

Neonatal SARS-CoV-2 Infections in Breastfeeding Mothers

Noa Ofek Shlomai, MD,^a Yair Kasirer, MD,^b Tzipora Strauss, MD,^c Tatiana Smolkin, MD, MSc,^d Ronella Marom, MD,^e Eric S. Shinwell, MD,^f Arye Simmonds, MD,^g Agneta Golan, MD,^h Iris Morag, MD,ⁱ Dan Waisman, MD,^j Clari Felszer-Fisch, MD,^k Dana G. Wolf, MD,^l Smadar Eventov-Friedman, MD, PhD^a

abstract

OBJECTIVES: To assess infection rates pre-discharge and post-discharge in breast milk-fed newborns with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-positive mothers who were separated post-delivery from their mothers and discharged from the hospital. Also, we aim to evaluate breastfeeding rates pre-discharge and post-discharge.

METHODS: Nasopharyngeal swabs for SARS-CoV-2 were obtained from symptomatic and high-risk women in the delivery room. Mothers with positive SARS-CoV-2 test results were separated from the newborns. Newborns were screened within 48 hours of delivery, and anti-infectious guidelines were imparted to the mothers before discharge. Rescreening took place ≥ 14 days post-discharge. Data regarding SARS-CoV-2-positive household members and breastfeeding were obtained by follow-up phone calls.

RESULTS: A total of 73 newborns of SARS-CoV-2-positive mothers were born in Israel during the ~ 3 -month period under study. Overall, 55 participated in this study. All neonates tested negative for the virus post-delivery. A total 74.5% of the neonates were fed unpasteurized expressed breast milk during the postpartum separation until discharge. Eighty-nine percent of the neonates were discharged from the hospital after their mothers were instructed in anti-infection measures. In 40% of the households, there were additional SARS-CoV-2-positive residents. A total of 85% of the newborns were breastfed post-discharge. Results for all 60% of the newborns retested for SARS-CoV-2 post-discharge were negative.

CONCLUSIONS: No viral infection was identified in neonates born to and separated from their SARS-CoV-2-positive mothers at birth and subsequently fed unpasteurized breast milk. All infants breastfed at home remained SARS-CoV-2 negative. These findings may provide insights regarding the redundancy of postpartum mother-newborn separation in SARS-CoV-2-positive women and, assuming precautions are adhered to, support the safety of breast milk.



^aDepartment of Neonatology and ^lClinical Virology Unit, Medical Center, Hadassah and Hebrew University, Jerusalem, Israel; ^bDepartment of Neonatology, Shaare Zedek Medical Center, Jerusalem, Israel; ^cAlbert Katz Department of Neonatology, Sheba Medical Center, Ramat Gan, Israel; ^dDepartment of Intensive Care in Premature Infants and Newborns, Baruch Padeh Medical Center, Poriya, Israel; ^eDepartment of Neonatology, Lis Maternity Center, Sourasky Medical Center, Tel Aviv, Israel; ^fNeonatal Intensive Care Unit, Ziv Medical Center and Azrieli Faculty of Medicine, Bar-Ilan University, Safed, Israel; ^gDepartment of Neonatology, Laniado Hospital, Netanya, Israel; ^hSoroka Medical Center and Ben Gurion University of the Negev, Be'er Sheva, Israel; ⁱDivision of Pediatrics, Shamir Medical Center, Zerifin, Israel; ^jDivision of Obstetrics and Newborn Medicine, Carmel Medical Center, Haifa, Israel; and ^kDepartment of Neonates, Ha'emek Medical Center, Afula, Israel

Dr Shlomai and Prof Eventov-Friedman conceptualized and designed the study, acquired and interpreted the data, drafted the initial manuscript, and revised the manuscript to conform with the comments of the coauthors; Prof Strauss, Drs Kasirer, Smolkin, Marom, Simmonds, Golan, Morag, Waisman, an Felszer-Fisch contributed substantially to the acquisition of the data and the revision of the manuscript for important intellectual content; Prof Shinwell contributed substantially to the acquisition and interpretation of the data and critically revised the manuscript for (Continued)

WHAT'S KNOWN ON THIS SUBJECT: The coronavirus disease 2019 (COVID-19) infection is a continuing pandemic and a major public health crisis. Most previous reports suggest no transplacental or transvaginal transmission of COVID-19.

