

# Analyzing the ophthalmic red reflex test in children with congenital Zika syndrome

## Análise do Teste do Reflexo Vermelho em crianças com Síndrome de Zika Congênita

Marcia Beatriz Tartarella<sup>1</sup> , Islane Maria Castro Verçosa<sup>1</sup> , Paloma Castro Verçosa<sup>1</sup> , Paula Carneiro<sup>1</sup> , Reno Castro Verçosa<sup>1</sup> , Eduarda Tartarella-Nascimento<sup>1</sup> , Luciano Pamplona de Goês Cavalcanti<sup>2</sup> , Erlane Marques Ribeiro<sup>3</sup> , João Borges Fortes Filho<sup>4</sup> 

<sup>1</sup> Centro de Aperfeiçoamento Visual Ver a Esperança Renascer, Fortaleza, CE, Brazil.

<sup>2</sup> Faculdade de Medicina, Universidade Federal do Ceara Rio Grande do Sul, Fortaleza, CE, Brazil.

<sup>3</sup> Setor de Pediatria, Hospital Infantil Albert Sabin, Fortaleza, CE, Brazil.

<sup>4</sup> Hospital de Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, Brazil.

### How to cite:

Tartarella MB, Verçosa IM, Verçosa PC, Carneiro P, Verçosa RC, Tartarella-Nascimento E, et al. Analyzing the ophthalmic red reflex test in children with congenital Zika syndrome. Rev Bras Oftalmol. 2025;84:e0032.

### doi:

<https://doi.org/10.37039/1982.8551.20250032>

### Keywords:

Red reflex test; Congenital Zika Syndrome; Zika virus infection; Optic nerve hypoplasia; Microcephaly; Child; Macular atrophy

### Descritores:

Teste do reflexo vermelho; Síndrome de Zika Congênita; Infecção por Zika vírus; Hipoplasia do nervo óptico; Microcefalia; Criança; Atrofia macular

Received on:  
Jan 5, 2024

Accepted on:  
Oct 30, 2024

### Corresponding author:

Marcia Beatriz Tartarella  
Rua Passo da Pátria, 1.678, apto. 92V  
Zip code 05085-000 – São Paulo, SP, Brasil  
E-mail: tartarella@yahoo.com

### Institution:

Centro de Aperfeiçoamento Visual Ver a  
Esperança Renascer (Caviver), Fortaleza  
(CE), Brazil.

### Conflict of interest:

Bayer Global Ophthalmology Awards  
Program in Retinal Diseases partially  
supported this project on retina and vision  
research, improving patient access to eye  
care.

### Financial support:

The Bayer Global Ophthalmology Awards  
Program provided funds and contributed  
to the acquisition of ophthalmic retinal  
imaging equipment.



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## ABSTRACT

**Objective:** To evaluate the red reflex test in children with congenital Zika syndrome in order to predict the occurrence of retinal lesion or optic nerve hypoplasia in these patients.

**Methods:** A descriptive cohort study was conducted in children with Congenital Zika Syndrome. The red reflex test was performed with a direct ophthalmoscope, and it was repeated after pupils' dilation. The patients underwent a comprehensive ophthalmological evaluation. Eye fundus was analyzed by binocular indirect ophthalmoscopy. The occurrence of macular atrophy or optic nerve hypoplasia was recorded.

**Results:** A total of 144 eyes from 72 infants were included. All children had microcephaly. The mean age ranged from 1 to 18 months of life (median = 10 months), and 54.2% were female. Congenital Zika syndrome ocular features (macular atrophy or optic nerve hypoplasia) were detected in a total of 50 eyes. In all of the 144 eyes, the red reflex was present, thus the red reflex test was considered normal without or with pupillary dilation, despite differences in the color nuances observed.

**Conclusion:** Red reflex test did not enhance the assessment of the occurrence of macular atrophic lesion or optic nerve hypoplasia in patients with congenital Zika syndrome.

