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Review Article

Zika virus - A Challenge for India

Zika virus: Epidemiology, Pathophysiology, Clinical Manifestations, Diagnosis, and Prevention- A Challenge for India.

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Abstract: This study aimed to assimilate findings related to the Zika virus from the scientific literature. Zika virus (ZIKV) is an emerging pathogen of huge public health significance to human beings. The recent outbreak has been associated with the increased incidence of congenital anomalies such as microcephaly & Guillain-Barre syndrome (GBS). In this review, we address the current concern with context to India. There is also a need to look for any such animal cycle/sylvatic involvement in India. The recently detected four cases in India show local transmission of ZIKV, suggesting that ZIKV might have been present in India for a long time. Therefore, ZIKAV might become a major public health concern in the future. Several entry and adhesion factors enable infection, and cellular autophagy, which is needed for flaviviral replication. Transmission is by an infected mosquito during a blood meal. ZIKAV is also transmitted via congenital, perinatal, and sexual, possibly by blood transfusion, animal bite, and intrauterine transmission. Transmission via breastfeeding has yet to be reported. The incubation period from mosquito bite to symptom commencement is 3-12 days. Infection is likely subclinical in 80% of cases. Symptoms that last for two to seven days include fever, conjunctivitis, arthralgia, myalgia, and pervasive rash, which may be itchy. Headache, retro-orbital pain, peripheral edema, and gastrointestinal struggle have also been witnessed. The symptoms and clinical signs do not have good positive or negative predictive value. Laboratory testing includes polymerase chain reaction (PCR) of ZIKAV RNA. There was neither vaccine against ZIKAV nor antiviral for managing ZIKAV in India. Treatment is suggestive. The review provides scientific evidence for public policy care, planning, and implementation.

Key Words: ZIKV, Epidemiology, Pathophysiology, Clinical manifestation, Diagnosis, Prevention

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1. INTRODUCTION

Zika Virus (ZIKV), a family member of the Flaviviridae and genus flavivirus, was first isolated in 1947 from a sentinel monkey in the Zika forest in Uganda, east Africa. ZIKV had a broad geographical distribution in Sub-Saharan Africa and South-East Asia, as suggested by subsequent epidemiological studies. In 1954, the first human infection was reported in Nigeria, but the identification of this virus was subsequently questioned and thought to be Spondweni virus infection. Later in 1962-63, the first confirmed human infection was reported in Uganda[1]. In 2015, in Brazil, the first aboriginal transmission occurred in the Northeastern region[2, 3]. The possibility of ZIKV arriving in Brazil was due to events involving foreign individuals. An existing history of epidemics by arboviruses stems from socioeconomic conditions, the predominantly tropical climate, extensive forest areas, and the country's marshy, closed, and caatinga regions. The persistent proliferation of vectors (Aedes species) in urban environments contributes to disseminating this ZIKV to other regions of Brazil with this environments[4]. In 2015, an explosive pandemic of ZIKV infection[5] surprised the world. On December 1, 2015, alerts were published by two major health organizations of world scilicet, the Pan American Health Organization (PAHO) and World Health Organization (WHO), about a possible association with increases in reports of congenital abnormalities and Guillain-Barre Syndrome (GBS)[6]. In recent years, reemerging infection of ZIKV has been responsible for the health problem at the global level. Dengue (DENV) and yellow fever viruses are closely related to other flaviviruses and distantly to the west nile virus[7, 8]. ZIKV is enveloped and icosahedral and has a non-segmented, single-stranded, 10-kb positive-sense RNA genome, similar to other flaviviruses. This virus genome encodes a single polyprotein of 3419 amino acids that are split by the serine and cellular furin proteases into the three functional domains, the capsid (C), precursor of the membrane (prM), and envelope (E), and seven nonstructural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS5)[9,10]. The NS1 protein is significant for viral replication and evasion of the immune system response. NS2 provides a chaperone-like function for NS3. NS4 is a major element of the virus replication complex, and NS5 has an N-terminal methyl-transferase domain that plays a role in necessary functions in viral RNA genome capping[11, 12]. On February 1, 2016, a Public Health Emergency of International Concern was declared by the WHO[13]. At birth, clinical findings of Microcephaly can include a range of brain malformations resulting from a failure of neurogenesis. Infections like cytomegalovirus and rubella acquired during pregnancy are established causes[14]. GBS is an immune-mediated ascending flaccid paralysis, which typically occurs within a month of an infection, such as Campylobacter jejuni or cytomegalovirus[15]. As of October 20, 2016, 67 countries have reported aboriginal transmission of the mosquito-borne flavivirus Zika since 2015, and 27 of these countries have reported cases of congenital brain abnormalities, GBS, or both[16]. They were increasing research and providing more rigorous scientific evidence of a causal relationship as a basis for the global health response by the emergency committee like the WHO[13].

