Thai Journal of Obstetrics and Gynaecology
January 2016, Vol. 24, pp. 2-5

EDITORIAL

Zika Virus Infection in Pregnancy

Vorapong Phupong, M.D.*

** Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand*

ABSTRACT

Zika virus is a mosquito-borne virus. It is transmitted to humans by infected Aedes spp. mosquitoes. Non-vector-borne transmission routes of Zika virus include blood transfusion-related transmission, sexual transmission, transplacental transmission, and perinatal transmission. Zika virus infection is asymptomatic in most cases. If symptoms occur, symptoms are generally mild and self-limited. Signs and symptoms, diagnosis and treatment of Zika virus infection in pregnant women are similar to non-pregnant women. Zika virus infection in pregnancy is associated with fetal structural brain abnormalities and microcephaly. The treatments are symptomatic and supportive. Prevention from mosquito bites is the best way to prevent Zika virus infection. Treatment of Zika virus infection in pregnant women is similar to non-pregnant women. However, obstetricians should be aware of congenital Zika virus infection when pregnant women infected with Zika virus especially in the first trimester.

Correspondence to: *Vorapong Phupong, M.D., Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand. Email: Vorapong.P@chula.ac.th*

Zika virus is a mosquito-borne virus. Zika virus is arbovirus (arthropod-borne virus) and is a member of family Flaviviridae, genus Flavivirus. It was discovered in 1947 from a rhesus monkey in the Zika forest in Uganda[1]. Zika virus is transmitted to humans by infected Aedes spp. mosquitoes such as Aedes egypti, Aedes africanus, Aedes albopictus[2, 3]. Zika virus is endemic to Africa and Southeast Asia[4]. Before 2007, few cases of human Zika virus infection had been reported. In 2007, an epidemic of Zika virus infection in humans occurred in Yap, Federated States of Micronesia, in the Pacific region[5]. In 2015, there was a dramatic increase in reports of Zika virus infection especially in pregnant women in Brazil[6]. Zika virus infection was also reported in travelers returning from Africa[7] or Southeast Asia[8].

Transmission

Zika virus is mainly transmitted by mosquitoes like other flaviviruses. Aedes (Stegomyia) mosquitoes appear to be the most important vector for Zika virus transmission. Non-vector-borne transmission routes of Zika virus have been reported. These include blood transfusion-related transmission[9], sexual transmission[7], transplacental transmission[10, 11], and perinatal transmission[12].

Signs and symptoms

The incubation period of flaviviruses, such as West Nile virus and dengue virus, is considered to be

from 3 to 7 days (range = 3–14 days)[13].

Zika virus infection is asymptomatic in most cases[5]. If symptoms occur, symptoms are generally mild and self-limited. Symptoms are similar to dengue and chikungunya[14]. It is characterized by mild fever (37.8°C–38.5°C), arthralgia, notably of small joints of hands and feet, myalgia, headache, retroorbital pain, conjunctivitis, and cutaneous maculopapular rash[5]. Rash has been reported 3–5 days after the febrile phase[7, 15]. A non-purulent conjunctivitis is a unique feature of Zika virus infections, and was found in 55% of cases[5].

Zika virus infection can be misdiagnosed during the acute viremic phase because of nonspecific influenza-like signs and symptoms. Hemorrhagic signs have not been reported in Zika virus infected patients[5, 7, 15]. However neurologic complications, including Guillain-Barré syndrome, have been reported[16].

Zika virus infection in pregnancy

Signs and symptoms, diagnosis and treatment of Zika virus infection in pregnant women are similar to non-pregnant women. Zika virus can cross the placenta and has been detected using RT-PCR analysis of amniotic fluid of pregnancies affected with fetal structural brain abnormalities and microcephaly[11], and Zika virus has been isolated post-mortem from the brain of a fetus with microcephaly[10]. These findings suggest a strong neurotropism of Zika virus. It is probable that Zika virus infection poses the greatest risk in early pregnancy, although effects throughout pregnancy cannot be excluded[17].

Diagnosis

Diagnostic tests for Zika virus infection include molecular test: reverse transcription PCR (RT-PCR) tests on acute-phase serum samples, which detect viral RNA, and other serologic tests: immunoglobulin M (IgM) ELISA and plaque reduction neutralization test (PRNT) to detect specific antibody against Zika virus in serum[4]. RT-PCR tests can be conducted on samples obtained less than 10 days after illness onset[18].

