Clinical Characteristics, Transmission Rate and Outcome of Neonates Born to COVID-19-Positive Mothers: A Prospective Case Series From a Resource-Limited Setting

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Background: Coronavirus disease (COVID-19) infection during pregnancy could damage the placenta, but data on neonates born to COVID-19-positive mothers is scarce. In this case series, we aim to describe clinical characteristics, transmission rate and outcomes at 3 months of age among neonates born to mothers with COVID-19 diagnosed near the time of delivery.

Methods: Prospective, multicenter case series from Suriname. We collected clinical data of neonates born to mothers with COVID-19 infection between June and August 2021. COVID-19 swabs were taken within 5 days and 2 weeks after birth. Follow-up took place at 3 months.

Results: We enrolled 18 neonates. However, 18/18 (100%) mothers were infected in the third trimester and 10/18 (55.6%) had severe COVID-19 infection requiring ICU admission and 2/10 (20%) died. In total 16/18 (77.8%) neonates were born after cesarean section and 13/18 (72.2%) were born preterm (median 35 weeks, Interquartile range 32 + 4–38 + 0). Neonatal intensive care unit admission was needed in 7/18 (38.9%) neonates. Respiratory symptoms occurred in 12/18 (66.7%), 5/18 (27.8%) were suspected of early-onset sepsis and 1/18(5.6%) of late-onset sepsis. One preterm neonate developed necrotizing enterocolitis. A nasopharyngeal swab was positive in 1/18 (5.5%) neonates within 5 days of life and in 9/11 (0%) neonates after 2 weeks. Follow-up showed mild neurodevelopmental delay in 2/14 (14.3%) patients.

Conclusion: We describe a high proportion of severely ill mothers due to COVID-19 infection with subsequent cesarean delivery and prematurity. Accounting for gestational age at birth, the neonatal clinical course and findings at follow-up appeared similar to neonates born to COVID-19-negative mothers. Maternal vaccination is recommended to prevent neonatal risks associated with prematurity and cesarean delivery.

Key Words: COVID-19, neonates, follow-up

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COVID-19 Protocols

We followed local and hospital-specific protocols concerning medical care. Neonates with the indication for admission to the neonatal intensive care, high care or medium care received standard medical care regardless of their COVID-19 status. Parents of the infants were allowed to visit their child once they were declared COVID-19 negative by the national public health institute, “Bureau voor Openbare Gezondheidszorg”. Neonates without indication for admission were, according to international guidelines of the WHO, allowed to room in with their mothers. Breastfeeding and skin-to-skin contact were permitted.

Ethical Aspects

The study protocol was approved by the Medical Ethical Committees “Commissie Mens gebonden Wetenschappelijk Onderzoek”, by the medical director of the Academic Hospital Paramaribo and by all the pediatric departments of the participating hospitals. Informed written consent was obtained from at least one of the parents or caregivers.

RESULTS

We enrolled 18 neonates born to COVID-19-positive mothers. Demographics and health profile of pregnant women are shown in Table 1. All pregnant women had singleton pregnancies and were diagnosed with COVID-19 infection during the third trimester of their pregnancy. Comorbidities were found in only 2 women: 1 woman suffered from pre-eclampsia and 1 with diabetes mellitus. All women had COVID-19 symptoms; 9/18 (50.0%) had mild to moderate severity of the disease and 8/18 (44.4%) had severe COVID-19 infection requiring ICU admission of which 2 (11.1%) died. The disease severity of 1 woman was unknown. Only 4/18 (22.2%) women gave birth through vaginal delivery. The remaining 14/18 (77.8%) neonates were born after cesarean section of which 12 were performed on the maternal indication. In 10/12 (83.3%) cases, the maternal indication was impending respiratory failure. The other 2 maternal indications were cesarean section in the medical history and placenta previa.

