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Vertical Transmission and Neonatal Outcomes Following Maternal SARS-CoV-2 Infection During Pregnancy

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Abstract: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has infected over 200 million people worldwide and has likely exposed millions of neonates to SARS-CoV-2 in utero. A large body of literature has examined the possibility of vertical transmission from pregnant women infected with SARS-CoV-2 to their neonates. In this chapter, we review mechanisms of—and evidence for—vertical transmission of SARS-CoV-2, including transplacental, through other biospecimens and breastfeeding, and discuss neonatal outcomes following in utero exposure. Based on the available literature, we conclude vertical transmission of SARS-CoV-2 is rare, and exposed neonates generally show favorable health outcomes.

Key words: SARS-CoV-2, COVID-19, neonatal, pregnancy, vertical transmission, breastfeeding

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Introduction

Since early 2020, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has overwhelmed the world's health care

resources, infecting over 200 million people worldwide and causing over 4 million deaths.[1] Considering the vast spread of SARS-CoV-2, it is likely that millions of neonates have been exposed to maternal SARS-CoV-2 infection in utero, and, despite efforts towards widespread social distancing and mass vaccination, the coronavirus disease 2019 (COVID-19) pandemic shows little sign of coming to an end in the near future. Given the vulnerable nature of the neonatal immune system, a major concern for many clinicians and researchers has been the possibility of vertical transmission of SARS-CoV-2 from infected mothers to their neonates and other adverse neonatal outcomes related to in utero viral exposure. Reassuringly, the evidence to-date has indicated a low risk of vertical transmission in exposed neonates.[2–8] In addition, the small number of neonates who do test positive for SARS-CoV-2 are healthy and do not show significant morbidities related to SARS-CoV-2 infection.[2,3,5,6] SARS-CoV-2 also appears to be unlikely to infect the placenta or other biospecimens, including breastmilk, and studies reporting on neonates who were breastfed and allowed to room-in with mothers report similar rates of vertical transmission as those in which neonates were isolated from their mothers.[3,4,6] In this chapter, we review the available literature surrounding mechanisms of vertical transmission of SARS-CoV-2, rates of infection, and early health outcomes in neonates exposed to SARS-CoV-2 in utero and through breastfeeding. We conclude that there is a need for future data related to viral variants and long-term child health outcomes.

Potential Mechanisms for Vertical Transmission of SARS-CoV-2

Numerous mechanisms of vertical transmission of SARS-CoV-2 from infected mother to newborn have been proposed, largely focused on transplacental transmission. SARS-CoV-2 enters host cells by binding its spike protein to angiotensin-2 converting enzyme (ACE2) receptors and uses cell surface protease TMPRSS2 for spike protein priming.[9] Because ACE2 and TMPRSS2 have been shown to be expressed on trophoblasts in the placenta,[10] thereby making the placenta theoretically susceptible to SARS-CoV-2 infection, transplacental transmission has been thought to be a plausible mechanism of vertical transmission. However, there have been conflicting reports of coexpression of ACE2 and TMPRSS2 by placental cells, with some groups reporting coexpression in syncytiotrophoblasts during the first trimester of pregnancy and in extravillous trophoblasts during the second trimester,[10] and others reporting negligible coexpression of ACE2 and TMPRSS2 throughout pregnancy.[11] Further, the presence of the virus in the blood is a necessary precursor to transplacental infection.[12] Although viremia was reported in a large majority of SARS-CoV-1-infected patients,[13] it occurs in a minority of mostly severely ill individuals infected with SARS-CoV-2,[14] and appears to be uncommon in pregnant SARS-CoV-2-infected patients.[15] Another mechanism that was briefly considered due to its relevance to other viruses is the cervicovaginal route of vertical transmission, involving neonatal exposure to infected cells during delivery,[12] but most studies that have tested vaginal fluid from SARS-CoV-2-infected pregnant women have shown that these samples test negative for the virus.[6] Altogether, placental infection seems to be the most plausible mechanism for vertical transmission of SARS-CoV-2, but the evidence to-date suggests that it is unlikely to occur.