An ELISA has been developed to detect specific IgM antibody to Zika virus[18]. Cross-reactive antibodies results in sera were demonstrated with other Flavivirus: dengue virus, yellow fever, Japanese encephalitis, Murray Valley encephalitis, and West Nile viruses[4]. This makes the difficult in diagnosis from antibodies result. Thus, it requires confirmation by neutralization assays. IgM was detectable as early as 3 days after onset of illness in some persons[18]. Neutralizing antibody developed as early as 5 days after illness onset[18]. In general, diagnostic testing for flavivirus infections should include an acute-phase serum sample collected as early as possible after onset of illness and a second sample collected 2 to 3 weeks after the first[4].

Zika virus RNA is detectable in urine by real-time RT-PCR at a higher load and with a longer duration than in serum. Zika virus RNA was detected ≤ 15 days (range 10 days to > 20 days) after onset of symptoms, which was > 7 days after it was not detected in serum samples. Thus, urine might be useful for confirmation of Zika virus infection because virus was detected at higher titers and for a longer period in urine samples than in serum samples[19].

Recommended management of pregnant women

Pregnant women should postpone travel to areas with ongoing local Zika virus transmission. Pregnant women and their partners should also be aware of the risk for Zika virus infection through unprotected sex with an infected male partner, and carefully follow CDC interim guidelines for preventing sexual transmission of Zika virus infection[20, 21].

Pregnant women who have a clinical illness consistent with Zika virus disease during or within 2 weeks of travel to areas with ongoing Zika virus transmission should have Zika virus testing. Zika virus testing of maternal serum includes RT-PCR testing for symptomatic patients with onset of symptoms during the previous week; IgM and PRNT testing should be performed on specimens collected ≥4 days after onset of symptoms[22, 23].

In pregnant women with Zika virus exposure and symptoms, positive Flavivirus serology or proven Zika

virus infection, or in those with exposure and/or symptoms but who have not had positive serology results, referral for detailed ultrasound assessment is appropriate. Measurement of head circumference (HC) to detect microcephaly (HC less than the third percentile for gestational age) and careful assessment of a fetal brain abnormality (such as intracranial calcifications or ventriculomegaly) should be performed[24].

Treatment

Most cases of Zika virus infections are self-limiting and without significant sequelae[5, 25]. There is no specific antiviral treatment for Zika virus infection. The treatments are symptomatic and supportive.

Prevention

There is no available vaccine to prevent Zika virus infection. When travelling to an affected area of Zika virus, prevention from mosquito bites is the best way to prevent Zika virus infection. Mosquito-bite prevention includes using air conditioning or window and door screens when indoors, wearing long sleeves and pants, using permethrin-treated clothing and gear, and using insect repellents[26].

