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Review Article

Zika virus: An informative note

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ABSTRACT
Recently Zika outbreak in Brazil highlighted itself to World Health Organization (WHO) and has been declared international emergency to public health. In this view, it has become mandatory to have one spot pool of knowledge i.e. its prevalence along with symptoms, transmission, diagnosis, prevention and other important data. Zika virus (ZIKV) is an emerging globally mosquito (Aedes) -borne pathogen belonging to family Flaviviridae and genus Flavivirus. It was first isolated in 1947 in Uganda. Zika cases were reported in Africa, Asia and predominantly in Pacific. Its symptoms demonstrate dengue like syndrome. Transmission of ZIKV occurs through infected mosquito bite, sexual intercourse, infected blood transfusion and mother to fetus. Zika symptoms include rash, myalgia, arthralgia, headache, fever, and edema. ZIKV infection during pregnancy cause congenital brain damage and microcephaly in new born. Mosquitoes and monkeys are main vectors of ZIKV. Zika diagnosis is mainly done by molecular techniques (RT-PCR)) and serological tests (ELISA or immuno-fluorescence). No treatment is available till now for ZIKV. Prevention strategies include insect repellant and eradication of mosquito vector. We, the authors feel this document as a preliminary informative source in overall related directions.

Keywords: Zika virus, RT-PCR, ELISA, World Health Organization

INTRODUCTION

Among many public health alerts, the global spread of ZIKV is of concern and alarm. Zika virus (ZIKV) is a globally emerging mosquito-borne pathogen belonging to family Flaviviridae and genus Flavivirus. The virus was first isolated in 1947 and described in 1952. It was isolated from a febrile sentinel rhesus monkey [1]. In 1948, ZIKV was also isolated from a pool of Aedes africanus mosquitoes from the Zika forest in Uganda during yellow fever study [2, 3]. Until 2007 only a small number of cases had been described in Africa and Asia. After that spread of ZIKV was observed in French Polynesia in October 2013. Approximately 29,000 people suspected for ZIKV were given medical help. The affected areas in the Pacific have expanded to include the Cook Islands, New Caledonia, and Easter Island [4, 5]. Virus transmission occurs via mosquito vectors from the Aedes genus of the Culicidae family in a sylvatic cycle involving nonhuman primates [6], although antibodies have also been detected in a number of other mammals i.e. water, buffalo, elephants, zebras etc [4]. However, in areas where there are no nonhuman primates, humans are the primary amplification hosts [7]. Virus infection many a times proved threat for the society. Previously Ebola virus emerged as a menace for population of West Africa, which has global consequences through risk of imported infections and mishandling for biological terrorism [8]. Likewise there are many diseases such as sarcoidosis [9], chikungunya [10], dengue, swine flu which established themselves as havoc for the society.

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Virology and pathogenesis

ZIKV genome is an approximately 10794 kb (length) single-stranded, positive sense ribonucleic acid (RNA) virus containing 10,794 nucleotides encoding 3,419 amino acids which is most closely related to Spondweni virus [11, 12]. Through phylogenetic analysis two major lineages have been identified i.e. African and Asian where, non-human primates (NHPs) were implicated as the vertebrates hosts of ZIKV [5, 13-15]. Pathogenesis of ZIKV infection is not clear yet, but it is hypothesized that mosquito born flaviviruses initially replicate in dendritic cells near the site of inoculation and then spread to lymph nodes followed by blood stream. Flaviviral replication is thought to occur in cellular cytoplasm [16]. The possible routes of transmission are shown in Figure 1. Musso et al showed in their study that ZIKV may also be transmitted through sexual intercourse as ZIKV was isolated from a patient's semen [17].