Vertical and/or Perinatal Transmission of SARS-CoV-2 From Infected Mother to Neonate is Rare

Consistent with inconclusive evidence for an effective mechanism, vertical transmission of

SARS-CoV-2 from infected mothers to their fetuses has thus far shown to be rare. A large body of literature, including meta-analyses and national registries reporting on thousands of pregnant women, has demonstrated that generally <5% of neonates exposed to SARS-CoV-2 in utero show evidence of infection.[2–8] A systematic review by Kotlyar et al[4] combined data on a total of 936 neonates born to SARS-CoV-2-infected mothers. Neonates included in the analysis were tested for SARS-CoV-2 viral RNA using nasopharyngeal swab within 48 hours after delivery, and a pooled proportion of 3.2% of neonates tested positive. The authors also calculated separate vertical transmission rates between studies from China and studies from outside of China and found that rates of vertical transmission were similar (2.0% in China vs. 3.5% outside of China),[4] which is notable given China's historically more stringent neonatal care recommendations for exposed neonates in comparison to many Western countries, including isolating neonates and prohibiting breastfeeding.[16] In a national cohort study from Sweden reporting on 2,323 neonates born to SARS-CoV-2-infected women, the rate of neonatal SARS-CoV-2 positivity was 0.9%, despite the encouragement of rooming-in between infected mothers and newborns, breastfeeding, and skin-to-skin care.[3] Similarly, a study coreporting on data from the United States and UK national registries of SARS-CoV-2-infected pregnant women and their neonates found vertical transmission rates of 1.8% in the United States cohort and 2.0% in the UK cohort.[2] On the higher end of reported vertical transmission rates to-date, Dhir et al[5] and Jafari et al[6] found neonatal positivity rates of 5.0% and 5.3% in meta-analyses of 1141 and 563 neonates, respectively, but neither group reported exclusion criteria based on the timing of testing postnatally, and Dhir et al[5] concluded that 41 of the 58 neonates who tested positive in their analysis had acquired SARS-CoV-2 during the postpartum period rather than vertically.

While the most accepted method of determining SARS-CoV-2 vertical transmission has relied on testing neonatal nasopharyngeal swabs using reverse transcription-polymerase chain reaction (RT-PCR), many studies report on testing other maternal and neonatal samples. Of particular importance to determining mechanisms by which SARS-CoV-2 vertical transmission may occur, several groups have tested placental samples, breastmilk, amniotic fluid, cord blood, and maternal vaginal secretions for viral RNA using RT-PCR. The meta-analysis by Jafari et al[6] reported that SARS-CoV-2 was detected in 12% of placental samples, 5% of breastmilk samples, 5.6% of amniotic fluid samples, 6% of cord blood samples, and 4.6% of vaginal secretions tested in the included studies. Kotlyar et al[4] also showed that placental samples seem to test positive for SARS-CoV-2 more frequently than other samples, with 7.7% of placenta samples in their analysis testing positive, as opposed to 0% of amniotic fluid samples and 2.9% of cord blood samples. However, neither analysis reported on the number of neonates with positive nasopharyngeal swabs and/or documented COVID-19 disease who also had positive placental, amniotic fluid, cord blood, or other samples. Therefore, whether biospecimen positivity is evidence of vertical transmission cannot be determined. Another systematic review reporting on 336 neonates exposed to and tested for SARS-CoV-2 infection found that only 4.4% were positive using pharyngeal swab RT-PCR.[17] Of these neonates, 5 had placental, amniotic fluid, and cord blood samples tested, and only 1 sample of amniotic fluid tested positive. Similarly, another group found that while 3 of 11 placental samples from SARS-CoV-2-infected women tested positive for the virus, none of the infants born to these women tested positive for SARS-CoV-2 during the first 5 days of life or showed any symptoms of COVID-19 disease.[18]

Together, the available evidence suggests that the presence of SARS-CoV-2 RNA in the placenta and other biospecimens at delivery is not only rare but also may not necessarily correlate with vertical transmission of SARS-CoV-2.