Clinical Characteristics of Neonates Born to COVID-19-Positive Mothers

Clinical characteristics, management and outcome of neonates born to COVID-19-positive mothers are summarised in Table 2. Of 18 neonates, 9 (50%) were male and 9 (50%) were female. In total 13/18 (72.2%) neonates were born preterm and only 5/18 (27.8%) were born at full-term gestation. The median gestational age was 35 weeks (Interquartile range 32 ± 4–38 ± 0). Among them, 17 neonates were born appropriate for their gestation and only 1 (5.6%) was born small for gestational age. However, 7 of the 18 (38.9%) neonates included had birth weights above 2.5 kg. 9/18 (50%) had 1.5–2.5 kg and 2 (11.1%) of the neonates weighed less than 1.5 kg. Appearance, Pulse, Grimace, Activity, Respiration (50%) had 1.5–2.5 kg and 2 (11.1%) of the neonates weighed less than 1.5 kg. Appearance, Pulse, Grimace, Activity, Respiration scores were >5 at 5 minutes for all neonates. No neonatal asphyxia occurred in the study cohort.

Seven of 18 neonates were admitted to the NICU. Six of 18 neonates were admitted to high-care units and 5/18 were sent home directly after birth. Respiratory symptoms occurred in 12/18 (66.7%) neonates. Although 4/18 (22.2%) neonates suffered from transient tachypnea of the newborn, of which one was supported with continuous positive airway pressure (CPAP) and the other 3 received low flow. In total 8/18 (44.4%) neonates developed neonatal respiratory distress syndrome, most of them received respiratory support with CPAP. Only for 1 neonate, with grade 3 Neonatal Respiratory Distress Syndrome, invasive ventilation was required. Also, 6/18 (33.3%) neonates did not develop any respiratory symptoms.

Infectious problems were seen in 7/18 (38.9%) neonates. Five were suspected of early-onset neonatal sepsis, for which empirical antibiotic therapy was given in different regimens because of different hospital guidelines among the participating centers. One neonate received antibiotics during 72 hours for suspected late onset sepsis. All blood cultures were negative. In one neonate, a urinary tract infection was suspected. Treatment with antibiotics was given for 72 hours. Negative urinary cultures were found. Four of 18 children had hyperbilirubinemia, for which phototherapy was administered.

One preterm neonate admitted to the NICU developed Necrotizing Enterocolitis, which was treated sufficiently with antibiotics and discontinued enteral feeding.

Two children were admitted with hematologic problems. One of them developed anemia after maternal blood loss during a cesarean section, this was corrected with one blood transfusion. The other preterm neonate developed anemia several weeks after birth, for which one transfusion was given.

None of the neonates died during the hospital stay.

The details of the 18 neonates and their mothers are shown in Table 3.
A nasopharyngeal swab to detect severe acute respiratory syndrome coronavirus-2 PCR was collected in all 18 newborns within the first 5 days of life before they had physical contact with their mother. One of the 18 neonates (5.5%) was positive. This neonate tested positive within 24 hours after delivery and was negative when retested at 2 weeks of age.

At 2 weeks postpartum, repeat PCR testing was performed in 11/18 (61.1%) included neonates. Swabs could not be collected in 7 neonates because of loss to follow-up or because no permission was obtained.

### TABLE 2. Clinical Characteristics, Management, SARS CoV-2 PCR Testing, and Outcome of Neonates Born to COVID-19-Positive Mothers—Summary Data