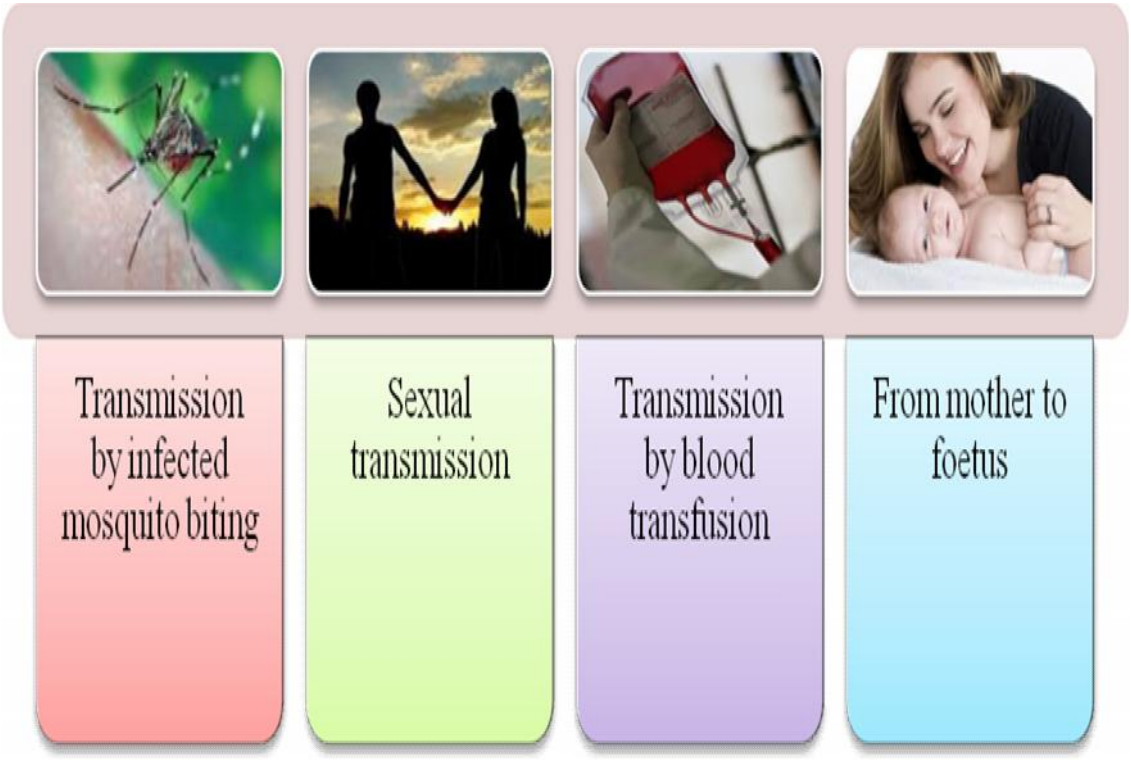

Figure 1. Routes of transmission of Zika virus in humans

Travellers are advised to use cover up clothing and insect repellent to protect them from mosquito biting. Public Health England advises travelers (women) who are pregnant, to avoid travel to an area where active Zika transmission is being reported, because of concerns about infection during pregnancy causing congenital brain damage and microcephaly in new born (Figure 2) [18, 19]. Authorities in Canada, the United States, Australia, and Taiwan are also providing same advices to their community. Public Health England advises that women, on returning to the UK, should avoid becoming pregnant for a further 28 days to avoid ZIKV transmission to new born baby [20].

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Figure 2. Picture of new born baby with microcephaly

The first Zika outbreak, associated with neonatal brain disorders and microcephaly, occurred in 2013-14 in French Polynesia. Again in 2015, Zika exploded in Brazil, followed by an ongoing epidemic of microcephaly. Malkar et al in their study found the presence of ZIKV in the fetal brain tissue, by performing reverse-transcriptase polymerase chain reaction (RT-PCR) assay, with consistent findings on electron microscopy. The complete genome of ZIKV was recovered from the fetal brain. Calcifications in the fetal brain and placenta were observed during ultrasonography carried out at 29 weeks of gestation exhibiting the presence of microcephaly [21]. Epidemiologic studies are still in process to track cases of microcephaly during 2016 in Brazil and countries affected later, such as Colombia (
Table 1) [22].

Table 1. Cases of congenital malformation potentially linked with Zika virus infection in Brazil (as of 18 January 2016) [23]

S. No.	Date of report & location	Clinical findings	Laboratory findings	Reference
1	17 Nov, 2015 Paraíba state	Foetus with microcephaly observed by ultrasound (US) exams a 30.1 weeks gestation Head circumference < 2.6 cm SD Lesions observed by US: -Brain atrophy with coarse calcifications involving the white matter of the frontal lobes, including the caudate, lentostriatal vessels and cerebellum. -Corpus callosal and vermian dysgenesis. - Enlarged cisterna magna Mother: symptoms compatible with Zika virus infection at week 18-19 of gestation	RT-PCR Zika virus positive in amniotic fluid (Instituto Oswaldo Cruz)	[18]

2	17 November 2015 Paraíba state	Foetus with microcephaly at ultrasound exams 29.2 weeks' gestation Head circumference < 3.1 cm SD Lesions observed by US: -cerebral hemispheres were markedly asymmetric (severe unilateral ventriculomegaly) -almost complete disappearance or failure to develop the thalami - thin pons and brainstem Mother: symptoms compatible with Zika virus infection at week 18-19 of gestation*	RT-PCR Zika virus positive in amniotic fluid (Instituto Oswaldo Cruz)	[18]
3	28 Nov, 2015 Ceara state	Newborn Born the 18 November 2015 (residing Tejuçuoca, Ceara State) No measurement of head circumference at birth Weight: 945 grams at birth Died within 5 min after birth Observed lesions (US, 13 Nov 2015): -microcephaly (head circumference 190 mm) - fetal anasarca - polydramnios	Presence of Zika viral genome in blood and tissue samples of the newborn (Evandro Chagas Institute)	[24]
4	5 Jan, 2015 Rio Grande do Norte state	Case: miscarriage, foetus with congenital malformations Observed lesions: - Congenital malformation Mother presented with rash and fever during pregnancy	Positive PCR test for Zika virus on foetal sample in samples of the placenta (US CDC laboratory)	[18]
14	15 Jan, 2016 Hawaii (USA)	Case: baby with congenital microcephaly who was born recently on Oahu island, Hawaii. Mother had a probable exposure to Zika virus when she was residing in Brazil in May 2015 (no further details provided)	Laboratory confirmation of a past Zika virus infection (no details) (US CDC laboratory)	[25]

Symptoms of ZIKV infection

On 1st February 2016 WHO's director general, Margaret Chan, convened a meeting of the International Health Regulations Emergency Committee due to the epidemic of ZIKV and there she declared Zika a public health emergency of international concern, as it is associated with growing clusters of microcephaly and other neurological disorders in French Polynesia and Brazil [22].

