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Ocular Assessments of a Series of Newborns Gestationally Exposed to Maternal COVID-19 Infection

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IMPORTANCE Congenital viral infections leading to ocular abnormalities are frequent and devastating. As ophthalmological manifestations of COVID-19 in newborns are still unknown, it is important to clarify if SARS-CoV-2 could be associated with ocular abnormalities.

OBJECTIVE To determine whether exposure to SARS-CoV-2 is associated with outcomes in 4the eyes of newborns.

DESIGN, SETTING, AND PARTICIPANTS This case series enrolled newborns from April to November 2020 from 3 different maternity hospitals in São Paulo, Brazil. The diagnosis of COVID-19 in mothers and newborns was based on real-time reverse transcriptase–polymerase chain reaction assays with material obtained from oronasopharyngeal swab sample; positive IGM serology was also considered as a diagnostic test for mothers. Newborns were excluded if they had any evidence of another congenital infection. All infants underwent external ocular examination and binocular indirect ophthalmoscopy.

EXPOSURES Serology test for COVID-19 and detection of SARS-CoV-2 from oronasopharyngeal specimen using a real-time reverse transcriptase–polymerase chain reaction assay on both mothers and newborns.

MAIN OUTCOMES AND MEASURES Screening for ophthalmologic manifestation in newborns after maternal COVID-19 infection.

RESULTS A total of 165 newborns (age range at examination, 1 to 18 days) were evaluated. Of these, 123 (74.5%) were born at full term, and 42 (25.4%) were born preterm. Maternal gestational age at the time of COVID-19–positive test varied from first to 40th gestational weeks. Six newborns (3.6%) had positive polymerase chain reaction findings for SARS-CoV-2. One newborn tested positive within 18 days (horizontal transmission), and 5 newborns tested positive in the first day of life (possible vertical transmission). None had ocular abnormalities. Concerning exposed newborns with negative test results, 1 presented with venous engorgement and vascular tortuosity, 7 had intraretinal hemorrhages, and 2 were diagnosed as having retinopathy of prematurity.

CONCLUSIONS AND RELEVANCE In this uncontrolled case series of Brazilian newborns of mothers with COVID-19 infection, a low rate of COVID-19 infection was found among newborns, and none had ocular abnormalities. Additional controlled studies may be warranted to confirm these findings.

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SARS-CoV-2 emerged in December 2019 and was isolated for the first time in China in January 2020.[1] With a high transmission rate, SARS-CoV-2 has spread to all continents and in March 2020, the World Health Organization declared COVID-19 a pandemic.[2]

Vertical transmission is one of the most serious complications of viral diseases occurring during pregnancy and very often may lead to ocular manifestations, mainly in the retina. A study evaluated 38 pregnant women with COVID-19 and found no association with increased morbidity and mortality or maternal transmission to the newborn.[1,3] Nevertheless, researchers in France and China reported 3 cases of vertical transmission.[4,5] However, regarding ophthalmological findings in newborns, there are still no published studies related to SARS-CoV-2 infection to date and to our knowledge. Because congenital viral infections such as cytomegalovirus and Zika virus can have devastating consequences to the eye of the newborn, it is important to determine if SARS-CoV-2 could also cause ocular manifestations in newborns.

Key Points

Question What are the ophthalmological manifestations in newborns after maternal COVID-19 infection?

Findings In this case series, 165 newborns exposed to SARS-CoV-2 went through ophthalmological evaluation. One exposed newborn presented with retinal vascular tortuosity and venous engorgement seen on ophthalmoscopy, 7 newborns showed intraretinal hemorrhages, and 2 newborns had retinopathy of prematurity.

Meaning These findings likely rule out a moderate or high increased risk of ocular involvement in newborns of mothers with SARS-CoV-2 infection regardless of gestational age.

