4. Cousins S. COVID-19 has "devastating" effect on women and girls. *Lancet (London, England)*. 2020;396:301–302.
5. Ferreira-Filho ES, Melo NRD, Sorpreso ICE, et al. Contraception and reproductive planning during the COVID-19 pandemic. *Expert Rev Clin Pharmacol*. 2020;13:615–622.
6. United Nations. *Transforming Our World: The 2030 Agenda for Sustainable Development*. New York, NY: United Nations; 2015.
7. Wang X, Zhou Z, Zhang J, et al. Novel Coronavirus in a pregnant woman with preterm delivery. *Clinical Infect Dis*. 2019;2020:71.
8. Ellington S, Strid P, Tong VT, et al. Characteristics of Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status - United States, January 22-June 7, 2020. MMWR Morbidity and mortality weekly report. 2020;69.
9. Collin J, Byström E, Carnahan A, Ahrne M. Public Health Agency of Sweden's Brief Report: Pregnant and postpartum women with severe acute respiratory syndrome coronavirus 2 infection in intensive care in Sweden. *Acta Obstet Gynecol Scand*. 2020;99:819–822.
10. Santos DS, Menezes MO, Andreucci CB, et al. Disproportionate impact of COVID-19 among pregnant and postpartum Black Women in Brazil through structural racism lens. *Clin Infect Dis*. 2020;ciaa:1–2.
11. Turan O, Hakim A, Dashraath P, Jeslyn WJL, Wright A, Abdul-Kadir R. Clinical characteristics, prognostic factors, and maternal and neonatal outcomes of SARS-CoV-2 infection among hospitalized pregnant women: A systematic review. *Int J Gynecol Obstet*. 2020;151:7–16.
12. Sciences TAAo. Research and Development goals for COVID-19 in Africa – World. 2020.
13. WHO, UNICEF, UNFPA, Division WBGatUNP. Maternal mortality: Levels and trends 2000 to 2017. Geneva, 2019.
14. Tang K, Gaoshan J, Ahonsi B, et al. Sexual and reproductive health (SRH): A key issue in the emergency response to the coronavirus disease (COVID-19) outbreak. *Reprod Health*. 2020;17:1–3.
15. Liu Y, Chen H, Tang K, Guo Y. Clinical manifestations and outcome of SARS-CoV-2 infection during pregnancy. *J Infect*. 2020. http://doi.org/10.1016/j.jinf.2020.02.028. [Epub ahead of print].
16. (IDRC) IDRC. Mobilizing an African research response to the COVID-19 pandemic 2020. https://www.idrc.ca/en/news/mobilizing-african-research-response-covid-19-pandemic. Accessed August 18, 2020.

Received: 5 February 2020 | Revised: 19 May 2020 | Accepted: 26 June 2020 | First published online: 10 August 2020
DOI: 10.1002/ijgo.13288

Obstetrics

Outcomes of subsequent pregnancies following Zika virus infection: A comparative case series

Adriana Melo[1,2,3,*] | Patrícia S. Oliveira-Szejnfeld[4] | Gustavo Malinger[5] | Jousilene S. Tavares[1] | Fabiana O. Melo[1] | Larissa Cristina Q. M. Coutinho[1] | Gabriela L. Gama[1,2] | Fernanda T. Moll[6] | Renato S. Aguiar[7] | Amílcar Tanuri[7] | Melania M. Amorim[1,3,8]

[1]Instituto de Pesquisa Professor Joaquim Amorim Neto, Campina Grande, Paraíba, Brazil
[2]UNIFACISA, Campina Grande, Paraíba, Brazil
[3]Federal University of Campina Grande (UFCG), Campina Grande, Paraíba, Brazil
[4]Department of Radiology, Federal University of São Paulo, UNIFESP, São Paulo, Brazil
[5]Lis Maternity Hospital, Tel Aviv Medical Center and Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel
[6]D'Or Institute of Research, Rio de Janeiro and São Paulo, Brazil
[7]Federal University of Rio de Janeiro, Rio de Janeiro, Brazil
[8]Instituto de Medicina Integral Professor Fernando Figueira (IMIP), Recife, Pernambuco, Brazil