Zika virus is related to other arboviruses such as yellow fever virus, Japanese encephalitis virus, dengue virus, and West Nile virus [12]. Symptoms of ZIKV infection are subclinical substantially. ZIKV infection is believed to be asymptomatic or mildly symptomatic in most cases. Hemorrhagic signs are yet not seen in ZIKV infected patients whereas neurological complications including Guillain-Barré syndrome, have been observed [4, 26-28]. Guillain-Barré syndrome is related to muscle weakness, which causes difficulty in walking, chewing, talking and swallowing and body aches especially severe lower back ache. The clinical symptoms of ZIKV infection are found to be similar to the infections caused by arbovirus such as dengue and chikungunya (Figure 3) [3, 7].

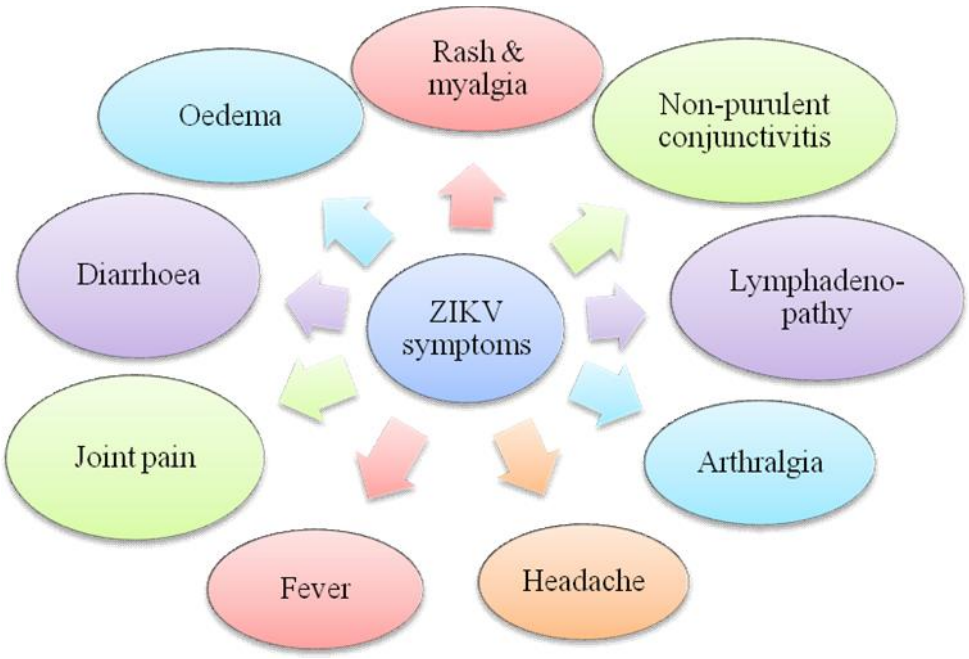

Figure 3. Symptoms of ZIKV infection

Prevalence of ZIKV

In humans, Zika virus was first detected in1952 using neutralizing antibody testing in sera from East Africa [1, 29]. In Nigeria (1964 to 1970), 15 types of arbovirus in human specimens were found among 171 isolations. The majority of isolations were from children below 4, among all age groups. Seasonal variation affects ZIKV isolation rates i.e. peaks in rainy seasons (June to August) and lowers down in dry seasons (January to February). Prevalence of Zika virus is high in Africa and tropical America, due to flavivirus super infections with high backgrounds of flavivirus immune responses [30]. In short span of time i.e. within a year Zika virus has spread to over 25 nations in the Americas, the Pacific islands, and Cape Verde in West Africa [22]. Brazil is the most affected country, with preliminary estimates of 440,000 to 1.3 million cases of autochthonous ZIKV infection reported through December 2015. Recent reports from the Ministry of Health of Brazil suggested that in the Northeast region of the country, cases of microcephaly have tremendously increased among newborns, indicating relation between ZIKV infection in pregnancy and fetal malformations [21].

Serological and entomological data indicated the prevalence of ZIKV infection mainly in two continents i.e. African continent and Asian continent [11]. In African continent cases were detected in Nigeria [31], Sierra Leone [32], Gabon [33], Uganda [34], Central African Republic [35], Senegal from [36] and Coˆ te d'Ivoire [37]. Whereas, in Asian continent, cases were found in Pakistan [38], Malaysia [39], Indonesia [40], Micronesia [7, 13] and Cambodia [6]. In Malaysia and Indonesia (1977 and 1978), many cases of Zika virus infection came into appearance towards the end of the rainy season [40].

