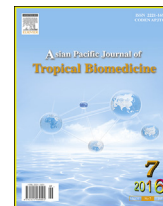


Contents lists available at [ScienceDirect](http://www.sciencedirect.com)

Asian Pacific Journal of Tropical Biomedicine

journal homepage: www.elsevier.com/locate/apjtbMini review <http://dx.doi.org/10.1016/j.apjtb.2016.03.014>

Emerging Zika virus infection: What should we know?

Viroj Wiwanitkit^{*1,2,3,4,5}¹Hainan Medical University, Haikou, China²Faculty of Medicine, University of Nis, Nis, Serbia³Joseph Ayobabalola University, Ikeji-Arakeji, Nigeria⁴Dr. DY Patil Medical University, Pune, India⁵Surin Rajabhat University, Surin, Thailand

ARTICLE INFO

Article history:

Received 22 Feb 2016

Accepted 20 Mar 2016

Available online 24 May 2016

Keywords:

Zika virus

Infection

Emerging

Epidemic

ABSTRACT

Zika virus infection is a new emerging viral disease that becomes the present public health threat. At present, this infection can be seen in several countries. The clinical presentation of this infection is a dengue-like illness. Nevertheless, the new information shows that the disease can be sexually transmitted and transplacentally transmitted. In addition, the recent evidence from the recent epidemic in South America shows that the infection in pregnancy can cause neonatal neurological defect. In this short review, the author summarizes and presents interesting data on clinical features of this new emerging infection.

1. Introduction

New emerging infection is the big topic in medicine in the present. There are many new problematic emerging infections. Zika virus infection is a new problematic emerging disease. It is classified as a new dengue-like viral infection [1,2]. As a new emerging disease, the knowledge on this viral disease is limited. At present, this infection can be seen worldwide in many countries and becomes the global concern. There are several questions in biomedicine on this new infection. The international concern on this disease is presently raised. World Health Organization has already declared Zika virus infection as a new emerging disease to be managed [3]. The clinical presentation of this infection is a dengue-like illness. Nevertheless, the new information shows that the disease can be sexually transmitted and transplacentally transmitted. In addition, the recent evidence from the recent epidemic in South

America shows that the infection in pregnancy can cause neonatal neurological defect. In this short review, the author summarizes and presents interesting data on clinical features of this new emerging infection.

2. Discovery of the Zika virus

In fact, Zika virus is not a new virus. It has been discovered and mentioned for more than 50 years [4–6]. Similar to many viruses, Zika virus was firstly discovered and reported in Africa. It was firstly detected in Zika forest area of Uganda. Monkey is believed to be the primary original host of this virus. After that, it is sporadically mentioned. Until the present time, the virus can be seen worldwide and becomes the new international health issue.

3. Virology of Zika virus

Zika virus is considered a flavivirus [5,7]. In 1956, Bearcroft firstly reported the pathogenicity of this virus in human volunteers [8]. In 2007, Kuno and Chang reported the full length sequence and genetic characteristics of the Zika virus [9]. The “open reading frames with respect to gene sizes, cleavage sites, potential glycosylation sites, distribution of

*Corresponding author: Professor Viroj Wiwanitkit, Wiwanitkit House, Bangkok, Bangkok 10160, Thailand.

Tel: +66 24132436

E-mail: vwiroj@yahoo.com

Peer review under responsibility of Hainan Medical University. The journal implements double-blind peer review practiced by specially invited international editorial board members.

cysteine residues, and unique motifs” are reported by Kuno and Chang [9]. According to PubMed nucleotide database, some records on complete genome of Zika virus isolates can be seen. The good examples are “Zika virus isolate SSABR1, complete genome” (10648 bp linear RNA; accession: KU707826.1) and “Zika virus strain Natal RGN, complete genome” (10808 bp linear RNA; accession: KU527068.1).

