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A Review on Zika Virus- A Global Threat

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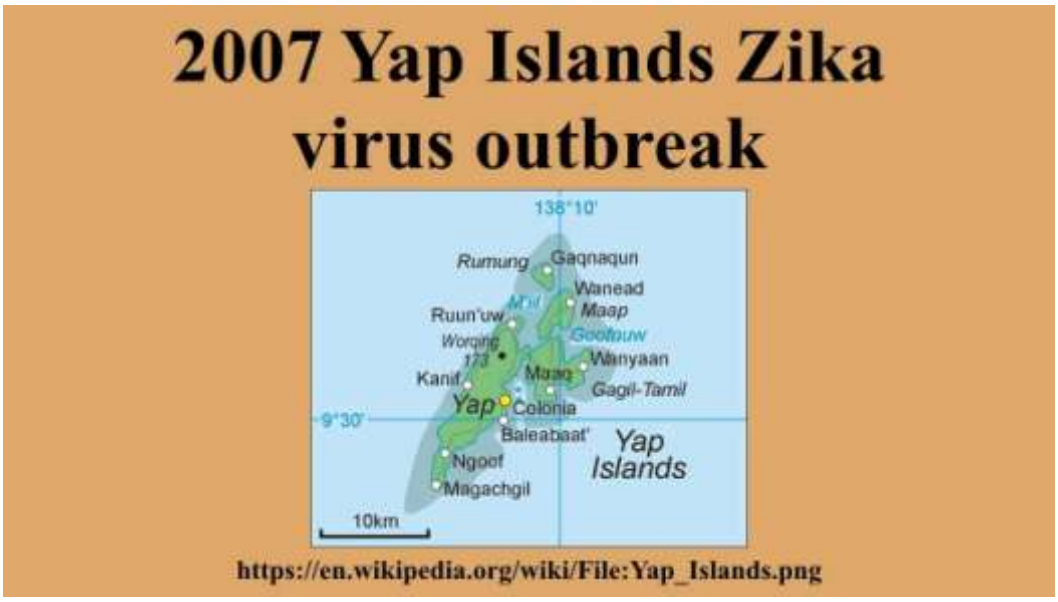
ABSTRACT
Zika virus is a flavivirus transmitted to humans primarily by Aedes (Stegomyia subgenus) mosquitoes.Here we extensively described the current understanding of the effecst of Zika virus on health and clinical manifestations. clinical manifestations of infection in adult cases are not severe and disease is not associated with high mortality rates. Zika virus infection can have an impact on fetal development and lead to severe neuro developmental abnormalities.

KEY WORDS;Aedes,Flavivirus,Zika virus

INTRODUCTION

Among many public health alerts,the global spread of arboviruses is of concern and alarm.Zika virus is an arbovirus in the Flavivirus family that includes yellow fever, West Nile, dengue, and Japanese encephalitis viruses. Zika virus is spread to people primarily through an infected Aedes species mosquito.Many people infected with virus wont have any symptoms or have only mild symptoms.Infection during pregnancy can cause microcephaly and other brain defects. Initially it is identified in 1947 in the Zika forest in Uganda in Rhesus macaque populatation initiative for research in yellow fever.Zika was later identified in humans in 1952.

The first large outbreak of disease caused by zika infection was reported from the islandof Yap in 2007. In India,the zika had first broken out in the western state of Gujarat and Tamilnadu in the south in January 2017.On 21st september 2018 The Ministry of Health and Family Welfare Government of India reported a confirmed case of zika virus infection in a 78 year old women in Jaipur(Rajastan state)



Previously limited to sporadic cases in Africa and Asia, the emergence of Zika virus in Brazil in 2015 heralded rapid spread throughout the Americas. Although most Zika virus infections are characterized by subclinical or mild influenza-like illness, severe manifestations have been described, including Guillain-Barre syndrome in adults and microcephaly in babies born to infected mothers. Neither an effective treatment nor a vaccine is available for Zika virus; therefore, the public health

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response primarily focuses on preventing infection, particularly in pregnant women. Despite growing knowledge about this virus, questions remain regarding the virus's vectors and reservoirs, pathogenesis, genetic diversity, and potential synergistic effects of co-infection with other circulating viruses. These questions highlight the need for research to optimize surveillance, patient management, and public health intervention in the current Zika virusepidemic.

