Neonatal management and outcomes during the COVID-19 pandemic: an observation cohort study

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Summary

Background The risk of vertical and perinatal transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2, which causes COVID-19), the most appropriate management, and the neonate’s risk of developing COVID-19 during the perinatal period are unknown. Therefore, we aimed to elucidate best practices regarding infection control in mother–newborn dyads, and identify potential risk factors associated with transmission.

Methods In this observational cohort study, we identified all neonates born between March 22 and May 17, 2020, at three New York Presbyterian Hospitals in New York City (NY, USA) to mothers positive for SARS-CoV-2 at delivery. Mothers could practice skin-to-skin care and breastfeed in the delivery room, but had to wear a surgical mask when near their neonate and practice proper hand hygiene before skin-to-skin contact, breastfeeding, and routine care. Unless medically required, neonates were kept in a closed Giraffe isolette in the same room as their mothers, and were held by mothers for feeding after appropriate hand hygiene, breast cleansing, and placement of a surgical mask. Neonates were tested for SARS-CoV-2 by use of real-time PCR on nasopharyngeal swabs taken at 24 h, 5–7 days, and 14 days of life, and were clinically evaluated by telemedicine at 1 month of age. We recorded demographics, neonatal, and maternal clinical presentation, as well as infection control practices in the hospital and at home.

Findings Of 1481 deliveries, 116 (8%) mothers tested positive for SARS-CoV-2; 120 neonates were identified. All neonates were tested at 24 h of life and none were positive for SARS-CoV-2. 82 (68%) neonates completed follow-up at day 5–7 of life. Of the 82 neonates, 68 (83%) roomed in with the mothers. All mothers were allowed to breastfeed; at 5–7 days of life, 64 (78%) were still breastfeeding. 79 (96%) of 82 neonates had a repeat PCR at 5–7 days of life, which was negative in all; 72 (88%) neonates were also tested at 14 days of life and none were positive. None of the neonates had symptoms of COVID-19.

Interpretation Our data suggest that perinatal transmission of COVID-19 is unlikely to occur if correct hygiene precautions are undertaken, and that allowing neonates to room in with their mothers and direct breastfeeding are safe procedures when paired with effective parental education of infant protective strategies.

Funding None.

Introduction COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has spread worldwide with substantial consequences for public health.1 New York City (NY, USA) has been particularly affected, with around 200 000 confirmed cases as of May 17, 2020. Adults with comorbidities are at greatest risk for severe disease and death; however, little is known about the consequences of SARS-CoV-2 infection in pregnant women and fetuses. Information regarding neonatal outcomes is scarce, and optimal management of the mother and neonate is unknown.

Respiratory viruses uncommonly result in intrauterine transmission of infection to fetuses; therefore, intrauterine transmission of SARS-CoV-2 is anticipated to be low. Two case reports describing isolation of SARS-CoV-2 from amniotic fluid and placental tissue and isolation of SARS-CoV-2 from the nasopharynx of the two neonates within 48 h of life suggested probable congenital infection; however, the rate of congenital infections of neonates born to SARS-CoV-2-positive mothers remains unknown. The risk of perinatal transmission, especially when breastfeeding, and the neonate’s risk of developing COVID-19 during the perinatal period are also unknown.2,3 Guidelines have been provided by various medical societies, but because of a scarcity of clinical data, they differ in recommended management strategies for mother–infant dyads.4

We aimed to follow up neonates born to mothers positive for SARS-CoV-2 at time of delivery, to elucidate best practices regarding infection control and identify potential risk factors associated with transmission.

Methods

Study design and participants For this observational cohort study, we identified all neonates born between March 22 and May 17, 2020, at New York Presbyterian—Komansky Children’s Hospital, Weill
Articles

Research in context

Evidence before this study

Little is known about the possible consequences of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in pregnant women and fetuses. There is scant information regarding neonatal outcomes, and optimal management of the mothers and neonates is unknown. We searched PubMed and LitCovid for all manuscripts published in English from Feb 1 to May 20, 2020, with the key terms “newborns and COVID-19”, “perinatal outcome COVID-19”. We found a few small case series advising separation from mothers and formula feeding for at least 14 days for all neonates born to a mother testing positive for SARS-CoV-2 at time of delivery. However, these interventions are mainly expert opinions and there is no prospective and actual data showing that these procedures are effective and needed.