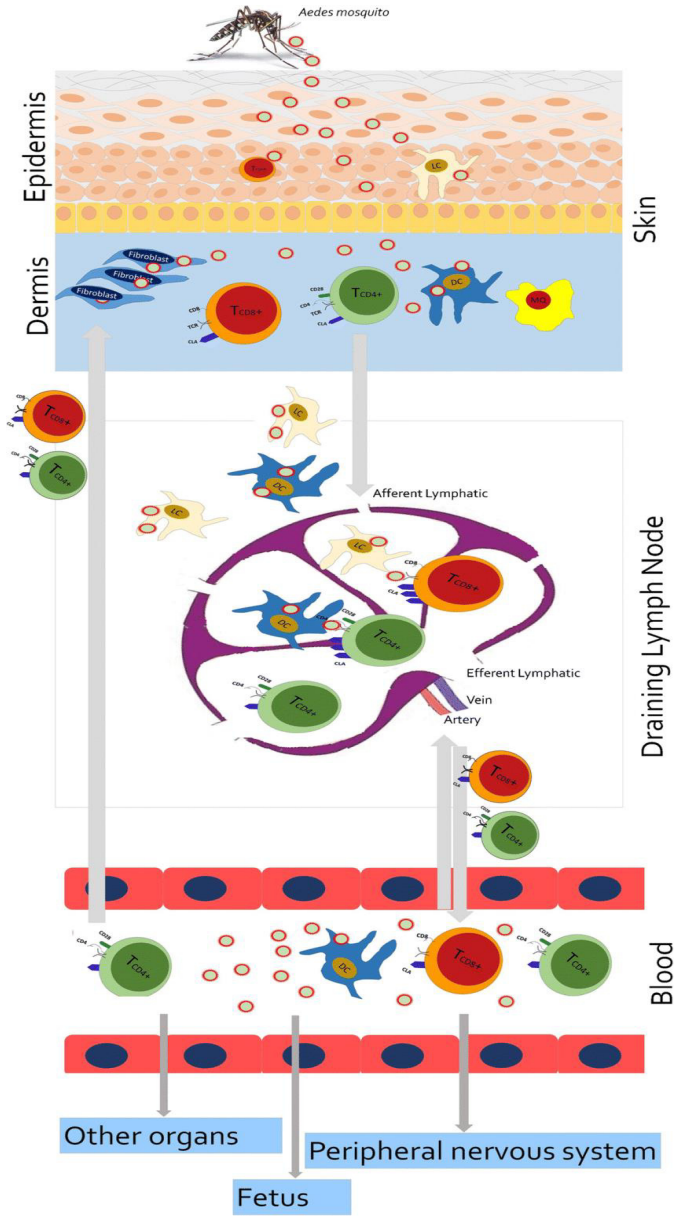

Fig. 1: Schematic representation of adaptive immunity to ZIKV infection. ZIKV enters Langerhans cells in the epidermis, migrating to lymph nodes. In lymph nodes, virus-specific T cells activate and express skin-homing receptor cutaneous lymphocyte-associated antigen (CLA) on the cell surface. These T cells return to the skin tissue, and over the bloodstream, the virus spreads to other tissues. Also, ZIKV displays tropism for neuronal cells of adults or neuronal progenitor cells in a fetus. DC, dendritic cells; LC, Langerhans cells; MQ, macrophage[17]