Methods

The study enrolled newborns with maternal COVID-19 infection who were admitted to 3 maternity hospitals in São Paulo, Brazil, from April to November 2020. This case series followed the principles outlined in the Declaration of Helsinki,[6] including informed consent (oral and written) provided by the parents, regarding the study data and the ophthalmological examination. This study was approved by the ethics committee at Federal University of São Paulo, Escola Paulista de Medicina. No compensation or incentives were offered to patients to participate in the study. This study follows the reporting guidelines for case series studies,[7] addressing the limitations of an uncontrolled design but also acknowledging the importance of such reports in a context of a pandemic, in which the characteristics of a new clinical entity needs to be promptly defined.

The diagnosis of COVID-19 in both mothers and newborns was based on real-time reverse transcriptase-polymerase chain reaction assays (PCR) with material obtained from oronasopharyngeal swab sample; positive IgM serology was also considered as a diagnostic test for mothers. Laboratory-confirmed maternal COVID-19 infection, regardless of gestational age, represented the inclusion criteria for the study. Newborns were excluded if they had evidence of another congenital infection. All infants underwent an external ocular examination and binocular indirect ophthalmoscopy with 28-diopter lens. Just before the newborn evaluation, a form was filled with data including the date of maternal COVID-19 infection, diagnostic test method for the mother (serology or reverse transcriptase-PCR), gestational age when infected, symptoms, gestational age at birth, delivery method (cesarean or vaginal birth), newborn weight and length, 1- and 5-minute Apgar score, and the result of the COVID-19 test of the newborn. Statistical analysis was performed through descriptive statistics, using measures of frequency and central tendency.

Results

This study enrolled 165 newborns with maternal COVID-19-positive test results (age range at ophthalmologic examination, 1 to 18 days). Of 165 newborns, 123 (74.5%) were born full term, while 42 (25.4%) were born preterm. One-minute Apgar score was less than 7 (moderately to severely depressed) in 11 newborns (6.6%), and, on the fifth minute, 6 newborns presented with Apgar score less than 7. The mean (SD) weight was 2921 (702) g (range, 745-4335 g). Twenty-nine newborns (17.6%) had low birth weight (less than 1500 g) and 2 newborns (1.2%) had extremely low birth weight (less than 1000 g). The mean (SD) length was 47.3 (3.9) cm (range, 34-53 cm).

Maternal COVID-19 diagnosis varied between first and 40th gestational weeks. Six newborns had positive PCR results for SARS-CoV-2. One infant tested positive within 18 days (horizontal transmission), and 5 tested positive in the first day of life (possible vertical transmission). None presented with ocular abnormalities. Infection occurred in the third trimester in 4 of 5 newborns (age, 31-38 gestational weeks) and in the first trimester in 1 newborn (age, 8 gestational weeks). Characteristics of COVID-19-positive newborns are seen in **Table 1**.

Despite the normal ophthalmoscopy findings of all infected newborns, some exposed infants with negative PCR assay results presented fundus abnormalities that may or may not be associated with the congenital disease (**Table 2**). Among exposed infants, 1 newborn presented with retinal vascular tortuosity and venous engorgement seen on ophthalmoscopy. Maternal infection occurred at 28 gestational weeks and other possible comorbidities were ruled out. Seven newborns presented with retinal hemorrhages. Two exposed newborns had retinopathy of prematurity. One newborn had the aggressive posterior form and needed treatment with anti-vascular endothelial growth factor injection. Clinically, 9 of 165 newborns (5.4%) presented with respiratory distress syndrome. Aside from that, 1 newborn with positive PCR results presented with tonic-clonic seizures, and, after brain imaging, the infant was diagnosed with COVID-19 encephalitis.

Table 1. Features of Newborns With COVID-19 Infection

Newborn	GA of maternal infection, wk	GA at birth, wk	Apgar score		Weight, g	Length, cm	Delivery method	Ocular abnormalities
			First min	Fifth min				
1	37	38	9	10	3790	49	Cesarean	None
2	18 d After birth	40	9	10	3125	49	Cesarean	None
3	30	31	7	9	1140	36.5	Cesarean	None
4	38	38	9	10	2835	48.5	Cesarean	None
5	38	38	9	10	2845	48	Cesarean	None
6	7	37.5	9	10	3210	47	Cesarean	None

Abbreviation: GA, gestational age.