Zika is nationally notifiable disease.Approximately one in four people infected with ZIKV are believed to develope symptoms.Most people fully recover without severe complications and hospitalisation rates are low.To date,there been no reported deaths associated with ZIKV infection.

1. Epidemiology

Zika virus was first discovered int the Zika forest of Uganda in 1947 in rhesus monkeys,but was not identified in humans until 1952 in Tanzania.Since then,outbreak shave occurred sporadically in Africa,the Americas,Asia,and the Pacific.Until 2007,only 14 cases had been documented in humans world wide. The firstlarge outbreak was reported on the islandof Yap (FederatedStatesofMicronesia) in 2007.The most likely source of this outbreakwas introduction of the virus by travel or trade involving an infected person or an infected mosquito.Another large outbreak was seen in the Pacific Islands (French Polynesia, Easter Island, the Cook Islands, New Caledonia) in 2013 to 2014.This was the first outbreak were the congenital maalformations(e.g.,microcephaly) and neurologic complications, including Guillain-Barresyndrome(GBS), were linked to the infection, although this association was made retrospectively.
In the current outbreak,the first reports of locally transmitted infection came from Brazil in May 2015 ,although there are data to suggest that the virus originated in the Americas in Brazil between October 2012 and May 2013.Eighty-sixcountries,territories,and sub nationa lareas have reported evidence of mosquito-borne Zika virus transmission.Transmission is ongoing in the Americas,the Western Pacific region,the South east Asia region, andAfrica. As of August1, 2018, 5716 cases have been reported in US states (5430 cases in returning 231 cases acquired through presumedlocal mosquito-borne transmission in Florida and Texas, and 55 cases acquired through other routes), and 37,262 cases havebeen reported in US territories (most via local mosquito-borne transmission).As of July 17, 2018, the US Zika Pregnancy Registry and the zika active pregnancy survilliance System in Puerto Ricohave reported 2474 pregnant women with any laboratory evidence ofctionin US states and theDistrict of Columbia ,and 4900 pregnant women in US territories.Among 478 confirmed cases in miami-dade country,Florida,6.9% of cases occurred in children ages 1to17 years. In the US ,local transmission has been previously reported in Florida andTexas.Pregnant women and people living in or traveling to either of these areas should consult current Centers for Disease Control and Prevention (CDC) guidance. The CDC classifies geographic areas in the US and Hawaii as either red (activetransmissionareas) or yellow (cautionaryareas),and this classification affects local guidance for pregnant women. Cases in returning travelers have been reported in but not limited to locations including the US, UK, Europe, Australia, NewZealand, Israel, Japan and China.
As of November 2017,305 cases were reported in the UK,all of them associated with travel.Between June 2015 and january 2017,21 countries in the European Union reported 2133 confirmed cases of infection(106 casesinpregnantwomen).

An association between Zika virus infection and fetal microcephaly,as well as other birth defects,was first reported in the current outbreak in October 2015.The prevalence of birth defects potentially related to Zika virus infection was reported to be 3 per 1000 live birth in an birth cohort of nearly 1million births in 2016.

Data from the US Zika Pregnancy Registry found that 10% of pregnancies with laboratory-confirmed infection resulted in fetuses/infants with birth defects.This figure increases to 15% when restricting the analysis to the first trimester.

This report covered cases reported in US states only.A more robust study of completed pregnancies in women with laboratory evidence of Zika virus infection in US territories found approximately 1 in 20 (5%)fetuses or infants had a possible Zika-associated birth defect.When the analysis was restricted to confirmed infection in the first trimester,the rate increased to 1 in 12(8%) An association between Zika virus infection and GBS was first reported in the current outbreak in July 2015.Current evidence estimates the incidence of GBS to be 24 cases per 100,000 persons infected with Zika.GBS has not reported in children.