2. EPIDEMIOLOGY

ZIKV was first discovered in 1947 in the Zika forest of Uganda in rhesus monkeys. Until 2007, there were only about 14 to 15 cases documented. In 2007 on Yap Island in Micronesia, the first big Zika outbreak was reported[18]. In May 2015, an alert regarding the first confirmed ZIKV infections in Brazil was issued by the Pan American Health Organization (PAHO) [19]. The outbreak has now spread to other South America, Central America, and Caribbean countries. World Health Organization (WHO) has reported as many as 23 countries and territories in America where local transmission of ZIKV has been reported[20]. The ZIKV arrived in Brazil from French Polynesia during the 2014 FIFA World Cup tournament, has been suggested by Brazilian researchers [21]. Maximum cases have been reported from Brazil, Colombia, Venezuela, Honduras, and El Salvador. Almost 1.3 million people worldwide have been affected, most in Brazil, which is battling its worst outbreak of Zika by the current outbreak. Around 35 cases of travel-acquired ZIKV infections were reported from the USA alone. The WHO declared ZIKV disease a Public Health Emergency of International Concern (PHEIC) on 1st February 2016. In the Epidemiological Update of the European Centre for Diseases Prevention and Control, 36 countries or territories have reported indigenous cases of ZIKV infection in the past nine months. These countries are all on the South American continents. The most affected country, the latest data regarding ZIKV according to the Ministry of Health weekly epidemiological update on the monitoring of microcephaly published on 2nd February, 4,783 suspected cases of microcephaly have been reported since week 43-2015, of which 1,132 (24%) were investigated and classified in Brazil. Of these cases, confirmed microcephaly 404 (36%) and central nervous system malformations, 17/404 (4%) were positive for ZIKV infection. Of 76 suspected deaths from

microcephaly and congenital central nervous system malformations, 15 were investigated and confirmed to have microcephaly and central nervous system malformations. ZIKV was detected in tissues from five of them[22]. For ZIKV, the environment in India is conducive because of the preponderance of the Ae. aegypti mosquitoes. These mosquitoes breed throughout the year in the surroundings of houses in potable water sources; the density increases during monsoon since more breeding sites become available. High humid environment and optimal temperature support their survival for many days; they can emplace eggs every 3-4 days and have multiple easy blood meals. As recommended by the authorities, "source reduction involving community participation" is the most effective and long-term preventive and control measure for Ae. aegypti. In India, it is difficult to achieve this due to perineal water shortage and other community constraints. The concept of preventing the disease using repellents, bed-net use, standing water treatment tablets, etc., has also been suggested. The four cases of ZIKV infection detected in India showed ZIKV local transmission with no travel history and suggested that ZIKV might have been present in India for a long time. The earlier vector-virus relationship studies with the chikungunya virus (CHIKV) suggested that ZIKV might become a major public health concern. ZIKV still does not have priority over other flaviviruses, such as DENV and CHIKV, in India. A foolproof program should be followed to estimate the extent of ZIKV's impact in India. A long-term, rigorous surveillance network is needed with the active participation of the concerned public health authorities at the local, regional, state, and central levels[23]. Pathophysiology of ZIKV infection In-vitro and in-vivo models ZIKV infects human embryonic cortical neural progenitor cells by inducing cell death and proving that human neurons are susceptible to the virus[24]. The virus mainly targets neuronal progenitor cells in the developing brain and some areas of the adult brain, in rare cases[25,26.] Earlier infection was associated with proliferation arrest and increased neuronal progenitor cell death. The same results were observed in cortical neurospheres[27.] Mouse and rhesus macaque experimental models supported a causal role for ZIKV in adverse pregnancy and neurological outcomes observed in people. ZIKV was recovered from fetal tissues after maternal peripheral infection in mice, suggesting materno-fetal transmission[27, 28]. Fetuses of infected mice had abnormalities similar to those described in humans[25, 27-30.] Vaginal infection in mice was associated with fetal defects[29.] ZIKV RNA was recovered in blood, semen, vaginal fluids, urine, saliva, and cerebrospinal fluid; after subcutaneous infection in primates[31-33] and viral RNA was recovered in blood, saliva, urine, lymph nodes, heart, spleen, uterus, vagina, and gastrointestinal tissues after intravenous inoculation in primates[34]. ZIKV RNA has been found to persist longer in whole blood than in plasma, which has been observed in people [35]. Due to an efficient adaptive immune response, the virus is rapidly cleared from the plasma34. Prolonged maternal viraemia and severe fetal brain malformations were observed after maternal infection in primates.[31, 33]