Minimal Evidence for Perinatal Transmission of SARS-CoV-2 Through Breastfeeding

In addition to a lack of evidence supporting vertical transmission of SARS-CoV-2 from infected mothers to neonates, there is also minimal evidence that SARS-CoV-2 is transmitted through breastfeeding during the perinatal period. Although some published guidelines still recommend that SARS-CoV-2-infected mothers withhold breastfeeding to prevent transmission,[16] several studies since the beginning of the COVID-19 pandemic have demonstrated that neonates who are breastfed by their infected mothers rarely acquire SARS-CoV-2. Available data has shown that a low proportion of breastmilk samples from SARS-CoV-2-infected women contain viral RNA. A recent systematic review analyzing samples from 116 infected women found that only 2.16% of samples tested positive using RT-PCR.[19] Further, a study on 55 neonates in Israel found no infections among neonates born to SARS-CoV-2 infected mothers who subsequently breastfed, and infants who continued breastfeeding at home remained SARS-CoV-2-negative at follow-up testing 14 to 21 days after hospital discharge.[20] Data from our group likewise found no evidence of COVID-19 disease in a cohort of 101 neonates born to SARS-CoV-2-infected women, 90.1% of whom were breastfed any amount neonatally and 40.6% of whom were mostly or exclusively breastfed neonatally.[7] Further, a large systematic review on breastfeeding women showed that a similar percentage of neonates who were fed breastmilk by SARS-CoV-2-infected mothers ultimately became infected with SARS-CoV-2 (15%) as those who were fed breastmilk substitutes (18%), suggesting that neonates who do become infected perinatally likely acquire SARS-CoV-2 from close contact with infected household members rather than feeding practices.[21]

In contrast to the lack of evidence of SARS-CoV-2 transmission via breastmilk, there is ample evidence highlighting the importance of direct breastfeeding and the ways in which breastfeeding aids neonatal immune development. Breastfeeding reduces rates of the upper and lower respiratory tract and gastrointestinal infections in newborns,[22] likely via mechanisms that stem from bioactive factors in breastmilk, such as maternal immune cells and healthy bacteria. These components of breastmilk support the development of the immune response, the mucosal barrier, and the microbiome in newborns.[23] Moreover, breastfeeding is known to provide protection against viruses that mothers have previously been infected with by transferring antibodies from mother to child.[24] Indeed, recent studies have found potential evidence for the transfer of SARS-CoV-2 antibodies through breastfeeding, indicating that breastfeeding may actually provide infants with protection against SARS-CoV-2 infection. A study from Israel including 84 women found evidence that the breastmilk of vaccinated mothers carries antibodies against SARS-CoV-2: there was strong production of immunoglobulin (Ig) A and IgG antibodies in breastmilk for 6 weeks after vaccination, with 97% of women showing elevated antibodies in their breastmilk.[25] The study also observed neutralizing effects in immune proteins, indicating that this elevation of antibodies could potentially exert protective effects against COVID-19 in breastfeeding infants. In another study

of 18 women who were diagnosed with COVID-19, 37 milk samples and 70 breast skin swabs were collected.[26] Only 1 conclusive positive viral RNA result was detected from the skin swabs, yet 76% of breastmilk samples contained SARS-CoV-2-specific IgA, and 80% had SARS-CoV-2-specific IgG. Further, 62% of these milk samples were capable of neutralizing SARS-CoV-2 infectivity in vitro, whereas milk samples collected before the COVID-19 pandemic were unable to do so.[26] Together, the available data suggest that breastmilk and breastfeeding do not transmit SARS-CoV-2 from mother to infant but rather may confer protective effects against infection for the neonate.

Neonatal Outcomes in Neonates Exposed to SARS-CoV-2 In Utero

Regardless of whether neonates born to SARS-CoV-2-infected women acquire COVID-19 disease themselves, viral exposure in utero may have the potential to impact neonatal health. In their study reporting on 92% of all births in Sweden from March 2020 through January 2021, Norman et al[3] compared a range of neonatal outcomes in 2323 neonates exposed to SARS-CoV-2 in utero to outcomes in 9275 unexposed case-matched neonates. The authors found that maternal SARS-CoV-2 infection was positively associated with some neonatal morbidities, including respiratory disorders and hyperbilirubinemia, but not with mortality or length of stay in neonatal care. The increased risk of respiratory disorders in SARS-CoV-2-exposed newborns was mediated by preterm delivery rates, which were found to be higher in the exposed group.[3] Increased rates of preterm delivery of SARS-CoV-2 exposed neonates as compared with general population rates have been reported in several studies, including 12.0% reported in the UK national registry,[2] 15.7% in the US national registry,[2] 21% reported by Jafari et al,[6] and 25% reported by Dhir et al.[5] These proportions are noticeably higher than the world preterm delivery rate of 11%,[27] and rates are generally even lower, below 10%, in the middle- and high-income countries in which most of these studies were performed.[27] Although rates of preterm delivery seem to be higher in SARS-CoV-2 exposed neonates, other measures of early health appear unaffected, with studies reporting that exposed neonates are not at increased risk for being small-for-gestational age[2] and that Apgar scores at delivery, a measure of the overall early neonatal condition, are not impacted by exposure to SARS-CoV-2.[3,6]

