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〔Mini Review〕

Need-to-know basics about Zika virus infection for dental professionals

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Abstract

Zika virus (ZIKV) infection, which spreads through the bite of an infected mosquito (*Aedes* species), is a global public health problem. Although about 80% of patients remain asymptomatic, infected individuals demonstrate common features such as fever, cutaneous rash, arthralgia, and conjunctivitis. ZIKV is known to be associated with neurological complications, such as microcephaly and Guillain–Barre syndrome. The virus spreads through contact with blood, semen, and vaginal fluids. However, it has been detected in many other human body fluids, including urine, amniotic fluid, breast milk, saliva, cerebrospinal fluid, and cervical mucous. As dental professionals frequently come in contact with saliva and blood, it is imperative that they protect themselves from ZIKV-infected patients and instruct them to avoid the transmission of this virus. In addition, saliva can be used as a diagnostic tool for ZIKV infection. A saliva-based test may prove effective, and dental professionals might be expected to play a key role in the future surveillance and detection of the virus.

Introduction

Zika virus (ZIKV) infection is an emerging pandemic viral disease that has been declared as a public health emergency by the World Health Organization (WHO, 2016). It has raised public concern from all around the globe due to the widespread nature of the infection at an alarming pace.

ZIKV infection is a mosquito-borne disease, which spreads primarily through the bite of an infected mosquito (*Aedes* species) (Fauci & Morens, 2016). The other routes of spread include intrauterine transmission, sexual contact, and blood transfusion (Besnard et al., 2014 ; D'Ortenzio et al., 2016 ; Musso et al, 2014). Although the majority of patients show mild symptoms such as fever, conjunctivitis, cutaneous rash, and arthralgia, this infection often causes birth defects, growth and developmental anomalies, including microcephaly, and some motor neurological manifestations in adults (Cao-Lormeau et al., 2016). Due to the increasing number of cases of microcephaly associated with ZIKV, it can significantly affect the dental and general health of the patient. Since the ZIKV might be transmitted through body fluids including blood and saliva (Musso et al, 2014 ; Musso et al., 2015), dental practitioners should be made aware of the risk of infection. Saliva obtained from patients may be useful for a diagnostic approach. Reports about the involvement of ZIKV infection in dentistry are limited. Therefore, this review aimed to demonstrate and discuss the importance of awareness about ZIKV infection in the dental setting.

Epidemiology

ZIKV originated from the Zika forest in Uganda and was isolated from a rhesus monkey in 1947 (Dick, 1953). The first human case of ZIKV was detected in 1952, after which it spread to other geographical regions such as Egypt (Smithburn KC et al., 1954), East Africa (Smithburn KC, 1952), Nigeria (Macnamara FN, 1954), India (Smithburn KC

et al, 1954), Japan (Taira M et al., 2017), Thailand (Pond WL, 1963), Vietnam (Smithburn KC et al, 1954), the Philippines (Hammon et al., 1958) and Malaysia (Smithburn KC et al, 1954), affecting more than 80 countries worldwide. During the outbreak of ZIKV in 2007 on several islands in the state of Yap, 5000 people were affected, while the outbreak in French Polynesia in 2013–2014 resulted in a total of 32,000 people who were affected by the virus (Schuler-Faccini et al., 2016). Thousands of babies were born with devastating birth defects after their mothers were infected in pregnancy. In 2015, a sudden increase in the cases of microcephaly in infants and the association of the Guillain–Barre syndrome was reported in Brazil (Schuler-Faccini et al., 2016). By 2016, almost 4300 cases of microcephaly had been recorded (Victora et al., 2016). However, by 2017, the number of infections had decreased owing to the several precautions that were taken into consideration. The WHO counted 12 outbreaks worldwide in 2015, 22 in 2016, and just one in early 2017. The Centers for Disease Control (CDC) and Prevention in the United States of America (US) recently deactivated its emergency response system for ZIKV that was launched in January 2016 (WHO, 2017). Although the number of infected cases has decreased, it is not completely controlled and can result in another outbreak in future. A revised guideline has been adapted by the European Centre for Disease Prevention and Control (ECDC) and WHO as a country-wise classification (WHO, 2017).