An outbreak of ZIKV was reported in Yap Island, Federated States of Micronesia in 2007 [7]. In 2013–2014, ZIKV also caused a major epidemic in the French Polynesia and New Caledonia [5, 26]. Travel alerts are issued by CDC for people traveling to the following regions and countries where Zika virus transmission is ongoing: the Commonwealth of Puerto Rico and the U.S. Virgin Islands, U.S. territories; American Samoa; Barbados; Bolivia; Brazil; Cape Verde; Colombia; Costa Rica; Curaçao; Dominican Republic; Ecuador; El Salvador; French Guiana; Guadeloupe; Guatemala; Guyana; Haiti; Honduras; Jamaica; Martinique; Mexico; Nicaragua; Panama; Paraguay; Saint Martin; Samoa; Suriname; Tonga; and Venezuela [41].

In Senegal (Nigeria), first evidence of ZIKV was collected in 1968 in the Saboya forest, 187 km from Dakar, in the western part of the country, from the *Ae. Luteocephalus* [42]. In 1970, the virus was also found in Bandia (65 km from Dakar), isolated from *Aedes luteocephalus, Ae. Furcifertaylori, Anopheles Gambiae s.l.* and human.

Table 2. Zika virus prevalence studies with location

Study year	Location of study	References
1947	Zika forest, Uganda, Nigeria, and East Africa	[1, 12]
1954	India	[43, 44]
1970-1975	Nigeria, Gabon	[44, 45]
1978	Malaysia, Indonesia	[40]
1988-1991	Senegal	[36]
1999	Ivory Coast	[37]
2001	Sabah, Malaysia	[15, 46]
2007	New World, Easter Islands, Nepal, Argentina, Hawaii, Scandinavia, Saudi Arabia	[14]
2007	Micronesia	[2, 7]
2008	Southeast Asia, Australia	[47]
2009	Southeast Asia	[48]
2008-2011	Senegal, Nigeria, Uganda, Egypt, India, Pakistan, North Vietnam, Malaysia, Indonesia, the Philippines, Borneo/Java, Micronesia, USA	[12, 13, 49]
2012-2013	Indonesia, Singapore, Australia, Tahiti, Germany	[50]
2013-2014	French Polynesia, New Caledonia	[2, 5, 26]
2014	Eastern Islands (Rapa Nui National Park, Chile) in the Pacific ocean	[51]
2015	Three states of Brazil: Bahia, Rio Grande do Norte and São Paulo	[51]
2016	Bolivia, Guyana, Ecuador, Guadeloupe, Guatemala, Paraguay, Puerto Rico, Barbados, Saint Martin and Haiti	[25]

In an entomological surveillance programme (1972 to 2011), 381 ZIKV isolates were collected in Kedougou (Southeastern Senegal) mainly from Ae. *africanus, Ae. luteocephalus, Ae. furcifer* and *Ae. taylori*, which was seven times from humans and twice from NHPs (e,g, Cercopithecus

aethiops, Erythrocebus patas) [3]. Serological studies conducted in 1988 and 1990 in Southeastern Senegal showed that 10.1 and 2.8 % of humans had Immunoglobulin M (IgM) antibodies to ZIKV respectively [36].

Surveillance of ZIKV infection

Surveillance of ZIKV fever should be based on the existing surveillance system for dengue and chikungunya, as the symptoms are similar to these infections. Surveillance system should monitor the epidemiological and entomological changes related to ZIKV infection and immediately communicated these to the national authorities if ZIKV introduction had been found in any area, in order to ensure timely decisions for actions as needed. If the infection traces has been found, surveillance of ZIKV should be focused.