While a majority of neonates born to SARS-CoV-2-infected women are born healthy and at term, the observed uptick in preterm delivery rates is concerning, and its mechanism remains largely unclear. One prevailing theory is that maternal disease severity contributes to increased preterm delivery rates, with the increased rates of preterm delivery seen in SARS-CoV-2-exposed neonates driven by mothers with severe or critical COVID-19 disease. Large databases have shown that pregnant women infected with SARS-CoV-2 are at higher risk of requiring respiratory support, requiring intensive care unit admission, and mortality than nonpregnant women infected with SARS-CoV-2.[28] Similarly, when pregnant women infected with SARS-CoV-2 are compared with other pregnant women who are not infected, infected women have a higher risk for mortality and intensive care unit admission.[29] This theory is consistent with studies on other respiratory diseases that have shown that disease severity is associated with preterm delivery,[30] an association which is thought to be related to the proinflammatory state induced by severe disease,[31] as well as drug treatments and medical interventions that are necessitated by severe illness.[30] Placental infection caused

by other viruses has also been linked to preterm delivery,[32] but as reviewed in the above sections, placental infection seems to be rare in SARS-CoV-2-infected women. Interestingly, however, increased COVID-19 disease severity has been associated with increased expression of placental ACE2 and interferon-induced transmembrane antiviral genes even in the absence of placental infection or vertical transmission,[33] suggesting that severe COVID-19 disease may alter the placental environment irrespective of placental infection or vertical transmission, potentially contributing to increased risk of preterm delivery.

In addition to considering outcomes in all neonates born to SARS-CoV-2-infected mothers, it is essential to track outcomes in the small subset of neonates who do become infected with SARS-CoV-2. Norman et al[3] showed that none of the 0.9% of neonates who tested positive for SARS-CoV-2 in their cohort had evidence of any morbidity related to COVID-19 disease, with 12 of the 21 neonates showing no symptoms, 9 with diagnoses with no clear relation to SARS-CoV-2, and zero exhibiting congenital pneumonia. Meta-analyses have similarly shown that about half of neonates with reported SARS-CoV-2 infection are asymptomatic, and that respiratory symptoms are the most common manifestation in those who are symptomatic.[5] While neonates may be at a slight increased risk of severe disease in comparison to older children, with early reports from China indicating that up to 10.6% of infants under 1-year-old had severe COVID-19 disease,[34] severe illness occurs in a small minority of patients and mortality is extremely rare in the neonatal population.[5,8]

Future Considerations and Conclusions

Although the evidence on vertical transmission and neonatal outcomes in neonates exposed to SARS-CoV-2 in utero has, to-date, been promising, the COVID-19 pandemic and the SARS-CoV-2 virus itself have proven to be ever-evolving. In recent months, the more contagious Delta variant has rapidly spread across the world, and much of the literature that has been gathered over the past 18 months regarding the effect of SARS-CoV-2 on pediatric populations has been called into question. While children were previously thought to be a group largely spared from symptomatic infection and severe disease, the Delta variant has caused an exponential surge in pediatric COVID-19 cases in the United States in recent weeks,[35] after becoming the dominant variant circulating throughout the country. Although severe illness still seems to be rare, with 0.1% to 2.0% of current child COVID-19 cases resulting in hospitalization as of September 16, 2021,[35] data from the CDC tracking rates of COVID-19-related hospital admissions in children aged 0 to 17 showed a peak in early September 2021 that was nearly double the rate of the previous peak from January 2021.[36] The Delta variant seems to be infecting children with a rate and severity not seen in other variants, which raises the question of whether vertical transmission and/or adverse neonatal outcomes will be more likely to occur if mothers are infected with this more contagious variant. Data from India, where the Delta variant has been circulating since Fall of 2020, may offer a preview as to the potential impact of this variant on neonatal populations. A recent report from the Indian National Neonatology Forum's registry of neonates born to SARS-CoV-2-infected women does show a slightly higher proportion of infected neonates (8%) compared with the estimates provided above, but the authors reported that the majority of infected neonates were asymptomatic, and symptomatic neonates mostly had symptoms related to prematurity and/or perinatal events rather than COVID-19 disease.[37]