WHAT THIS STUDY ADDS: This study reveals the lack of infection among neonates who were fed the breast milk of their severe acute respiratory syndrome coronavirus 2-positive mothers after discharge, many to homes where other residents were infected. The findings are relevant to public policy relating to the continuing COVID-19 pandemic.

To cite: Shlomai NO, Kasirer Y, Strauss T, et al. Neonatal SARS-CoV-2 Infections in Breastfeeding Mothers. *Pediatrics*. 2021;147(5):e2020010918

Since the first case of coronavirus disease 2019 (COVID-19)-related pneumonia was reported in Wuhan, Hubei Province, China, in December 2019, the disease has spread throughout China and worldwide, thereby constituting a pandemic and a major international health crisis.¹⁻⁴ COVID-19 was first diagnosed in Israel on February 20, 2020, in 2 of 11 Israeli citizens returning from Japan. Two days later, pilgrims from South Korea visiting Israel were diagnosed with the virus, and 5 days thereafter, the infection was detected in a healthy Israeli man who returned from a trip to Italy and subsequently spread the virus to 4 other people.

Initially, the majority of COVID-19 cases in Israel were diagnosed in Jerusalem, an ethnically, linguistically, and religiously diverse city with communities that maintain distinct ways of life. Given Israel's small size and unrestricted movement, by May 30, the disease had spread throughout the country. At that time, there were 16 987 patients with confirmed COVID-19 (1.69 cases per 1 million people), of whom 14 776 recovered and 284 died. The infection rate per 1000 people varied among regions, ranging from 0.22 to 9.93, reflecting differences in population density and compliance with the Israel Ministry of Health prevention guidelines.⁵

During the period from March 5 to May 30, 2020, ~45 000 women gave birth nationwide. Of these, 73 mothers tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Most presented with no or mild symptoms, allowing a typically brief postpartum hospitalization of 2 to 3 days.

Significantly, the infection rate of SARS-CoV-2-positive women who arrived at the delivery room of the Israeli centers (0.16%) was extremely low compared to the 13.7% detection rate found among pregnant women admitted for delivery in New York

during the same time period.⁶ This may suggest differences in the respective populations' susceptibility to the virus and/or reflect compliance levels with prophylactic infection control policies or other factors.

In the current study, we aim to evaluate predischarge and postdischarge infection status in neonates born to SARS-CoV-2-positive mothers who gave birth in 11 of 26 perinatal-neonatal centers in Israel during the first pandemic phase and who were routinely separated from their infected mothers after birth. In this study, we focused on whether (1) separation of the neonate from his or her mother after delivery reduces the risk of infection, and (2) in light of equivocal data in the literature, we sought to determine if, after anti-infectious guidance has been imparted to their mothers, infants can be safely breastfed before and after discharge from the hospital.

METHODS

SARS-CoV-2-positive women delivered in 12 of the 26 Israeli birth centers during the study period (March to May 2020), and 11 of these centers participated in this study.

At the Hadassah Medical Center, which comprises 2 Jerusalem hospitals, universal screening for the virus was conducted for all women admitted for delivery from April 1, 2020. The other centers tested only in cases in which there were clinical grounds for suspecting infection or in women at high risk for SARS-CoV-2 infection.

Clinical symptoms of the mothers were assessed before, during, and after delivery. At this initial phase of the pandemic, neonates were separated from their mothers with SARS-CoV-2 at birth until discharge, and data regarding their clinical course were obtained. During hospitalization, the newborns received either formula or their mothers' unpasteurized breast milk.

