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Review of maternal COVID-19 infection: considerations for the pediatric ophthalmologist



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SUMMARY

With the increasing number of COVID-19 cases in the United States, more data is being reported on transmission, symptomatology, clinical course, and treatment of the virus. Research has focused on the trends and unique characteristics in at-risk populations, including pregnant women. This report summarizes the current data on considerations in pregnancy and postpartum period for mother and neonate to elucidate potential transmission risks for pediatric ophthalmologists. (J AAPOS 2020;24:209-211)

Pregnancy Considerations and Vertical Transmission

Because of the physiologic adaptive changes of pregnancy and its immunosuppressive state, pregnant women are at a relatively higher risk of contracting viral respiratory infections and may develop more severe infection compared to the general population.¹ In general, maternal infections in pregnancy are associated with adverse outcomes, including non-reassuring fetal status, premature labor or rupture of membranes, neonatal intensive care unit admission, and stillbirth.² The predominant clinical features of COVID-19 in pregnant women are similar to those in nonpregnant individuals and include fever, cough, dyspnea, and lymphopenia.³ There are reports of significant respiratory morbidity in pregnant women with COVID-19, including prolonged hospitalization, intensive care unit (ICU) admission, intubation, and extracorporeal membrane oxygenation.^{3,4} Although initial studies showed no differences in nonpregnant and pregnant COVID-19 patients, recent data illustrates that pregnancy is associated with higher risk of severe disease.⁵

Asymptomatic carriers of COVID-19 can be seen even in the pregnant cohort. In New York City, two affiliated hospitals implemented universal testing on labor and delivery, and a cohort study of 215 women revealed an asymptomatic carrier rate of 13.7% (n = 29).⁶

By definition, vertical transmission of an infection occurs through transplacental passage, neonatal contact with cervicovaginal sections, and/or breast milk. The data on verti-

cal transmission with COVID-19 is limited and controversial. Some studies have shown samples from amniotic fluid, cord blood, and breast milk are negative from symptomatic COVID-19 positive mothers, whereas more recent data has identified the virus in these fluids.^{7,8} Further, COVID-19 RNA has been documented on the fetal side of the placenta in affected mothers leading to the possibility of vertical transmission.⁹ Given the recent developments of this virus, there is currently limited data on perinatal outcomes when pregnant women are asymptomatic or when the infection is acquired in the first and second trimester of pregnancy. If a neonate is infected with COVID-19, clinical symptoms have ranged in severity, including fever, gastrointestinal distress, pneumonia, feeding intolerance, and lethargy.^{10,11}

Recommendations for Labor and Delivery and Neonatal Care

Centers for Disease Control (CDC) guidelines recommended that hospital visitors should be restricted for women who test positive for COVID-19 or are persons under investigation (PUI). Some hospitals have a no-visitor policy for these women. Women with COVID-19 or PUI should be placed in isolation rooms with droplet and contact precautions. Airborne infection isolation rooms should be used for vaginal deliveries as this is considered an aerosolizing procedure. All providers caring for these patients should wear proper protective equipment including N95 masks, gown, and eye protection. Infection with COVID-19 is not an indication for delivery, and cesarean delivery is reserved for usual obstetric indications. COVID-19 infection is not a contraindication to delayed cord clamping.¹²

The CDC and the American Academy of Pediatrics have made recommendations regarding neonatal care that are continually updated as more information becomes available. Infants born to mothers with known COVID-19 at the time of delivery should be suspected to have COVID-19 and isolated from healthy newborns. They should be bathed to remove virus from the skin, then tested at 24 and 48 hours post-delivery. Testing should continue

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at 48-72 hour intervals until two consecutive negative tests. Although the benefits of skin-to-skin contact are well understood, the risk and benefits must be weighed in the setting of maternal COVID-19 and generally not recommended. Neonatal separation from the mother should be determined through shared decision making, because this will greatly affect maternal-neonatal bonding.¹² If not strictly isolated, then a distance of at least 6 feet should be maintained, and any interaction with the neonate requires good hand hygiene and face mask protection. Neonatal feeding with breast milk is encouraged, ideally through maternal expression and feeding by a healthy caregiver.¹²

