of America. Specific diagnostic tools and methods for vector control system should be developed for the identification as well as minimization and elimination of ZIKV. A detail host pathogen and host vector interaction must be carried out in order to understand how zika virus interacts with various factors that may or may not be responsible for the pathogenicity of zika virus infection. Due to lack of proper treatment of this virus, ZIKV infection becomes enormously fatal. Various Anti-viral drug designing, antiviral compounds synthesis and production of vaccine should be encouraged for betterment of human race.

7. Ethical Approval

Neither any human samples was used nor any animal was involved in this review study. All clinical data was collected from various sources like IDSP, PAHO, WHO, ECDC etc.

8. Data Availability

All relevant are within the manuscript and with supplementary tables and figures.

9. Consent to Participate

Authors have declared no potential conflict of interest regarding authorship

10. Consent for Publication

No objection from authors end regarding publication of this article.

11. Source of Funding

None.

12. Conflict of Interest

None.

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