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Changes in Clinical Care of the Newborn During COVID-19 Pandemic

From the Womb to First Newborn Visit



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KEYWORDS

• SARS-CoV-2 • Newborn • Perinatal transmission • Pandemic

KEY POINTS

- Perinatal transmission of SARS-CoV-2 is mainly horizontal, necessitating strict control measures for preventing spread of infection to newborns.
- Universal screening for SARS-CoV-2 for all pregnant women is necessary to guide delivery room preparation and postdelivery care of newborns and mothers.
- Newborns infected with SARS-CoV-2 are usually asymptomatic or have mild clinical disease; therefore, other causes need to be investigated in case of severe illness.
- Breast feeding and bonding between newborn and SARS-CoV-2 infected mother can be encouraged with proper education and infection control measures.
- All newborns should have routine newborn care irrespective of their SARS-CoV-2 status as early discharge has not shown to reduce the spread of infection.

INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which was first reported in the Wuhan region of China in December in 2019 has struck the world, affecting humans across all age groups.¹ Initially, it was thought to affect mainly the respiratory system causing a “pneumonia of unknown etiology,”² but it was soon discovered that it affects multiple organ systems with significant morbidity and mortality. SARS-CoV-2 has been demonstrated to be transmitted by respiratory droplets, contact, and fomites.^{3–5} SARS-CoV-2 has

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proven to be highly contagious with a reproduction number of 2.2 to 5.7, which means that 1 person with SARS-CoV-2 infection can infect on an average 2 to 5 people around him or her if no precautions are followed.⁶ SARS-CoV-2 gains entry into the lungs and gut by binding to the angiotensin-converting enzyme receptor 2 present abundantly on the type 2 pneumocytes and gastrointestinal epithelium. There is controversy regarding in utero transmission of SARS-CoV-2. However, there is increasing evidence of horizontal transmission from mother to neonate. There is a scarcity of data regarding pregnant women affected with COVID-19, and its implications during pregnancy: prenatal visits, antenatal scans, testing, and management of symptomatic women, and delivery, as well as delivery room preparedness, logistics, and postnatal care of newborns.⁷⁻¹⁰ In this review, we highlight major changes in clinical practice implemented during delivery and postnatal care of newborns born to mothers with confirmed or suspected SARS-CoV-2 infection during the pandemic, based on various expert opinions and evolving evidence.

SARS-CoV-2 INFECTION IN PREGNANCY

Early speculations regarding SARS-CoV-2 infection in pregnancy were concerning owing to changes in cellular immunity during pregnancy along with an array of physiologic changes in the cardiovascular, respiratory, and coagulation systems. Few studies have investigated whether SARS-CoV-2 infection poses additional risk during pregnancy.¹¹ Studies so far have shown similar COVID-19 symptoms in pregnant and nonpregnant women.^{12,13} Surveillance data from the Centers for Disease Control and Prevention (CDC) including 91,412 women of reproductive age group (15–45 years of age) with laboratory-confirmed SARS-CoV-2 infection showed no difference between pregnant (8207) and nonpregnant women (83,205) in terms of cough and shortness of breath.¹⁴ Headache, fever, chills, diarrhea, and muscle aches were in fact less frequently noted in pregnant women compared with nonpregnant women. Initial studies from New York showed a significant asymptomatic carrier rate ($\leq 33\%$) in pregnant women.^{15,16} Therefore, universal screening for SARS-CoV-2 infection in all pregnant women during hospitalization or at the time of delivery was proposed and soon became the standard of care. In a series of 54 pregnant women with confirmed ($n = 38$) and suspected ($n = 16$) SARS-CoV-2 infections reported by Sentilhes and colleagues,¹⁷ oxygen supplementation was required in 24.1%, intensive care unit admission in 9.3%, and severe illness was observed in those over the age of 35 years or those with comorbidities, such as asthma and obesity. A recent report by the CDC's Coronavirus Disease 19-Associated Hospitalization Surveillance Network surveillance team found that, of the 598 pregnant women hospitalized in 13 states across the country with COVID-19 between March 1 and August 22, 2020, the majority of them (55%) were asymptomatic.¹⁸ However, severe illness was observed in symptomatic women that included intensive care admission in 16%, mechanical ventilation in 8%, and mortality in 1%.¹⁸ In an analysis of approximately 400,000 women aged 15 to 44 years with symptomatic COVID-19 by the CDC's Surveillance for Emerging Threats to Mothers and Babies Network (SET-NET), intensive care unit admission, invasive ventilation, extracorporeal membrane oxygenation, and death were more likely in pregnant women than in nonpregnant women.¹⁹ In a 35-year-old woman infected with COVID-19, placental pathology showed inflammation and the presence of SARS-CoV-2 by immunohistochemistry at 22 weeks gestation, possibly contributing to the development of early-onset preeclampsia, hypertension, and disseminated coagulopathy.²⁰ Hence, a multidisciplinary team of maternal and fetal medicine specialists and neonatologists is essential in the care of pregnant women with SARS-CoV-2 infection and their infants.