Added value of this study

To the best of our knowledge, this is the largest cohort of neonates born to mothers positive for SARS-CoV-2 at the time of delivery, with prospective follow-up up to 1 month of life. In our cohort, 68 (83%) of 82 neonates with complete follow-up data roomed in with the mothers and all were allowed to breastfeed. Prospective real-time PCR testing for SARS-CoV-2 was negative in all neonates tested at 1 week and 2 weeks of life. None of the neonates had symptoms of COVID-19 as of 1 month of age.

Implications of all the available evidence

Our findings support the published literature and confirm that perinatal transmission of COVID-19 is unlikely to occur if correct hygiene precautions are undertaken. In view of the benefits of early mother–neonate bonding and breastfeeding, rooming in with the mother and direct breastfeeding are safe and should be promoted, but these procedures need to be paired with effective parental education of infant protective strategies, such as use of surgical masks when near the neonate and frequent hand hygiene.

Cornell Medicine, New York Presbyterian—Lower Manhattan Hospital, and New York Presbyterian—Queens in New York City to mothers who tested positive for SARS-CoV-2 from a nasopharyngeal swab sample at the time of delivery. As a result of inadvertent exposure of health-care professionals to SARS-CoV-2 from asymptomatic women in labour, and concern that symptoms of labour can mimic those of COVID-19, universal screening of all pregnant women presenting in labour was implemented in our Labour and Delivery units on March 25, 2020.

Neonates were referred to newly created neonatal COVID-19 outpatient clinics from the three hospitals from March 22, 2020.

This study was approved by the Weill Cornell Medicine institutional review board, protocol number 20-04021816. It was approved as exempt from consent as our testing and clinical follow-up was created as part of standard medical care for this population. Institutional Review Board approval was obtained to retrospectively collect the data obtained as part of clinical care.

Procedures

Testing for SARS-CoV-2 was done by use of real-time PCR (rtPCR; RealStar SARS-CoV-2 RT-PCR Kit, [Altona Diagnostics USA, Plain City, OH], cobas SARS-CoV-2 Test [Roche Molecular Systems, Branchburg, NJ], and Xpert Xpress SARS-CoV-2 [Cepheid, Sunnyvale, CA]). Turnaround time from specimen collection to result reporting was 24 h for the Altona and Roche tests and 1–2 h for Cepheid Xpert. Neonates were tested for SARS-CoV-2 by rtPCR on a nasopharyngeal swab sample at 12–24 h, 5–7 days, and 14 days of life and as indicated at subsequent visits. These timepoints were chosen to provide an opportunity for repeat testing and routine neonatal care. The 5–7-day timepoint was used to allow for routine neonatal follow-up, because many paediatricians’ offices were not seeing patients in person; thus, a visit to our clinic at that time allowed for repeat testing along with routine neonate evaluation. The 14-day timepoint was decided on the basis of what was known about viral shedding and antibody responses at that time, and we purported that mothers were unlikely, if asymptomatic, to remain infectious at that time. Thus, if the neonate remained SARS-CoV-2 rtPCR-negative at 14 days, the likelihood of continued risk of transmission from the mother was unlikely.