3. IMMUNITY AGAINST ZIKV

The antibody response is often monotypic, allowing serological identification of the infecting virus in primary flavivirus infections. In secondary flavivirus infections, which commonly occur in endemic ZIKV areas, the antibody response becomes broadly heterotypic, cross-reacting with multiple flavivirus antigens, making reliable identification of the infecting virus by serology-based assays challenging. There is one ZIKV serotype, despite two lineages (African and Asian) and three genotypes (west African, east African, and Asian)[36, 37]. Although, like other flaviviruses, ZIKV induces a humoural antibody response that is thought to provide lifelong protection against re-infection. However, this assumption should be further confirmed across the investigated human cohorts. The amount of background immunity required in the population to prevent the emergence or recirculation of the virus is unknown. Heterologous cross-reacting anti-flavivirus antibodies can enhance in-vitro cell infection with ZIKV (like other flaviviruses) through the Fc receptor, a phenomenon called antibody-dependent enhancement, which is postulated to play a part in DENV pathogenesis[38.] Although In-vitro studies have shown that pre-existing DENV antibodies might drive increased ZIKV replication, there is no evidence that this phenomenon plays a part in viral pathogenesis[39, 40.] Studies in rhesus macaques suggest that immunity against the ZIKV African lineage confers immunity against the heterologous Asian lineage and vice versa[41].The innate and cellular immune responses to ZIKV, which are probably similar to those triggered by other flaviviruses, are very little known[42-44.]

4. ZIKV TRANSMISSION

4.1. Vector-borne

ZIKV is part of the mosquito-borne group of flaviviruses mainly transmitted in the urban environment by Aedes (subgenus stegomyia) mosquitoes, which also transmit DENV, CHIKV, and yellow fever virus[36]. Approximately 3.6 billion people are infested with Aedes aegypti, Aedes albopictus, and other Aedes mosquitoes. They are at risk for ZIKV, DENV, CHIKV, and yellow fever virus infection and epidemic transmission in all tropical and subtropical populations worldwide[45]. Between April 2007, and March 2017, ZIKV transmission had only been reported in 84 countries worldwide[46]. Studies suggest that mosquitoes belonging to other genera, mainly culex mosquitoes, which transmit West Nile and Japanese encephalitis viruses, might be involved in ZIKV transmission were conflicting[47, 48.] More investigations are needed concerning whether culex is a viable vector substantially affecting operational prevention and control programs. In addition, vertical transmission of the virus has been shown in Ae aegypti mosquitoes[49.]

4.2. Non-vector borne

4.2.1. Sexual

In 2008, sexual transmission of ZIKV was suspected when a scientist infected in Senegal transmitted the virus to his wife upon returning to the USA, and in 2013 when infectious viral particles were detected in the semen of a French Polynesian patient [36, 50]. ZIKV sexual transmission has since been documented when people living in non-endemic areas became infected after sexual intercourse with partners returning from endemic areas. Both asymptomatic and symptomatic infections through genital, oral, and anal intercourse, and male-to-male, male-to-female, and female-to-male contact through sexual transmission are possible[51]. Sexual transmission is reported to have occurred up to 44 days after symptom onset; infectious viral particles have been

isolated up to 69 days after symptom onset in semen and up to 2 days after symptom onset in the female genital tract[52, 53.] ZIKV RNA has been detected for up to 6 months after symptom onset in semen and up to 13 days after symptom onset in the female genital tract, 53 which does not necessarily associate with infectious virus[54.] The exact duration of infectivity of genital fluids is unknown[53]. The effect of ZIKV infection on male fertility is unknown. Sexual transmission of the virus can impact assisted reproductive technology and gamete or embryo banking. A validated RT-PCR to detect ZIKV in semen should be implemented to screen donors[54]. Sexual transmission might play a part in non-endemic areas; the main mode of ZIKV transmission is through mosquito bites[55.] The effect of sexual transmission in endemic areas is impossible to assess because the entire population is exposed to mosquitoes. As many as 13 countries have reported evidence of non-vector person-to-person virus transmission in March 2017[46.]