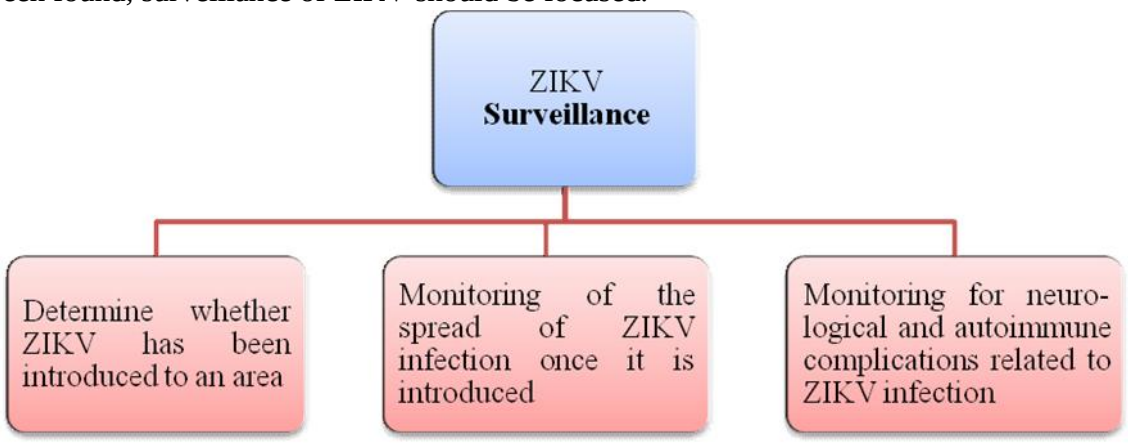

Figure 4. ZIKV Surveillance

To maintain and develop effective control measures to prevent the transmission of ZIKV infection following recommendations (Figure 4) should be followed by the countries with or without ZIKV transmission. Countries **without** ZIKV transmission should set up and strengthen the event-based surveillance systems to detect the cases having symptoms of ZIKV infection (fever, rashes, malaise, conjunctivitis etc). These should be based on the experiences of Brazil and Colombia in which dengue, chikungunya, measles, rubella, and parvovirus B19 have been ruled out. Health authorities must be on alert for the emergence of clusters of rash febrile syndrome of unknown etiology and test for ZIKV infection. Countries **with** ZIKV transmission should set up the surveillance systems to monitor the geographical spread of the virus to detect the introduction into new areas and potential neurological and autoimmune complications, as well as the impact on public health. These systems should be able to identify the risk factors associated with Zika virus infection and circulating Zika virus lineages [31, 45].

Vectors of ZIKV

It includes:

1) Mosquitoes
2) Monkeys
3) Additional Species

I. Mosquitoes

Aedes mosquitoes play a significant role in transmission of ZIKV. In Sierra Leone (1972), during an entomological and serologic survey, sera from children up to 14 years were analyzed for 12 antigens from viruses including Zika, Chikungunya, West Nile and yellow fever. Among these

arboviruses (ZIKV) prevalence was found to be much greater [32]. Between November 1961 and June 1963, on a 120-ft long tower, twelve Zika virus strains were isolated and pools of mosquitoes (*Aedes africanus*) from Zika forest were used for the virus isolations (Table 3) [52].

Table 3. Isolation of ZIKV from different species of mosquito in different cities

S. no.	Species	Country/city	Year	Reference
1.	*Aedes africanus* & *Ae. Apicoargenteus*	Uganda	1947	[34, 53]
2.	*Ae. aegypti*	Malaysia	1964	[39]
3.	*Ae. luteocephalus*	Nigeria	1969, 1972	[31]
4.	*Ae. vittatus, Ae. furcifer,* & *Ae. aegypti*	Cote d'Ivoire	1999	[37]

II. Monkeys

Zika virus was originally isolated in 1947 from a febrile sentinel monkey during a yellow fever study in Uganda [1]. In Uganda, monkeys serve as two types of hosts for yellow fever i.e.

1) As an enzootic state in the Zika forest in Western Uganda (Bwamba County)
2) As epizootics in central Uganda zone of savannas forest.

Among these two an epizootic for Zika virus occurred in two episodes in the Zika forest. One epizootic for Zika virus was happened in 1969 with consequent accumulation of non-immune monkeys (post epizootic of 1962–1963). Second one was occurred in 1970, when biting densities increased for *Aedes africanus*. After eighteen months, an intensive epizootic for Yellow Fever developed. This contradicted the hypothesis that subsequent Yellow Fever epizootics would be subdued by Zika virus infections in nature for red-tail monkeys. During the yellow fever epizootic in Zika forest (1972), several other arbovirus antibodies were discovered as well in monkeys near Entebbe, Uganda [34].

III. Additional species

Several other different species are also implicated in susceptibility to Zika virus, e.g. buffalo, elephants, zebras etc [4].

Diagnosis of ZIKV infection

Diagnosis of Zika virus infection is difficult as it is easily mistaken for other arbovirus infections including Chikungunya and dengue fever [6]. For patients with symptoms such as fever, rash, arthralgia, body aches etc. and person who has travelled to an area with ongoing transmission of Zika, laboratory testing is important to confirm the etiology of the symptoms. For the diagnosis of Zika virus infection mainly molecular techniques (such as Conventional or real-time reverse transcription-polymerase chain reaction (RT-PCR)) and serological tests (ELISA or immuno-fluorescence) are performed (Figure 5). RT-PCR is used to detect the viral Ribonucleic Acid (RNA) whereas ELISA or immuno-fluorescence is performed to detect the specific IgM or IgG. Testing Algorithm for detection of suspected case of ZIKV infection is given below in Figure 6. During the first 7 days of symptoms, molecular technique (RT-PCR) is used to identify viral RNA in serum. A positive RT-PCR indicates confirmation of virus and if it is negative then

antibody (IgM) testing is performed but sample should be taken within 4 days after onset of symptoms. Due to cross reactivity with other arbovirus such as chikungunya, dengue etc, positive test is further confirmed by PRNT (plaque reduction neutralization test) for the presence of Zika virus [54].