IMPACT ON ROUTINE ANTENATAL VISIT AND SCANS

Since the declaration of SARS-CoV-2 as a pandemic by World Health Organization (WHO), the American College of Obstetrics and Gynecology (ACOG) has proposed various modifications in the existing guidelines of antenatal visits and ultrasounds. These modifications were primarily made to decrease the amount of contact between the pregnant women and health care facilities as well as to decrease the transmission of SARS-CoV-2 throughout the general population.²¹ Minimal data are available on the impact on maternal and fetal health after these guideline changes. In a 28-year-old pregnant woman with gestational diabetes mellitus and chronic hypertension who was found to be COVID-19 positive at 34 weeks gestation, her routine nonstress testing and amniotic fluid index testing were delayed owing to her COVID-19-positive status. Ultimately, her nonstress testing revealed category 2 tracing persistently, requiring urgent cesarean section.²² This case highlights that the frequency of antenatal visits and testing should be decided on an individualized basis, especially for high-risk pregnancies.

TRANSMISSION FROM MOTHER TO NEWBORN

The first case of SARS-CoV-2 infection in a neonate was reported in February 2020. The infant presented at 17 days of age with a fever, cough, runny nose, and vomiting.²³ This presentation led to suspicion of vertical transmission in utero because the mother of the newborn had tested positive for SARS-CoV-2. Early studies conducted in China were unable to isolate SARS-CoV-2 from amniotic fluid, vaginal mucus, cord blood, placenta, urine, feces, or breast milk. Similarly, Silva and colleagues did not find SARS-CoV-2 by reverse transcriptase polymerase chain reaction (RT-PCR) in 18 samples of amniotic fluid, umbilical cord, and placenta obtained from COVID-19-positive mothers.²⁴ Therefore, the risk of vertical transmission was considered highly unlikely.^{25–29} However, in a retrospective cohort study of 3497 respiratory, urine, stool, and serum samples from adults analyzed for SARS-CoV-2 viral load, the median duration of the virus in stools (22 days; interquartile range [IQR], 17–31 days) was significantly longer than in respiratory (18 days; IQR, 13–29 days; $P = .02$) and serum samples (16 days; IQR, 11–21 days; $P < .001$).³⁰ In a study by Zeng and colleagues,⁹ 3 of the 33 neonates born to COVID-19-positive mothers tested positive by RT-PCR from nasopharyngeal and anal swabs by 2 days of age despite strict isolation of the newborn soon after delivery. Two of the 3 neonates were born at full term with mild symptoms such as fever, vomiting, and lethargy; the third neonate was born at 31 weeks of gestation and developed respiratory distress syndrome and pneumonia, along with leukocytosis and thrombocytopenia requiring noninvasive positive pressure ventilation and antibiotics because his blood culture was positive for *Enterobacter* spp. Hence, the contribution of SARS-CoV-2 in causing symptoms in the third neonate was dubious. However, in a case reported by Dong and colleagues³¹ of a neonate born to a SARS-CoV-2-positive mother was found to have high levels of SARS-CoV-2-specific IgM antibodies at 2 hours of age despite negative pressure room delivery and strict adherence to precautions. Her PCR results were negative on 5 consecutive samples during the first 16 days of life. Her IgM and IgG levels were still elevated at 16 days of life, but were trending down. Because IgM antibodies are elevated only after 3 to 7 days after the infection, high IgM levels in the infant only at the 2 hours of age strongly suggested an intrauterine infection. In a review of 217 neonates born to SARS-CoV-2-infected mothers, only 7 (3%) tested positive.³² Of the 7, 3 had positive serum IgM and IgG levels with negative PCR and the remaining 4 had a positive PCR from nasopharyngeal or anal swabs. In the national registry of perinatal