4.2.2. Transfusion

In 2014, the potential for ZIKV transfusion-transmitted infection was suspected in French Polynesia after viral RNA was detected in 2.8% of asymptomatic blood donors[36] and in 2016; in Puerto Rico, 1.1% of blood donors were identified as viraemic[56]. In 2017, ZIKV RNA-positive asymptomatic blood donors were detected in Florida and Texas57-59. In 2016, transfusion-transmitted infection was confirmed in Brazil60. In endemic areas, it is difficult to prove whether infection occurred with the sexual transmission or transfusion transmitted61. With the poor availability of molecular biology-based assays and the challenges associated with the interpretation of serology data, the number of documented cases of transfusion-transmitted infection is probably underestimated. ZIKV is a new challenge for the blood supply[62, 63.] A recommendation has been issued to prevent transfusion-transmitted infections by the WHO, the US Food and Drug Administration (FDA), and the American Association for Blood Banks. Most infections are asymptomatic; the most effective mitigation strategies to prevent transfusion-transmitted infection are nucleic acid testing of blood donations or pathogen inactivation[57.] Pathogen-inactivation systems have been shown to inactivate many pathogens, including ZIKV, after photochemical treatment of plasma and platelets are commercially available [64-66.] Robust inactivation of ZIKV has also been shown with a pathogen inactivation system under development for the chemical treatment of red blood cells[67]. ZIKV transmission has not been reported through organ transplantation; the FDA has also issued guidance for donors of other substances of human origin.

4.2.3. Materno-fetal

During the French Polynesian outbreak in 2013, perinatal transmission of ZIKV was first reported [68]. The Brazilian outbreak subsequently confirmed intrauterine transmission[69, 70]. Detected viral RNA in the amniotic fluid of pregnant women suffering from symptoms compatible with ZIKV infection, and later in fetal brains and products of miscarriages, supports maternal-fetal transmission of the virus[71-73.] The placental immunological barrier has been described and implicated in destruction in chronic placentitis (TORCH type-Toxoplasmosis or Toxoplasma gondii; Other infections; Rubella; Cytomegalovirus; Herpes simplex virus-2 or neonatal herpes simplex). ZIKV does not cause a massive inflammatory response within the placenta but still induces severe damage in the fetal brain, unlike TORCH pathogens. Therefore, the vertical transmission will not occur in all pregnant women infected with ZIKV, and symptomatic congenital infection will not be observed in all exposed fetuses, similar to cytomegalovirus and toxoplasmosis [74, 75.] The exact rate of vertical transmission and congenital infection remains to be identified. Neonatal transmission by breastfeeding has not yet been described, but infectious viral particles have been detected in breast milk[76]. Transmission of the virus relies on preventing mosquito bites and practicing safe sex for maternal-fetal infections[77, 78]. All pregnant women returning with possible ZIKV exposure should be tested, despite symptom status per the USA Centers for Disease Control and Prevention[79]. Avoid pregnancy for women living in areas of active virus circulation; those living in non-endemic areas should not travel to endemic areas or countries. All pregnant women should avoid sexual contact with partners with the same exposure risks. Recommendations are experimental and based on detecting ZIKV RNA up to 6 months after exposure in semen and 2 weeks after exposure in the female genital tract.

4.2.4. Contact with infected body fluids

Only once through contact with body fluids of a highly viraemic non-sexual direct person-to-person transmission has been reported in severely ill patients, but this mode of transmission remains to be confirmed[80.]

4.2.5. Diagnosis

The clinical picture of ZIKV infection is similar to that of DENV and CHIKV, former mosquito-borne viral diseases. The differential diagnosis of ZIKV infection is wide. Diagnosis is directed by history (travel, sexual behaviors, and interaction with other infection causes) and consideration. In additionally to DENV and CHIKV, other diagnoses that should be considered include HIV seroconversion, measles, scarlet fever, rickettsial infection, leptospirosis, parvovirus, enterovirus, rubella, and secondary syphilis. The symptoms and clinical signs do not have good positive or negative predictive value; therefore, laboratory testing is needed for dependable diagnosis[81.]