Mode of transmission of ZIKV

ZIKV is mainly transmitted by the bite of the *Aedes* mosquito (Marchette et al., 1969). Transplacental transmission or transmission during delivery by an infected mother has also been reported (Besnard et al., 2014). Zika viral RNA has been detected in breast milk, which raises the concern of potential transmission by breastfeeding (Besnard et al., 2014). Sexual transmission was reported in a few instances (Musso et al., 2015 ; Fig.1). The Zika viral RNA has also been detected in urine at higher loads, which may hint at possibility of a person-to-person transmission route ; in addition, it indicates the possibility of testing the urine after the early symptoms of viraemia have subsided (Fauci & Morens, 2016). The virus has been found to be transmitted via blood transfusion (Musso et al., 2014). A recent study indicated that the viral RNA was detected in blood samples from asymptomatic donors, and the number of positive results was unexpectedly high (3% ; Musso et al., 2014). On February 16, 2016, the Food and Drug Administration in the US recommended the deferral of blood donations from individuals who had traveled to areas with active ZIKV transmission, were potentially exposed to the virus, or had experienced a confirmed ZIKV infection (Zuanazzi et al., 2017).

Signs, symptoms, and complications

ZIKV is characterized as an asymptomatic or mild dengue-like disease with fever, headache, myalgia, muscle and joint aches, conjunctivitis, and maculopapular rashes, with an incubation period of 3 to 12 days (Zuanazzi et al., 2017 ; CDC, 2016 ; Fig.1). Only about 20% of cases are symptomatic (CDC, 2016). There is no specific anti-viral treatment for this condition, and the management of symptoms may include the use of analgesics and antipyretics. However, over the period of 60 years of observation, ZIKV has not been reported to cause hemorrhagic fever or death (Fauci & Morens, 2016). The most significant public health concern is the recently confirmed association between ZIKV infection during pregnancy and microcephaly or other severe fetal brain defects (Schuler-Faccini et al., 2016). The relationship between ZIKV infection and microcephaly has long been suspected, based on the detection of Zika viral RNA in mothers and in amniotic fluid samples from fetuses, which indicates the potential of this virus to infect fetuses. Incomplete viral autophagy, centrosome abnormalities, and chromosomal instability have been observed in Zika-infected cells. Notably, no other flavivirus has been associated with teratogenic effects in humans. Guillain-Barré syndrome, an autoimmune disease causing acute or subacute flaccid paralysis, has also been found to be associated with ZIKV infection (Cao-Lormeau et al., 2016 ; Zuanazzi D et al., 2017 ; CDC, 2016).

Detection of ZIKV in saliva

Although the transmission of ZIKV through saliva has not been substantiated so far, its presence in saliva has been detected (Musso et al., 2015). Exposure to the saliva of infected patients can be considered as a possible, yet unlikely, route of infection. The virus has been recovered in cell cultures from the saliva of infected patients and has also been detected in saliva from patients with Zika fever, especially during the acute phase of the disease (Musso et al., 2015 ; Bonaldo et al., 2016). ZIKV peptides can be detected in the