Table 2. Features of Exposed Newborns With Ocular Abnormalities

Newborn	GA of maternal infection, wk	GA at birth, wk	Apgar score		Weight, g	Length, cm	Delivery method	Ocular abnormalities
			First min	Fifth min				
1	35	36	6	8	2560	42	Cesarean	Retinal hemorrhages
2	38	39	9	9	3605	50	Cesarean	Retinal hemorrhages
3	36	38	7	8	2990	47	Cesarean	Retinal hemorrhages
4	20	38	9	10	3090	46	Cesarean	Retinal hemorrhages
5	21	40	9	10	3260	49.5	Cesarean	Retinal hemorrhages
6	26	39	9	10	3090	47	Cesarean	Retinal hemorrhages
7	26	38	9	10	3085	49	Cesarean	Retinal hemorrhages
8	28	38	9	10	2900	48	Cesarean	Retinal vascular tortuosity and venous engorgement
9	25	26	7	8	1070	35	Cesarean	Retinopathy of prematurity
10	29	29	1	2	1245	41.5	Cesarean	Retinopathy of prematurity

Abbreviation: GA, gestational age.

Discussion

Although the World Health Organization reported no evidence on vertical transmission when infection occurs in the third trimester,[8] our study showed a possible different scenario. Also, a recent publication reported the case of a possible mother-to-child transmission occurring at 35 weeks of gestational age.[9]

Given the appearance compatible with postpartum hemorrhages in this study, it is hard to tell whether retinal hemorrhages are secondary to COVID-19 or just incidental findings, since the rate we found (4.2% [7 of 165]) is within the published cross-sectional reports (6.7%).[10] In addition, our study found that 2 newborns had retinopathy of prematurity. This means a rate of 333% among infants born with weight less than 1250 g, which is also in line with expected rates of retinopathy of prematurity in COVID-19–naive populations.[11]

The high rate found of newborns with respiratory distress syndrome in our sample (9 of 165 [5.4%]) is notable because this complication is usually seen in about 1% of infants.[12] We wonder if there is an association between newborn respiratory distress and exposure to SARS-CoV-2 to justify these numbers.[13]

Bwire et al[14] found in a systematic review that 6.3% of newborns exposed to COVID-19 infection tested positive at birth, and they argue that there is low possibility of vertical transmission of COVID-19. Our study found 3% of SARS-COV-2 positivity among newborns, suggesting that vertical transmission of the virus may occur at low rates.

Limitations

Considering the lack of a control group owing to the design of the study, the reported findings cannot be generalized. The lack of standardized imaging also represents a limitation for this study.

Conclusions

The low rate of ocular abnormalities found in this study, likely within the range of anticipated findings in the absence of COVID-19, suggests that there is not a moderate or high increased risk of ocular abnormalities in newborns of mothers with COVID-19. Additional controlled and larger-sized studies with standardized imaging (fundus images and optical coherence tomography imaging) and standardization of ophthalmologists would be needed to rule out a low increased risk. Although more data are needed, vertical transmission of SARS-CoV-2 seems to be possible and should be a concern, especially in a condition that could be asymptomatic that is so widespread in the population and that could bring a substantial burden to patients and to the health care system even at low rates of congenital infection. Considering the noninvasive nature of fundus examination, retinal changes should be further investigated in prospective studies to understand their possible applications in the diagnosis and management of COVID-19.

ARTICLE INFORMATION

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Concept and design: Kiappe.
Acquisition, analysis, or interpretation of data: Kiappe, Cruz, Rosa, Arrais.
Drafting of the manuscript: Kiappe, Cruz, Arrais.
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