|         | All Patients (n = 18) | Preterm <37 Weeks (n = 13) | Term ≥37 Weeks (n = 5) |
|---------|-----------------------|----------------------------|------------------------|
| **Clinical characteristics** | | | |
| Birthweight (g) | Median: 2261 | 1870 | 2920 |
| | IQR: 1765–2903 | 1740–2290 | 2850–3250 |
| Head circumference (cm) | Median: 31.5 | 31.0 | 34.0 |
| | IQR: 31.0–33.5 | 30.0–31.9 | 32.0–34.0 |
| APGAR at 5 min | <5: 0/18 (0%) | 0/13 (0.0%) | 0/5 (0.0%) |
| | ≥5: 17/18 (94.4%) | 12/13 (92.3%) | 5/5 (100.0%) |
| Respiratory disorder | Yes: 12/18 (66.7%) | 10/13 (76.9%) | 2/5 (40.0%) |
| | No: 6/18 (33.3%) | 3/13 (23.1%) | 3/5 (60.0%) |
| Circulatory disorder | Yes: 1/18 (5.5%) | 1/13 (7.7%) | 0/5 (0.0%) |
| | No: 17/18 (94.4%) | 12/13 (92.3%) | 5/5 (100.0%) |
| Gastrointestinal disorder | Yes: 2/18 (11.1%) | 2/13 (15.4%) | 0/5 (0.0%) |
| | No: 16/18 (88.9%) | 11/13 (84.6%) | 5/5 (100.0%) |
| Metabolic disorder | Yes: 5/18 (27.8%) | 5/13 (38.5%) | 0/5 (0.0%) |
| | No: 13/18 (72.2%) | 8/13 (61.5%) | 5/5 (100.0%) |
| Hematologic disorder | Yes: 2/18 (11.1%) | 2/13 (15.4%) | 0/5 (0.0%) |
| | No: 16/18 (88.9%) | 11/13 (84.6%) | 5/5 (100.0%) |
| Infectious disorder | Yes: 7/18 (38.9%) | 5/13 (38.5%) | 2/5 (40.0%) |
| | No: 11/18 (61.1%) | 8/13 (61.5%) | 3/5 (60.0%) |
| Neurologic disorder | Yes: 0/18 (0.0%) | 0/13 (0.0%) | 0/5 (0.0%) |
| | No: 18/18 (100.0%) | 13/13 (100.0%) | 5/5 (100.0%) |
| **Management** | | | |
| Admission | NICU: 7/18 (38.9%) | 7/13 (53.8%) | 0/5 (0.0%) |
| | High-care: 6/18 (33.3%) | 4/13 (30.8%) | 2/5 (40.0%) |
| | No hospital admission: 5/18 (27.8%) | 2/13 (15.4%) | 3/5 (60.0%) |
| Hospital length of stay (days) | Median: 8 | 9 | 4 |
| | IQR: 5–10 | 7–9 | 4–5 |
| Respiratory support | Invasive ventilation: 1/18 (5.6%) | 1/13 (7.7%) | 0/5 (0.0%) |