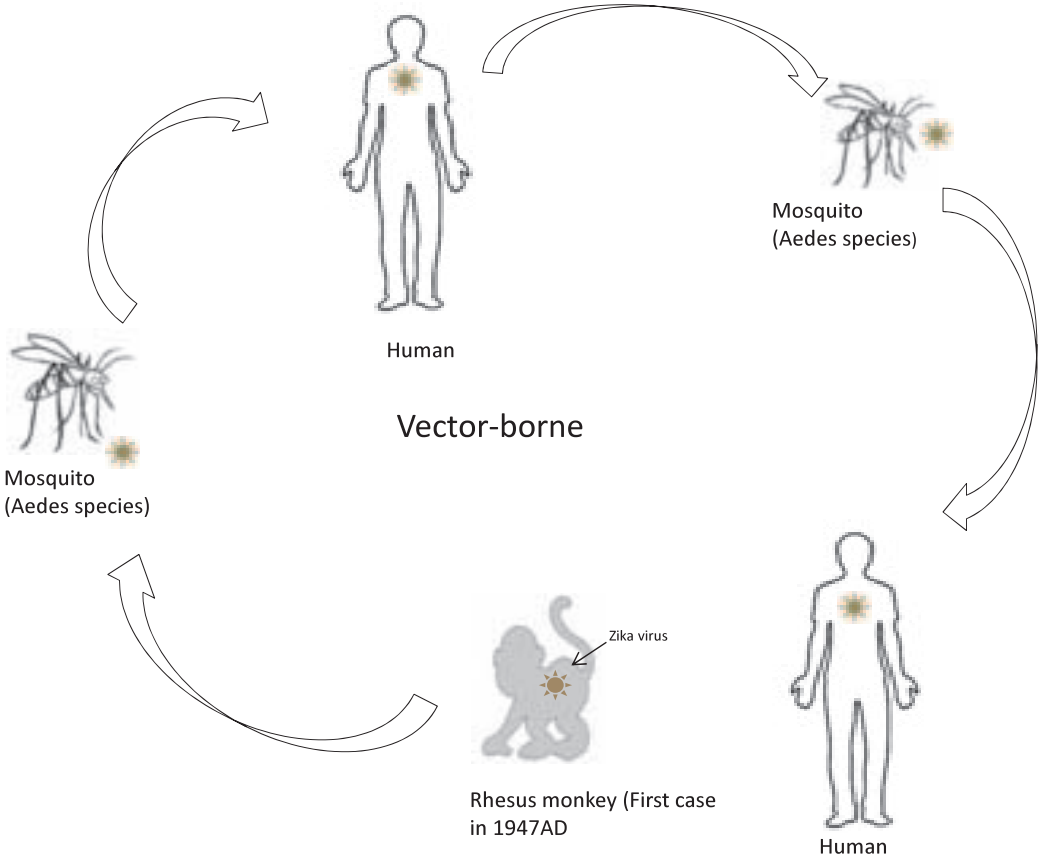
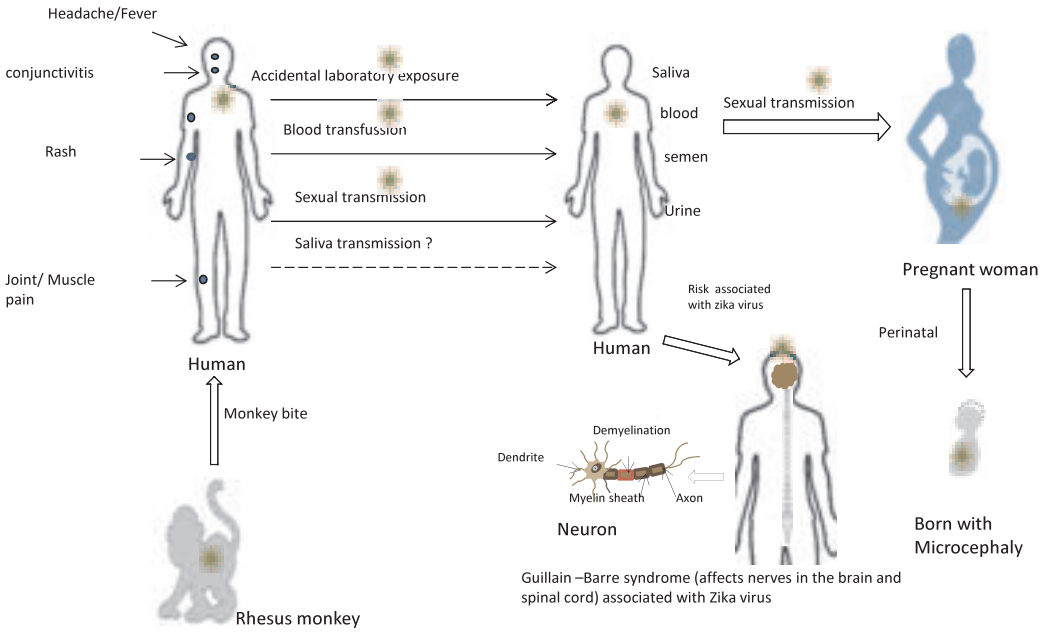


Figure 1. Mode of transmission of Zika virus

a. Vector borne transmission. Zika virus is transmitted by the bite of the *Aedes* mosquito. When a healthy mosquito bites a Zika infected patient/monkey, it sucks the virus−infected blood. The virus replicates inside mosquito gut, and is then transmitted to a healthy human when it is bitten by the carrier mosquito.