While additional data on the Delta variant will need to be tracked in the coming months, overall, the existing evidence suggests that neonates born to mothers infected with SARS-CoV-2 are at low risk of vertical transmission and adverse neonatal outcomes. Mechanistically, the only plausible route of SARS-CoV-2 vertical transmission seems to be transplacental infection, but analysis of placental samples has shown that placental infection is rare and does not necessarily predict neonatal infection. Several large studies and meta-analyses have shown that generally <5% of neonates exposed to SARS-CoV-2 in utero test positive for the virus neonatally and that biospecimen samples at delivery also rarely test positive. Rates of vertical transmission do not appear to be increased by postnatal care practices such as breastfeeding, skin-to-skin care, and rooming-in, and breastfeeding likely bolsters neonatal immunity and should be encouraged. Further, neonates exposed to SARS-CoV-2 in utero, including neonates infected with SARS-CoV-2 themselves, are generally healthy and have favorable outcomes, although exposed neonates are slightly more likely to be born preterm for unclear reasons that may be driven by mothers with severe COVID-19 disease. In sum, the existing literature on outcomes in neonates born to SARS-CoV-2-infected women is encouraging and indicates that these neonates fare well. Additional follow-up data in the coming months and years will be essential to detect the impact of new variants and surveil long-term child health outcomes in exposed neonates.

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References

1. World Health Organization. WHO Coronavirus (COVID-19) Dashboard; 2021. Available at: https://covid19.who.int/. Accessed September 30, 2021.
2. Mullins E, Hudak ML, Banerjee J, et al. Pregnancy and neonatal outcomes of COVID-19: coreporting of common outcomes from PAN-COVID and AAP-SONPM registries. *Ultrasound Obstet Gynecol*. 2021;57:573–581.
3. Norman M, Navér L, Söderling J, et al. Association of maternal SARS-CoV-2 infection in pregnancy with neonatal outcomes. *JAMA*. 2021;325:2076–2086.
4. Kotlyar AM, Grechukhina O, Chen A, et al. Vertical transmission of coronavirus disease 2019: a systematic review and meta-analysis. *Am J Obstet Gynecol*. 2021;224:35.e3–53.e3.
5. Dhir SK, Kumar J, Meena J, et al. Clinical features and outcome of SARS-CoV-2 infection in neonates: a systematic review. *J Trop Pediatr*. 2021;67:fmaa059.
6. Jafari M, Pormohammad A, Sheikh Neshin SA, et al. Clinical characteristics and outcomes of pregnant women with COVID-19 and comparison with control patients: a systematic review and meta-analysis. *Rev Med Virol*. 2021;31:e2208.
7. Dumitriu D, Emeruwa UN, Hanft E, et al. Outcomes of neonates born to mothers with severe acute respiratory syndrome coronavirus 2 infection at a large medical center in New York City. *JAMA Pediatr*. 2021;175:157–167.
8. Kyle MH, Glassman ME, Khan A, et al. A review of newborn outcomes during the COVID-19 pandemic. *Semin Perinatol*. 2020;44:151286.
9. Shang J, Wan Y, Luo C, et al. Cell entry mechanisms of SARS-CoV-2. *ProcNatl Acad Sci USA*. 2020;117:11727.
10. Ashary N, Bhide A, Chakraborty P, et al. Single-cell RNA-seq identifies cell subsets in human placenta that highly expresses factors driving pathogenesis of SARS-CoV-2. *Front Cell Dev Biol*. 2020;8:783.
11. Pique-Regi R, Romero R, Tarca AL, et al. Does the human placenta express the canonical cell entry mediators for SARS-CoV-2? *eLife*. 2020;9:e58716.
12. Egloff C, Vauloup-Fellous C, Picone O, et al. Evidence and possible mechanisms of rare maternal-fetal transmission of SARS-CoV-2. *J Clin Virol*. 2020;128:104447.