## RESUMO

**Objetivo:** Avaliar o teste do reflexo vermelho em crianças com Síndrome de Zika Congênita e correlacionar com a presença de lesões retinianas ou hipoplasia de nervo óptico nestes pacientes.

**Métodos:** Um estudo descritivo foi conduzido em crianças com Síndrome de Zika Congênita. O teste do Reflexo Vermelho foi realizado através do oftalmoscópio direto e repetido após a dilatação medicamentosa das pupilas. Os pacientes foram submetidos a exame oftalmológico. O fundo de olho foi analisado através da oftalmoscopia binocular indireta para detecção de atrofia macular e hipoplasia de nervo óptico.

**Resultados:** Um total de 144 olhos de 72 crianças foram incluídos. Todas as crianças apresentavam microcefalia. A idade variou de 1 a 18 meses (mediana = 10 meses), e 54.2% eram do sexo feminino. Alterações oculares compatíveis com Síndrome de Zika Congênita (atrofia macular e hipoplasia de nervo óptico) foram detectadas em 50 olhos. Nos 144 olhos analisados o reflexo vermelho estava presente e normal, com ou sem a dilatação das pupilas, mesmo na presença de diferentes nuances de coloração.

**Conclusão:** O Teste do reflexo vermelho não se mostrou capaz de detectar a ocorrência de atrofia macular ou hipoplasia de nervo óptico nos pacientes com Síndrome de Zika Congênita.

## INTRODUCTION

Red reflex test (RRT), or the Brückner test, is an important ophthalmological screening test for babies. It is a simple, feasible, non-invasive and low-cost test that can detect congenital or acquired eye abnormalities soon after birth or during early childhood. It can be performed by pediatricians, ophthalmologists, family doctors, nurses, medical students, and health personnel.

Congenital Zika syndrome (CZS) was reported among neonates in Brazil from the year of 2015.<sup>(1)</sup> Clinical characterization of the CZS includes the presence of microcephaly, severe central nervous system malformation, arthrogryposis, and atrophic retinal lesions.<sup>(1,2)</sup>

This study aimed to evaluate the RRT in children with CZS in order to predict the occurrence of retinal lesion or optic nerve hypoplasia in these patients.

## METHODS

This is an institutional descriptive cohort study conducted at *Centro de Aperfeiçoamento Visual Ver a Esperança Renascer* (Caviver), Fortaleza (CE), Brazil, during December 2016. Patients with microcephaly (defined as cephalic circumference < 32 cm at birth) and clinical diagnosis of CZS were included. A multidisciplinary team approach conducted by ophthalmologists, pediatricians, geneticists, orthopedists, and physical therapists evaluated all of the patients included.

Red reflex test was performed by the same team of ophthalmologists before and after pupillary dilation with tropicamide 1% eye drops. The RRT was considered normal when the ocular media or structures allowed the reflection of the choroidal blood vessels through the pupillary opening.

A direct ophthalmoscope was placed between 30 to 50 cm away of the children's eyes in a semi-dark room and RRT was evaluated. A comprehensive ophthalmic evaluation was performed. Eye fundus was analyzed by binocular indirect ophthalmoscopy and retina digital imaging was obtained with RetCam (RetCam Shuttle, Clarity Medical Systems).

The main outcomes were the detection of retinal or optic nerve abnormalities by the use of the screening test of the RRT performed before or after pupillary dilation.

The results of the RRT were correlated with the occurrence of macular atrophic lesion or optic nerve hypoplasia observed at the eye fundus evaluation.

Statistical analysis was conducted using Epi-Info, and qui-squared test was used for categorial variables.

The study protocol was approved by the Ethics Committee of the *Hospital Infantil Albert Sabin* in

Fortaleza. The protocol also conforms to the provisions of the Declaration of Helsinki in 1995, as revised in Edinburgh in 2000.

