

## Zika Virus Infection in Assisted Reproduction; Current Scenario and Future Prospects

Aamir Javed<sup>1\*</sup>, Ashim Roy<sup>1</sup>, Muralidhar, T. S.<sup>1</sup> & Ajay Kumar<sup>2</sup>

<sup>1</sup>Centre for R and D in Life Sciences, Biotechnology Research Laboratory, Dayananda Sagar Institutions, S.M. Hills, Kumaraswamy Layout, Bangalore, India

<sup>2</sup>Department of Biotechnology Faculty of Engineering & Technology, MR International University, Faridabad, India

\***Correspondence to:** Dr. Aamir Javed, Centre for R and D in Life Sciences, Biotechnology Research Laboratory, Dayananda Sagar Institutions, S.M. Hills, Kumaraswamy Layout, Bangalore, India.

### Copyright

© 2018 Dr. Aamir Javed, *et al.* This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Received: 04 May 2018

Published: 25 May 2018

**Keywords:** *Assisted Reproduction; Egg Donation; IVF; Sperm Donation; Zika Virus*

### Abstract

#### Rationale of Review

It is well known that Zika infection can be sexually transmitted; there is a potential hazard for malady transmission at a few phases of assisted reproduction. Such plausibility represents a genuine test to couples tightening infertility with regenerative innovations. Here, we talk about what is known with respect to Zika infection contamination concerning sexual transmission and associate this information with later suggestions in the domain of infertility treatment.

### Current Verdicts

Zika infection can be transmitted from infected men and ladies through vaginal, oral or butt-centric intercourse. Zika infection RNA has been distinguished in blood, semen, cervical bodily fluid and vaginal liquid. Presently, the Places for Ailment Control prescribes that contaminated men hold up a half year, and infected ladies two months, before endeavoring pregnancy. Conceptive tissue contributors should hold up a half year before giving an example.

### Outline

Additionally investigation of Zika infection transmission in various conceptive tissues and foundation of approved testing strategies for viral malady transmissibility are direly required. Conceptive technologists need to build up screening, testing and research center conventions meant to lessen the danger of Zika infection transmission amid helped propagation.

## Introduction

Dissimilar to numerous mosquito-borne diseases, the Zika infection has as of late developed as a sexually transmitted contamination with exceptionally critical outcomes in the setting of pregnancy [1]. As viral contaminations turn out to be more across the board, the pregnancy-related dangers associated with Zika infection disease may posture issues for expanding quantities of patients craving treatment of infertility. Since the Zika infection can be sexually transmitted, there are special transmission chances that must be considered amid the procedure of helped proliferation. Viral transmission represents a genuine test to conceptive endocrinologists to guarantee the security of infertility patients. This survey will basically look at what is known in regards to Zika infection contamination concerning sexual transmission and to connect this learning with late recommendations for patients and suppliers engaged with infertility treatment [2].

## Epidemiology

In the course of recent years, ZIKV has been watched flowing among African and Asian populaces [1], yet has gotten close to nothing consideration from mainstream researchers. The main instances of human disease were recognized through the identification of killing antibodies against ZIKV in ~13% of people in Uganda in 1952 [2]. The infection was then found in three patients with jaundice in African countries [3]. For a large portion of a century, ZIKV was restricted to sporadic contaminations disseminated all through a lot of East and West Africa and Southeast Asia [4]. ZIKV rose outside Asia and Africa without precedent for 2007. In this manner, the primary known scourge happened on Yap Island in Micronesia in the Pacific Sea zone, where 180 associated cases were accounted for out with a populace of 7380 tenants [5]. The greater part of the announced cases was considerate, and there was no cover focal sensory system (CNS) impedance, conceivable fetopathy or results for pregnancy. The extent of contaminated individuals in the populace was evaluated to be 73%, exhibiting a huge number, ~80%, of asymptomatic or paucisymptomatic cases. Just sporadic instances of ZIKV were connected in the vicinity of 2007 and 2013. In a year expansive plague was accounted for in French Polynesia, with an expected 19000 symptomatic diseases [6].