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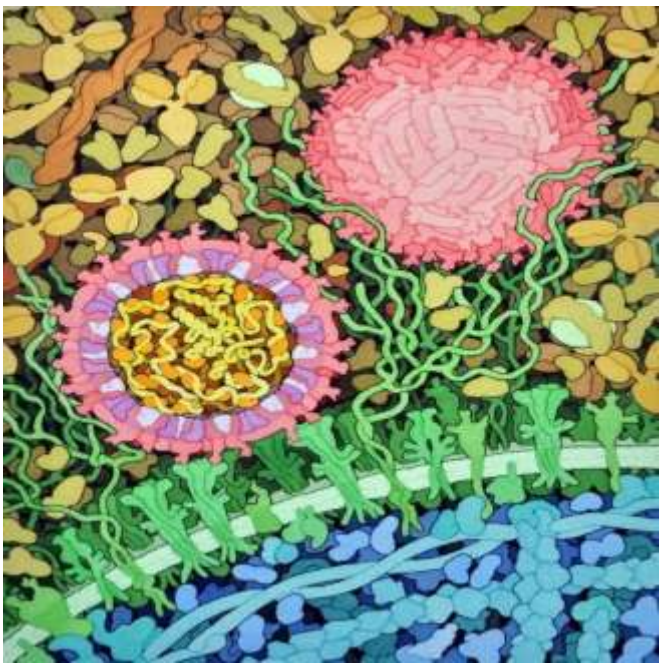
2. Virology



Zika virus belongs to the family Flaviviridae family and the genus Flavivirus, thus is related to the dengue, yellow fever, Japanese encephalitis, and West Nile viruses. Like other flaviviruses, Zika virus is enveloped and icosahedral and has a nonsegmented, single-stranded, 10-kilobase, positive-sense RNA genome. It is most closely related to the Spondweni virus and is one of the two known viruses in the Spondweni virus clade Cross-section of Zika virus, showing the viral envelope composed of envelope proteins (red) and membrane proteins (purple) embedded in the lipid membrane (white): The capsid proteins(orange) are shown interacting with the RNA genome (yellow) at the center of the virus.

A positive-sense RNA genome can be directly translated into viral proteins. As in other flaviviruses, such as the similarly sized West Nile virus, the RNA genome encodes seven nonstructural proteins and three structural proteins. One of the structural proteins encapsulates the virus. This protein is the flavivirus envelope glycoprotein, that binds to the endosomal membrane of the host cell to initiate endocytosis. The RNA genome formsa nucleocapsid along with copies of the 12-kDa capsid protein. The nucleocapsid, in turn, is enveloped within a host-derived membrane modified with two viral glycoproteins. Viral genome replication depends on the making of double-stranded RNA from the single-stranded, positive-sense RNA (ssRNA(+)) genome followed by transcription and replication to provide viral mRNAs and new ssRNA(+) genomes.] A longitudinal study shows that 6 hours after cells are infected with Zika virus, the vacuoles and mitochondria in the cells begin to swell. This swelling becomes so severe, it results in cell death, also known as paraptosis. This form of programmed cell death requires gene expression. IFITM3 is a trans-membrane protein in a cell that is able to protect it from viral infection by blocking virus attachment. Cells are most susceptible to Zika infection when levels of IFITM3 are low. Once the cell has been infected, the virus restructures the endoplasmic reticulum, forming the large vacuoles, resulting in cell death.

There are two Zika lineages: the African lineage and the Asian lineage.Phylogenetic studies indicate that the virus spreading in the Americas is 89% identical to African genotypes, butis most closely related to the Asian strain that circulated in French Polynesia during the 2013–2014 outbreak. The Asian strain appears to have first evolved around 1928]

3. ETIOLOGY

Zika virus is a single - stranded RNA virus of the Flaviviridae family (genusflavivirus), and is related to the dengue, yellow fever, west Nile, and Japanese encephalitis viruses. Transmission to humans is primarily through the bite of an infected

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Aedes species mosquito. It is most commonly transmitted by the A aegypti species which lives in tropical regions, but can also be carried by A albopictus which lives in temperate regions. Nonvector transmission events in utero, sexual, and transfusion transmission have also been reported.

