

Pregnancy in Time of Zika Virus: Report of Ophthalmological Findings

¹Geraldo de Barros Ribeiro and ²Paulo Franco Taitson

¹Department of Ophthalmology, Universitario de Belo Horizonte (Uni-BH),
Service at Hospital Infantil Sao Camilo, Belo Horizonte, Brazil

²Director Secretary of the Brazilian Society of Assisted Reproduction (SBRA), Irvine, California

Abstract: The outbreak of Zika virus in several countries has been associated with microcephaly and congenital eye problems. With this, women have been oriented to delay pregnancy due to the risk of contamination and maternal-fetal transmission. Questionnaires were applied to couples and records analysis of children born from October-December 2015 in the city of Olinda, Pernambuco, Brazil. This region was an endemic area of Zika virus, making it a suitable place to compute findings from the disease in newborns. The questionnaire was applied in partnership with the Brazilian Society for Assisted Reproduction (SBRA) which set up a nucleus of reproductive health guidance in the city, once the epidemic expanded. The mean gestational age was 37.4±0.5 weeks. The mean fetal birth weight was 3.120 (±432.2) g. The mean age of the child on the day of the ophthalmologic examination was 2.1 (±0.8) months. Twenty babies of mothers who had Zika virus infection in the first trimester of pregnancy were examined. Of the children examined, 4 presented ocular alterations. The main findings were abnormalities of the optic nerve (3 cases: 2 females and 1 males) and 1 female case with chorioretinal atrophy. One of the children with ocular alterations had no microcephaly and another had no central nervous system anomaly. Recently, a strong relationship of congenital infection with Zika virus with ocular problems, mainly alterations in the retina and optic nerve was established. It is important, therefore, the multidisciplinary follow-up for cases of microcephaly, including the presence of the ophthalmologist in order to prevent, diagnose and treat eye diseases as well as to stimulate vision and rehabilitation of patients.

Key words: Zika virus, ophthalmology, health care, human reproduction, microcephaly, rehabilitation of patients

INTRODUCTION

The Zika virus was first discovered in a forest called Zika in Uganda in 1947. The 5 years later, the first human cases of Zika were detected and since, then Zika's outbreaks have been reported in tropical Africa, Southeast Asia and the Pacific Islands (Petersen *et al.*, 2016). In Brazil, the first cases were reported 2015. Since, then 48 countries in the Americas have confirmed transmission by the mosquito. The Zika virus is transmitted to people mainly through the bite of infected *Aedes aegypti* and *Aedes albopictus* mosquitoes. These are the same mosquitoes that spread the Dengue and Chikungunya viruses. Mosquitoes become infected when they feed on a person already infected with the virus. In this way, they can spread the virus to several people through other bites (Ai *et al.*, 2016; Petersen *et al.*, 2016).

Many people infected with the Zika virus will be asymptomatic or only have mild symptoms. The most

common symptoms of Zika are fever, rash, headache, joint pains, red eyes and muscle pain. Symptoms can last for several days to a week. People with symptoms do not usually get sick enough to seek medical care (Petersen *et al.*, 2016). However, in countries with outbreaks of Zika they associate it with the increase in cases of Guillain-Barre syndrome (Parra *et al.*, 2016). A person who has been infected by Zika will probably develop immunity and be protected from future infections. There is no vaccine against the Zika virus. Prevention is done by avoiding the bite of the infected mosquito. Zika can also be sex-transmitted and condoms can reduce the chance of contamination (McCarthy, 2016).

The Zika virus can be transmitted from a pregnant woman to the fetus. Infection during pregnancy can cause microcephaly and other serious problems in the fetus (Mehta *et al.*, 2018). Therefore, the so called congenital Zika virus syndrome has the following characteristics: microcephaly with decreased brain tissue; ocular changes, mainly damage to the retina and optic nerve; joint

problems with limited movement and increased muscle tone. Recognition of Zika virus contamination during pregnancy does not mean that the baby will have birth defects. This means that Zika infection during pregnancy increases the chances of these problems (Gregory *et al.*, 2017). Some children who are infected do not have microcephaly soon after birth but may have slow head growth and develop postnatal microcephaly (Mehta *et al.*, 2018; De Freitas *et al.*, 2016; Honein *et al.*, 2017; Moore *et al.*, 2017).