COVID-19 infection established by the American Academy of Pediatrics Section on Neonatal Perinatal Medicine (AAP SONPM NPC-19 registry), which includes 295 centers, 139 of 6229 infants (2.2%) born to COVID-19–positive mothers tested positive as of February 20, 2021.³³ More than one-third (2888) of these newborns had contact, droplet, and air-borne isolation, 2303 (28%) had contact and droplet isolation, 1677 (20%) had contact, droplet, air-borne, and negative pressure isolation, 466(6%) had unspecified form of isolation, and 873 (11%) had no isolation.³³ Because the evidence for vertical transmission is weak, newborns are most likely infected via horizontal transmission after delivery from mother or other caregivers. Therefore, implementing strict infection control measures during and after delivery, quarantine of infected mothers, and close monitoring of neonates in the perinatal period was essential in decreasing horizontal transmission. The CDC’s SET-NET had information of 2869 newborns delivered from 13 jurisdictions between March 29 and October 14, 2020. They reported 610 infants (21.3%) who were tested and 16 (2.6%) of them were positive for SARS-CoV-2. They were primarily those born to women with infection at delivery.³⁴ This result led to the development and implementation of essential delivery preparedness strategies across various birthing centers to curb the spread of SARS-CoV-2.

COVID-19 VACCINATION DURING PREGNANCY

The US Food and Drug Administration recently approved 2 vaccines against SARS-CoV-2 (Pfizer-BioNtech mRNA vaccine and Moderna mRNA-1273 vaccine) under the context of an Emergency Use Authorization in high-risk priority groups. The CDC’s Advisory Committee on Immunization Practices and the ACOG have recommended their use in pregnant and lactating women.^{35,36} However, the data are lacking regarding the benefits (to the mother and transplacental passage of passive immunity to the fetus) and side effects of these vaccines in this subset of patients because pregnant women were not involved in the studies during vaccine development.³⁷ In a study by Flannery and colleagues³⁸ involving 1714 mothers who delivered from April to August 2020 in the northeastern United States, 83 (6%) had detectable IgG and/or IgM antibodies at delivery. However, the majority of infants born to these seropositive mothers (72/83) had detectable IgG levels at birth, suggesting transplacental transfer during pregnancy. For Moderna mRNA-1273 vaccine, the WHO revised the recommendation on January 29, 2021, stating that “pregnant women at high risk of exposure to SARS CoV-2 (e.g. health workers) or who have comorbidities which add to their risk of severe disease, may be vaccinated in consultation with their health care provider.”³⁹ Although immunization may be the best available options for pregnant and lactating mothers to protect themselves and their infants, longitudinal clinical studies are necessary to implement safe vaccination guidelines.

DELIVERY ROOM AND NEWBORN RESUSCITATION PRACTICES

Much of delivery room preparedness recommendations depended on the COVID-19 status of the mother. Therefore, a short turnaround time of the test was crucial for optimal preparedness during delivery. If resources were available, all mothers were tested for SARS-CoV-2 at delivery, regardless of their clinical profile, to prevent nosocomial spread to other patients and health care workers.⁴⁰ All mothers whose COVID-19 status was unknown either owing to a lack of resources, testing refusal, or in whom the test results were not back by the time they delivered were considered positive owing to the high asymptomatic carrier state.¹⁵ Important aspects of delivery room preparedness included the availability of KN95 masks, appropriate personal

protective equipment, medical professionals experienced in neonatal resuscitation to minimize aerosolization during newborn resuscitation, and separation of the mother from the newborn.^{15,40} Discussion and planning between the obstetric and neonatal teams guided maternal and newborn care, such as the use of maternal steroids (dexamethasone for COVID-19–related lung injury in mother vs betamethasone for fetal lung maturity), magnesium sulfate for preterm delivery, unfractionated heparin for thromboembolism prophylaxis, and the use of remdesivir.⁴¹ Positive pressure ventilation using bag and mask, endotracheal intubations, and high-flow nasal cannula have the potential to aerosolize the respiratory droplets, allowing SARS-CoV-2 to remain in air for more than 3 hours and propagate for more than 2 months.⁴² Pregnant women who are COVID-19 positive or unknown should deliver preferably in a negative pressure room, if available, with an adjoining room for neonatal resuscitation.^{40,43,44} If not available, a single room with minimal entry and exit of essential caregivers from the room is paramount.^{43,44} Earlier, delayed cord clamping was deferred owing to the unknown risk of vertical transmission.⁸ However, according to recent recommendations from the ACOG and the AAP SONPM, delayed cord clamping can be practiced in suspected or confirmed COVID-19–positive mothers because there is no strong evidence to suggest transplacental viral transmission at this time.^{43,45}