Pediatric Considerations

Pediatric COVID-19 infection seems to be distinct from adult disease because of its usual mild clinical course, with relatively fewer children requiring hospitalization and ICU admission compared with adult patients.¹³ In studies investigating pediatric presentation, fever and cough remain the most common symptoms, but upper respiratory and gastrointestinal symptoms, such as nasal discharge, vomiting, and diarrhea, may also be present.^{13,14} Among 2,572 pediatric COVID-19 cases, 398 (15%) occurred in children <1 year of age, and this cohort, along with children with underlying conditions, accounted for the highest percentage of hospitalizations.¹³

Based on limited number of cases, there is a concern of an association of COVID-19 and multisystem inflammatory syndrome which resembles Kawasaki disease in the pediatric population.¹⁵ Kawasaki disease is an acute vasculitis whose exact etiology is unknown, but is thought to be the result of an infectious agent that triggers an immune response of a cytokine storm and macrophage activation.¹⁶ In two cohort studies of Kawasaki-like disease among children the COVID-19 pandemic, symptoms and clinical findings included fever, erythema/induration of hands and feet, polymorphic rash, laterocervical lymphadenopathy, bulbar non-exudative conjunctivitis, mucocutaneous involvement, meningitis, and coronary artery aneurysm.^{16,17}

Ophthalmic Considerations

Conjunctivitis is a reported symptom of COVID-19 infection, and the virus has been identified in ocular secretions.^{18,19} Additionally, ocular symptoms include epiphora, conjunctival congestion, and chemosis, although they are more common in patients with severe illness.¹⁸ Currently the duration and infectivity of positive viral conjunctiva is unknown. Conjunctival transmission is not well elucidated yet, but a recent study has shown COVID-19 in conjunctival swabs.²⁰ No reports of neonatal conjunctivitis have been reported in infants with COVID-19, although this may be a concern especially with vaginal delivery and neonatal exposure to cervicovaginal secretions. Kawasaki disease may present with

conjunctivitis and should be considered an illness that requires urgent treatment.

Given limited data on vertical transmission, it is recommended that all providers, including ophthalmologists who care for infants from mothers with asymptomatic and symptomatic COVID-19 infection, assume that the child of a mother who has tested positive is infected. At a minimum, examination procedure must include wearing of mask and gloves, with hand washing between patients. When an infant has known COVID infection, then personal protective equipment, including gown and face protection, must be used as much as possible. The indirect ophthalmoscope can be fashioned with plexiglass that hangs from the scope and protects the examiner's face. An N95 mask better protects the examiner than does a cloth or paper mask. Retinopathy of prematurity examinations usually begin at 4 weeks of age, by which point the COVID status of an infant may be known. If not, assume the infant is COVID positive. The examiner should wash hands, don gloves for the examination, then remove gloves after the examination has been completed and wash again. Avoid touching the face and clean equipment after each examination. Older children should be screened before examination, either in- or outpatient. At a minimum, this would include taking a history of symptoms (fever, sore throat, cough, family history of illness, and travel to involved areas). The child's temperature should be taken prior to the visit. Ideally, this can be accomplished for the most part before the child is brought to the examination. Any child who could be infected should have his/her examination deferred if the problem is an elective one.