The data used in this study were collected from inpatient medical records at time of birth and the outpatient medical record at the neonatal COVID-19 clinic visits on days 5–7 and 14 and by telemedicine visits at 1 month of life. Data collected included demographics, neonatal and maternal clinical presentation at time of delivery, during hospitalisation, and once discharged, microbiology results (SARS-CoV-2 rtPCR testing), and infection control practices in the hospital and at home. Neonates were assessed at all timepoints for fever, hypothermia, respiratory distress, lethargy, cough, rhinorrhea, irritability, rash, diarrhoea, and feeding intolerance. Mothers were assessed at each outpatient clinic visit for self-reported symptoms of fever, cough, anosmia, ageusia, shortness of breath, sore throat, rhinorrhea, myalgias, vomiting, and diarrhoea. Infection control practices included in the data collection were disposition of the neonate at delivery (allowed to room in with mother or admitted to a dedicated isolation room), feeding method (direct breastfeeding or expressed breast milk or formula), and self-reported frequency of hand hygiene, breast cleansing, and use of surgical masks at home.
Standard of care at all participating institutions is to initiate newborn skin-to-skin contact with mothers in the first hour of life if medically appropriate. This practice was not altered during the pandemic. Mothers who were positive for SARS-CoV-2 could practice skin-to-skin care and breastfeed in the delivery room with some modifications to usual processes. Among the precautions, mothers donned a surgical mask when near their neonate and practiced proper hand hygiene before skin-to-skin contact, breastfeeding, and routine care. All neonates who roomed in with their mothers were kept in a closed Giraffe isolette (General Electric Healthcare, Chicago, IL) and were held by mothers for feeding after appropriate hand hygiene, breast cleansing, and placement of a surgical mask. Only mothers were allowed to be present on the postpartum unit for the duration of the neonate’s stay. All mothers were allowed to breastfeed their neonate while in the hospital and after being discharged home. Mothers of neonates admitted to the NICU were allowed to visit once 14 days had elapsed after they tested positive and if they were afebrile for at least 72 h.

Statistical analysis
We did a descriptive analysis with results presented as proportions for categorical variables and median and simple ranges for continuous variables. Stata 13 software was used for all analyses.

Role of the funding source
There was no funding source for this study.

Results
Between March 22 and May 17, 2020, there were 1481 deliveries, with 116 (8%) mothers testing positive for SARS-CoV-2. Of the 120 neonates identified, 106 (88%) were referred to our outpatient clinic (figure). 14 (12%) of 120 neonates were lost to follow-up, because some providers were not aware of the follow up clinic and did not make referrals. Only the 82 (69%) neonates with completed follow-up data at day 5–7 of life were included in the final analysis of this study; however, the immediate peripartum data is provided for the 24 neonates who were referred but had no subsequent follow-up (table 1).

Of the 82 neonates, 41 (50%) were female, 36 (44%) were born by caesarean section, 68 (83%) were born at term, 14 (17%) were preterm, and the median gestational age was 38 weeks (range 27–41). The most common indications for caesarean sections were arrest of labour (12 [33%] of 36) and non-reassuring fetal tracing (6 [17%] of 36). Mode of delivery was not affected by SARS-CoV-2 test results. 12 (15%) neonates were admitted to the neonatal intensive care unit (NICU) and 70 (85%) received routine neonatal care.

20 (26%) of 78 mothers reported never being symptomatic, and 58 (74%) were symptomatic; 27 (46%) of these 58 mothers had symptoms onset more than 2 weeks before delivery and were asymptomatic at delivery, and 31 (54%) had symptoms onset within 2 weeks before delivery or during labour (table 2). Of the 22 mothers who reported symptoms within 7 days of delivery, 18 (82%) had cough, nine of whom also reported a fever. Mothers with symptom onset more than 2 weeks before delivery were more prevalent during the last weeks of the study period.

Of the 82 neonates, 68 (83%) roomed in with the mothers (table 1). Of these 68 neonates who roomed in, three (4%) were separated from their mothers after 24 h per clinical indications; one required 3 days of phototherapy, one remained under brief observation in the NICU for prolonged QT syndrome, and one had clinically significant feeding intolerance and short bowel syndrome requiring prolonged NICU admission. 14 (17%) neonates were separated from their mothers immediately after birth; four were kept in a dedicated isolation room in the newborn nursery owing to maternal medical condition or maternal preference, and ten were directly admitted to the NICU. Of the 12 neonates admitted to the NICU, five had a length of stay of 2–4 days and reasons for admission were prolonged QT syndrome, mild respiratory distress, and tachycardia. Median length of hospital stay for all 82 neonates was 2 days (range 1–21).

By 5–7 days of life, 73 (89%) of 82 neonates were discharged home to parents, and the remaining nine (11%) remained hospitalised. 44 (60%) of these 73 neonates were discharged home to an environment
where a household member, other than mother, had reported symptoms consistent with COVID-19. In most cases, the symptomatic household member was an adult, and in multiple cases, more than one household member was ill (table 2).

Self-reported use of masks and hand hygiene practices were done always by 62 (85%) of 73 parents, frequently or sometimes by six (8%), and never by three (4%), despite recommendations given at time of hospital discharge; data were not available for two families (table 2).