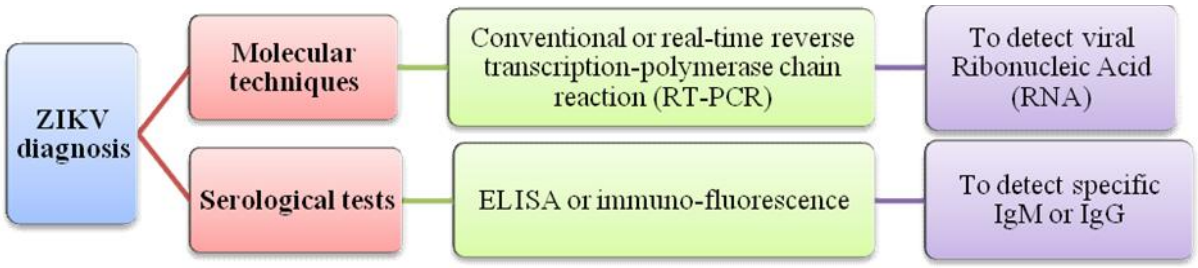

Figure 5. Diagnostic techniques for ZIKV

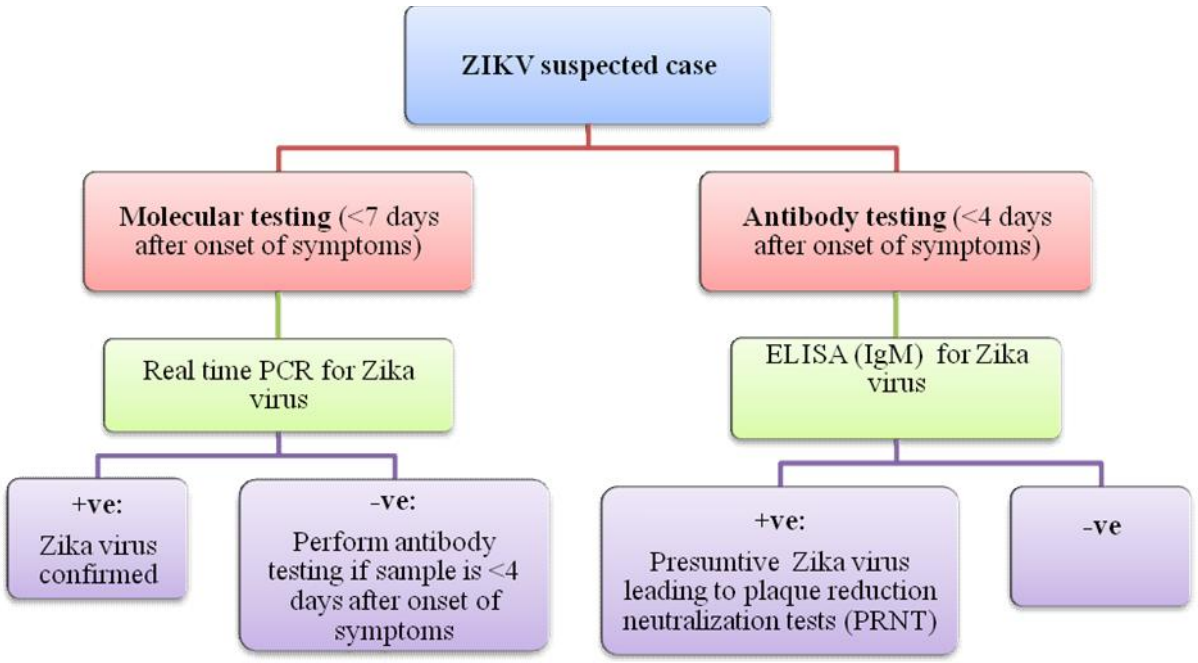

Figure 6. Testing Algorithm for detection of suspected case of ZIKV

Management of ZIKV infection

- No specific antiviral treatment for Zika virus is available, so symptomatic relief should be given to the patient.
- Patient should be isolated from the others. Symptomatic and supportive treatment include rest and the use of acetaminophen or paracetamol to relieve fever. The use of antihistamines to control pruritus usually associated with the maculo-papular rash could be recommended.
- Patient should be advised to take plenty bed rest.

- Aspirin and other Non-steroidal Anti-inflammatory Drugs (NSAIDs) are contraindicated due to risk of bleeding and cause of the clinical symptoms could be dengue or chikungunya respectively.
- Patients should be advised to take plenty of fluids to replenish fluid lost from sweating, vomiting and other losses. Affected patient should avoid being bitten by *Aedes* mosquitoes during the first week of illness to prevent infection of other persons.
- Physicians or health care workers who attend to Zika virus-infected patients should protect against mosquito bites by using insect repellent and wearing long sleeves and pants [25, 55].