Due to the outbreak of the Zika virus and its complications, especially, in children who were contaminated during pregnancy, the hypothesis of counseling has emerged that women postpone their plans to become pregnant. However, according to the institution's clinical and epidemiological research protocol for microcephaly there is no formal recommendation to avoid pregnancy. The decision to become pregnant is a personal decision of each woman and her family. The representation of the Anonymous (2016) in Brazil adopts the same position. Women who choose to wait may have their cryopreserved oocytes, thus giving them a chance to take advantage of biological motherhood later in life (De Carvalho *et al.*, 2016).

Children with congenital Zika infection can have damage to the eyes (retinal and optic nerve damage) and/or regions of the brain responsible for vision which can affect visual development. Babies with and without microcephaly may have eye problems. If your baby was born with Zika's congenital infection, he should undergo eye exams to check for eye problems, even if he does not have neurological changes (Ventura *et al.*, 2016a, b; Zin *et al.*, 2017).

Children who have had congenital Zika virus infection require a multidisciplinary follow-up, including the ophthalmologist, to prevent, diagnose and treat eye diseases as well as to stimulate the vision and rehabilitation of patients (Parra *et al.*, 2016). Our study analyzes the prevalence of problems ocular congenital infections related to Zika virus in a region in Brazil where an outbreak of the disease occurred.

MATERIAL AND METHODS

Research project approved by the Research Ethics Committee of the Pontificia Universidade Catolica (PUC-MG). CAAE 54529916.70000.5137. Semi-structured questionnaires were applied to couples and records analysis of children born between October and December 2015 in the city of Olinda, Pernambuco. As the metropolitan area of Olinda was an endemic area of Zika virus became a conducive place to compute findings arising from the disease in newborns. The questionnaire

was applied in partnership with the Brazilian Society for Assisted Reproduction (SBRA) which set up a nucleus of reproductive health guidance in the city, once the epidemic expanded. The present study will present the ophthalmological findings.

RESULTS AND DISCUSSION

The charts showed that during the "Zika Time Pregnancy" campaign of the SBRA, 20 babies from mothers who had Zika virus infection in the first trimester of pregnancy were submitted to ophthalmologic examination. Mean gestational age: 37.4±0.5 weeks. The mean fetal birth weight was 3.120 (±432.2) g. The mean age of the child on the day of the ophthalmologic examination was 2.1 (±0.8) months. Of the children examined, 4 presented ocular alterations that threatened visual development. The main findings were abnormalities of the optic nerve (3 cases: 2 females and 1 male) and 1 female case with chorioretinal atrophy. One of the children with ocular alterations had no microcephaly and another had no central nervous system anomaly.

In Brazil, in November 2015, the Ministry of Health declared the outbreak of the Zika virus a public health emergency after the increase of cases of microcephaly in the northeast region of the country. In 2015 and 2016, 15 states in Brazil had confirmed cases in Zika virus transmission laboratory and an increase in the prevalence of microcephaly (2.8 cases per 10,000 live births), significantly exceeding the prevalence in four states without confirmed transmission (0.6/10,000) (Zin *et al.*, 2017).

Our study corroborates the ocular changes related to infection by Zika virus transmitted to the fetus by the pregnant woman, especially in the beginning of pregnancy. Twenty babies were examined and four (20%) presented ocular alterations. Other studies performed in the states of Rio de Janeiro, Bahia, Pernambuco and also in the United States showed ocular involvement in infants of mothers infected with Zika virus in 21.4, 29.3, 63.6 and 15%, respectively (De Oliveira *et al.*, 2016, Shapiro-Mendoza *et al.*, 2017, Cragan *et al.*, 2017, Reynolds *et al.*, 2017).