Transmission via platelet transfusion has been reported in brazil. Infection has been reported in a small series of hepatic and renal transplant recipients, and infection with Zika was strongly suspected in a pediatric patient who developed Guillain - Barre syndrome after Zika virus RNA has been detected in body fluid other than blood and semen, including amniotic fluid, CSF, urine, Saliva, Vaginal secretions, and, ocular fluids; however, transmission via these body fluids has not yet been fully elucidated. The virus may persists for up to 80 days in the blood, and persists in the blood longer than plasma. The virus has been detected in the genital tract of an infected women, which may have implications for vertical transmission. It has also been detected in fetaltissue.

Occupational exposure in healthcare personnel is possible via a percutaneous injury, or direct contact of mucous membrane with blood, tissue or other body fluids that are infectious. Theoretically, the viruses mat be transmitted through blood transfusions or organ donations, although to date there are no reports of this type of transmission; there are numerous reports of Zika transmissions through sexula contact.

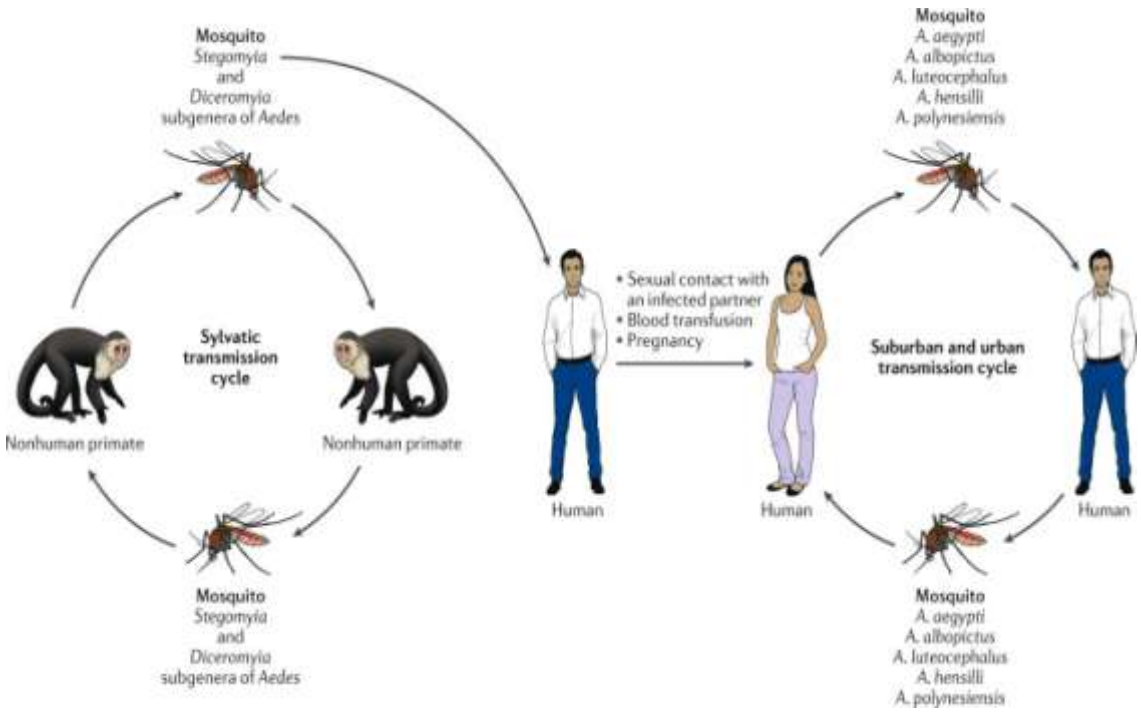
The major risk factor to get the infection are being in areas where infected mosquitoes reside, having unprotected sex with a person who has recently been diagnosed with Zika, and not taking precautions to prevents mosquito bites.

INCUBATION PERIOD

The incubation period for Zika viruses is about three to twelve days, after the mosquito bite. Symptoms may last for about four to seven days. approximately 60% to 80% of infection do not produce any symptoms or signs. the incubation period for the virus infection usually transmitted by sexual contact is under investigation.