| | CPAP: 8/18 (44.4%) | 8/13 (61.5%) | 2/5 (40.0%) |
| | Low-flow: 3/18 (16.7%) | 1/13 (7.7%) | 0/5 (0.0%) |
| | None: 6/18 (33.3%) | 3/13 (23.1%) | 3/5 (60.0%) |
| Caffeine | Yes: 5/18 (27.8%) | 5/13 (38.5%) | 0/5 (0.0%) |
| | No: 13/18 (72.2%) | 8/13 (61.5%) | 5/5 (100.0%) |
| Antibiotics | Yes: 7/18 (38.9%) | 5/13 (38.5%) | 2/5 (40.0%) |
| | No: 11/18 (61.1%) | 8/13 (61.5%) | 3/5 (60.0%) |
| Blood transfusion | Yes: 2/18 (11.1%) | 2/13 (15.4%) | 0/5 (0.0%) |
| | No: 16/18 (88.9%) | 11/13 (84.6%) | 5/5 (100.0%) |
| Phototherapy | Yes: 4/18 (22.2%) | 4/13 (30.8%) | 0/5 (0.0%) |
| | No: 14/18 (77.8%) | 9/13 (69.2%) | 5/5 (100.0%) |
| Cranial ultrasound | Indication: 2/18 (11.1%) | 2/13 (15.4%) | 0/5 (0.0%) |
| | Abnormalities: 0/2 (0.0%) | 0/2 (0.0%) | 0/2 (0.0%) |
| Outcome at 3 months | Symptoms | Yes: 3/18 (16.7%) | 3/13 (23.1%) | 0/5 (0.0%) |
| | No: 15/18 (83.3%) | 10/13 (76.9%) | 5/5 (100.0%) |
| Weight (g) | Median: 4255 | 4230 | 4940 |
| | IQR: 4083–4618 | 3940–4400 | 4560–5250 |
| | Unknown: 6/18 (33.3%) | 4/13 (30.8%) | 2/5 (40.0%) |
| Head circumference (cm) | Median: 37.3 | 37.0 | 38.8 |
| | IQR: 36.6–37.6 | 36.5–37.5 | 37.7–38.9 |
| | Unknown: 6/18 (33.3%) | 4/13 (30.8%) | 2/5 (40.0%) |
| General physical examination | Abnormalities: 1/18 (5.6%) | 1/13 (7.7%) | 0/5 (0.0%) |
| | No abnormalities: 12/18 (66.7%) | 8/13 (61.5%) | 4/5 (80.0%) |
| | Unknown: 5/18 (27.8%) | 4/13 (30.8%) | 1/5 (20.0%) |
| Neurodevelopment | Abnormalities: 2/18 (11.1%) | 2/13 (15.4%) | 0/5 (0.0%) |
| | No abnormalities: 11/18 (61.1%) | 7/13 (53.8%) | 4/5 (80.0%) |
| | Unknown: 5/18 (27.8%) | 4/13 (30.8%) | 1/5 (20.0%) |
| SARS-CoV-2 PCR | ≤5 days positive: 1/18 (5.6%) | 1/13 (7.7%) | 0/5 (0.0%) |
| | 2–3 weeks positive: 0/11 (0.0%) | 0/9 (0.0%) | 0/2 (0.0%) |