Ocular impairment in our study was more common when maternal-fetal transmission of the Zika virus occurs in the first trimester of pregnancy, similar to findings in other studies (De Freitas *et al.*, 2016, Zin *et al.*, 2017). Ocular changes are not always associated with microcephaly or neurological changes which reinforces the need for ophthalmologic examination in all children born with suspected infection by Zika congenital virus (Zin *et al.*, 2017).

The Brazilian Ministry of Health has assisted in the elaboration of programs to monitor the health and development of children with microcephaly. Most of these children have significant impairment in motor development, seizures, disturbances in hearing and vision and also sleep difficulties. In this way, they need specialized multidisciplinary care.

Data collection on the Zika virus and its effects are extremely important for the formulation of public health guidelines for the guidance of pregnant women. The aim is to improve patient counseling about risks during pregnancy, to inform best practices for the care of pregnant women with Zika virus and their infants to identify and refer the affected children to specialized services as soon as possible (Zin *et al.*, 2017).

A pregnant woman infected with the Zika virus can pass the virus to the fetus during pregnancy or around the time of birth. Zika virus was found in breast milk and there were several reports of Zika virus infection in breastfed babies. However, there were no reports of health problems in infants resulting from the mother's milk of a mother with Zika virus. Because the benefits of breastfeeding outweigh the risk of the Zika virus being transmitted through breast milk, the US Centers for Disease Control and prevention (CDC) continues to encourage mothers to breastfeed, even in areas at risk of Zika (Blohm *et al.*, 2017, Gregory *et al.*, 2017, Colt *et al.*, 2017).

CONCLUSION

The ocular changes found in our study, chorioretinal lesion and optic disc abnormalities, suggest the possibility that pregnant women, even asymptomatic, infected with Zika virus may have newborns with microcephaly and ophthalmoscopic lesions. An important issue is the need for ophthalmologic examination even in patients without microcephaly for the investigation of ocular lesions.

REFERENCES

- Ai, J.W., Y. Zhang and W. Zhang, 2016. Zika virus outbreak: A perfect storm. *Emerging Microbes Infect.*, 5: 1-3.
- Anonymous, 2016. Timeline of emergence of Zika virus in the Americas. Pan American Health Organization, Washington, D.C., USA. https://www.paho.org/hq/index.php?option=com_content&view=article&id=11959:timeline-of-emergence-of-zika-virus-in-the-americas&Itemid=41711&lang=en
- Blohm, G.M., J.A. Lednicky, M. Marquez, S.K. White and J.C. Loeb *et al.*, 2017. Evidence for mother-to-child transmission of Zika virus through breast milk. *Clin. Infect. Dis.*, 66: 1120-1121.
- Colt, S., M.N. Garcia-Casal, J.P. Pena-Rosas, J.L. Finkelstein and P. Rayco-Solon *et al.*, 2017. Transmission of Zika virus through breast milk and other breastfeeding-related bodily-fluids: A systematic review. *PloS Negl. Trop. Dis.*, 11: 1-14.
- Cragan, J.D., C.T. Mai, E.E. Petersen, R.F. Liberman and N.E. Forestieri *et al.*, 2017. Baseline Prevalence of birth defects associated with congenital Zika Virus Infection-Massachusetts, North Carolina and Atlanta, Georgia, 2013-2014. *MMWR. Morbidity Mortality Weekly Rep.*, 66: 219-222.
- De Carvalho, B.R., P.F. Taitson, K.S.A.G. Brandao, R.A. Ferriani and H.M. Nakagawa *et al.*, 2016. Reproductive planning in times of Zika: Getting pregnant or the delay plans? The opinion of the Brazilian society of assisted reproduction committee-the basis is the bioethical discussion. *JBRA. Assisted Reprod.*, 20: 159-164.
- De Freitas, B.P., J.R.O. de Dias, J. Prazeres, G.A. Sacramento and A.I. Ko *et al.*, 2016. Ocular findings in infants with microcephaly associated with presumed Zika virus congenital infection in Salvador, Brazil. *JAMA. Ophthalmol.*, 134: 529-535.
- De Oliveira, W.K., J. Cortez-Escalante, W.T.G.H. de Oliveira, G.M.I. do Carmo, C.M.P. Henriques, G.E. Coelho and G.V.A. de Franca, 2016. Increase in reported prevalence of microcephaly in infants born to women living in areas with confirmed Zika virus transmission during the first trimester of pregnancy-Brazil, 2015. *Morbidity Mortality Weekly Rep.*, 65: 242-247.
- Gregory, C.J., T. Oduyebo, A.C. Brault, J.T. Brooks and K.W. Chung *et al.*, 2017. Modes of transmission of Zika virus. *J. Infect. Dis.*, 216: S875-S883.
- Honein, M.A., A.L. Dawson, E.E. Petersen, A.M. Jones and E.H. Lee *et al.*, 2017. Birth defects among fetuses and infants of US women with evidence of possible Zika virus infection during pregnancy. *Jam.*, 317: 59-68.
- McCarthy, M., 2016. Zika virus was transmitted by sexual contact in Texas, health officials report. *BMJ.*, 352: 1-1.
- Mehta, R., C.N. Soares, R. Medialdea-Carrera, M. Ellul and M.T.T. da Silva *et al.*, 2018. The spectrum of neurological disease associated with Zika and chikungunya viruses in adults in Rio de Janeiro, Brazil: A case series. *PloS Negl. Trop. Dis.*, 12: 1-20.