We also examined the breastfeeding rates and infection in the neonates who were fed breast milk after delivery and after discharge from the hospital. Before discharge, all mothers were thoroughly instructed regarding anti-infection precautions and preventive hygiene to reduce the risk of infecting their infants. Follow-up by phone took place ≥ 2 weeks after birth.

All newborns were screened for SARS-CoV-2 by nasopharyngeal swab samples tested by real-time polymerase chain reaction (RT-PCR) at 24 and 48 hours postdelivery. The samples were collected in 2-mL viral transport medium and mixed at a 1:1 ratio with a double-concentrated lysis buffer (DNA/RNA Shield; Zymo Research, Irvine, CA). Viral RNA was extracted by using the QIASymphony DSP Virus/Pathogen Kit on Qiasymphony platform (Qiagen) in accordance with the manufacturer's specifications. RNA was eluted into 60 μ L, of which 10 μ L was used for a 30- μ L reverse transcription RT-PCR by using a Real-Time Fluorescent RT-PCR kit for Detecting SARS-CoV-2 ORF1ab gene (BGI).

Specimens from the newborns who were rescreened were obtained by nasopharyngeal swab 14 to 21 days postdischarge.

Information regarding the infant's postdischarge health, whether they were fed breast milk, and concerning SARS-CoV-2-positive household members was assembled by the researchers using a questionnaire (Supplemental Information) in the course of a telephone interview that took place 14 to 21 days after discharge.

RESULTS

During the study period (March 5 to May 30, 2020), 73 SARS-CoV-2-positive women were identified from ~45 000 mothers who delivered at 12 Israeli birth centers. Data from 11 of these centers were collected,

and 55 neonates and 53 SARS-CoV-2–positive mothers participated in this study (Table 1).

Of the 51 singletons and 2 sets of twins, the majority were born at term (gestational age mean: 39 ± 1 weeks; gestational age range: $31 + 1/7$ – $41 + 1/7$ weeks), whereas 5 were preterm infants (gestational age range: $31 + 1/7$ – $36 + 6/7$ weeks). Average birth weight was 3136 g (range: 1290–4000 g).

Four newborns required treatment in the NICU, 1 because of prematurity-related respiratory distress syndrome, another owing to a congenital heart defect, and 2

because of low birth weight. One of these, a 35-week preterm infant who was small for gestational age (birth weight: 1680 g) died of necrotizing enterocolitis.

Two other infants required special treatment in the nursery, 1 presenting with transient tachypnea and treated with intravenous antibiotics and a second infant with neonatal jaundice who received phototherapy and intravenous fluids.

In 52 of 55 (95%) women, the mother's SARS-CoV-2 status was known before birth and, consequently, the infant was separated from the mother

immediately at birth as a prophylaxis measure. In 3 cases, the mother's positive status was available within a few hours of delivery. In these 3 cases, mother–infant skin-to-skin contact took place before the results of positive infection were received.

Of the 53 mothers, 41 (74.5%) expressed breast milk during the initial mother-infant separation period, which in most cases lasted 2 to 3 days.

Before discharge, all neonates, including the preterm infant who died of necrotizing enterocolitis, had negative SARS-CoV-2 polymerase chain reaction (PCR) results.

All but 6 neonates were discharged from the hospital after their mothers received detailed preventive instructions for hand hygiene, protective measures while breastfeeding (hand hygiene and masking), neonatal care, and recommended timing of circumcision.⁷ The remaining 6 neonates were discharged to SARS-CoV-2–negative households, separated from their infected mothers.

The households to which the infants were discharged had an average of 3 to 5 children, with an age range of 0 to 11 years, in addition to the newborn. In 40% of these homes (22 of 55), there was at least 1 SARS-CoV-2–positive member in addition to the mother.

Follow-up with the infants' families took place in the form of phone calls conducted 14 to 60 days (average: 38.8 days) after discharge. Information was collected from the replies of the informants to the questionnaire.