CPAP, continuous positive airway pressure; NICU, NICU, neonatal intensive care unit; PCR, polymerase chain reaction.
TABLE 3. Clinical Characteristics and Outcomes of Neonates Born to COVID-19-Positive Mothers (n = 18), Specified by Neonate

| Case 1 | Case 2 | Case 3 | Case 4 | Case 5 | Case 6 | Case 7 | Case 8 | Case 9 |
|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| **Maternal characteristics** |        |        |        |        |        |        |        |        |
| Age (years) | 37 | 23 | 43 | 36 | 46 | Unknown | 32 | 36 | 37 |
| Trimester of COVID | 3rd | 3rd | 3rd | 3rd | 3rd | 3rd | 3rd | 3rd | 3rd |
| Severity disease* | Severe | Moderate | Severe | Moderate | Mild | Moderate | Moderate | Mild | Severe |
| Comorbidity† | No | No | No | No | No | No | No | No | No |
| Dexamethasone | Yes | Yes | Yes | Yes | No | Yes | Yes | Yes | Yes |
| Gestational age (weeks) | 33 + 0 | 32 + 4 | 28 + 3 | 38 + 2 | 40 + 3 | 32 + 4 | 33 + 0 | 35 + 3 | 31 + 0 |
| Mode of delivery ‡ | CS, maternal indication | CS, maternal indication | CS, maternal indication | CS, maternal indication | CS, neonatal indication | VD | CS, maternal indication | CS, neonatal indication | CS, maternal indication |
| **Clinical characteristics neonate** |        |        |        |        |        |        |        |        |        |
| Sex | Male | Female | Female | Male | Female | Male | Female | Male | Male |
| Birthweight (gram) with P-value | 2014 (p50) | 1745 (p44) | 1290 (p82) | 2850 (p19.3) | 3780 (p80.3) | 1825 (p52) | 2231 (p71) | 3265 (p96) | 1740 (p69) |
| Head circumference (cm) with P-value | 31.5 (p79) | 31.0 (p96) | 28.0 (p97) | 31.5 (p2.2) | 35.0 (p66.4) | 30.0 (p67) | 33.5 (p98) | 34.0 (p93) | 31.0 (p96) |
| APGAR score | 8–9–10 | 8–9–10 | 10–7–10 | 10–10–10 | 9–10–10 | 9–10–10 | Transient | Neonatal Tachyphnea of the Newborn | 2–9–9 |
| Respiratory disorder | NRDS, grade unknown | NRDS, grade 2 | Apnea | NRDS, grade 3 | No | No | No | NRDS, grade 1 | Apnea |
| Circulatory disorder | No | No | No | No | No | No | No | No | No |
| Gastrointestinal disorder | No | No | No | No | No | No | No | No | No |
| Metabolic disorder | Un-conjugated hyperbilirubinemia, physiological | Un-conjugated hyperbilirubinemia, physiological | Acute Kidney Injury, prerenal | No | No | No | No | No | No |
| Infectious disorder | Urinary Tract Infection, suspected (UC unknown) | Anemia | Late Onset Sepsis, suspected (BC negative) | No | No | No | Early onset neonatal sepsis, suspected (BC unknown) | No | No |
| Neurologic disorder | No | No | No | No | No | No | No | No | No |
| Management | Yes, NICU | Yes, NICU | Yes, NICU | No admission | No admission | Yes, NICU | Yes, NICU | Yes, NICU | Yes, NICU |
| ICU admission | Unknown | Unknown | Unknown | No admission | No admission | Unknown | Unknown | Unknown | 10 |
| Hospital length of stay (days) | CPAP | Invasive ventilation | No | No | No | No | No | No | No |
| Maximum respiratory support | CPAP | Invasive ventilation | No | No | No | No | No | No | No |
| Caffeine§ | Augmentin; stopped after 72 u with negative UC | Augmentin/Aminocain; stopped after 72 u with positive BC | No | No | No | No | No | No | No |
| Antibiotics§ | Augmentin/Aminocain; stopped after 72 u with negative BC | Augmentin/Aminocain; stopped after 72 u with positive BC | No | No | No | No | No | No | No |
| Transfusion blood products | No | No | No | No | No | No | No | No | No |
| Phototherapy | No | No | No | No | No | No | No | No | Yes |
| Cranial ultrasound | No indication | No abnormalities | No abnormalities | No indication | No indication | No indication | No indication | No indication | No indication |
| SARS-2-COVID PCR ≤5 days | Negative | Negative | Negative | Negative | Negative | No executed | Negative | Negative | No executed |
| 2–3 weeks | Negative | Negative | Negative | Negative | Negative | No executed | Negative | Negative | No executed |
| Outcome 3 months | Un-executed | Un-executed | Un-executed | Un-executed | Un-executed | Un-executed | Un-executed | Un-executed | Un-executed |
| Reported symptoms | Unknown | Unknown | Unknown | Unknown | Unknown | Unknown | Unknown | Unknown | Unknown |
| Weight (gram) with P-value | 4230 (p0.9) | 2370 (p7) | 2370 (p7) | 4280 (p6.6) | 4550 (p8.6) | Unknown | Unknown | 4820 (p0.9) |
| Head circumference (cm) with P-value | Unknown | 37.5 (p7.0) | 32.8 (p31) | Unknown | 36.6 (p6.9) | 38.0 (p22.8) | Unknown | 37.5 (p0.5) |
|-----------------------------------|---------|------------|-----------|---------|------------|------------|---------|------------|