Mode of Delivery

Varied speculations have been made on the mode of delivery in pregnant women with SARS-CoV-2.^{46–49} Cesarean section was performed for routine obstetric indications or worsening respiratory distress and exhaustion owing to COVID-19.⁴⁰ Some centers also preferred cesarean section for decreasing the total hospital stay of the mother and to minimize cross-infection.^{40,47} However, in a case reported by Iqbal and colleagues,⁴⁸ a full-term female infant who was born by vaginal delivery to a SARS-CoV-2–infected mother was asymptomatic and discharged home on the 6th day of life. A retrospective cohort study among adults found that SARS-CoV-2 was present in stool samples for a longer duration compared with serum and respiratory mucosa.³⁰ Therefore, caution should be taken in mothers with diarrhea during vaginal delivery. In a systematic review by Khan and colleagues⁴⁹ that which included 8 studies, comprising a total of 100 women with COVID-19, cesarean section was noted in 85%, premature deliveries in 29%, and low birthweight infants in 16%. However, there is a shift in this trend; recent data from the AAP SONPM NPC-19 registry showed that of 7486 suspected or confirmed COVID-19–positive pregnant women, 4872 (65%) delivered vaginally and the remaining 2614 (35%) underwent cesarean section as of February 20, 2021.³³

BREAST MILK AND BREASTFEEDING

The AAP, along with other academic organizations such as the Academy of Breast Feeding, the CDC, and the WHO recommend breastfeeding in mothers with confirmed or suspected COVID-19 while taking the necessary precautions.^{45,50–53} Mothers can either pump breast milk or directly nurse the baby while wearing a face mask and performing breast and hand hygiene.⁵² The mother can either wash her hands with soap and water or use sanitizer with at least 60% alcohol before touching the baby. Preferably, expressed breast milk should be fed by an uninfected healthy caregiver not at risk of developing severe illness from SARS-CoV-2.⁵⁴ Earlier studies were unable to detect SARS-CoV-2 in breast milk.^{13,25,27,55,56} However, in few studies SARS-CoV-2 was detected in breast milk.^{57,58} A case was reported of a 32-week gestational age preterm baby who was breastfed SARS-CoV-2–positive breast milk but did not

become infected. The baby was inadvertently fed expressed breast milk from the mother who later tested positive for SARS-CoV-2. Her expressed milk also tested positive by RT-PCR despite using a face mask and standard personal protective equipment while expressing the milk. However, the newborn tested negative for SARS-CoV-2 nasopharyngeal swab as well as for antibodies at 30 days after the exposure.⁵⁹ Similarly, in a series of 14 infants breast fed by SARS-CoV-2–positive mothers, breast milk tested positive in only 1 case. Four of the 14 infants (including the one fed the infected breast milk) tested positive for SARS-CoV-2, but the clinical course of all the infants was uneventful. The repeat testing of these 4 infants was negative for SARS-CoV-2 at 6 weeks.⁶⁰ Although there is no clear evidence that infants fed breast milk from COVID-19–positive mothers are protected from SARS-CoV-2 infection, breast milk may contain antibodies against SARS-CoV-2 providing passive immunity and protecting the baby. The Human Milk Banking Association of North America milk banks provide heat-treated pasteurized donor breast milk that has been shown to inactivate viruses similar to SARS-CoV-2.⁶¹ Hence, human donor milk could be used in preterm and term neonates admitted to the nursery and neonatal intensive care unit (NICU) for longer durations.