4. Epidemiology of Zika virus infection

At first, Zika virus epidemiology is limitedly studied in Africa. The well-known pioneer report is from Nigeria. Fagbami studied sero-epidemiology in Oyo State, Nigeria in 1950s and revealed “a high prevalence of antibodies to Zika and three other flaviviruses used. The percentages of positive sera were as follows: Zika (31%), yellow fever (50%), West Nile (46%), and Wesselsbron (59%) [6]”. Fagbami also mentioned that “the percentage of neutralizing antibodies to other flaviviruses in Zika virus immune sera was 81% to dengue type 1, 58% to yellow fever, 7% to Wesselsbron, 6% to West Nile and 3% to Uganda S [6].” After the pioneer report from Nigeria, there are some sporadic reports on epidemiology of Zika virus worldwide. Iosos *et al.* noted that since the “first identified in Uganda in 1947, few human cases were reported until 2007, when a Zika outbreak occurred in Yap, Micronesia, even though Zika virus activity had been reported in Africa and in Asia through virological surveillance and entomological studies [10].” Until present, the virus can be seen in several tropical countries and it can also be seen in returning travelers to non-tropical areas [11,12]. However, the big concern is the recent epidemics in South America [13]. The reports on neonatal problem in neonate born to infected mother leads to the present urgent concern on the public health threat of Zika virus at present [14].

5. How Zika virus can be transmitted

As already noted, Zika virus infection is a dengue-like infection. It is firstly classified as an arboviral disease. The *Aedes* mosquito is believed to be the main mosquito vector.

Aedes aegypti, the same as dengue virus, is the main vector for transmission of Zika virus [15]. In addition to transmission by mosquito vector, there are also evidences of other modes of transmission of Zika virus. The transplacental transmission is confirmed and it is the present global concern on the infected newborn with neurological problems [13]. Nevertheless, the newest concern is on the possibility of sexual transmission of Zika virus [16]. Musso *et al.* reported that “During a Zika virus outbreak in French Polynesia, a patient in Tahiti sought treatment for hematospermia, and Zika virus was isolated from his semen. Zika virus transmission by sexual intercourse has been previously suspected [16].” Oster *et al.* also recently mentioned guidelines for prevention of sexual transmission of Zika virus [17]. Another important concern is on the possibility of transmission by blood transfusion [18]. Musso *et al.* noted that “42 (3%) of 1505 blood donors, although asymptomatic at the time of blood donation, were found positive for Zika virus by PCR [18]” and concluded that their “results serve to alert blood safety authorities about the risk of post-transfusion Zika fever [18].” Aubry *et al.* also mentioned the detected seropositivity among donated blood samples in the endemic

area of Zika virus [19]. Hence, Zika virus becomes the present hot issue in transfusion medicine.

6. Clinical features of Zika virus infection

Clinically, Zika virus infection is a virus infection that causes acute febrile illness. The clinical problem is not different from dengue virus infection [1,2]. To diagnose and differentiate Zika virus infection from dengue virus infection, specific PCR test is required [1,2]. Focusing on the other interesting clinical problem, neurological disease in affected infants born to infected mother is the big problem. At present, this problem is widely noted. Petersen *et al.* [20] reported that “outbreak in Brazil, has also been associated with a significant rise in the number of babies born with microcephaly and neurological disorders, and has been declared a global emergency by the World Health Organization.” In fact, the neurological problem can be seen in general, non-infant cases but it is the simple neurological problem as seen in dengue, not the congenital neurological defect [10]. In addition, it is confirmed that Zika virus infection can result in Guillain–Barre syndrome [21], which is believed to be due to the immunopathology process [18,22,23].