| General physical examination      | Unknown | No abnormalities | No abnormalities | Unknown | No abnormalities | No abnormalities | Unknown | No abnormalities |
| Neurodevelopment ¶                | Unknown | No abnormalities | Delay (does not follow) | Case 12 | Unknown | No abnormalities | Unknown | No abnormalities |
| Maternal characteristics          | Case 10 | Case 11 | Case 12 | Case 13 | Case 14 | Case 15 | Case 16 | Case 17 | Case 18 |
| Age (years)                       | 23      | 26        | 38        | 33      | 25        | 22        | 36      | 33        | 33 |
| Gestational age (weeks)           | 3rd     | 3rd       | 3rd       | 3rd     | 3rd       | 3rd       | 3rd     | 3rd       | 3rd |
| Severity disease*                 | Moderate | Unknown | Severe, died. | Moderate | Unknown | No abnormalities | Unknown | No abnormalities |
| Comorbidity†                      | Unknown | No abnormalities | No abnormalities | Unknown | No abnormalities | No abnormalities | Unknown | No abnormalities |
| Dexamethasone                     | No      | Unknown | Yes       | No      | Yes       | Yes       | Yes     | Yes       | Yes |
| Gestational age (weeks)           | 39+0    | 35+3      | 31+5      | 38+0    | 33+5      | 35+0 (Ballard-score) | 39+0 | 36+3 |
| Mode of delivery ‡                | CS, maternal indication | CS, maternal indication | CS, maternal indication | CS, maternal indication | CS, maternal indication | CS, maternal indication | CS, maternal indication | CS, maternal indication |
| Clinical characteristics neonate  |         |           |           |         |           |           |         |           |           |
| Sex                               | M       | M         | F         | M       | F         | F         | M       | F         | M |
| Birthweight (gram) with P-value   | 2850 (p14.2) | 2455 (p37) | 1700 (p95) | 3250 (p42.1) | 1870 (p32) | 1402 (p1) | 2290 (p32) | 2920 (p24.1) | 3027 (p68) |
| Head circumference (cm) with P-value | 34.0 (p35.8) | 31.0 (p20) | Unknown | 32.0 (p2.6) | 30.0 (p40) | 29.5 (p9) | 31.0 (p27) | 34.0 (p51) | 33.0 (p51) |
| APGAR score                       | 9-9-9   | 7-9-10    | Unknown | 7-8      | Transient Tachypnea of the Newborn | Transient Tachypnea of the Newborn | Transient Tachypnea of the Newborn | Transient Tachypnea of the Newborn | Transient Tachypnea of the Newborn |
| Respiratory disorder              | No      | No        | Tachycardy, | No      | No        | No        | No      | No        | No |
| Circulatory disorder              | No      | No        | No        | No      | No        | No        | No      | No        | No |
| Gastrointestinal disorder         | No      | No        | No        | No      | No        | No        | No      | No        | No |
| Metabolic disorder                | No      | No        | No        | No      | No        | No        | No      | No        | No |
| Hematologic disorder              | No      | No        | No        | No      | No        | No        | No      | No        | No |
| Infectious disorder               | Infection, suspected (BC unknown) | No | No | No | Early onset neonatal sepsis, suspected (BC negative) | No | No | No | No |
| Neurologic disorder               | No      | No        | No        | No      | No        | No        | No      | No        | No |
| Management                        | Head Circumference | Head Circumference | Head Circumference | Head Circumference | Head Circumference | Head Circumference | Head Circumference | Head Circumference | Head Circumference |
| ICU admission                     | Unknown | 7         | 9         | 7       | 14        | No admission | No        | No        | No |
| Hospital length of stay (days)    | 3       | 4         | Unknown   | 5       | 9         | 7         | 14      | No admission | No admission |
| Maximum respiratory support       | Low-flow | No        | CPAP      | Low-flow | CPAP      | Low-flow | No       | No       | No |
| Caffeine                          | No      | No        | Yes       | No       | Yes       | No       | No       | No       | No |
| Antibiotics                       | Augmentin, duration unknown | No | No | Augmentin, stopped after 5 days | No | No | Augmentin, stopped after 7 days | No | No |
| Transfusion blood products        | No      | Yes       | No        | No      | No        | No       | No      | No       | No |
| Phototherapy                      | No      | No        | No        | No      | Yes       | No       | No      | No       | No |
| Cranial ultrasound findings       | No indication | No indication | No indication | No indication | No indication | No indication | No indication | No indication | No indication |