***Correspondence**
Adriana Melo, Rua Salvino de Oliveira Neto 87, 58402-040 Campina Grande, Paraíba, Brazil.
Email: asomelo@gmail.com

Funding Information
Improvement of Higher Education Personnel (CAPES); Ministry of Education (MEC); National Council for Scientific and Technological Development (CNPq); Ministry of Science, Technology, Innovation and Communication (MCTI); Department of Science and Technology (Decit); Secretariat of Science, Technology and Strategic Supplies (SCTIE); Ministry of Health

KEYWORDS: Congenital abnormalities; Microcephaly; Pregnancy; Zika; Zika virus

TABLE 1 Clinical, laboratory, and neuroimaging findings in fetuses/newborn infants with congenital Zika syndrome and in the subsequent pregnancy in eight women followed up at IPESQ, Campina Grande, Paraíba, Brazil.

Case	Mother's Age	Zika symptoms	1st/5th min Apgar	Gestational age (weeks)	Weight[a] g/ (Z-score[e])	Length[b] cm/ (Z-score[e])	HC[c] cm/ (Z-score[e])	Micro-cephaly	Neuroimaging findings[d]	qPCR ZIKV	IgM Mother and newborn	IgG Mother and newborn	Condition at hospital discharge	Denver II	Type of delivery	Interval between pregnancies
#1																
1st Pregnancy	28	Yes (10 wk)	9/10	39	2,970/ (−0.4)	47.5/ (−0.7)	31.5/ (−1.7)	No	Moderate reduction in brain parenchyma, lissencephaly, subcortical and basal ganglia calcifications, ventriculomegaly, corpus callosum dysgenesis, hypoplastic cerebellum, hypoplastic and segmented brain stem	Mother: Negative Cord blood and placenta: Positive	Not tested	Not tested	Alive	Abnormal	Vaginal Birth	12 mo
2nd Pregnancy	29	No	9/9	38	3,400/ (−0.8)	47/ (−0.9)	35.5/ (1.6)	No	Normal	Mother and newborn: Negative	Mother and newborn: Negative	Mother and newborn: Positive	Alive	Normal	Vaginal Birth	
#2																
1st Pregnancy	22	Yes (8 wk)	9/9	38	2,780/ (−0.5)	50/ (1.2)	31/ (−1.8)	No	Moderate reduction in brain parenchyma, lissencephaly, subcortical calcifications, ventriculomegaly, corpus callosum dysgenesis	Mother: Negative Cord blood: Positive	Not tested	Not tested	Alive	Abnormal	Vaginal Birth	14 mo
2nd Pregnancy	23	No	9/9	38	3,620/ (1.5)	50/ (1.2)	35/ (1.7)	No	Normal	Mother and newborn: Negative	Mother and newborn: Negative	Mother and newborn: Positive	Alive	Normal	Cesarean	
#3																
1st Pregnancy	17	No	8/9	41	3,050/ (−1.2)	47/ (−2.1)	30/ (−3.8)	Yes	Mild reduction in brain parenchyma, gyral simplification, subcortical calcifications	Mother: Negative Cord blood: Positive	Not tested	Not tested	Alive	Abnormal	Cesarean	14 mo

(continued)