References

1. Dick GW, Kitchen SF, Haddow AJ. Zika virus. I. Isolations and serological specificity. Trans R Soc Trop Med Hyg 1952;46(5):509-20.
2. Haddow AJ, Williams MC, Woodall JP, Simpson DI, Goma LK. Twelve Isolations of Zika Virus from Aedes (Stegomyia) Africanus (Theobald) Taken in and above a Uganda Forest. Bull World Health Organ 1964;31:57-69.
3. Wong PS, Li MZ, Chong CS, Ng LC, Tan CH. Aedes (Stegomyia) albopictus (Skuse): a potential vector of Zika virus in Singapore. PLoS Negl Trop Dis 2013;7(8):e2348.
4. Hayes EB. Zika virus outside Africa. Emerg Infect Dis 2009;15(9):1347-50.
5. Duffy MR, Chen TH, Hancock WT, Powers AM, Kool JL, Lanciotti RS, et al. Zika virus outbreak on Yap Island, Federated States of Micronesia. N Engl J Med 2009;360(24):2536-43.
6. Brasil P, Pereira JP, Jr., Raja Gabaglia C, Damasceno L, Wakimoto M, Ribeiro Nogueira RM, et al. Zika Virus Infection in Pregnant Women in Rio de Janeiro - Preliminary Report. N Engl J Med 2016.
7. Foy BD, Kobylinski KC, Chilson Foy JL, Blitvich BJ, Travassos da Rosa A, Haddow AD, et al. Probable non-vector-borne transmission of Zika virus, Colorado, USA. Emerg Infect Dis 2011;17(5):880-2.
8. Shinohara K, Kutsuna S, Takasaki T, Moi ML, Ikeda M, Kotaki A, et al. Zika fever imported from Thailand to Japan, and diagnosed by PCR in the urines. J Travel Med 2016;23(1).
9. Marano G, Pupella S, Vaglio S, Liumbruno GM, Grazzini G. Zika virus and the never-ending story of emerging pathogens and transfusion medicine. Blood Transfus 2015:1-6.
10. Mlakar J, Korva M, Tul N, Popovic M, Poljsak-Prijatelj M, Mraz J, et al. Zika Virus Associated with Microcephaly. N Engl J Med 2016.
11. Oliveira Melo AS, Malinger G, Ximenes R, Szejnfeld PO, Alves Sampaio S, Bispo de Filippis AM. Zika virus intrauterine infection causes fetal brain abnormality and microcephaly: tip of the iceberg? Ultrasound Obstet Gynecol 2016;47(1):6-7.
12. Besnard M, Lastere S, Teissier A, Cao-Lormeau V, Musso D. Evidence of perinatal transmission of Zika virus, French Polynesia, December 2013 and February 2014. Euro Surveill 2014;19(13).
13. Rudolph KE, Lessler J, Moloney RM, Kmush B, Cummings DA. Incubation periods of mosquito-borne viral infections: a systematic review. Am J Trop Med Hyg 2014;90(5):882-91.
14. Phupong V. Dengue fever in pregnancy: a case report. BMC Pregnancy Childbirth 2001;1(1):7.
15. Kwong JC, Druce JD, Leder K. Zika virus infection acquired during brief travel to Indonesia. Am J Trop Med Hyg 2013;89(3):516-7.
16. Oehler E, Watrin L, Larre P, Leparc-Goffart I, Lastere S, Valour F, et al. Zika virus infection complicated by Guillain-Barre syndrome--case report, French Polynesia, December 2013. Euro Surveill 2014;19(9).
17. Schuler-Faccini L, Ribeiro EM, Feitosa IM, Horovitz DD, Cavalcanti DP, Pessoa A, et al. Possible Association Between Zika Virus Infection and Microcephaly - Brazil, 2015. MMWR Morb Mortal Wkly Rep 2016;65(3):59-62.
18. Lanciotti RS, Kosoy OL, Laven JJ, Velez JO, Lambert AJ, Johnson AJ, et al. Genetic and serologic properties of Zika virus associated with an epidemic, Yap State, Micronesia, 2007. Emerg Infect Dis 2008;14(8):1232-9.
19. Gourinat AC, O'Connor O, Calvez E, Goarant C, Dupont-Rouzeyrol M. Detection of Zika virus in urine. Emerg Infect Dis 2015;21(1):84-6.
20. Meaney-Delman D, Hills SL, Williams C, Galang RR, Iyengar P, Hennenfent AK, et al. Zika Virus Infection Among U.S. Pregnant Travelers - August 2015-February 2016. MMWR Morb Mortal Wkly Rep 2016;65(8):211-4.
21. Oster AM, Brooks JT, Stryker JE, Kachur RE, Mead P, Pesik NT, et al. Interim Guidelines for Prevention of Sexual Transmission of Zika Virus - United States, 2016. MMWR Morb Mortal Wkly Rep 2016;65(5):120-1.
22. Petersen EE, Staples JE, Meaney-Delman D, Fischer M, Ellington SR, Callaghan WM, et al. Interim Guidelines for Pregnant Women During a Zika Virus Outbreak - United States, 2016. MMWR Morb Mortal Wkly Rep 2016;65(2):30-3.

23. Oduyebo T, Petersen EE, Rasmussen SA, Mead PS, Meaney-Delman D, Renquist CM, et al. Update: Interim Guidelines for Health Care Providers Caring for Pregnant Women and Women of Reproductive Age with Possible Zika Virus Exposure - United States, 2016. MMWR Morb Mortal Wkly Rep 2016;65(5):122-7.
24. Papageorghiou AT, Thilaganathan B, Bilardo CM, Ngu A, Malinger G, Herrera M, et al. ISUOG Interim Guidance on ultrasound for Zika virus infection in pregnancy: information for healthcare professionals. Ultrasound Obstet Gynecol 2016.
25. Heang V, Yasuda CY, Sovann L, Haddow AD, Travassos da Rosa AP, Tesh RB, et al. Zika virus infection, Cambodia, 2010. Emerg Infect Dis 2012;18(2):349-51.
26. Staples JE, Dziuban EJ, Fischer M, Cragan JD, Rasmussen SA, Cannon MJ, et al. Interim Guidelines for the Evaluation and Testing of Infants with Possible Congenital Zika Virus Infection - United States, 2016. MMWR Morb Mortal Wkly Rep 2016;65(3):63-7.