4. PATHOGENESIS

Virus life cycle and infection dynamics in humans



Little is known about the life cycle of ZIKV and most of the information is extrapolated from the knowledge of the other closely related flaviviruses. ZIKV is transmitted between humans in the urban cycle through the bite of female Aedes spp. mosquitoes. The virus is acquired by the mosquito during a blood meal, and upon replication in the body of the arthropod, it reaches

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the salivary gland and is injected atthe subsequent meal into the skin of the new host The human skin at the site of inoculation thus represents the first site of viral replication, and human primary dermal fibroblasts, epidermal keratinocytes and immature dendritic cells have been demonstrated to be permissive to ZIKV infection and replication. From the skin the virus spreads to the draining lymph node, where it is amplified, resulting in viraemia and haematogenous dissemination to peripheral tissues and visceral organs. There are few cell types for which ZIKV tropism has been proven so far.

In humans, ZIKV RNA is detectable in blood typically within the first 10 days after infection (i.e. during the first 3–5 days after the onset of symptoms), with viral load peaks occurring at the onset of symptoms In the blood, the virus appears to be cell- associated, since viral load is higher in whole blood than in plasma and serum.Viraemia is typically low titre (about 1000–10 000 ZIKV RNA copies/mL); however, high level(up to ~107–109 copies/mL) and/or prolonged viraemia may occur During the first weeks post-infection, the virus is excreted at relatively high load in urine, saliva and other bodily fluids consistent with a systemic infection. Viral shedding in saliva and urine has been reported also for other flaviviruses, while a peculiar feature of ZIKV isthe tropism for testicular tissue and excretion in semen even for months after clearance from blood The mechanisms of infection and the cellular reservoir for ZIKV in the testis are unknown.

Following infection, an antibody- and cell-mediated immune response is induced. Specific IgM antibodies against ZIKV have been estimated to appear at 9days after infection i.e. approximately 4–7 days after symptom onset, followed by the appearance of IgG antibodies after 2–3 days. IgM antibodies against flaviviruses are usually detectable for 2–3 months, but may also persist for over 1 year, while IgG antibodies usually remain detectable for months or years and probably confer lifelong protection

5. SYMPTOMS

An estimated three out off our people infected with Zika virus do not have symptoms at all.In symptomatic patients,Zika virus generally causes a mild illness that lasts from2 to 7 days.The incubation period is between 3 and 12days.Serious complications from zika virus infection are uncommon.The most common symptoms include:

- Itching/pruritis(verycommon)
- non-purulent conjunctivitis
- muscle or joint pains(quitecommon)
- headache(inabouthalfofcases)
- mildfever(inonlyaminorityofcases)
- Lower backpain
- Retro-orbitalpain

ZIKA VIRUS LABOROTORY TESTING

Zika virus has been detected in whole blood(alsoserumandplasma),urine,cerebrospinal fluid,amnioticfluid,semen,vaginalfluids and

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saliva.There is accumulating evidence that Zika virus is present in urine,blood or saliva.

Types required. Nucleic acid testing: Within 0-7 days of onset of symptoms,Zika virus infection can often be diagnosed by detecting Zika virus RNA in blood by performing nucleic acid testing(NAT). Within 0-10 days of onset of symptoms,urine should also be collected for zika virus RNA testing using NAT. Serological testing Serological testing within 0-7 days of symptom onset could result in a "falsenegative"result as the antibody response may not yet have developed.As Zika virus-specific IgM and IgG typically develop toward the end of the first week of illness,blood samples are recommended to be collected between 7 days and 12 weeks post symptom onset for Zika virus-specific IgM and IgG serologicaltesting.

Blood samples are suitable only for Zika-specific IgG testing.Samples taken after days post symptom onset should also be tested for other flaviviruses(e.g.Dengue virus and Yellow Fever virus)to out rule cross reactivity between Zika and serological assay for other flaviviruses.Chikungunya serological testing will be performed based upon relevant travel history,as the clinicalpresentation is similiar that of Zikavirus infection.

6. TREATMENT

- There is no specific medicine or vaccine for Zika virus.
- Treat the symptoms
- Get plenty of rest.
- Drink fluids to prevent dehydration.
- Take medicine such as acetaminophen (Tylenol®) to reduce fever and pain.
- Do not take aspirin or other non-steroidal anti-inflammatory drugs (NSAIDS) like ibuprofen until dengue can be ruled out to reduce the risk of bleeding.
- If you are taking medicine for another medical condition or if you are pregnant, talk to your doctor or other healthcare provider before taking additional medication.