Case	Mother's Age	Zika symptoms	1st/5th min Apgar	Gestational age (weeks)	Weight[a] g/ (Z-score[e])	Length[b] cm/ (Z-score[e])	HC[c] cm/ (Z-score[e])	Micro-cephaly	Neuroimaging findings[d]	qPCR ZIKV	IgM Mother and newborn	IgG Mother and newborn	Condition at hospital discharge	Denver II	Type of delivery	Interval between pregnancies
2nd Pregnancy	18	No	9/9	39	3,260/ (0.1)	50/ (0.4)	34/ (0.1)	No	Normal	Mother and newborn: Negative	Mother and newborn: Negative	Mother and newborn: Positive	Alive	Normal	Cesarean	
#4																
1st Pregnancy	22	Yes (18 wk)	3/3	41	2,770/ (−1.9)	49/ (−1.0)	36.5/ (1.6)	No	Severe reduction of the brain parenchyma, subcortical calcifications, severe ventriculomegaly, agenesis of the corpus callosum, thalamus not visualized, severe hypoplastic cerebellum, hypoplastic and non-segmented brain stem.	Mother: Negative Amniotic fluid: Positive	Not tested	Not tested	Dead (Respiratory failure)	Not evaluated	Cesarean	16 mo
2nd Pregnancy	23	No	9/9	41	3,780/ (0.6)	51/ (0.3)	36/ (1.1)	No	Normal	Mother and newborn: Negative	Mother and newborn: Negative	Mother and newborn: Positive	Alive	Normal	Cesarean	
#5																
1st Pregnancy	22	Yes (20 wk)	8/9	39	2,555/ (−1.5)	46/ (−1.6)	31/ (−2.1)	Yes	Moderate reduction in brain parenchyma, lissencephaly, subcortical calcifications, ventriculomegaly, corpus callosum dysgenesis	Mother: Negative Cord blood: Positive	Not tested	Not tested	Alive	Abnormal	Vaginal Birth	16 mo
2nd Pregnancy	24	No	9/9-8/9	37	2,460/ (−1.1) 1,960/ (−2.3)	45/(−1.6) 43/ (−2.5)	33.5/(0.4) 31/(−1.6)	No	Normal	Mother and newborn: Negative	Mother and newborn: Negative	Mother and newborn: Positive	Alive	Normal	Vaginal Birth	

(continued)

Case	Mother's Age	Zika symptoms	1st/5th min Apgar	Gestational age (weeks)	Weight[a] g/ (Z-score[e])	Length[b] cm/ (Z-score[e])	HC[c] cm/ (Z-score[e])	Micro-cephaly	Neuroimaging findings[d]	qPCR ZIKV	IgM Mother and newborn	IgG Mother and newborn	Condition at hospital discharge	Denver II	Type of delivery	Interval between pregnancies
#6																
1st Pregnancy	20	Yes (8 wk)	9/10	38	2,100/ (−2.3)	38/ (−4.6)	27/ (−4.4)	Yes	Severe reduction in brain parenchyma, lissencephaly, subcortical and basal ganglia calcifications, ventriculomegaly, corpus callosum dysgenesis	Mother: Negative Cord blood: Positive	Not tested	Not tested	Alive	Abnormal	Cesarean	18 mo
2nd Pregnancy	22	No	9/9	38	2,800/ (−0.7)	48/ (−0.4)	33/ (−0.4)	No	Normal	Mother and newborn: Negative	Mother and newborn: Negative	Mother and newborn: Positive	Alive	Normal	Vaginal Birth	
#7																
1st Pregnancy	30	Yes (10 wk)	8/9	39	2,750/ (−1.0)	46.5/ (−1.3)	29/ (−3.6)	Yes	Moderate reduction in brain parenchyma, lissencephaly, subcortical calcifications, ventriculomegaly, corpus callosum dysgenesis	Mother: Negative Placenta: Positive	Not tested	Not tested	Alive	Abnormal	Cesarean	19 mo
2nd Pregnancy	32	No	9/9	40	3,445/ (−0.5)	49/ (−0.2)	33.1/ (0.60)	No	Normal	Mother and newborn: Negative	Mother and newborn: Negative	Mother and newborn: Positive	Alive	Normal	Cesarean	
# 8																
1st Pregnancy	37	Yes (12 wk)	8/9	39	3,188/ (−0.1)	46/ (−1.9)	34/ (0.1)	No	Mild reduction in brain parenchyma, gyral simplification, subcortical calcifications	Mother: Negative Cord blood: Positive	Not tested	Not tested	Alive	Abnormal	Cesarean	22 mo
2nd Pregnancy	39	No	8/9	39	3,470/ (0.6)	50/ (0.4)	36/ (1.7)	No	Normal	Mother and newborn: Negative	Mother and newborn: Negative	Mother and newborn: Positive	Alive	Normal	Cesarean	

[a]Birthweight (g).
[b]Birth length (cm).
[c]Head circumference at birth (cm).
[d]Obstetric ultrasonography, fetal and neonatal magnetic resonance and neonatal computed tomography.
[e]Intergrowth-21.