## Clinical Diagnosis

The most usually detailed manifestations amid ZIKV disease are a maculopapular rash (75%), fever (66%), arthralgia (66%), myalgia (52%) and conjunctival hyperaemia (at first depicted as conjunctivitis in the principal distributions) (42%) [7]. Different side effects incorporate cerebral pain (14%), retro-orbital agony (4-39%), oedema (8%), pruritus (8%), gastrointestinal side effects (8-10%), asthenia (0-5%), lymphadenopathy (0-5%), ear, nose and throat side effects (1.5%) and discombobulation (0.5%). These side effects are normally mellow and keep going for 2-7 days. In this manner, while the basic clinical picture is very like different arbovirus contaminations, for example, dengue, a few indications are more suggestive of ZIKV, for example, conjunctival hyperaemia, rash and the recurrence of the afebrile frame. Amid the French Polynesia pandemic, atypical appearances of neurological entanglements were accounted for, and these were optionally affirmed amid the plague in the Americas. GBS was the most much of the time detailed CNS disability, be that as it may, a few others have been accounted for, for example, meningoencephalitis, encephalopathy, encephalitis, intense myelitis and optic neuropathy [8].

## Review of the Zika Infection Pandemic

In February 2016, the WHO pronounced the Zika infection pandemic as a general wellbeing crisis of between national concerns [9]. At first limited to few reasonably disconnected pestilences in French Polynesia in two years and the Easter Islands in Chile in 2014, the infection has quickly and generally spread eastbound. Since 2015, an aggregate of 49 nations and domains have encountered new episodes [10]. Starting at 28 December 2016 in the Assembled States, 214 privately procured mosquito-borne cases, 4574 travel-related cases, and one research center gained case and 38 sexually transmitted cases have been accounted for [11].

## Fetal Anomalies and Unfavorable Results Related with Zika Contamination

The most impeding effect of Zika infection contamination happens in pregnancy. Innate Zika contamination is related with fetal microcephaly and other unfriendly results, for example, brainstem and cerebellar hypoplasia, deferred myelination, extreme ventriculomegaly, net calcification of the mind parenchyma, lissencephaly, cerebrum decay, visual imperfections, scalp rugae and joint contractures [12]. The long-standing wellbeing sway for singular infants conceived with inherent Zika contamination, and additionally the general wellbeing effect of expanding number of children with Zika disease, warrants an endless supply of transmission, especially inside the domain of human proliferation [13].

## Zika Infection Within the World of Propagation: What We Know Almost Chance of Disease and Infectivity in Different Regenerative Tissues

Although Zika contamination essentially happens through the chomp of contaminated *Aedes* species mosquitos, transmission has too been found to happen vertically, from mother to child and on a level plane, by means of verbal,butt centric and vaginal intercut and through blood transfusions. The resulting discourse will audit the potential vectors for viral transmission that seem influence helped reproduction [14].

## Male Gamete

Zika infection by means of sperm amid helped proliferation. The Zika infection is an individual from the Flaviviridae family; hence, a few investigations of disease by means of hepatitis C infection, likewise a Flavivirus, can furnish knowledge into hypothetical dangers related with Zika in sperm tests utilized for intra-uterine insemination of fruitless couples, cryopreservation or in vitro. Extrapolation from thinks about archiving the transmission of human papilloma infection, hepatitis C infection and cytomegalovirus through infected sperm demonstrate that viral trans-mission by means of sperm is conceivable [15]. As of now, there is no industrially accessible strategy by which to test contamination with or infectivity of Zika infection in sperm tests. In particular, it isn't right now known whether sperm washing will diminish the likelihood of disease. Additionally contemplates are justified to decide the potential dangers of contamination by means of sperm, given that techniques expected to wash these examples could possibly be adequate to counteract transmission amid IVF [16].