MOTHER AND NEWBORN SEPARATION

Owing to the unknown infective properties of the virus, the Chinese Neonatal 2019-nCoV expert working Group published its first consensus statement in February 2020 soon after the first case of SARS-CoV-2 was reported in a neonate.⁸ They recommended separation of mother and child based on a systematic review of the adult literature on SARS-CoV-2 as well as previous reports of Middle East respiratory syndrome-related coronavirus and severe acute SARS-CoV infections.⁸ As more cases were reported from China and around the world affecting newborns as early as few hours, separation of the mother with suspected or confirmed SARS-CoV-2 from newborn was strongly recommended by other health organizations such as the AAP, ACOG, and CDC.^{43,45,62} However, separation may not be always feasible owing to the lack of infrastructure and resources available in other parts of the world. Recent amendments to the CDCs guidelines allow a case-by-case approach and takes into account decision made between the health care provider and mother, the clinical condition of the mother and infant, availability of testing, staffing, space, personal protective equipment, and test results of the newborn.⁶² As of August 3, 2020, the CDC recommends mothers to remain separated for at least 10 days after the occurrence of first symptoms (20 days if critically ill or the mother is immunocompromised), and at least 24 hours after the last fever without use of antipyretics and improvement in other symptoms.⁶² If the newborn is tested COVID-19 positive, there is no need for separation. If the mother refuses separation, the newborn and mother should be placed in a negative pressure room with 6 feet or more distance between the two. In addition, the newborn should be placed in a temperature-regulated isolette to minimize droplet spread from mother. The Italian Society of Neonatology guidelines endorsed by the Union of European Neonatal and Perinatal Societies suggest that rooming-in of mother and newborn is workable if a mother is SARS-CoV-2 positive, or is a person under investigation, or is asymptomatic, or has minimal symptoms at delivery, but with strict infection control measures.⁶³ Ample research-based evidence has concluded that early maternal–newborn bonding positively impacts the growth and development in term and preterm neonates.^{64,65} Early separation may negatively affect the bonding, breast milk production, and mental health of the mother during the hospital stay and after discharge with uncertain short- and long-term implications. In a

recent study of 45 newborns born to SARS-CoV-2–positive mothers, 33 (73%) roomed-in with the mother. Thirty-one of the 33 newborns were breastfed within the 1 hour of birth. All 33 newborns tested negative for SARS-CoV-2, did not require NICU admission, and remained asymptomatic at their 2-week telemedicine follow-up visit.⁶⁶

CLINICAL FEATURES OF SARS-CoV-2 INFECTION IN NEONATES

Various clinical studies have concluded that newborns and infants are less susceptible to SARS-CoV-2 infection and have a fairly mild clinical course with lower mortality compared with adults. A few theories have been proposed explaining this difference in clinical susceptibility. These include immature angiotensin-converting enzyme receptor 2 in neonates, which may prevent or decrease binding of the virus to the epithelial cells and naïve immune system of newborn mounting a poor inflammatory response.^{67,68} However, the exact pathogenesis of COVID-19 is still being investigated. Neonates and children are usually asymptomatic or develop mild symptoms such as respiratory distress and feeding difficulties. A clinical finding of COVID-19 specific to newborns has not been recognized. The first few case series from China reported that the majority of newborns born to SARS-CoV-2–confirmed positive mothers were unaffected.^{25,26} Later, a few publications reported varied presentations such as respiratory distress, shock, tachycardia, sepsis, thrombocytopenia, and occasionally death in neonates.^{8,9,32,69} Other presenting symptoms include temperature instability, poor feeding, diarrhea, vomiting, and abdominal distension. Associated risk factors such as prematurity, prolonged rupture of membranes, and sepsis were also present in these neonates. In another case series of 4 neonates ranging between 30 hours and 17 days of age with a confirmed SARS-CoV-2 positive result by nucleic acid testing, 2 had fever, 1 developed respiratory distress, 1 had cough, and 1 had no symptoms.⁶⁹ Recently, another case of a SARS-CoV-2–positive neonate was reported who developed cyanosis and hypoxemia with respiratory distress at 48 hours of life. His chest radiograph showed ground glass opacity and he improved on high-flow nasal cannula with a 30% FiO_2 .⁷⁰ Aghdam and colleagues⁷¹ reported a 15-day-old neonate who presented with fever, tachycardia, and respiratory distress who improved quickly and was discharged 6 days later. In China, a greater proportion of infants less than 1 year of age had severe or critical disease compared with older children (10.6% vs 4.8%).⁷² Owing to the high incidence of asymptomatic cases, other causes should be investigated in newborns with confirmed SARS-CoV-2 infection who demonstrate clinical deterioration. However, in a recent review of 18 PubMed articles that included 25 SARS-CoV-2–positive confirmed newborns less than 28 days of age, with a mean age of 8.2 ± 8.5 days, a gestational age of 37.4 ± 4.0 weeks, and a birth weight of 3041.6 ± 866.0 grams, the clinical features included fever in 28%, vomiting in 16%, cough or shortness of breath in 12%, diarrhea, lethargy or respiratory difficulty in 8% or cyanosis, feeding intolerance, hyperpnea, mild intercostal retractions, mottling, sneezing, nasal stuffiness, and paroxysmal episodes in 4%; only 16% of these newborns were completely asymptomatic.⁷³ Deaths were not reported in any of the newborns and 8 of 25 (32%) required intensive care. The mean length of hospital stays of 15.8 ± 10.8 days.⁷³ In another review of 26 articles published from December 1, 2019, to May 12, 2020, that included 38 SARS-CoV-2–positive confirmed neonates, 26 (68%) were symptomatic at a median age of 10 days (IQR, 2–19 days).⁷⁴ Clinical findings included fever in 50%, gastrointestinal symptoms in 26%, hypoxia in 20%, and cough in 20%. All newborns were discharged home after a median length of stay of 10 days (IQR, 6–14 days).⁷⁴ In a study by the national surveillance registry of

