

Ophthalmologic evaluation in infants of mothers with Zika: A report from Colombia

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Dear Editor

Zika virus (ZIKV) is an emerging perinatal infection, that can be included in the group of pregnancy risk infections such as cytomegalovirus and *Toxoplasma* (STORCH). They can lead to neurological sequelae, including microcephaly and congenital ZIKV syndrome (CSZ) in ZIKV infections. Previously, we have discussed and reported about this situation [1], but we would like to extend this discussion and consider and assess the potential damage to other organs, including the eyes. Then, we would like to take the opportunity to report possible ophthalmologic alterations in a child born to mothers with a high suspicion of ZIKV infection during pregnancy in Colombia.

Thirty nine pregnant women during November 2015–July 2016, in the municipality Aguachica, Cesar, Colombia, were evaluated [2]. ZIKV test (RT-PCR) was performed in 16 (out of 39), yielding results only five pregnant women, all of them positive. Therefore, clinical criteria were defined based on maternal symptoms (Table 1) and epidemiological characteristics [3]. At birth, telephone contact was made to schedule an ophthalmologic screening, through funduscopy to all the children of mothers with ZIKV and suspected ZIKV infection during pregnancy.

Aguachica had an incidence of ZIKV of 0.1–129.7 cases/100,000 inhabitants, and an accumulated incidence ranging 81.4 to 333.4 cases/100,000 pregnant women [4]. During pregnancy, prenatal care consultations were done according to medical criteria. All the patients had suggestive symptoms of ZIKV infection (Table 1). Distributed by trimester as follows, 21 from the first trimester (53.85%), 16 (41.03%) from the second, and 2 (5.13%) from the third.

The children were evaluated by ophthalmologists, in the first six months of life. The evaluation protocol established was done with phenylephrine and tropicamide. Variables such as gravidity age at the diagnosis time for ZIKV infection, type of birth, gestational age at birth, weight, height, TORCH serology (*Toxoplasma*, rubella, CMV, herpes), and hepatitis B, VDRL, HIV, and ZIKV, hospitalization in Neonatal ICU, perinatal hypoxia, family ophthalmological background syndromic association and head circumference, were collected from clinical registries. There was no detection of another perinatal infection or relevant family history. Besides, other alterations related to other possible infections of the TORCH complex were evaluated.

From 55 pregnant women with clinical characteristics of ZIKV

infection, two pregnant women lost their pregnancy during the first trimester; one fetus had perinatal death due to multiple malformations, another pregnant woman changed her residence. Additionally, eight patients were not evaluated because they could not be contacted or missed the evaluation. Finally, a total of 39 children with ages between 0 and 7 months were evaluated.

We detected three neonates with microcephaly (head circumference of 29, 30 and 30 cm) And also, we found two cases of children with ophthalmological alterations. Case 1: Left eye: pink optic nerve, small intraretinal hemorrhages at the level of the temporal arches with the involvement of the macular area without affecting the fovea and attached retina. Follow-up a month, both eyes were healthy. Right eye without alterations. Case 2: Retinal area affected in the macula and the peripapillary area with hypo and hyperpigmented lesions without foci of active chorioretinitis. (Fig. 1). This baby had microcephaly.

We found a one case with ocular alterations in children whose mothers suffered ZIKV infection in pregnancy (clinical case confirmed by PCR). That one was associated with microcephaly and severe neurological compromise, according to previous reports with ocular involvement and the presence of microcephaly [5]. That is considered a risk factor for ocular compromise, besides the infection during the first trimester in the pregnancy. It is essential to mention that normocephalic neonates can have ocular involvement [6].

Although ophthalmological alterations associated with ZIKV infection have been characterized [5,6], some reports are describing different types of damage or compromised function, including pigmentary maculopathy, chorioretinal macular atrophy associated with hyperpigmentation, vascular tortuosity, sub-retinal hemorrhages, peripheral pigmentary changes, the involvement of the optic nerve, coloboma, asymmetry in ocular size, intraocular calcifications and subluxation of the crystalline [5,6].

A complete evaluation can be performed through optical coherence tomography, where other alterations have been determined such as loss of the ellipsoidal area, increased retinal pigment epithelial reflectivity, thinning of the retina and choroidal and colobomatous excavation [5,6]. The other case corresponds to a neonate (8 days-old) with a history of vaginal delivery who presented a unilateral retinal hemorrhage. At medical re-consultation, we find a resolution of the hemorrhages probably post-partum. In this neonate, there were no family risk

Table 1
Clinical findings of mothers with confirmed or suspected Zika virus infection.