Focusing on the interesting neurological defect in infant with congenital Zika virus infection, micrencephaly was observed, with almost complete agyria, hydrocephalus, and multifocal cortical dystrophic calcifications with focal inflammation [24], which are the pathological findings in autopsy cases [24,25]. In addition, the problem of optic nerve is also found in the affected infants with microcephaly [26,27]. Ventura *et al.* studied the infected infants born to infected mother in Brazil during recent epidemics and found that there were many ophthalmological problems [27]. Direct viral invasion to the brain tissue is confirmed [24,25]. The similar underlying pathogenesis as described for brain involvement is proposed. Nevertheless, in infected mothers, Ventura *et al.* reported that at the time of examination, no ophthalmological abnormalities were identified in the mothers and they did not report ocular symptoms during pregnancy [27].

7. Management of Zika virus infection

As a new emerging viral infection, there is still no specific antiviral drug and vaccine for treatment and prevention of Zika virus infection [28]. To manage the cases, the similar means used in dengue are usually used. In fact, some cases might be asymptomatic or have a few clinical problems and can be successfully managed [1,2]. Indeed, some cases might also be misdiagnosed as dengue and already completely managed as dengue [1,2].

For prevention of disease, the simple concept for prevention of arboviral infection, avoidance of mosquito bite is suggested. For the vaccine, it is still under research and development [29]. Since the pregnant subject is considered risk for giving birth to infected infant with birth defects, it is suggested that special prevention and care has to be given to this population [30]. Also, it is suggested for special preparedness in infection control for the mass gatherings events [21,31].

8. Conclusion

There are several interesting clinical problems in Zika virus infection that lead to the present global concern on this new

emerging viral infection. Since it is very difficult to diagnose and highly similar to dengue, the incorrect diagnosis is possible. The concern of the practitioner is needed. Use of proper diagnostic tool and prompt management are the key factors for success in management of disease.

Conflict of interest statement

I declare that I have no conflict of interest.