The results revealed that 47 neonates (85%) were exclusively breastfed at the time of follow-up. Two of the mothers had not intended to breastfeed, a decision that was unrelated to their SARS-CoV-2 infection or the mother–infant

TABLE 1 Maternal and Neonatal Characteristics at Delivery and After Discharge

Characteristics	Value
Maternal characteristics, <i>n</i> = 53 unless specified	
Age, y, mean \pm SD (range)	29.7 \pm 7.3 (20–44)
Gravida, mean \pm SD (range)	4.6 \pm 3.6 (1–15)
Parity, mean \pm SD (range)	3 \pm 2.7 (0–10)
Maternal SARS-CoV-2 status known before delivery, <i>n</i> (%)	52 (96.2)
Vaginal delivery, <i>n</i> (%)	43 (81)
Symptoms	
No symptoms	40 (76.1)
Fever >100 °F	10 (18.8)
Cough and sore throat	10 (18.8)
Shortness of breath	6 (11.3)
Loss of taste or smell	5 (9.5)
Fatigue	5 (9.5)
Pneumonia	2 (3.8)
Need for assisted ventilation	2 (3.8)
Neonatal characteristics, <i>n</i> = 55 unless specified	
Gestational age, wk, mean \pm SD (range)	39 \pm 1 (31 + 1–41 + 1)
Birth wt, g, mean \pm SD (range)	3136 (1290–4000)
Gestational size, <i>n</i> (%)	
AGA	43 (78.1)
LGA	7 (12.7)
SGA	5 (9)
Sex, <i>n</i> (%)	
Male	30 (54.5)
Female	25 (45.5)
Immediate separation from the mother, <i>n</i> (%)	47 (85)
NICU stay (unrelated to COVID-19), <i>n</i> (%)	4 (7.2)
Neonatal mortality, %	1.8 (1 neonate, because of necrotizing enterocolitis)
Breast milk during separation, <i>n</i> (%)	41 (74.5)
Discharge with the mother, <i>n</i> (%)	49 (89)
Postdischarge follow-up, <i>n</i> = 55 unless specified	
No. household residents, average (range)	3.41 (0–11)
Households with additional SARS-CoV-2–positive residents besides the mother, <i>n</i> (%)	22 (40)
Postdischarge breastfeeding, <i>n</i> (%)	47 (85.4)
Postdischarge neonatal nasopharyngeal swab, % (<i>n</i> of <i>M</i>)	60 (33 of 55)
SARS-CoV-2–positive neonatal nasopharyngeal swabs, %	0

AGA, average for gestational age; LGA, large for gestational age; SGA, small for gestational age.

separation initiated for all dyads either at delivery or as soon as the mother's SARS-CoV-2 positive status became known.

Follow-up specimens by nasopharyngeal swabbing were obtained from 33 of 55 (60%) newborns 14 to 21 days postdischarge. All of the PCR test results were negative, notwithstanding that the newborns were cared for by their SARS-CoV-2-positive mothers and that 3 of the infants had skin-to-skin contact with their mothers after delivery before their mothers' positive viral results were received.

None of these neonates had fever, cough, or any other symptoms of disease, according to the information received during follow-up phone conversations. To the best of our knowledge (from the phone calls and a review of pediatric emergency department reports), none of these infants were hospitalized because of SARS-CoV-2 infection or any other cause for at least 14 and up to 21 days after discharge.

DISCUSSION

Our findings indicating the absence of neonatal infection in a large group of infants born to SARS-CoV-2-positive mothers in 11 birth centers throughout Israel corroborate some of the previous research in which no evidence of transplacental or transvaginal transmission of COVID-19 was found.⁸⁻¹¹ However, population susceptibility to the virus among obstetrical patients and preexisting comorbidities may influence perinatal outcome¹² and supports the need for local COVID-19 screening to guide policy concerning prophylactic infection control measures.¹³

At an early stage of the pandemic, Yan et al¹ presented a case series of 116 SARS-CoV-2-positive women in China. The incidence of severe respiratory disease in these mothers was 8%,

which matches the rates of severe COVID-19 infection in the nonpregnant population in their region in China. This contrasts with only 2 women in our study who had COVID-19 pneumonia, 1 of whom was intubated for a cesarean delivery and remained ventilated for a few days. Other than that, these 2 women did not require invasive respiratory support.