## Semen

Reports of patients known to have transmitted Zika malady to sexual accomplices have archived positive culture of irresistible Zika infection inside those people's semen, involving this liquid in the transmission of the infection [17]. Supporting this hypothesis, Zika RNA has been identified in semen following determination of recognize capable RNA in the blood, and without Zika RNA distinguished in the pee. These discoveries additionally suggest that the Zika infection may have a tropism for the male conceptive tract and this may clarify sexual transmission of Zika [18]. Extra concerns with respect to a potential long-term effect of Zika infection contamination on male generation emerged from murine models evil presence starting the infection specially recreated in both the mind and the testis, the last of which could hypothetically bring about sexual transmission in the long haul [19]. The day and age in which Zika infection can be sexually transmitted after starting disease of the man isn't unequivocally known and in truth shows up to some degree variable in light of ebb and flow data. Reports to date have recorded sexual trans-mission 41 days after beginning of side effects [20]. Viral culture the best quality level for distinguishing replicative/irresistible infection - has affirmed nearness of irresistible infection up to 69 days after side effect beginning [21], while Zika viral RNA has been identified in human semen a half year after indication beginning [22]. These information show that viral trans-mission through semen could happen for no less than 69 days, and potentially a half year after malady beginning. Be that as it may, invert transcriptase RT-PCR to distinguish viral RNA isn't approved in semen. All the more vitally, it is obscure whether the nearness of viral RNA alone is prescient of infectivity, and the potential time course of viral shedding of irresistible infection in semen over these more drawn out periods isn't known [23]. Additionally investigation of these components is expected to outline sane screening and testing procedures to anticipate viral transmissibility by means of semen.

## Oocytes and Embryo Development

It is realized that the two oocytes and embryo development can possibly wind up infected with certain infections. In particular, viral diseases of oocytes with human papilloma infection and of developing lives with cow-like herpes infection have been archived [24].

This infers Zika infection could conceivably contaminate human oocytes as well as developing lives. In any case, it isn't known whether human disease at the season of oocyte or sperm gift could bring about the gift of infected examples [25]. In considering an infection all the more firmly identified with Zika, there is information showing that oocytes got from transporters of hepatitis C may not convey hepatitis C viral contaminations. In particular, investigations of ladies with hepatitis C experiencing egg recovery archived high rates of infection in follicular liquid which was later imperceptible in developing life culture media following washing of oocytes [26]. As of now, there is no institutionalized or considered strategy to test human oocytes or embryo development got from ladies who experienced oocyte recovery during a period of a positive serum Zika PCR result. Subsequently, there is no confirmation to recommend that testing of developing lives for Zika disease through trophoblast biopsy is useful or would give helpful data [27].

### **Infertile Females and Gestational Bearers**

Zika infection has been recorded to be transmitted through the placenta as right on time as the primary trimester, and in addition by transmission amid conveyance [28]. Creature models of Zika contamination amid pregnancy give additional confirmation to infection transmission through the placenta, with antagonistic impacts on placental blood stream and additionally on the fetal cerebrum by means of direct immunization of those tissues [29]. Besides, one late case additionally covered transmission from an influenced female to her male accomplice [30]. All in all, these information demonstrate that viral transmission could happen amid the way toward accomplishing pregnancy (i.e. through the cervix/vagina) or later through the gestational transporter's blood or the placenta [31]. Consequently, the two ladies experiencing infertility treatment and gestational transporters are in danger for transmission of Zika infection either assumption or postconception, on the off chance that they have been or are infected with Zika Transmission by means of the cervix or vagina is most pertinent to previously established inclination strategies, including intrauterine insemination, oocyte recovery, developing life exchange or coordinated intercourse after controlled ovarian hyperstimulation. Zika infection RNA has been distinguished in genital, endocervical and cervical bodily fluid of a symptomatic lady 3 days after side effect beginning, and a cervical swab stayed positive 11 days after indications started [32]. Such discoveries have suggestions for sexual transmission to male partners and in addition vertical transmission to babies - a capacity known to be related with hepatitis C infection [33]. It isn't yet known whether the infection can be transmitted past 11 days after manifestations or after an asymptomatic disease. Following origination, maternal transmission by means of blood or placenta is conceivable. Zika RNA can be distinguished in the blood of nonpregnant ladies 11-13 days after indication beginning and for up to 10 weeks in pregnant ladies [34]. In any case, it isn't yet con-solidified that blood-borne vertical transmission is conceivable, and, assuming this is the case, by what instrument.