References

- [1] Joob B, Wiwanitkit V. Zika virus infection and dengue: a new problem in diagnosis in a dengue-endemic area. *Ann Trop Med Public Health* 2015; **8**: 145-6.
- [2] Wiwanitkit S, Wiwanitkit V. Acute viral hemorrhage disease: a summary on new viruses. *J Acute Dis* 2015; **4**: 277-9.
- [3] Gulland A. Zika virus is a global public health emergency, declares WHO. *BMJ* 2016; **352**: i657.
- [4] Weinbren MP, Williams MC. Zika virus: further isolations in the Zika area, and some studies on the strains isolated. *Trans R Soc Trop Med Hyg* 1958; **52**(3): 263-8.
- [5] Dick GW, Kitchen SF, Haddock AJ. Zika virus. I. Isolations and serological specificity. *Trans R Soc Trop Med Hyg* 1952; **46**(5): 509-20.
- [6] Fagbami AH. Zika virus infections in Nigeria: virological and seroepidemiological investigations in Oyo State. *J Hyg (Lond)* 1979; **83**(2): 213-9.
- [7] Dick GW. Zika virus. II. Pathogenicity and physical properties. *Trans R Soc Trop Med Hyg* 1952; **46**(5): 521-34.
- [8] Bearcroft WG. Zika virus infection experimentally induced in a human volunteer. *Trans R Soc Trop Med Hyg* 1956; **50**(5): 442-8.
- [9] Kuno G, Chang GJ. Full-length sequencing and genomic characterization of Bagaza, Kedougou, and Zika viruses. *Arch Virol* 2007; **152**(4): 687-96.
- [10] Iosifidis S, Mallet HP, Leparac Goffart I, Gauthier V, Cardoso T, Herida M. Current Zika virus epidemiology and recent epidemics. *Med Mal Infect* 2014; **44**(7): 302-7.
- [11] Summers DJ, Acosta RW, Acosta AM. Zika virus in an American recreational traveler. *J Travel Med* 2015; **22**(5): 338-40.
- [12] Fonseca K, Meatherall B, Zarra D, Drebot M, MacDonald J, Pabbaraju K, et al. First case of Zika virus infection in a returning Canadian traveler. *Am J Trop Med Hyg* 2014; **91**(5): 1035-8.
- [13] Zika virus outbreaks in the Americas. *Wkly Epidemiol Rec* 2015; **90**(45): 609-10.
- [14] McCarthy M. Zika virus outbreak prompts US to issue travel alert to pregnant women. *BMJ* 2016; **352**: i306.
- [15] Thomas DL, Sharp TM, Torres J, Armstrong PA, Munoz-Jordan J, Ryff KR, et al. Local transmission of Zika virus – Puerto Rico, November 23, 2015–January 28, 2016. *MMWR Morb Mortal Wkly Rep* 2016; **65**(6): 154-8.
- [16] Musso D, Roche C, Robin E, Nhan T, Teissier A, Cao-Lormeau VM. Potential sexual transmission of Zika virus. *Emerg Infect Dis* 2015; **21**(2): 359-61.
- [17] 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.
- [18] Musso D, Nhan T, Robin E, Roche C, Bierlaire D, Zisou K, et al. Potential for Zika virus transmission through blood transfusion demonstrated during an outbreak in French Polynesia, November 2013 to February 2014. *Euro Surveill* 2014; **19**(14): 20761.
- [19] Aubry M, Finke J, Teissier A, Roche C, Brout J, Paulous S, et al. Sero-prevalence of arboviruses among blood donors in French Polynesia, 2011–2013. *Int J Infect Dis* 2015; **41**: 11-2.
- [20] Petersen E, Wilson ME, Touch S, McCloskey B, Mwaba P, Bates M, et al. Rapid spread of Zika virus in the Americas – implications for public health preparedness for mass gatherings at the 2016 Brazil Olympic Games. *Int J Infect Dis* 2016; **44**: 11-5.
- [21] Oehler E, Watrin L, Larre P, Leparac-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): 20720.
- [22] Gatherer D, Kohl A. Zika virus: a previously slow pandemic spreads rapidly through the Americas. *J Gen Virol* 2016; **97**: 269-73.
- [23] Pinto Junior VL, Luz K, Parreira R, Ferrinho P. [Zika virus: a review to clinicians]. *Acta Med Port* 2015; **28**(6): 760-5. Portuguese.
- [24] Mlakar J, Korva M, Tul N, Popović M, Poljšak-Prijatelj M, Mraz J, et al. Zika virus associated with microcephaly. *N Engl J Med* 2016; **374**: 951-8.
- [25] 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.
- [26] de Paula Freitas B, de Oliveira Dias JR, Prazeres J, Sacramento GA, Ko AI, Maia M, et al. Ocular findings in infants with microcephaly associated with presumed Zika virus congenital infection in Salvador, Brazil. *JAMA Ophthalmol* 2016; <http://dx.doi.org/10.1001/jamaophthalmol.2016.0267>.
- [27] Ventura CV, Maia M, Ventura BV, Linden VV, Araújo EB, Ramos RC, et al. Ophthalmological findings in infants with microcephaly and presumable intra-uterus Zika virus infection. *Arg Bras Oftalmol* 2016; **79**(1): 1-3.
- [28] Valeyrie-Allanore L. [What's new in clinical dermatology?]. *Ann Dermatol Venerol* 2015; **142**: S1-7. French.
- [29] O'Dowd A. UK is safe from Zika virus and is helping towards a vaccine, MPs hear. *BMJ* 2016; **352**: i692.
- [30] Meaney-Delman D, Rasmussen SA, Staples JE, Oduyebo T, Ellington SR, Petersen EE, et al. Zika virus and pregnancy: what obstetric health care providers need to know. *Obstet Gynecol* 2016; **127**: 642-8.
- [31] Elachola H, Gozzer E, Zhuo J, Memish ZA. A crucial time for public health preparedness: Zika virus and the 2016 Olympics, Umrah, and Hajj. *Lancet* 2016; **387**(10019): 630-2.