Preventive measures for ZIKV infection

IV. Personal prevention measure:

Patients infected with dengue, chikungunya or Zika virus should minimize the contact with the vector to prevent the spread of the virus and therefore the disease. Patients, his/her family members and the community must be educated about the ways to minimize this risk of transmission by reducing vector population and human-vector contact. Vector-patient contact could be minimized by following the given recommendations:

- Mosquito nets (bed nets) treated with or without insecticide should be used.
- Clothes that cover the extremities should be used by the patient and family to avoid the mosquito biting.
- Wire-mesh screens on doors and windows should be used.
- Repellents containing DEET, IR3535 or Icaridin should be applied on the exposed skin or clothing. It must be used strictly in accordance with the instructions indicated on the product label.

These recommendations should be followed by everyone to avoid the transmission of infection to healthy community.

Blood safety authorities should consider donors with a relevant travel history to areas with active Zika virus transmission, in line with measures defined for dengue virus. In unaffected areas with competent vectors for Zika virus, a preparedness plan for prevention and control of outbreaks of Zika virus infection should cover the continuity of blood supply.

Awareness should be increased among health professionals who provide prenatal care of the possible association of Zika virus and microcephaly and adapt prenatal monitoring in accordance with the exposure to the vector [25].

V. Preventive measures for travelers

Prior to departure to the places documented with dengue, chikungunya and/or Zika virus transmission

Health authorities should inform travelers about the symptoms and the necessary measures to protect themselves from mosquito bites, such as using repellents, wearing appropriate clothing to minimize skin exposure and using insecticides or nets, who are heading to any country with documented circulation of dengue, chikungunya, Zika virus etc.

Pregnant women and women who are trying to become pregnant, and who plan to travel to the areas experiencing transmission of Zika virus, should discuss their travel plans with their healthcare providers and consider postponing their travel to affected areas, especially to areas with increasing or widespread transmission [23]

Upon returning from places with dengue, chikungunya and/or Zika virus transmission

Travelers are advised to contact their physician/healthcare provider if they suspect to have symptoms of dengue, chikungunya or Zika virus upon returning home.

VI. Integrated Vector Management (IVM)

As the ZIKV infection is transmitted by the same mosquito (*Ae. Aegypti*) as that of dengue and chikungunya, so an effective and operational dengue and chikungunya vector control program should be followed for the integrated vector management. The success of the IVM program relies on:

- intersectoral participation and collaboration at all levels of government, including health, education, environment, social, development and tourism sectors, among others
- support of non-governmental organizations (NGOs) and private organizations

Communication channels should provide clear and quality information to the public about these diseases via communication campaigns. Prevention and control measures by national authorities should include the following:

- To prevent or minimize vector propagation and human contact with the vector-mosquito, vector breeding sites in household and common areas (e.g. parks, schools, cemeteries, etc.) must be eliminated. This can be achieved by organizing mass sanitation campaigns for the elimination of breeding sites, specifically in areas where routine garbage collection has been interrupted.
- Breeding site control measures through physical, biological and chemical methods should be implemented. Mosquitoes should be removed from the places where people gather (e.g., schools, transport terminals, hospitals, health centers, etc.).
- It is suggested to use adulticide treatment primarily through spraying, especially in areas where autochthonous or imported cases of dengue, chikungunya, and/or Zika virus are detected, to remove infected adult mosquitoes and interrupt transmission. Spraying is the primary manner to interrupt transmission and obtain time to consolidate the removal of larval breeding sites intensively.
- Spraying equipment should be maintained in an appropriate manner and intensified monitoring (e.g., quality control) of fieldwork operators both during larval control and adult insecticide treatment (fumigation) should be ensured [55].

VII. Preventive measures for pregnant women

A pregnant woman could become infected with ZIKV during any trimester. Pregnant women should be tested for Zika virus infection, who report two or more symptoms consistent with Zika virus disease (acute onset of fever, maculopapular rash, arthralgia, or conjunctivitis) with a history of travel to an area with Zika virus transmission, during or within 2 weeks of travel, or who have ultrasound findings of fetal microcephaly or intracranial calcifications, in consultation with their state or local health department. In pregnant women with laboratory evidence of Zika virus infection, Serial ultrasound examination should be considered in pregnant women with laboratory evidence of ZIKV infection to monitor fetal growth and anatomy and referral to a maternal-fetal medicine or infectious disease specialist with expertise in pregnancy management is recommended [54]. A pregnant woman should avoid traveling in the areas with ZIKV introduction. In case of travelling, she should cover her body with long sleeves clothes and should use mosquito repellant.