13. Chen W, Xu Z, Mu J, et al. Antibody response and viraemia during the course of severe acute respiratory syndrome (SARS)-associated coronavirus infection. *J Med Microbiol*. 2004;53:435–438.
14. Li Y, Schneider AM, Mehta A, et al. SARS-CoV-2 viremia is associated with distinct proteomic pathways and predicts COVID-19 outcomes. *J Clin Invest*. 2021;131:e148635.
15. Edlow AG, Li JZ, Collier A-rY, et al. Assessment of maternal and neonatal SARS-CoV-2 viral load, transplacental antibody transfer, and placental pathology in pregnancies during the COVID-19 pandemic. *JAMA Netw Open*. 2020;3:e2030455.
16. Fang F, Chen Y, Zhao D, et al. Recommendations for the diagnosis, prevention, and control of coronavirus disease-19 in children—the Chinese perspectives. *Front Pediatr*. 2020;8:553394.
17. Tolu LB, Ezeh A, Feyissa GT. Vertical transmission of severe acute respiratory syndrome coronavirus 2: a scoping review. *PLoS One*. 2021;16:e0250196.
18. Penfield CA, Brubaker SG, Limaye MA, et al. Detection of severe acute respiratory syndrome coronavirus 2 in placental and fetal membrane samples. *Am J Obstet Gynecol MFM*. 2020;2:100133.
19. Kumar J, Meena J, Yadav A, et al. SARS-CoV-2 detection in human milk: a systematic review. *J Matern Fetal Neonatal Med*. 2021:1–8. [Online ahead of print].
20. Shlomai NO, Kasirer Y, Strauss T, et al. Neonatal SARS-CoV-2 infections in breastfeeding mothers. *Pediatrics*. 2021;147:e2020010918.
21. Centeno-Tablante E, Medina-Rivera M, Finkelstein JL, et al. Transmission of SARS-CoV-2 through breast milk and breastfeeding: a living systematic review. *Ann N Y Acad Sci*. 2021;1484:32–54.
22. Ip S, Chung M, Raman G, et al. Breastfeeding and maternal and infant health outcomes in developed countries. *Evid Rep Technol Assess (Full Rep)*. 2007;153:1–186.
23. Lawrence RM, Lawrence RA. Breastfeeding: more than just good nutrition. *Pediatr Rev*. 2011;32:267–280.
24. Jackson KM, Nazar AM. Breastfeeding, the immune response, and long-term health. *J Am Osteopath Assoc*. 2006;106:203–207.
25. Perl SH, Uzan-Yulzari A, Klainer H, et al. SARS-CoV-2–specific antibodies in breast milk after COVID-19 vaccination of breastfeeding women. *JAMA*. 2021;325:2013–2014.
26. Pace RM, Williams JE, Järvinen KM, et al. Characterization of SARS-CoV-2 RNA, antibodies, and neutralizing capacity in milk produced by women with COVID-19. *mBio*. 2021;12:e03192.
27. Walani SR. Global burden of preterm birth. *Int J Gynecol Obstet*. 2020;150:31–33.
28. Zambrano LD, Ellington S, Strid P, et al. Update: characteristics of symptomatic women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status—United States, January 22-October 3, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69:1641–1647.
29. Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ*. 2020;370:m3320.
30. Bánhidy F, Acs N, Puhó EH, et al. Maternal acute respiratory infectious diseases during pregnancy and birth outcomes. *Eur J Epidemiol*. 2008;23:29–35.
31. Silasi M, Cardenas I, Kwon JY, et al. Viral infections during pregnancy. *Am J Reprod Immunol*. 2015;73:199–213.
32. Cardenas I, Means RE, Aldo P, et al. Viral infection of the placenta leads to fetal inflammation and sensitization to bacterial products predisposing to preterm labor. *J Immunol*. 2010;185:1248–1257.
33. Mourad M, Jacob T, Sadovsky E, et al. Placental response to maternal SARS-CoV-2 infection. *Sci Rep*. 2021;11:14390.
34. Dong Y, Mo X, Hu Y, et al. Epidemiology of COVID-19 among children in China. *Pediatrics*. 2020;145:e20200702.
35. American Academy of Pediatrics. Children and COVID-19: State-Level Data Report; 2021.
36. Centers for Disease Control and Prevention. New admissions of patients with confirmed COVID-19 per 100,000 population by age group, United States. US Department of Health & Human Services; 2021. Available at: https://covid.cdc.gov/covid-data-tracker/#new-hospital-admissions. Accessed September 25, 2021.
37. More K, Chawla D, Murki S, et al. Outcomes of neonates born to mothers with coronavirus disease 2019 (COVID-19)—National Neonatology Forum (NNF) India COVID-19 Registry. *Indian Pediatr*. 2021;58:525–531.