At 5–7 days of life, 18 (22%) of 82 neonates were exclusively formula fed, whereas the remaining 64 (78%) were receiving breastmilk, through direct latching or bottle administration, with or without addition of formula (table 1).

rtPCR results from a nasopharyngeal swab obtained at birth were available for all 120 neonates initially identified. 119 (99%) neonates had a negative rtPCR and one result was reported as invalid (table 3). 79 (96%) of the 82 neonates included in the final analysis had a repeat rtPCR at 5–7 days of life and all were negative, including the infant whose initial rtPCR result was reported as invalid. 72 (88%) neonates had repeat rtPCR testing at day 14 of life, of whom 70 (97%) had a negative test result. Two (3%) results were reported as invalid and testing was not repeated, because both neonates were clinically well.

Three (4%) of 82 neonates had a telemedicine visit at days 7 and 14 of life and were asymptomatic during the entire observation period, but they were not retested.

Aside from seven (8%) preterm neonates admitted to NICU for standard care for prematurity, all other neonates were asymptomatic at birth, except four who had transient tachypnoea of neonate in two and antibiotic administration for 48 h owing to maternal fever in one. 32-term neonates who reached 1 month of age as of May 17, 2020 (follow-up ongoing).

Table 1: Demographics and neonatal characteristics

<table>
<thead>
<tr>
<th>Sex</th>
<th>Neonates referred who completed follow-up (N=82)</th>
<th>Neonates referred with no follow-up (N=24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>41 (50%)</td>
<td>14 (58%)</td>
</tr>
<tr>
<td>Female</td>
<td>41 (50%)</td>
<td>10 (42%)</td>
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</tbody>
</table>

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<thead>
<tr>
<th>Race</th>
<th>Neonates referred who completed follow-up (N=82)</th>
<th>Neonates referred with no follow-up (N=24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>30 (37%)</td>
<td>12 (50%)</td>
</tr>
<tr>
<td>Black</td>
<td>10 (12%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Asian</td>
<td>14 (17%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Other or declined to answer</td>
<td>28 (34%)</td>
<td>10 (42%)</td>
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</table>

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Neonates referred who completed follow-up (N=82)</th>
<th>Neonates referred with no follow-up (N=24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hispanic, Latino, or Spanish</td>
<td>23 (28%)</td>
<td>6 (25%)</td>
</tr>
<tr>
<td>Not Hispanic, Latino, or Spanish</td>
<td>32 (39%)</td>
<td>14 (58%)</td>
</tr>
<tr>
<td>Other or declined to answer</td>
<td>27 (33%)</td>
<td>4 (17%)</td>
</tr>
</tbody>
</table>

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<thead>
<tr>
<th>Insurance</th>
<th>Neonates referred who completed follow-up (N=82)</th>
<th>Neonates referred with no follow-up (N=24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Private</td>
<td>45 (55%)</td>
<td>11 (46%)</td>
</tr>
<tr>
<td>Public</td>
<td>37 (45%)</td>
<td>11 (46%)</td>
</tr>
<tr>
<td>NA</td>
<td>0</td>
<td>2 (8%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Born by</th>
<th>Neonates referred who completed follow-up (N=82)</th>
<th>Neonates referred with no follow-up (N=24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caesarean section</td>
<td>36 (44%)</td>
<td>7 (29%)</td>
</tr>
<tr>
<td>Vaginal delivery</td>
<td>46 (56%)</td>
<td>17 (71%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gestational age, weeks</th>
<th>Neonates referred who completed follow-up (N=82)</th>
<th>Neonates referred with no follow-up (N=24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preterm (&lt;37 weeks)</td>
<td>14 (17%)</td>
<td>0</td>
</tr>
<tr>
<td>34–36 weeks</td>
<td>11 (13%)</td>
<td>-</td>
</tr>
<tr>
<td>32–33 weeks</td>
<td>2 (2%)</td>
<td>-</td>
</tr>
<tr>
<td>28–31 weeks</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>&lt;28 weeks</td>
<td>1 (1%)</td>
<td>-</td>
</tr>
<tr>
<td>Term</td>
<td>68 (83%)</td>
<td>-</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Birthweight, grams</th>
<th>Neonates referred who completed follow-up (N=82)</th>
<th>Neonates referred with no follow-up (N=24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥2500</td>
<td>71 (87%)</td>
<td>23 (96%)</td>
</tr>
<tr>
<td>1500-2499</td>
<td>10 (12%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>1000-1499</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>&lt;1000</td>
<td>1 (1%)</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 1 continues in next column
ongoing). 77 (94%) of 82 infant’s parents were symptom-free at the day 14 of life visit and were instructed to discontinue mask precautions at home when around the neonate. Five (6%) of 82 infant’s parents were still symptomatic and were instructed to continue wearing a mask for an extra week.