(Continued)
TABLE 3.

| SARS-2-COVID PCR | Case 10 | Case 11 | Case 12 | Case 13 | Case 14 | Case 15 | Case 16 | Case 17 | Case 18 |
|------------------|---------|---------|---------|---------|---------|---------|---------|---------|---------|
| ≤ 5 days         | Negative| Negative| Negative| Negative| Positive| Negative| Negative| Negative| Negative|
| 2–3 weeks        | Negative| Negative| Negative| Not executed| Not executed| Negative| Negative| Not executed| Not executed|
| Weight (gram)    | 4940 (p18.0) | Unknown | 3940 (p0.6) | 5560 | 4400 (p5.9) | 5560 | (p15.1) | 36.6 (p13.7) | Unknown |
| Head circumference cm with P-value | 49.4 (p18.0) | Unknown | Unknown | Unknown | Unknown | Unknown | Unknown | Unknown | Unknown |
| General physical examination | No abnormalities | Unknown | No abnormalities | No abnormalities | No abnormalities | No abnormalities | No abnormalities | No abnormalities | No abnormalities |
| Neurodevelopment | No abnormalities | Unknown | No abnormalities | No abnormalities | No abnormalities | No abnormalities | No abnormalities | No abnormalities | No abnormalities |

CPAP, continuous positive airway pressure; CS, cesarean section; NICU, neonatal intensive care unit; PCR, polymerase chain reaction; VD, vaginal delivery.

*Severe = ICU-admission; moderate = oxygen requirement with nasal cannula, venturi mask and/or non-rebreather mask, mild = no treatment needed and/or asymptomatic.
†Diabetic mellitus/gravidarum, hypertension/pregnancy induced hypertension/pre-eclampsy, epilepsy, sickle cell; serology (VDRL, HbsAg, HIV).
‡VD = vaginal delivery; CS = cesarean section.
¶Neurodevelopment according to "Van Wiechen" at 3 months (follows with eyes and head, smiles back, raises head in prone position at 45 degree.

We report a vertical transmission rate of 5.5% and a horizontal transmission rate of 0%. However, we did not confirm vertical transmission via other means, such as placental transfer, amniotic fluid or serologic evidence. Previous studies reported COVID-19-positive rates of 0%–10.8% in swabs taken within 72 hours after birth. We hypothesized that horizontal transmission could occur because of COVID-19-positive members in the household, potentially leading to delayed infection and complications of COVID-19. However, none of the neonates in our study were COVID-19-positive at the age of 2 weeks. Our findings support the current WHO guidelines of breastfeeding and skin-to-skin contact for neonates of parents was obtained to repeat the testing. None of the 11 (0/11) (0.0%) PCR tests were positive, indicating no horizontal transmission in this study.

Three Months Follow-Up

A total of 13 of 18 infants were seen by a pediatrician for follow-up at the outpatient clinic. Of the 5 infants who were not seen by a pediatrician, 1 infant could not come because of travel distance and costs, therefore a consult by phone was performed; 4 infants were lost to follow-up.

At the age of 3 months, 1 infant was diagnosed with bronchiolitis and obstipation; 2 infants reported complaints of reflux. From 12 of the 13 infants with follow-up at 3 months, weight and head circumference were noted. For 11 of 12 infants, weight and head circumference curves were according to the expected growth curve or did increase. Only 1 of 12 children, case 3, had a decrease in the growth curve for both weight and head circumference. With general physical examination, no infants had any abnormalities. One infant had a cardiac murmur at the age of 2 weeks, at follow-up the murmur was not found anymore with no cardiac abnormalities on cardiac ultrasound.

Twelve of 14 infants had normal neurodevelopment according to Van Wiechen; 2 infants had a neurodevelopmental delay. One of them, an ex-preterm infant born at 28 weeks, also had deviating growth of the skull.

The neonate with a positive nasopharyngeal swab, who was born preterm and received CPAP and phototherapy in the neonatal period, suffered from gastro-esophageal problems as reflux at 2–3-month follow-up. No other problems were observed or reported at follow-up.

DISCUSSION

In this case series, we describe the clinical characteristics, transmission rate and middle-term outcome of infants born to infected women during the severe acute respiratory syndrome coronavirus-2 pandemic.