UK that included 66 newborns who tested positive, 16 (24%) were born preterm. The incidence of SARS-CoV-2 was estimated to be 5.6 per 10,000 live births. The most common symptoms were hyperthermia (35%), poor feeding/vomiting (33%), and coryza (26%). In terms of respiratory support, 33% required supplemental oxygen, 15% required noninvasive ventilation, and 5% required intubation.⁷⁵ In a large single-center study in New York including 101 newborns born to SARS-CoV-2–positive mothers, maternal severe or critical COVID-19 disease was associated with birth approximately 1 week before the due date (median gestational age, 37.9 weeks [IQR, 37.1–38.4 weeks] vs median, 39.1 weeks [IQR, 38.3–40.2 weeks]; $P = .02$) and an increased risk of requiring phototherapy (3 of 10 [30.0%] vs 6 of 91 [7.0%]; $P = .04$) compared with newborns of mothers with asymptomatic or mild COVID-19.⁷⁶ Interestingly, a preterm newborn delivered at 34 weeks of gestation developed late-onset fever, thrombocytopenia, and elevated inflammatory markers concerning for fetal inflammatory response syndrome, which was attributed to maternal SARS-CoV-2 infection. The neonate tested negative for SARS-CoV-2 by RT-PCR twice 24 hours apart. He subsequently developed pulmonary hypertension requiring inhaled nitric oxide with significant improvement and discharge home at 22 days of age.⁷⁷

DEFINITION OF COVID-19 IN NEONATES

In February 2020, the Chinese Perinatal-neonatal 2019-nCoV Committee proposed the definition of suspected and confirmed neonatal cases after a systematic review of current and previous literature in their consensus statement.

Suspected COVID-19

All newborns born to SARS-CoV-2–positive confirmed mothers within 14 days before birth and 28 days after birth or newborns exposed directly to SARS-CoV-2–infected individuals (including family members, caregivers, medical staff, and visitors) are considered to be suspected cases.⁸

Confirmed COVID-19

Newborn in whom respiratory tract or blood specimens tested by RT-PCR are positive for SARS-CoV-2;

OR

Virus gene sequencing of the respiratory tract or blood specimens is highly homologous to that of the known SARS-CoV-2 specimens.⁸

Management

The majority of newborns with suspected and confirmed SARS-CoV-2 who require medical attention do so because of associated comorbidities of the perinatal period. All newborns with suspected or confirmed SARS-CoV-2 should be quarantined with droplet and contact precautions for at least 14 days. The management of these newborns is mainly supportive. Owing to a lack of evidence of the efficacy and safety profile of pharmaceutical agents such as hydroxychloroquine, azithromycin, and remdesivir in newborns, their use is not recommended.^{5,8} Similarly, there is no evidence for the effectiveness of gamma globulin, hormonal therapy or interferon therapy.⁸ However, owing to the widespread use of the COVID-19 vaccine, we expect to see an increase in the titers of anti-COVID-19 antibodies in intravenous immunoglobulin pooled from plasma donors that could be used for treating SARS-CoV-2 in the near future. Modifications in clinical practice made while caring for newborns with SARS-CoV-2 in terms of respiratory support, isolation, appropriate use of personal

protective equipment, and KN95 masks by health care providers, laboratory and radiology staff and for discharge planning is summarized elsewhere in this article.