- Moore, C.A., J.E. Staples, W.B. Dobyns, A. Pessoa and C.V. Ventura *et al.*, 2017. Characterizing the pattern of anomalies in congenital Zika syndrome for pediatric clinicians. *JAMA. Pediatr.*, 171: 288-295.
- Parra, B., J. Lizarazo, J.A. Jimenez-Arango, A.F. Zea-Vera and G. Gonzalez-Manrique *et al.*, 2016. Guillain-Barre syndrome associated with Zika virus infection in Colombia. *N. Engl. J. Med.*, 375: 1513-1523.
- Petersen, L.R., D.J. Jamieson, A.M. Powers and M.A. Honein, 2016. Zika virus. *N. Engl. J. Med.*, 374: 1552-1563.
- Reynolds, M.R., A.M. Jones, E.E. Petersen, E.H. Lee and M.E. Rice *et al.*, 2017. Vital signs: Update on Zika virus-associated birth defects and evaluation of all US infants with congenital Zika virus exposure-US Zika Pregnancy Registry, 2016. *MMWR. Morbidity Mortality Weekly Rep.*, 66: 366-373.
- Shapiro-Mendoza, C.K., M.E. Rice, R.R. Galang, A.C. Fulton and K. van Maldeghem *et al.*, 2017. Pregnancy outcomes after maternal Zika virus infection during pregnancy-US territories. *MMWR. Morbidity Mortality Weekly Rep.*, 66: 615-621.
- Ventura, C.V., M. Maia, B.V. Ventura, V.V.D. Linden and E.B. Araujo *et al.*, 2016a. Ophthalmological findings in infants with microcephaly and presumable intra-uterus Zika virus infection. *Arquivos Brasileiros Oftalmologia*, 79: 1-3.
- Ventura, C.V., M. Maia, S.B. Travassos, T.T. Martins and F. Patriota *et al.*, 2016b. Risk factors associated with the ophthalmoscopic findings identified in infants with presumed Zika virus congenital infection. *JAMA. Ophthalmol.*, 134: 912-918.
- Zin, A.A., I. Tsui, J. Rossetto, Z. Vasconcelos and K. Adachi *et al.*, 2017. Screening criteria for ophthalmic manifestations of congenital Zika virus infection. *JAMA. Pediatr.*, 171: 847-854.