Non vector-borne

b. Non−vector born transmission. Human−to−human transmission through sexual transmission, perinatal and blood transfusion. Monkey to human transmission through the bite of a Zika−infected monkey. The clinical features include headache/fever, conjunctivitis, and muscle/joint pain. Complications such as microcephaly in new−born babies and Guillain−Barre syndrome in adults may occur.

saliva of patients previously diagnosed with Zika fever, indicating that ZIKV may be latent in the salivary gland (Balthesen et al., 1994). Viruses such as herpes simplex virus types 1 and 2 (HSV1, HSV2) and cytomegalovirus (CMV) can be transmitted through saliva (Barzon et al., 2016). Saliva may play a critical role in the human-to-human transmission of ZIKV. Nevertheless, to the best of our knowledge, there is no information about the transmission of Zika via saliva in the literature. Thus, further studies are needed to determine this phenomenon.

From another point of view, saliva can be used as a diagnostic sample for ZIKV infection (Bonaldo et al., 2016). In fact, it has been already used as a source for ZIKV diagnostics when the first cases were reported during the 2014 outbreak in French Polynesia (Barzon et al., 2016). Recently, many reports confirmed that viral load (as determined by RNA levels) is significantly higher in saliva than in plasma ; ZIKV RNA could be detected for a much longer period in saliva than in plasma (Barzon et al., 2016). Moreover, it was detected in the saliva of the patient even during the convalescent phase (Balthesen et al., 1994). A saliva-based test may be effective, and dental professionals may play a key role in the future surveillance and detection of this virus (Balthesen et al., 1994).

Oral manifestations in patients with ZIKV infection

Several dental problems such as delay in the eruption of deciduous dentition, hypersalivation, higher chances of caries development, and the presence of enamel alterations consistent with dental hypoplasia have been observed in children with microcephaly associated with prenatal ZIKV infection (Cavalcanti, 2017). Therefore, it is essential for the dental professional to provide proper attention to the patient during dental care and adequate information regarding oral hygiene and eating habits to the caretakers and family. Severe neurological complications associated with Guillain-Barre syndrome have been described in postnatal ZIKV infections (Passi et al., 2017). Patients with Guillain-Barre syndrome present with muscle weakness caused due to the damage of the peripheral nervous system by the immune system. Facial muscle weakness with disorders of muscle movement and swallowing are often observed in these patients (Rajabally et al., 2012). Nonetheless, no specific orofacial manifestations have been reported so far. A recent paper reported the presence of hyperemia and petichae in the hard palate of a patient with ZIKV. Since ZIKV are neurotropic viruses, which are capable of infecting and replicating in neural cells (Brasil et al., 2016), they may persist in the latent state and are reactivated at a later period, as in the cases of HSV that cause recurrent ulcerations in the oral mucosa. ZIKV could invade endothelial cells, fibroblasts, and keratinocytes via receptors in the oral mucosal tissues (Brasil et al., 2016), causing specific oral pathogenic conditions. However, further investigations are needed to determine the presence of oral specific manifestations.

Role of dental professionals for ZIKV infection control

No appropriate treatment strategy or vaccine for ZIKV is available thus far. Protection of dentists from the infection and avoiding the transmission of this condition to other patients is crucial. Both saliva and blood are known to be the routes for transmission of ZIKV infection during dental procedures. Active participation of dental professionals for the screening of ZIKV infected patients and their adherence to infection control guidelines are of utmost importance in controlling the dissemination of ZIKV infection. It is advisable for dental professionals, who encounter suspected patients with ZIKV infections, to report them to the local health department for further investigations (CDC, 2016).

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