Zika virus Transmission

Through mosquito bites

Zika virus is transmitted to people primarily through the bite of an infected Aedes species mosquito (Ae. aegypti and Ae. albopictus). These are the same mosquitoes that spread dengue and chikungunya viruses.

These mosquitoes typically lay eggs in or near standing water in things like buckets, bowls, animal dishes, flower pots, and vases. They prefer to bite people, and live indoors and outdoors near people.

Mosquitoes that spread chikungunya, dengue, and Zika bite during the day and night. A mosquito gets infected with a virus when it bites an infected person during the period of time when the virus can be found in the person's blood, typically only through thefirst week of infection.Infected mosquitoes can then spread the virus to other peoplethrough bites.

From mother to child

A pregnant woman can pass Zika virus to her fetus during pregnancy. Zika is a cause of microcephaly and other severe fetal brain defects. We are studying the full range of other potential health problems that Zika virus infection during pregnancy may cause. A pregnant woman already infected with Zika virus can pass the virus to her fetus during the pregnancy or around the time of birth.

Zika virus has been found in breast milk. Possible Zika virus infections have been identified in breastfeeding babies, but Zika virus transmission through breast milk has not been confirmed. Additionally, we do not yet know the long-term effects of Zika virus on young infants infected after birth. Because current evidence suggests that the benefits of breastfeeding outweigh the risk of Zika virus spreading through breast milk,CDC continues to encourage mothers to breastfeed, even if they were infected or livedin or traveled to an area with risk of Zika. CDC continues to study Zika virus and the ways it can spread and will update recommendations as new information becomes available.

Through sex

Zika can be passed through sex from a person who has Zika to his or her partners. Zikacan be passed through sex, even if the infected person does not have symptoms at the time. Learn how to protect yourself during sex.

It can be passed from a person with Zika before their symptoms start, while they have symptoms, and after their symptoms end.

Though not well documented, the virus may also be passed by a person who carries the virus but never develops symptoms.

Studies are underway to find out how long Zika stays in the semen and vaginal fluids of people who have Zika, and how long it can be passed to sex partners. We know that Zika can remain in semen longer than in other body fluids, including vaginal fluids, urine, and blood.

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Through blood transfusion

To the date, there have not been any confirmed blood transfusion transmission cases in theUnited States.

There have been multiple reports of possible blood transfusion transmission cases in Brazil. During the French Polynesian outbreak, 2.8% of blood donors tested positive for Zika and in previous outbreaks, the virus has been found in blood donors.

Through laboratory and healthcare setting exposure

There are reports of laboratory acquired Zika virus infections, although the route of transmission was not clearly established in all cases.

To date, no cases of Zika virus transmission in healthcare settings have been identified in the United States. Recommendations are available for healthcare providers to help prevent exposure to Zika virus in healthcare settings.

Risks

Anyone who lives in or travels to an area with risk of Zika and has not already been infected with Zika virus can get it from mosquito bites. Once a person has been infected, he or she is likely to be protected from future infections.

7. FOLLOW-UP CARE

The long-term prognosis for infants with congenital Zika virus infection is currently unknown. CDC's infant guidance includes recommendations for testing infants for congenital Zika infection and clinical management recommendations for infants with evidence of Zika virus infection, both with and without apparent birth defects, to ensure careful screening and monitoring of infant development. For infants with congenital Zika virus infection, care is focused on diagnosing and managing conditions that are present andaddressing problems as they arise.

Overall, families and caregivers of infants with congenital Zika virus infection will require ongoing psychosocial assessment and support. As a critical component of patient care and to facilitate early identification of developmental delays, families should be empowered to be active participants in their child's monitoring and care.