### **Suggestions for Advising Patients in the Conceptive Endocrinology and Infertility Center**

The Places for Sickness Control (CDC), Sustenance and Medication Organization (FDA) and WHO have all as of late distributed rules for all people of regenerative age with respect to safe sexual practices to stay away from intrinsic Zika contamination.

Such recommendations depend on gives an account of time from potential or known contamination with Zika to sickness transmission. In September 2016, the American Culture of Regenerative Drug (ASRM) distributed an arrangement of rules adjusted from joined CDC, FDA and WHO productions, with a concentration after nurturing patients with infertility [35]. Given the way that asymptomatic people may harbor Zika infection in conceptive tissues, in spite of the fact that not as of now prescribed, the creators recommend that all suppliers watching over patients wanting pregnancy consider screening patients for Zika presentation with a Zika infection survey, and tailor persistent advising in regards to timing of pregnancy in view of those dangers [36].

## General Rules for All Patients Endeavoring Pregnancy

The latest CDC rules prescribe a similar time postponement to pregnancy for people with symptomatic contaminations as they do patients with asymptomatic exposures. In particular, ladies who have ventured out to a territory with Zika infection, had sex with a person with known or conceivable Zika contamination or encountered a symptomatic Zika disease are encouraged to abstain from endeavoring pregnancy until two months after either the last conceivable presentation or side effect beginning [37]. Men in any of the above circumstances are encouraged to defer endeavoring pregnancy with their accomplices until a half year after side effect beginning or last potential introduction [38]. Such rules depend on the abovementioned data on Zika infection RNA identified in regenerative tissues. Couples dwelling in a territory with dynamic transmission of Zika infection ought to be guided in regards to the potential dangers of Zika infection disease in pregnancy. Patients ought to be educated that information respecting DEET use in pregnancy are consoling and there is no known relationship with distortions notwithstanding when utilized as a part of the principal trimester [39]. On the off chance that symptomatic, testing ought to be performed per CDC rules and pregnancy ought to be deferred for a half year (for male contamination) and two months (for female disease) [40]. For asymptomatic people, consideration of getting to be pregnant ought to be individualized and in view of patient equality, age, wellbeing status, qualities and inclinations should manage the choice to endeavor pregnancy and mosquito chomp avoidance ought to be accentuated [41]. For people dwelling in a territory without known Zika transmission, it is prescribed to evade go to zones with dynamic Zika infection transmission [42]. Late information from the US Zika Pregnancy Registry demonstrates that, starting at 30 November 2016, a sum of 32 newborn children and five lost babies have had birth surrenders owing to Zika disease [43]. At last, albeit most instances of sexual transmission of Zika infection answered to date include transmission from a symptomatic individual. Announced an instance of a couple showing for deducibility treatment after movement to the endemic zone of Martinique in which the lady tried positive for Zika RNA by RT-PCR in blood pee and the man tried positive in pee and original plasma [44]. Patients ought to be educated with respect to the likelihood concerning asymptomatic, likely undetected, viral spread amid this day and age, especially in those living in zones of dynamic transmission of Zika by mosquitoes.

## Issues in Regards to Zika Disease Testing

As indicated by ASRM rules, all patients seeking after infertility treatment who have had a potential Zika introduction however are asymptomatic ought to be offered serum testing for viral RNA utilizing RT-PCR, because of the hazard that the nearness of viral RNA in blood may associate with viral nearness in the male or female conceptive tract liquids [45].

Patients ought to be educated that immediate viral RNA testing with RT-PCR can bring about both false negative and false positive outcomes. Testing outside of the season of treatment for infertility does not demonstrate viral irresistible status at the season of treatment. What's more, a negative serum RNA result can't preclude disease in reproductive tissues [45]. In spite of the way that asymptomatic people have been found to spread Zika infection disease, and viral RNA has been distinguished in semen, cervical bodily fluid and vaginal liquid, momentum rules don't suggest testing semen and cervical/vaginal liquids.