At the telemedicine visit at 1 month of life, three sets of parents were still using masks when next to the neonate despite our recommendation, mainly because of parental fear of still being contagious.

Of the 53 neonates, 45 (85%) were still breastfeeding and eight (15%) were exclusively formula fed.

Parents reported new-onset congestion without fever for three neonates. These three infants were retested for SARS-CoV-2 by nasopharyngeal PCR, all of which were negative. One neonate had 1 day of fever and was evaluated in the emergency department, where blood and urine cultures and repeat SARS-CoV-2 PCR were negative; he was discharged home without admission. All neonates continued to be clinically well and are growing appropriately.

**Discussion**

To our knowledge, this is the largest US cohort of neonates born to mothers who tested positive for SARS-CoV-2 at time of delivery and who were subsequently followed with serial testing and clinically up to 1 month of life. In our case series, no infant had SARS-CoV-2 virus detected by a nasopharyngeal swab in the immediate postnatal period (24 h), nor at 5–7 or 14 days of life. Additionally, all infants remained asymptomatic during the study period. This finding supports the previous reports of a low risk of perinatal transmission with strict infection control practices.

To date, there are several case reports of neonates who have tested positive for SARS-CoV-2 within 48 h. Zeng and colleagues\(^1\) reported on three of 33 neonates, born to SARS-CoV-2-positive mothers, with positive nasopharyngeal swabs on days 2 and 4 of life. Two individual case reports suggestive of probable congenital infection have been published. Zamaniyan and colleagues\(^5\) described a preterm neonate born to a mother with severe COVID-19; the neonate tested positive by nasopharyngeal swab at 48 h and amniotic fluid was also positive for SARS-CoV-2 by rtPCR. Kirtsman and colleagues\(^6\) reported a term neonate born to a mother with 1 day of fever and cough at time of delivery. The mother’s placental tissue was rtPCR-positive for SARS-CoV-2 on both the parenchymal and chorionic sides. The infant tested positive for SARS-CoV-2 at birth by nasopharyngeal swab. In a study from the UK,\(^17\) six neonates were positive within 12 h after birth; however, whether this represented a false positive from maternal contamination has not been confirmed, because testing was obtained very soon after birth and was not repeated at a later time to confirm. In two reports from China,\(^18,19\) three neonates born to mothers with COVID-19 pneumonia were positive for IgG and IgM; however, presence of IgM alone is not a
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of Pediatrics,11 the US Centers for Disease Control and Prevention,12 and the recommendations of the American Academy of Pediatrics, which advocate for the promotion of breastfeeding and the initial mother–infant relationship rather than in the respiratory tract in congenitally infected neonates. However, neonates positive for SARS-CoV-2 at birth reported in the published literature so far had a positive nasopharyngeal swab. Finally, we relied solely on parental report regarding hand hygiene and mask usage at home, so there is the potential for recall bias.

In conclusion, our data suggest that perinatal transmission is unlikely to occur if correct hygiene precautions are undertaken and that rooming in and breastfeeding are safe procedures when paired with effective parental education of infant protective strategies.

Contributors

CMS and PD, examined the infants and contributed to the design, data organisation, analysis, discussion, main interpretation of results, and writing of the article. JYH, KPA, and JD examined the children and contributed to the discussion of results and writing of the article. PT, JH,
MB, CC, LG, and AP contributed with epidemiological information and infant referrals and to writing of the article.

Declaration of interests
We declare no competing interests.

Data sharing
The de-identified dataset supporting the conclusions of this Article can be made available from the corresponding author upon reasonable request.

Acknowledgments
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References