## RESULTS

A total of 144 eyes of 72 children with CZS were included and the RRT was evaluated before and after pupil dilation. The age of the cohort ranged from 1 to 18 months of age (median = 10 months), and 41 patients were female. Cephalic perimeter at birth varied from 21.5 cm to 32 cm (mean = 29.1, median = 30 cm), as seen in table 1.

**Table 1.** Demographic characteristics of the population and results

Number of children	72 patients
Number of eyes	144 eyes
Median age at the study	10 months
Median cephalic perimeter at birth	30 cm
Normal red reflex test	144 eyes
Abnormal red reflex test	None
Macular atrophy and optic nerve hypoplasia	35 eyes
Macular atrophy	10 eyes
Optic nerve hypoplasia	5 eyes
Strabismus	32 patients
Nystagmus	20 patients

Anatomical ocular abnormalities were detected in 50 eyes. Thirty-five eyes had circumscribed macular atrophy associated with optic nerve hypoplasia, ten eyes presented isolated macular atrophy, and five eyes had isolated optic nerve hypoplasia. Strabismus was detected in 32 patients. Nystagmus was present in 20 children.

No leukocoria or absence of red reflex was observed. All 144 eyes had normal and symmetric red reflex observed without or with pupil's dilation despite differences in the color nuances observed. Pupillary dilation did not influence RRT results.

## DISCUSSION

The RRT is routinely performed to provide important information on the ocular health status in infants. It can provide an easy and feasible way to detect ocular anomalies that block the visual axis. It is an effective screening test to detect leukocoria or congenital cataract in newborns. Other ocular features as retinoblastoma, retinal detachment, intraocular hemorrhage, Coats' disease, corneal leukoma, congenital glaucoma, and pupillary membranes can affect the RRT results. The RRT is a screening method of great importance because many congenital eye abnormalities need prompt treatment to avoid irreversible amblyopia or blindness in early childhood.<sup>(3,4)</sup>

The color of the normal eye fundus reflex through the pupil may vary from red to many nuances or gradients of red, orange, and yellow color according to specific individual conditions as: ethnicity, and ocular refractive errors.<sup>(5)</sup>

The clinical characterization of CZS includes severe ocular abnormalities that affect the eye fundus, as circumscribed macular atrophy (colobomatous-like) and optic nerve hypoplasia. These ocular conditions can cause poor vision that affects quality of life of the children and their families. Low vision and blindness in babies cause motor and global delay in early childhood, and affected children need special rehabilitation and education.<sup>(6,7)</sup>

A red reflex, or a pupillary reflex with variable color gradients, was detected in all eyes in this study, and the RRT results could not predict the occurrence of ocular abnormalities in this group of children with CZS. It is recommended that newborns with microcephaly or other signs of CZS should have their eye fundus evaluated by an ophthalmologist to detect ocular manifestations of CZS infection. Retinal digital imaging can be obtained, and it is a helpful tool for ophthalmologists to analyze retinal abnormalities in situations that telemedicine is necessary.

## CONCLUSION

The red reflex test was normal in all patients, and it could not predict the occurrence of intraocular abnormalities in this group of children with congenital Zika syndrome. In conclusion, children with microcephaly should have their eye fundus evaluated in order to detect ocular manifestations of congenital Zika syndrome.

## AUTHORS' CONTRIBUTION

Tartarella MB, Verçosa I: Study design; Tartarella MB, Verçosa I, Verçosa P, Carneiro P, Verçosa R, Tartarella-Nascimento E: Clinical evaluation of the patients; Cavalcanti LP: Statistical analysis; Tartarella MB, Tartarella-Nascimento E, Fortes Filho JB: Text contribution; Tartarella MB, Marques Ribeiro EM, Fortes Filho JB, Verçosa I: Reference analysis;

Tartarella MB, Verçosa I, Verçosa P, Carneiro P, Verçosa R, Tartarella-Nascimento E; Cavalcanti LP, Ribeiro EM, Fortes Filho JB: Text review and final approval.

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