## **Suggestions for Safe Practices in ART**

Notwithstanding advising of patients as examined beforehand, helped regenerative care suppliers must think about the inclusion of extra outsiders in the treatment of infertility. In particular, as per FDA rules, givers of sperm, oocytes and embryo organisms must hold up to give until a half year after a known Zika contamination, living arrangement or go to a territory of dynamic infection transmission or sexual experience with a conceivably infected man [46]. Remarkably, proposals for gestational transporters are the same as those for any ladies endeavoring to accomplish infertility [47]. A related issue is that research facility methods inside infertility centers must address the potential for Zika infection transmission amid helped reproductive advancements. The thought of potential chance for Zika disease in beforehand put away examples from possibly Zika contaminated benefactors ought to be resolved [48], and choices and directing ought to be custom fitted properly. In taking care of new examples from conceivably Zika-uncovered contributors, treatment of sperm ought to take after that for sperm gave from HIV-positive benefactors, notwithstanding the way that these have not been demonstrated to counteract Zika transmission. It has been recommended that conventions to keep away from Zika introduction amid the procedure of helped propagation be created [49].

## **Future Prospective**

Despite these dangers, which were maybe particularly undermining in light of the fact that they were ineffectively assessed, general wellbeing and scientific experts have expounded systems and suggestions, to a great extent in view of a preparatory standard, with the underlying point of keeping the danger of ZIKV contamination amid pregnancy. Consequently, putting off any pregnancy designs, particularly in a pandemic region, has been a consensual proposal. In the following couple of years, a noteworthy change will be to absolutely decide the genuine frequencies in people of the distinctive pathogenic possibilities that have been ascribed to ZIKV and their individual outcomes for fertility and progeny. Therefore, the circumstance will keep on rapidly develop. Experts looking after individuals wishing to imagine ought to stay mindful of the progressions concerning pestilence regions, primary screening, demonstrative techniques and proposals in regards to sexuality and multiplication to have the capacity to give satisfactory data to their patients. ART professionals have put resources into advancing information about the pandemic and the outcomes of ZIKA contamination to better control the dangers of the medicalization of origination for the type, as in different settings, for example, a hereditary pathology of one individual from the couple. Thought of dangers to the hatchling includes multidisciplinary choices. Other basic advances will be the improvement of systems and antibodies to stop the spread of the infection and keep its most extreme impacts.

Applicants ZIKA immunizations have demonstrated defensive viability in preclinical examinations did in animal models and a few antibodies have entered clinical trials. This aggregate experience ought to be utilized to better expect reactions to future episodes of irresistible specialists that are transmissible through a few courses.

## **Conclusion**

All in all, the Zika infection plague calls for more stringent screening of patients and other participants in assisted regenerative technology, persistent directing and research center example dealing with. The potential danger of Zika transmission through human conceptive tissues, especially semen, notwithstanding blood and cervical/vaginal tissues, warrants further think about. Similarly, the exact systems of sexual and vertical transmission, and also the ideal testing methods for viral infectivity, remain issues needing research.

## **Acknowledgement**

The authors are extremely thankful to Dr. Hemechandra Sagar (Chairman), Dr. Premchandra Sagar (Vice Chairman), Dr. Krishna Gowda, Director, Dayananda Sagar College of Biological Sciences, Dr. C.D. Sagar Centre for Life Sciences, Bangalore-560078, INDIA, for their colossal guidance.

## **Availability of Data and Materials**

The datasets supporting the conclusions of this article are included within the article.

## **Funding**

This project was a non funded project.

## **Ethics Approval and Consent to Participate**

Not applicable.

## **Consent for Publication**

Not applicable.

## **Competing Interests**

The authors declare that they have no competing interests.