Recent research into congenital Zika syndrome (CZS) has focused on further characterizing microcephaly, central nervous system (CNS) abnormalities, arthrogryposis, hearing loss, ophthalmological and digestive abnormalities, seizures, delayed motor/cognitive development,[1,2] and possible viral persistence.[3,4] Nevertheless, the risk to a second pregnancy in women who delivered an infant with CZS remains unknown.

This prospective case series, conducted at a specialist center for children with CZS in Campina Grande, Paraiba, Brazil, describes and compares data from eight women infected by Zika virus (ZIKV) whose children were born with CZS and who subsequently conceived and delivered a second child. Variables from the two groups of pregnancies were evaluated: maternal age, symptoms of ZIKV infection, first/fifth minute Apgar scores, gestational age, weight, length, head circumference (HC) and microcephaly at birth, type of delivery, neuroimaging findings, laboratory diagnosis of ZIKV, the infant's status at discharge (alive/dead), and neurological evaluation (Denver II). This study was approved by the Alcides Carneiro Hospital Ethics Committee and all patients signed an informed consent form.

Mean interpregnancy interval was 16 months (range 12–22 months). Table 1 summarizes the clinical, imaging, and laboratory data. HC (P=0.02), birthweight (P=0.02), and microcephaly at birth (P=0.03) differed significantly between the two sets of pregnancies (Student's t-test).

The virus appears to persist for a mean of 14 days in blood and 34 days in semen; nonetheless, this window could reach 80 and 125 days, respectively.[2,3] ZIKV displays tropism for the CNS[4]; however, how long it can remain in the CNS or eyes is unknown.

A 2018 study described a child with CZS who died aged 5 months. Of the organs evaluated at autopsy, ZIKV was detected in the brain, indicating viral persistence.[4] However, since viral persistence has been found only in the brain and not in the other fluids or tissues of individuals with CZS, these findings cannot be extrapolated to individuals with an acute ZIKV infection. A search of the PubMed, Scopus and Lilacs/SciELO databases yielded no publications on the risk to a fetus conceived soon after the delivery of an affected sibling.

In this case series, neither microcephaly nor brain abnormalities were found in children born from a pregnancy subsequent to one in which the mother was exposed to ZIKV and delivered a child with CZS. Since the sample size in this case series was small, a larger cohort study is required to establish the safety of a subsequent pregnancy following ZIKV infection.

AUTHOR CONTRIBUTIONS

AM, PSOS, AT, FTM and MMRA designed and planned the study. AM, PSOS, GM, FOM, LCQMC, FTM and RSA carried out the study. AM, GM, JST, GLG, FTM, RSA and MMRA analyzed the data. AM, PSOS, JST, FOM, GLG, AT, FTM, RSA and MMRA contributed to writing the manuscript. All authors approved the final version of the manuscript and agree to be accountable for all aspects of the work.

ACKNOWLEDGMENTS

Coordination for the Improvement of Higher Education Personnel (CAPES)/Ministry of Education (MEC); National Council for Scientific and Technological Development (CNPq)/Ministry of Science, Technology, Innovation and Communication (MCTI); and Department of Science and Technology (Decit)/Secretariat of Science, Technology and Strategic Supplies (SCTIE)/Ministry of Health (grants 443372/2016-0, 425136/2016-7, 440488/2016-8 and 428837/2016-6).

CONFLICTS OF INTEREST

The authors have no conflicts of interest.

REFERENCES

1. Melo A, Gama GL, Da Silva Junior RA, et al. Motor function in children with congenital Zika syndrome. *Dev Med Child Neurol*. 2020;62:221–226.
2. Almeida KJ, Martins AC, Almendra IC, et al. Clinical aspects of congenital microcephaly syndrome by Zika virus in a rehabilitation center for patients with microcephaly. *Rev Assoc Med Bras*. 2019;65:1249–1253.
3. Sánchez-Montalvá A, Pou D, Sulleiro E, et al. Zika virus dynamics in body fluids and risk of sexual transmission in a non-endemic area. *Trop Med Int Health*. 2018;23:92–100.
4. Chimelli L, Moura Pone S, Avvad-Portari E, et al. Persistence of Zika virus after birth: clinical, virological, neuroimaging, and neuropathological documentation in a 5-month infant with congenital Zika syndrome. *J Neuropathol Exp Neurol*. 2018;77:193–198.