Follow-Up Care for Infants Born to Women with Possible Zika Virus Exposure during Pregnancy

Infants with birth defects consistent with congenital Zika syndrome (e.g., microcephaly, intracranial calcifications or other brain or eye abnormalities) who are born to mothers withpossible Zika virus exposure during pregnancy (regardless of maternal test results) require a multidisciplinary team and established medical home to facilitate the coordination of care. Follow-up care for these infants include the following:

A standard evaluation with routine preventive pediatric care and immunizations at each subsequent well-child visit

Additional eye exams should be as recommended by ophthalmologists

Referral for automated auditory brainstem response (ABR) testing by 1 month, if infant passed the newborn hearing screen using only the otoacoustic emissions (OAE) method

Referral to specialists for management of clinical abnormalities.

Infants without birth defects consistent with congenital Zika syndrome but who were born to mothers with laboratory evidence of possible Zika virus infection during pregnancy should receive the following care:

A standard evaluation with routine preventive pediatric care (including growth parameters) and immunizations at each subsequent well-child visit

Additional eye exams should be as recommended by ophthalmologists

Referral for automated auditory brainstem response (ABR) testing by 1 month, if infant passed the newborn hearing screen using only the otoacoustic emissions (OAE) method

Refer to specialists for any signs associated with congenital Zika virus infection (e.g., impaired visual acuity/function, hearing problems, developmental delay, delay of head growth)

For infants in this group who test positive for Zika virus infection, healthcare providers should follow recommendations for infants with clinical findings even in the absence of clinically apparent abnormalities.

For infants in this group who have adequate laboratory testing but without laboratory evidence of congenital infection and a normal clinical evaluation, congenital Zika virus infection is unlikely. Healthcare providers should continue routine pediatric care but remain alert for any new findings of possible congenital Zika virus infection.

Infants without birth defects consistent with congenital Zika syndrome but who were born to mothers with possible Zika virus exposure but without laboratory evidence of possible Zika virus infection during pregnancy should receive the following care:

A standard evaluation with routine preventive

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pediatric care and immunizations at each subsequent well-child visit

Further evaluation beyond the initial evaluation and preventive care is not routinely indicated unless abnormalities are noted at any time. If findings are identified, referral to appropriate specialists should occur and the infant should receive further evaluation, including testing and evaluation for congenital Zika virus infection.

8. PREVENTION

There is no vaccine to prevent Zika. The best way to prevent diseases spread by mosquitoes is to protect yourself and your family from mosquito bites and from getting Zika through sex..

Here's how:

- Wear long-sleeved shirts and long pants
- Stay in places with air conditioning and window and door screens to keep mosquitoes outside.
- Take steps to control mosquitoes inside and outside your home
- Treat your clothing and gear with permethrin or buy pre-treated items.
- Use Environmental Protection Agency (EPA)-registered insect repellents. Always follow the product label instructions.
- When used as directed, these insect repellents are proven safe and effective even forpregnant and breastfeeding women.
- Do not use insect repellents on babies younger than 2 months old.
- Mosquito netting can be used to cover babies younger than 2 months old in carriers, strollers, or cribs to protect them from mosquito bites.
- Do not use products containing oil of lemon eucalyptus or para-menthane-diol on children younger than 3 years old.
- Sleep under a mosquito bed net if air conditioned or screened rooms are not available orif sleeping outdoors.
- Prevent sexual transmission of Zika by using condoms or not having sex.

CONCLUSION

Together with Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS), Zika virus infection qualifies as a "newly emerging" infectious disease, with the potential to cause serious public health issues. Unlike the other "newly emerging" infections which can lead to severe morbidity and mortality in infected adults or pediatric hosts, Zika infection does not pose a significant threat to infected adults and its risk is more due to the potential to cause fetal abnormalities, provided that the infection occurs during pregnancy.

Indeed, among the four recent PHEIC declarations by WHO (i.e. 2009 Swine flu declaration, 2014 Polio and Ebola declarations and 2016 Zika virus declaration), Zika is unique in the sense that it is a member of the TORCH group of infections; i.e. the group of pathogens with the ability to lead to congenital infections/anomalies.

This might influence both disease prevention and management strategies as well as raising ethical and sociological issues. Thus, increased awareness of the medical community together with improvements in vector control and disease surveillance systems are of utmost importance for controlling any potential Zika virus-related threats in different countries.

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