## Bibliography

1. Hayes, E. B. (2009). Zika virus outside Africa. *Emerg Infect Dis.*, *15*(9), 1347-1350.
2. Smithburn, K. C. (1952). Neutralizing antibodies against certain recently isolated viruses in the sera of human beings residing in East Africa. *J Immunol.*, *69*(2), 223-234.
3. Brooks, R. B., Carlos, M. P., Myers, R. A., White, M. G., Bobo-Lenoci, T., *et al.* (2016). Likely Sexual transmission of Zika virus from a man with no symptoms of Infection-Maryland. *Morb Mortal Wkly Rep.*, *65*(34), 915-916.
4. Ming, G. L., Tang, H. & Song, H. (2016). Advances in Zika virus research: stem cell models, challenges, and opportunities. *Cell Stem Cell*, *19*(6), 690-702.
5. Miranda-Filho Dde, B., Martelli, C. M., Ximenes, R. A., Araújo, T. V., Rochas, M. A., *et al.* (2016). Initial description of the presumed congenital Zika syndrome. *Am J Public Health.*, *106*(4), 598-600.
6. Honein, M. A., Dawson, A. L., Petersen, E. E., Jones, A. M., Lee, E. H., *et al.* (2017). Births defects among fetuses and infants in US Women with evidence of possible Zika Virus infection during pregnancy. *JAMA.*, *317*(1), 59-68.
7. Dick, G. W., Kitchen, S. F. & Haddock, A. J. (1952). Zika virus: Isolations and serological specificity. *Trans R Soc Trop Med Hyg.*, *46*(5), 509-520.
8. D'Ortenzio, E., Matheron, S., Yazdanpanah, Y., de Lamballerie, X., Hubert, B., *et al.* (2016). Evidence of sexual transmission of Zika virus. *N Engl J Med.*, *374*(22), 2195-2198.
9. Aubry, M., Teissier, A., Huart, M., Merceron, S., Vanhomwegen, J., *et al.* (2017). Zika virus seroprevalence, French Polynesia, 2014-2015. *Emerg Infect Dis.*, *23*(4), 669-672.
10. Epelboin, L., Boullé, C., Ouar-Epelboin, S., Hanf, M., Dussart, P., *et al.* (2013). Discriminating malaria from dengue fever in endemic areas: clinical and biological criteria, prognostic score and utility of the C-reactive protein: a retrospective matched-pair study in French Guiana. *PLoS Negl Trop Dis.*, *7*(9), e2420.
11. Epelboin, L., Douine, M., Carles, G., Villemant, N., Nacher, M., *et al.* (2016). Zika virus outbreak in Latin America: What are the challenges for French Guiana in April 2016? *Bull SocExot.*, *109*(2), 114-125.
12. Torjesen, I. (2016). Zika Virus outbreaks prompt warnings to pregnant women. *BMJ.*, *352*, i500.
13. Driggers, R. W., Ho, C. Y., Korhonen, E. M., Kuivanen, S., Jääskeläinen, A. J., *et al.* (2016). Zika virus infection with prolonged maternal viremia and fetal brain abnormalities. *N Engl J Med.*, *374*, 2142-2151.