4.2.6. Laboratory Testing

The final diagnosis is based on recognizing ZIKV RNA in the blood (serum or, ideally, EDTA-treated plasma) and other body fluids by polymerase chain reaction (PCR). In the acute phase, diagnosis made by antibody detection in serum samples is conceded by substantial cross-reactivity with antibodies to other flaviviruses; false positive results can be comprehended with past DENV infection or previous yellow fever vaccination[83]. Details are shown in Table No 01 below.

Table No 1: Diagnosis is based on recognition of ZIKV RNA.

Sample	Test	Timing
Blood	PCR	Less than 5 days (Sometimes up to 8 days) from symptom onset[82].
Serum	IgM antibody detection	Measurable 4-7 days from symptom beginning and continues for 2-12 weeks[83].
Saliva	PCR	Less than 5 days (rare up to 8 days) from the beginning of symptom[82].
Semen	PCR	Very limited data: RNA was spotted 62 days after symptom onset in one case [84].
Urine	PCR	Very limited data: Single study (6 patients)-positive in 6/6 at 10 days from the beginning of symptom and 1/6 quite positive at 30 days[85].

4.3. Clinical features and complications of ZIKV infections

The clinical presentation of uncomplicated ZIKV infection has been described extensively[36]. Because of its non-specific nature, infection is often not detected or needs to be misdiagnosed. Up to 80% of asymptomatic infections have been reported; a retrospective serosurvey in French Polynesia showed that, among patients who were seropositive for the virus, the percentage of asymptomatic infections was about 30% in infants and 50% in adults[86]. These results emphasize that the virus strain can influence flavivirus infections' asymptomatic to symptomatic ratio.

4.4. Complications in fetuses and neonates

In October 2015 in Brazil, a potential link between maternal ZIKV infection and a congenital syndrome was identified when neurologists and physicians in Pernambuco found a significant increase in microcephaly cases. As a result, the Brazilian Ministry of Health declared a national health emergency in November, 2015[87,88]. In February 2016, WHO declared the microcephaly epidemic a public health emergency of international concern[89]. The temporal association between the ZIKV outbreak and severe congenital CNS malformations was also reported in a retrospective analysis conducted in French Polynesia. The risk ratio of developing brain anomalies was approximately 50 compared to uninfected people in French Polynesia and Recife, Brazil[90], [91]. The ZIKV and microcephaly epidemics in these countries and in returning travelers in the USA analysis suggested that the greatest risk of fetal brain anomalies was during the first trimester[88, 91, 92].

4.5. Complications in adults

Guillain-Barre syndrome (GBS) was the first reported severe complication of ZIKV infection in adults. ZIKV and GBS link was confirmed by a case-control study conducted in French Polynesia[93]. The increased incidence of GBS during ZIKV outbreaks varied by country and was up to a 20-times baseline in French Polynesia and a 10-times baseline in Venezuela[36, 94]. In the largest series of ZIKV-associated GBS (French Polynesia and Colombia), the main characteristics of GBS were a rapid progression to nadir (about 1 week), a short plateau phase (median 4 days), and a high proportion of facial palsy. Electrophysiological findings showed different results for different places. Most French Polynesian cases were of GBS's acute motor axonal neuropathy subtype. In contrast, the predominant subtype in Colombia was acute inflammatory demyelinating polyradiculoneuropathy, the most common subtype of GBS[93, 95]. The pathogenesis of ZIKV-associated GBS is still unknown: direct neuropathogenic mechanisms, hyperacute immune response, immune deregulation, and molecular mimicry against nervous antigens are all hypotheses[96]. Treatment of GBS, which requires intensive care facilities, plasma exchange, and intravenous immuno-globulins, can be challenging in remote areas and low-resource countries. In March 2017, 23 countries or territories reported an increased incidence of GBS or laboratory confirmation of a ZIKV infection among GBS cases[46].