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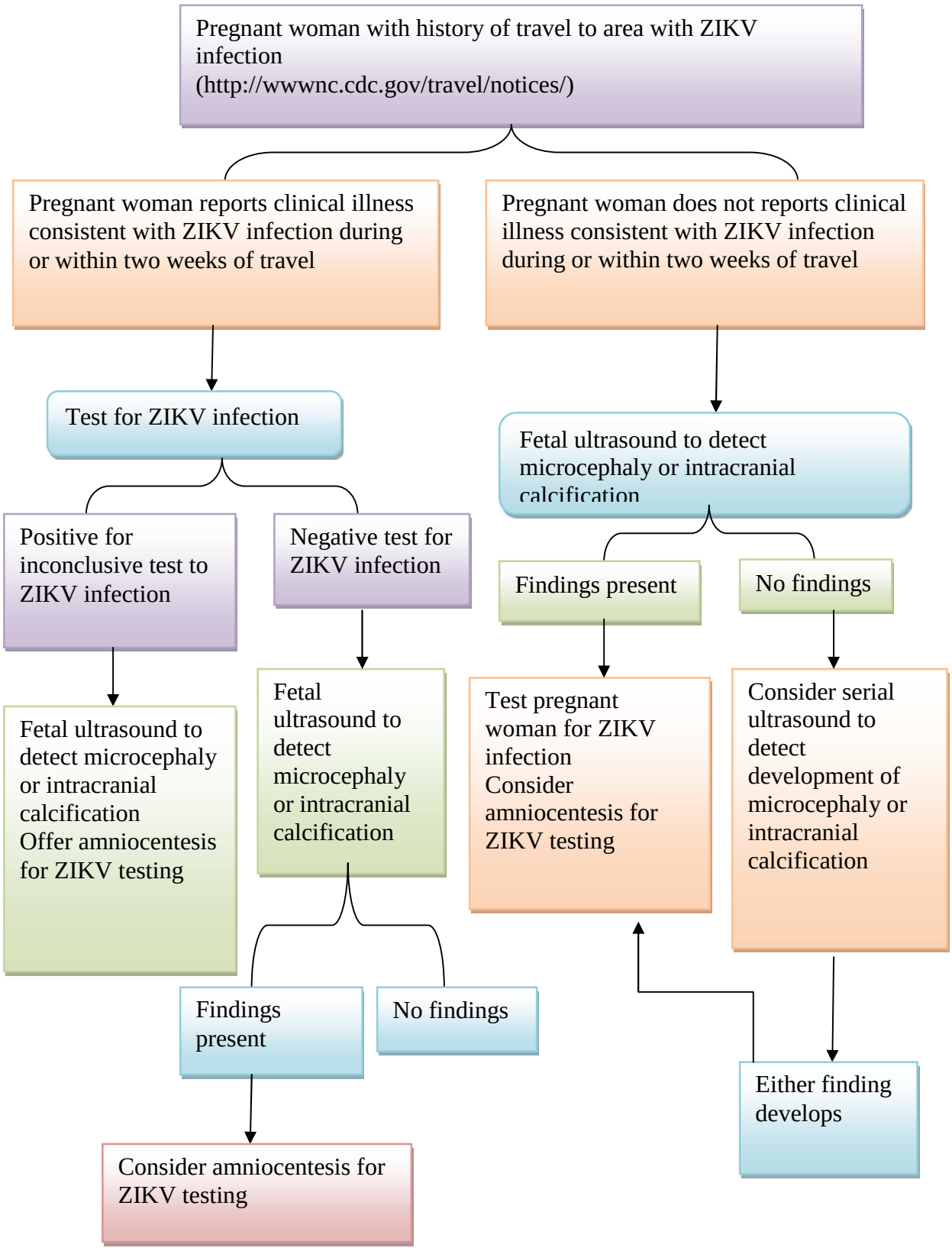

Figure 7. Recommendations for the pregnant women with or without clinical illness [54]
Epidemic Developments in 2016

ZIKV infection continues to spread in the Americas. In Rapid Risk Assessment till 19 January 2016, 13 additional countries or territories have reported laboratory confirmed autochthonous transmission including 12 countries in the Americas: Barbados, Bolivia, Ecuador, France (French Guiana, Guadeloupe, Martinique and Saint-Martin), Guyana, Haiti, Honduras, Puerto Rico, and Suriname, as well as one country in Asia: Thailand. In addition, autochthonous transmission was reported retrospectively in the Maldives through a travel-related case returning to Finland in June 2015 [25]. After 19 January, eight new countries have reported autochthonous transmission that are American Samoa, Costa Rica, Curaçao, Dominican Republic, Jamaica, Nicaragua, Tonga and US Virgin Islands [56]. Thirty-five countries or territories have reported autochthonous cases of Zika virus infection within the past nine months [25].

Current scenario

Several companies are trying for a vaccine which can fight against Zika, but no one reached to success till now. One of the Pharmaceutical company, Inovio Pharmaceuticals in collaboration with GeneOne Life Sciences (manufacturer of DNA plasmid-based agents), found a vaccine called SynCon, which showed promising results in mice. SynCon constructs were administered in mice using Inovio's CELLECTRA® electroporation delivery technology. Inovio's Zika DNA vaccine resulted in seroconversion, or the development of detectable specific antibodies in the blood, in all vaccinated mice. It was also found that vaccination generated robust and broad T cell responses as analyzed by the standardized T cell ELISPOT assay. These findings are vital given the potential importance of neutralizing antibodies in preventing infection and the role T cells play in clearing infection by killing cells that harbor the virus. The vaccine will next be tested in non-human primates and then phase-I human trials will be done for Zika vaccine [23].

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