14. Van der Eijk, A. A., Van Genderen, P. J., Verdijk, R. M., Reusken, C. B., Mögling, R., *et al.* (2016). Miscarriage associated with Zika Virus infection. *N Engl J Med.*, 375(10), 1002-1004.
15. Uraki, R., Hwang, J., Jurado, K. A., Householder, S., Yockey, L. J., *et al.* (2017). Zika Virus causes testicular atrophy. *Sci Adv.*, 3(2), e1602899.
16. Brasil, P., Pereira, J. P. Jr., Moreira, M. E., Ribeiro Nogueira, R. M., Damasceno, L., *et al.* (2016). Zika virus infection in pregnant women in Rio de Janeiro. *N Engl J Med.*, 375(24), 2321-2334.
17. Frank, C., Cadar, D., Schlaphof, A., Neddersen, N., Günther, S., Schmidt-Chanasit, J. & Tappe, D. (2016). Sexual transmission of Zika virus in Germany, April 2016. *Euro Surveill.*, 21(23), 30252.
18. Fréour, T., Mirallié, S., Hubert, B., Splingart, C., Barrière, P., *et al.* (2016). Sexual transmission of Zika virus in an entirely asymptomatic couple returning from a Zika epidemic area, France, April 2016. *Euro Surveill.*, 21(23), 30254.
19. Hamer, D. H., Barbre, K. A., Chen, L. H., Grobusch, M. P., Schlagenhaut, P., *et al.* (2017). Travel associated Zika virus disease acquired in the americas through February 2016: a geo sentinel analysis. *Ann Intern Med.*, 166(2), 99-108.
20. Osuna, C. E., Lim, S. Y., Deleage, C., Griffin, B. D., Stein, D., *et al.* (2016). Zika viral dynamics and shedding in rhesus and cynomolgus macaques. *Nat Med.*, 22(12), 1448-1455.
21. Atkinson, B., Thorburn, F., Petridou, C., Bailey, D., Hewson, R., *et al.* (2017). Presence and persistence of Zika virus RNA in semen, United Kingdom, 2016. *Emerg Infect Dis.*, 23(4), 161692.
22. Harrower, J., Kiedrzyński, T., Baker, S., Upton, A., Rahnama, F., *et al.* (2016). Sexual transmission of Zika Virus and persistence in semen, New Zealand, 2016. *Emerg Infect Dis.*, 22(10), 1855-1857.
23. Oehler, E., Watrin, L., Larre, P., Leparc-Goffart, I., Lastere, S., *et al.* (2014). Zika virus infection complicated by Guillain- Barré syndrome—case report, French Polynesia. *Euro Surveill.*, 19(9).
24. Paz-Bailey, G., Rosenberg, E. S., Doyle, K., Munos-Jordan, J., Santiago, G. A., *et al.* (2017). Persistence of Zika virus in body fluids—preliminary report. *N Engl J Med.*, 379(13), 1234-1243.
25. Roa, M. (2016). Zika Virus outbreak: reproductive health and rights in Latin America. *Lancet*, 387(10021), 843.
26. Olson, J. G., Ksiazek, T. G., Suhandiman & Triwibowo. (1981). Zika Virus, a cause of fever in Central Java, Indonesia. *Trans R Soc Trop Med Hyg.*, 75(3), 389-393.
27. Roberts, D. J. & Frosch, M. P. (2016). Zika and histopathology in first trimester infections. *Lancet*, 388(10047), 847-849.