The relatively minor symptoms experienced by the SARS-CoV-2-positive women in our study before birth, coupled with low rates of preterm births, compared with other countries¹ may be attributed to differences in population health and antenatal care.¹⁴ The option of COVID-19 vertical transmission has been examined in several studies.

Zeng et al¹⁵ described a cohort of 33 SARS-CoV-2-positive women at the time of delivery. Three of these 33 infants (9%) presented with early-onset COVID-19 infection. The authors argued that since strict infection control and prevention procedures were implemented during delivery, it is likely that the sources of SARS-CoV-2 in the neonates' upper respiratory tracts or rectal swabs were maternal in origin. Of these neonates, 1 had meconium aspiration syndrome, 1 had lethargy and fever, and 1 was a 31-week preterm infant.

Kirtsman et al¹⁶ described a neonate with a probable congenital COVID-19 infection despite separation at delivery. However, this conflicts with recent studies that presented negative SARS-CoV-2 PCR results in amniotic fluid and breast milk,¹⁷ suggesting that there is no vertical transmission of COVID-19. Piersigill et al¹⁸ presented a case report of a preterm infant born at 26 weeks who tested positive for SARS-CoV-2 several days after birth, after several days of skin-to-skin contact with his positive-status and symptomatic mother. After the mother's breast milk proved negative for SARS-CoV-2

by PCR, the authors concluded that this case resulted from horizontal rather than vertical transmission.

In a recent systematic review of 11 studies, Muhidin et al¹⁹ concluded that there is no evidence of intrauterine or transplacental transmission of SARS-CoV-2 to the fetus during the third trimester of pregnancy. However, Vivanti et al²⁰ describe a case of transplacental transmission of SARS-CoV-2 in a neonate born to a mother who became infected in the last trimester. The transmission was confirmed by comprehensive virological and pathologic investigation, revealing that of 179 newborns tested for SARS-CoV-2 at birth from mothers who tested positive for the virus, vertical transmission was suspected in 8 infants. In a recent meta-analysis of 74 articles,²¹ researchers found confirmed transplacental and intrapartum transmission of SARS-CoV-2 in 5.7% and 3.3% of the cases examined, respectively.

This conflicts with the findings of Mahyuddin et al,²² who found that the laboratory results for the 40 SARS-CoV-2-positive pregnant women they studied did not find evidence of the coexpression of the angiotensin-converting enzyme 2 receptor and TMPRSS2 protease. Such coaction is required for SARS-CoV-2 to gain cytoplasmic entry, and it was not observed in cells at the maternal-fetal interface, which reduces the possibility of viral entry into the cells.

This corroborates available clinical data wherein no consistent and conclusive features of congenital infections have been documented and coheres with other clinical reports that have not found well-supported, consistent, and conclusive evidence of congenital infections. Nonetheless, clear evidence exists of histopathological changes in the placenta of SARS-CoV-2-positive women, reflecting maternal vascular malperfusion and inflammatory

changes.²³ It remains unclear whether these pathologic changes can cross the maternal-placental interface and enable transplacental transmission of the SARS-CoV-2 virion. Even if this is possible, however, it is unlikely to be a frequent occurrence.

In a study of 38 SARS-CoV-2-positive women, Schwartz et al²⁴ found no confirmed cases of intrauterine transmission of SARS-CoV-2, and all neonatal specimens, including several placentas, had negative test results for SARS-CoV-2 by RT-PCR.

Against this background, the possibility and rates of transplacental transmission of SARS-CoV-2 remain unclear, as does a central research question addressed here: Can the SARS-CoV-2 virus be transmitted to the newborn by breast milk?

A recent correspondence²⁵ reports COVID-19 infection in 1 of 2 SARS-CoV-2-positive women whose breast milk was tested several times after they had received appropriate instruction concerning infection prevention. One woman's breast milk tested negative for the virus, whereas the other's returned with positive results, and the infant presented mild COVID-19 symptoms and a positive viral PCR test. It is unknown whether the newborn was infected through the milk or other modes of infection.