References

1. Wong SF, Chow KM, Leung TN, et al. Pregnancy and perinatal outcomes of women with severe acute respiratory syndrome. *Am J Obstet Gynecol* 2004;191:292-7.
2. Schwartz DA, Graham AL. Potential maternal and infant outcomes from (Wuhan) coronavirus 2019-nCoV infecting pregnant women: lessons from SARS, MERS, and other human coronavirus infections. *Viruses* 2020;12:194.
3. Dashraath P, Wong JL, Lim MX, et al. Coronavirus disease (COVID-19) pandemic and pregnancy. *Am J Obstet Gynecol* 2020;222:521-31.
4. Valeria S, Parisi F, Patane L, et al. Clinical findings and disease severity in hospitalized pregnancy women with coronavirus disease 2019 (COVID-19). Epub ahead of print. *Obstet Gynecol* 2020.
5. Ellington S, Strid P, Tong V, 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. *CDC Morbidity and Mortality Weekly Report*, June 26, 2020. Available at: <https://www.cdc.gov/mmwr/volumes/69/wr/mm6925a1.htm>.
6. Sutton D, Fuchs K, D'Alton M, Goffman D. Universal screening for SARS-CoV-2 in women admitted for delivery. *N Engl J Med* 2020; 382:2163-4.
7. Kirtsman M, Diambomba Y, Poutanen SM, et al. Probable congenital SARS-CoV-2 infection in a neonate born to a woman with active SARS-CoV-2 infection. *CMAJ Can Med Assoc J Assoc Medicales Can* 2020;192:E647-50.
8. Zamaniyan M, Ebadi A, Mir SA, Rahmani Z, Haghshenas M, Azizi S. Preterm delivery, maternal death, and vertical transmission in a pregnant woman with COVID-19 infection. *Prenat Diagn* 2020; <https://doi.org/10.1002/pd.5713>.

9. Patane L, Morotti D, Giunta M, et al. Vertical transmission of coronavirus disease 2019: severe acute respiratory syndrome coronavirus 2 RNA on the fetal side of the placenta in pregnancies with coronavirus disease 2019–positive mothers and neonates at birth. Epub ahead of print. *Am J Obstet Gynecol* 2020.
10. Zeng L, Xia S, Yuan W, et al. Neonatal early-onset infection with SARS-CoV-2 in 33 neonates born to mothers with COVID-19 in Wuhan, China. *JAMA Pediatr* 2020;174:722-5.
11. Zhu H, Wang L, Fang C, et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. *Transl Pediatr* 2020;9:51-60.
12. Wyckoff A. AAP updates guidance on newborns whose mother have suspected or confirmed COVID-19. American Academy of Pediatrics News. Available at: <https://www.aappublications.org/news/2020/05/21/covid19newborn052120>. Accessed June 20, 2020.
13. Centers for Disease Control and Prevention. Coronavirus disease 2019 in children—United States, February 12–April 2, 2020. *Morbidity and Mortality Weekly Report*. Available at: <https://www.cdc.gov/mmwr/volumes/69/wr/mm6914e4.htm>. Accessed June 20, 2020.
14. Dong Y, Mo X, Hu Y, et al. Epidemiological characteristics of 2143 pediatric patients with 2019 coronavirus disease in China. Epub ahead of print. *Pediatrics* 2020.
15. Jones VG, Mills M, Suarez D, et al. COVID-19 and Kawasaki disease: novel virus and novel case. *Hosp Pediatr* 2020;10:537-40.
16. Verdoni L, Mazza A, Gervasoni A, et al. An outbreak of severe Kawasaki-like disease at the Italian epicenter of the SARS-CoV-2 epidemic: an observational cohort study. *Lancet* 2020;395:1771-8.
17. Pouletty M, Borocco C, Ouldali N, et al. Paediatric multisystem inflammatory syndrome temporally associated with SARS-CoV-2 mimicking Kawasaki disease (Kawa-COVID-19): a multicentre cohort. *Ann Rheum Dis* 2020;79:999-1006.
18. Wu P, Duan F, Luo C, et al. Characteristics of ocular findings of patients with coronavirus disease 2019 (COVID-19) in Hubei Province, China. *JAMA Ophthalmol* 2020;138:575-8.
19. Colavita F, Lapa D, Carletti F, et al. SARS-CoV-2 isolation from ocular secretions of a patient with COVID-19 in Italy with prolonged viral RNA detection. *Ann Intern Med* 2020. M20-1176.
20. Valente P, Iarossi G, Federici M, et al. Ocular manifestations and viral shedding in tears of pediatric patients with coronavirus disease 2019: a preliminary report. *J AAPOS* 2020;24. 000-000.