28. Rodriguez-Morales, A. J. (2016). Zika and microcephaly in Latin America: an emerging threat for pregnant travelers? *Travel Med Infect Dis.*, *14*(1), 5-6.
29. Victora, C. G., Schuler-Faccini, L., Matijasevich, A., Ribeiro, E., Pessoa, A. & Barros F. C. (2016). Microcephaly in Brazil: how to interpret reported numbers? *Lancet*, *387*(10019), 621-624.
30. Cuevas, E. L., Tong, V. T., Rozo, N., Valencia, D., Pacheco, O., *et al.* (2016). Preliminary report of microcephaly potentially associated with Zika Virus infection during Pregnancy-Colombia, January-November 2016. *Morb Mortal Wkly Rep.*, *65*(49), 1409-1413.
31. Tang, H., Hammack, C., Ogden, S. C., Wen, Z., Qian, X., *et al.* (2016). Zika Virus infects human cortical neural progenitors and attenuates their growth. *Cell Stem Cell*, *18*(5), 587-590.
32. Meltzer, E., Lustig, Y., Leshem, E., Levy, R., Gottesman, G., *et al.* (2016). Zika virus disease in traveler returning from Vietnam to Israel. *Emerg Infect Dis.*, *22*(8), 1521-1522.
33. Tetro, J. A. (2016). Zika and microcephaly: causation, correlation or coincidence? *Microbes Infect*, *18*(3), 167-168.
34. Ventura, C. V., Maia, M., Ventura, B. V., Linden, V. V., Araújo, E. B., *et al.* (2016). Ophthalmological findings in infants with microcephaly and presumable intra-uterus Zika Virus infection. *Arq Bras Oftalmol.*, *79*(1), 1-3.
35. Zare, M. M., Poretti, A. & Keshavarz, E. (2017). Neuroimaging findings of zika virus infection: emphasis of congenital versus acquired aspects. *Jpn J Radiol.*, *35*(1), 41-42.
36. Penot, P., Brichtler, S., Guilleminot, J., Lascoux-Combe, C., Taulera, O., *et al.* (2017). Infectious Zika Virus in vaginal secretions from an HIV-infected woman, France, August 2016. *Euro Surveill.*, *22*(3), 30444.
37. CitiDogan, A., Wayne, S., Bauer, S., Ogunyemi, D., Kulkarni, S. K., *et al.* (2016). The Zika virus and pregnancy: evidence, management, and prevention. *J Matern Fetal Neonatal Med.*, *30*(4), 386-396.
38. Arsuaga, M., Bujalance, S. G., Díaz-Menéndez, M., Vázquez, A. & Arribas, J. R. (2016). Probable sexual transmission of Zika virus from a vasectomised man. *Lancet Infect Dis.*, *16*(10), 1107.
39. Kwong, J. C., Druce, J. D. & Leder, K. (2013). Zika virus infection acquired during brief travel to Indonesia. *Am J Trop Med Hyg.*, *89*(3), 516-517.
40. Faria, N. R., AzevedoRdo, S., Kraemer, M. U., Souza, R., Cunha, M. S., *et al.* (2016). Zika virus in the Americas: early epidemiological and genetic findings. *Science*, *352*(6283), 345-349.
41. Fréour, T., Mirallié, S., Hubert, B., Splingart, C., Barrière, P., *et al.* (2016). Sexual transmission of Zika virus in an entirely asymptomatic couple returning from a Zika epidemic area, France, April 2016. *Euro Surveill.*, *21*(23), 30254.

42. Froeschl, G., Huber, K., Von Sonnenburg, F., Nothdurft, H. D., Bretzel, G., *et al.* (2017). Long-term kinetics of Zika virus RNA and antibodies in body fluids of a vasectomized traveler returning from Martinique: a case report. *BMC Infect Dis.*, *17*(55), 2123-2139.
43. Chan, J. F., Zhang, A. J., Chan, C. C., Yip, C. C., Mak, W. W., *et al.* (2016). Zika virus infection in Dexamethasone-immunosuppressed mice demonstrating disseminated infection with multi-organ involvement including orchitis effectively treated by recombinant type I Interferons. *E Bio Medicine.*, *14*, 112-122.
44. American Society for Reproductive Medicine. Guidance for Providers Caring for Women and Men of Reproductive Age with Possible Zika Virus Exposure.
45. Carvalho, F. H., Cordeiro, K. M., Peixoto, A. B., Tonni, G., Moron, A. F., *et al.* (2016). Associated ultrasonographic findings in fetuses with microcephaly because of suspected Zika virus (ZIKV) infection during pregnancy. *PrenatDiagn.*, *36*(9), 882-887.
46. Jaenisch, T., Rosenberger, K. D., Brito, C., Brady, O., Brasil, P. & Marques, E. T. (2017). Risk of microcephaly after Zika virus infection in Brazil, 2015 to 2016. *Bull World Health Organ.*, *95*(3), 191-198.
47. Jouannic, J. M., Friszer, S., Leparc-Goffard, I., Garel, C. & Eyrolle-Guignot, D. (2016). Zika virus infection in French Polynesia. *Lancet*, *387*(10023), 1051-1052.
48. Krauer, F., Riesen, M., Reveiz, L., Oladapo, O. T., Martínez-Vega, R., Porgo, T. V., Haefliger, A., Broutet, N. J., Low, N., WHO Zika Causality Working Group. (2017). Zika virus infection as a cause of congenital brain abnormalities and Guillain-Barré syndrome: systematic review. *PLoS Med.*, *14*(1), e1002203.
49. Cao-Lormeau, V. M., Blake, A., Mons, S., Lastère, S., Roche, C., *et al.* (2016). Guillain-Barré syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study. *Lancet*, *387*(10027), 1531-1539.