Lackey et al²⁶ reported 9 mothers with confirmed COVID-19 whose breast milk samples consistently tested negative for SARS-CoV-2 by RT-PCR. To date, there are no convincing data revealing that the virus is able to penetrate the mammary gland cells or that human milk can be a source of SARS-CoV-2 infection.²⁷

Accordingly, the Italian Society of Neonatology guidelines,²⁸ as well as those of the World Health

Organization,²⁷ include a recommendation for breastfeeding by SARS-CoV-2-positive mothers, either directly or by freshly expressed breast milk, depending on the mother's health. The Italian Society of Neonatology states that pasteurization is not necessary because human milk is not believed to be a vehicle for SARS-CoV-2 transmission.²⁹

The results of this study are based on nationally extensive data, extending from delivery to at least 2 weeks postdischarge, and characterized by a high retention rate of participation among patients. Our findings reveal no neonatal infection among newborns of SARS-CoV-2-positive mothers. Most of these neonates were asymptomatic, and in those who had clinical symptoms, these were related to perinatal or prematurity causes. These results suggest a promising prognosis for newborns of SARS-CoV-2-positive mothers.

Our results further reveal that breastfeeding does not lead to viral transmission from mothers to their infants, as long as hygienic and related precautions are taken. Moreover, we demonstrated that neonates remained asymptomatic and healthy while being fed with unpasteurized expressed breast milk, both during postdelivery separation from their mothers and at home. This concurs with a report by Patil et al³⁰ and contrasts with the negative influence on breastfeeding after in-hospital short separations described by Popofsky et al.³¹ Even so, we believe that this cannot be used to advise the separation of the newborn-mother dyad but rather to acknowledge that if separation occurs, it does not necessarily eliminate the possibility of breastfeeding after discharge.

Susceptibility to the virus among obstetrical patients may differ internationally, which highlights the need for local SARS-CoV-2 screening to guide prophylactic infection-control measures. Differential locational impact is suggested, for example, when considering the discrepancy in rates of severe respiratory disease between the Israeli women described here and Chinese mothers described by Yan et al.¹ Similarly, the relatively light symptoms experienced by the SARS-CoV-2-positive women before delivery who participated in our study, and the low rates of preterm births compared with other countries,¹ may also be attributable to global differences in population health and antenatal care.

With our study results, we suggest that neonates born to SARS-CoV-2-positive mothers can have an excellent prognosis. With all the neonates testing negative for SARS-CoV-2, ongoing separation after delivery appears unnecessary, as long as careful anti-infection measurements are taken. Furthermore, under these conditions, our study reveals that breastfeeding by a SARS-CoV-2 mother is safe.

These conclusions, we believe, can serve to inform public policy during the ongoing crisis.

ABBREVIATIONS

COVID-19: coronavirus disease 2019

PCR: polymerase chain reaction

RT-PCR: real-time polymerase chain reaction

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

important intellectual content; Prof Wolf provided the analysis of coronavirus disease 2019 polymerase chain reaction data and revised the manuscript; and all authors approved the final version of the manuscript as submitted and agreed to be accountable for all aspects of the work.

DOI: <https://doi.org/10.1542/peds.2020-010918>

Accepted for publication Dec 23, 2020

Address correspondence to Noa Ofek Shlomai, MD, Department of Neonatology, Hadassah and Hebrew University Medical Center, Jerusalem, Israel. E-mail: noaofek@hadassah.org.il

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

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FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

COMPANION PAPER: A companion to this article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-049772.

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Pediatrics 2021;147;

DOI: 10.1542/peds.2020-010918 originally published online April 13, 2021;

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Felszer-Fisch, Dana G. Wolf and Smadar Eventov-Friedman

Pediatrics 2021;147;

DOI: 10.1542/peds.2020-010918 originally published online April 13, 2021;

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