4.6. Vaccines and drugs against ZIKV

International funding agencies have been supporting vaccine development against ZIKV. A DNA vaccine has entered Phase I clinical trials and other more than 40 vaccine candidates are in the pipeline, some of them are being fast-tracked for license[97]. However, a vaccine may not be available for at least 2 years. It is also not known if ZIKV infections lead to lifelong immunity[98]. Although using large screening strategies, several compounds have been found to have in-vitro activity against ZIKV; no antiviral drugs have shown activity against the virus in vivo[99].

4.7. Management

Currently, there are no drugs or vaccines available for ZIKV Infection. Therefore, the management of affected individuals is symptomatic; the following things should be taken into consideration:

a. Adequate fluid intake.
b. Rest.
c. Antipyretics in the form of paracetamol to treat fever, avoiding aspirin and NSAIDs.
d. Prevent mosquito bites during the infected stage to prevent the spread of the disease.
e. If the patient is extra pregnant, care has to be taken to monitor for congenital disabilities and adverse pregnancy outcomes. Only after documented congenital disabilities during pregnancy termination should be considered.

4.8. Prevention Strategies

As vaccination has entered Phase, I clinical trials and more than 40 vaccine candidates are in the pipeline, some are being fast-tracked for license[97], indicating that progress in developing full flagged may require more time. Hence prevention of this disease becomes the most crucial method to control the outbreak and its spread. Therefore, people should take care to prevent themselves from getting infected with ZIKV, which could be undertaken through the following routes:

a. Preventing mosquito bites by
(i.) wearing full-sleeved shirts and long pants indoors.
(ii.) Use of Environmental Protection agency registered Insect repellents.

(iii) Use mosquito nets at home to prevent biting during sleep[100].

b. Avoid unnecessary travel to countries currently facing the wrath of ZIKV infection.

c. Particularly pregnant women should avoid travel to affected countries.

d. Avoid getting pregnant while residing in affected countries has been advised due to the surge of microcephaly cases till endemic crises are over.

e. Travel precautions should be followed; travelers to affected areas should take extra care to avoid mosquito bites by using recommended insect repellents. In addition, in case of the development of any symptoms suggestive of ZIKV infection should immediately report to healthcare facilities by travelers who visited affected territories.

f. Vector control by vector surveillance, environmental manipulation and modification, biological and chemical control, and personal protective measures must be strengthened.

g. Educating healthcare professionals and the population at large is essential to create awareness about ZIKV and remove panic broadcasting information to the people by various methods like billboards at airports and hospitals.

h. To prevent the spread of this outbreak and control the infection, surveillance at various stages is essential. Pediatricians, obstetricians, and physicians should be sensitized towards monitoring cases and keeping a tab on numbers. In cases of GBS, atypical unexplained neurological manifestations, newborns with congenital disabilities, and microcephaly, the healthcare providers should keep a high degree of suspicion and elicit travel histories and report accordingly.

i. To prevent the control of the outbreak of ZIKV, international and national collaboration at various levels is an equally essential element[101].

5. CONCLUSION

Zika virus (ZIKV) is a flavivirus with RNA in the form of a core genetic material encased inside a fatty membrane, which sits within a 20-sided protein shell covered in carbohydrates. The virus's genetic structure provides a map of potential sites of the virus that therapeutic agents could target, used to create an effective vaccine or improve our ability to diagnose and distinguish ZIKV infection from that of other related viruses. In 2016, WHO declared ZIKV a public health emergency of international concern, but in November 2016, it was no longer. However, in May 2017, more than 200 000 infections and 3000 congenital syndromes associated with ZIKV infections were confirmed in America. The presence of ZIKV in areas where other flaviviruses have already been observed can lead to an increase in mortality due to issues related to differential diagnosis and the unavailability of commercial diagnostic kits. Therefore, vector control measures should be increased, healthcare actions should be taken, and ZIKV should be diagnosed by serological and molecular tests (RT-PCR). There is no specific treatment for ZIKV infection; the best strategies to deal with this disease are personal protection from mosquito bites and vector control.

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7. AUTHORS CONTRIBUTION STATEMENT

Naveen Kumar B., Asief M, And Qadrie ZL reviewed the literature and wrote the review paper. The corresponding author makes the necessary corrections and communications.

8. CONFLICT OF INTEREST

Conflict of interest declared none.

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