Symptoms	Frequency (%)
Rash	39 (97.5)
Joint pain	27 (67.5)
Asthenia	25 (62.5)
Fever	23 (57.5)
Headache	23 (57.5)
Conjunctivitis	22 (55.0)
Muscle pain	20 (50.0)
Lack of appetite	16 (40.0)
Retroarticular pain	13 (32.5)
Inflammation	13 (32.5)
Diarrhea	10 (25.0)
Stomach pain	9 (22.5)
Vomiting	5 (12.5)

factors for ophthalmological compromise, however the follow-up should be performed.

In addition to the affectations previously described, since the beginning of the epidemic, other clinical conditions have been found, such as low weight, anasarca, and arthrogryposis, among other characteristics similar to TORCH infections. We were extensive in our search of possible ophthalmological commitment in neonates with microcephaly because this condition with the acquisition of the infection in the first trimester of gestation seem to be risk factors for ocular involvement [5,6].

It is still unknown if the pathophysiological mechanism of development of ocular alterations is due to the microcephaly development process or directly to the viral infection. There are some reports of

ophthalmological alterations in neonates without microcephaly from mothers with positive serological tests for ZIKV, and some of these mothers were asymptomatic. Also, central nervous system and chorioretinal impairment have been described with other flaviviral infections [5,6].

Given the current uncertainties, we believe that all infants whose mothers have ZIKV infection or suspected infection during their pregnancy, even if there was no microcephaly, should have an ophthalmological assessment. The ophthalmological findings are relevant. Also, additional studies must be implemented to evaluate the long-term visual impairment in ZIKV infection to describe its possible chronic sequelae.

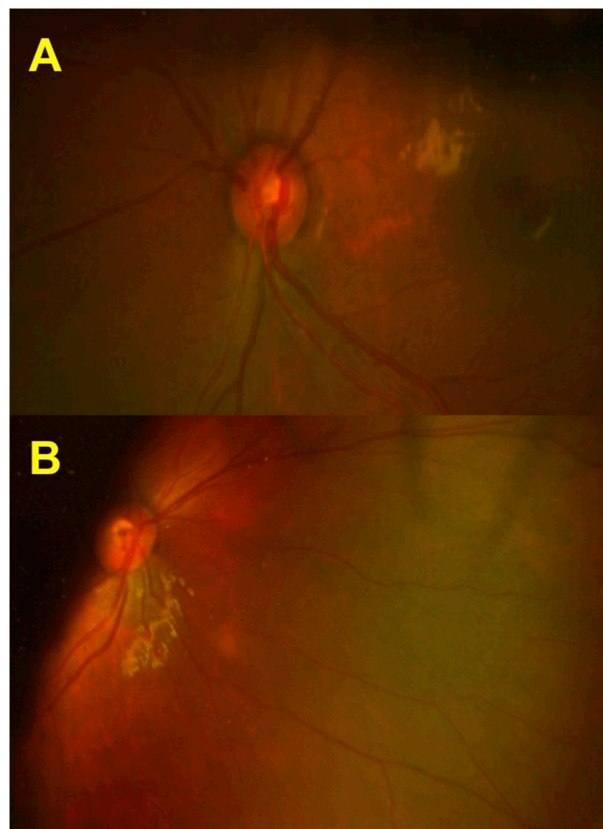


Fig. 1. Ophthalmological alterations in ZIKV patients. A. Disc with Excavation of 0.2×0.2 , pink neuroretinal ring, in macular area hypopigmented lesions less than 1-disc diameter near the foveal area without compromising it. Vessels without alterations. B. Disc with the excavation of 0.2×0.2 pink neuroretinal ring, at the level of the nasal edge of the disk hyperpigmented and hypopigmented lesions of 1-and-a-half-disc diameter, are evident. Vessels without alterations. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

CRedit authorship contribution statement

Jorge L. Alvarado-Socarras: Conceptualization, Formal analysis.
David R. Murillo-García: Writing - original draft. **Alfonso J. Rodríguez-Morales:** Conceptualization, Formal analysis, Writing - original draft.

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