We observed that more than 2/5 of the mothers with COVID-19 infection were severely ill, of which 2 women died. In our study period, COVID-19 vaccination in pregnant women was not actively recommended yet. The severity of the COVID-19-disease resulted in our study population of almost 80% in cesarean section and in more than 70% in preterm births. These findings of a higher incidence of cesarean section and preterm births are in line with previous systematic reviews.22–24 Both, cesarean delivery and prematurity are important observations because of the possibility of adverse events in neonates.24–26 Moreover, our data underscore the importance of vaccination in pregnant women, to prevent severe illness and to prevent potential complications of cesarean section and/or prematurity.

Despite increased risk of adverse events, none of the neonates suffered from asphyxia. Respiratory symptoms occurred in almost 70% of neonates, which was higher than reported in a systematic review of Dhir, et al.1 However, this review involved less premature babies, which could partly explain less frequent respiratory symptoms.

We report a vertical transmission rate of 5.5% and a horizontal transmission rate of 0%. However, we did not confirm vertical transmission via other means, such as placental transfer, amniotic fluid or serologic evidence. Previous studies reported COVID-19-positive rates of 0%–10.8% in swabs taken within 72 hours after birth. We hypothesized that horizontal transmission could occur because of COVID-19-positive members in the household, potentially leading to delayed infection and complications of COVID-19. However, none of the neonates in our study were COVID-19-positive at the age of 2 weeks. Our findings support the current WHO guidelines of breastfeeding and skin-to-skin contact for neonates of
COVID-19 positive mothers. Separating neonates after birth from COVID-19-positive mothers brings more harm than the risk of horizontal transmission.

Viral infections are known to cause long-term morbidity. Although, the long-term outcome of COVID-19 infection in adults has been described, little is known about the outcome of neonates. At follow-up, 3 months after birth, we did not observe any COVID-19-related problems. Neither we observed more/other non-COVID related problems compared to neonates born to COVID-19-negative mothers. No other literature was found on follow-up at 3 months or longer. The longest time to follow-up of neonates born to COVID-19-positive mothers was 4 weeks, showing adequate growth and outcome at 1 month of life. Our study shows no COVID-19-related problems even at the age of 3 months.

The 1 neonate who tested positive on a nasopharyngeal swab, did not reveal any important clinical findings during the first 3 months of life. This is consistent with the current literature. A systematic review of Trevisanuto et al. with a median follow-up of 10 days, shows that most neonates with COVID-19 infection are asymptomatic or presented with mild symptoms.

We hypothesize that longer follow-up of neonates born to COVID-19-positive mothers will not reveal new findings. However, in some cases of congenital infections, symptoms may appear after years. Therefore, future research on COVID-19-positive neonates should monitor neurodevelopment.

This study is limited by the relatively low number of included cases. Based on the number of COVID-19-positive PCR tests in the country, we estimate that approximately 24 neonates were born to mothers with a COVID-19 infection during the study period. We may have missed pregnant women who did not need hospital admission and COVID-19-positive pregnant women who were asymptomatic (pregnant women admitted to the hospital were only tested in case of symptoms). Also, all maternal COVID-19 infections occurred in the third trimester, whereas it is possible that an infection earlier in pregnancy could result in more severe outcome. We also did not take into account different COVID-19 strains which could cause different phenotypes in the neonate. Nevertheless, this prospective, country-wide case series from a resource-limited setting is the first to study potential horizontal transmission and outcome at 3 months, thereby contributing to current knowledge of neonates from COVID-19-infected mothers.

In conclusion, this case series shows a high rate of severely ill pregnant women due to COVID-19 infection with direct consequences on neonates because of preterm birth and delivery through cesarean section. More attention is needed on maternal vaccination, to prevent neonatal risk due to preterm birth and cesarean section. The neonatal clinical course and findings at follow-up at 3 months did not seem to differ from neonates born to COVID-19-negative mothers. Furthermore, we show vertical transmission rates of 5% and no horizontal transmission at the age of 2 weeks. Future studies should investigate neonatal outcomes after maternal COVID-19 infection in the 1st or 2nd trimester, preferably with subtyping of different COVID-19 strains.

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