Respiratory support, personal protective equipment, and isolation

There are few neonates reported with suspected or confirmed SARS-CoV-2 requiring respiratory support so far.^{9,78} Aerosolization of SARS-CoV-2 can be decreased by limiting and/or cautiously performing procedures such as ventilation (bag and mask, invasive and noninvasive), endotracheal intubation, and insertion of orogastric or nasogastric tubes.^{5,15,40,79} For bag and mask ventilation, high-efficiency particulate air filters should be used between the mask and CO₂ detector to minimize aerosolization.^{80,81} Dual limb conventional ventilators are a closed circuit containing in-built high-efficiency particulate air filters near the endotracheal tube and, therefore, are safer than bag and mask ventilation.^{80,81} Suctioning should be performed using an in-line suction catheter.⁸⁰ The use of personal protective equipment, including a face mask, face shield, and gloves, while performing these aerosolization procedures and even otherwise is essential for health care workers to protect themselves and minimize spread while taking care of these newborns as recommended by the CDC.⁸² Depending on the availability of infrastructure and resources, isolation or cohorting of confirmed newborns in a designated enclosed space in NICU is recommended.^{8,40} Reusable monitoring tools such as stethoscope and thermometers should not be shared among patients.

Laboratory evaluation

Both the AAP and the CDC recommend testing for SARS-CoV-2 for all newborns delivered by suspected or confirmed SARS-CoV-2–positive mothers because it guides ongoing infection prevention and control, clinical observation of newborn, the need for isolation, discharge planning, and newborn outpatient follow-up visits.^{45,82} The timing of first testing is usually between 24 and 48 hours after delivery, depending on the discharge plan for the newborn. If the results of the first test at 24 hours are negative, the AAP recommends repeat testing at 24 hours or later after the first test result because some tests in newborns become positive at a later time. If the first test performed at 24 hours is positive, then repeat testing at least 24 hours apart should be performed until 2 test results are negative.^{45,82} This process will suggest clearance of the virus from the mucosal sites. RT-PCR from nasopharyngeal and throat swabs are recommended. Presently, the diagnostic role of antibody testing has not been well-established owing to inconclusive data.

Radiologic studies

A chest radiograph should be performed if clinically indicated. Radiologic findings in newborns are not specific and may include ground glass opacities, unilateral and bilateral subsegmental opacities and pneumothorax.^{8,9,26} In a national surveillance registry from the UK, of the 26 newborns who were SARS-CoV-2 positive and had chest radiographs, 14 (56%) had abnormal findings, with ground-glass changes reported in 7 (28%); in addition, 4 of these 7 babies were born preterm.⁷⁵

ROUTINE NEWBORN SURVEILLANCE AND NEWBORN/NEONATAL INTENSIVE CARE UNIT VISITATION BY FAMILY MEMBERS

In April 2020, the Vermont Oxford Network, in partnership with the AAP SONPM, conducted an audit to assess the impact of SARS-CoV-2 on neonates and their families.⁸³ Of the 332 hospitals, 54% reported shortages of equipment, testing, or personnel, 73% reported minor disruptions to care for infants and families, and 3% reported

an inability to provide care to some, most, or all infants.⁸⁴ Owing to the ever-evolving evidence of SARS-CoV-2 transmission between asymptomatic carriers, varying policy changes have been made by many NICUs and newborn nurseries across the world to limit the entry of healthy family members. Owing to vulnerability of the infant's health in the NICU, the AAP recommends restricting parents and family members with COVID-19 for 14 to 20 days from the onset of disease symptoms or the first positive test.⁴⁵ Some NICUs made strict visitation policies with exceptions on a case-by-case basis. This difference led to disparities in the NICU visitation by family members and lack of parental participation in family-centered rounds.⁸³ The AAP strongly advocated that "any policy restricting visitors for pediatric patients should be applied equally regardless of children's race, ethnicity, socioeconomic status, culture, and religion" to minimize health disparities.⁸⁵ Nonetheless, various social, emotional, and psychological challenges were faced by family members during the separation of neonates staying for an extended duration in the NICU.⁸³ Parental stress arising from NICU admission has been associated with poor neurodevelopmental outcomes in preterm babies.⁸⁶ Especially in the pandemic, parental stress can worsen owing to restricted visitation. Owing to growing evidence of low transmission risk in the NICU, these restrictions have been alleviated to some extent in most NICUs and newborn nurseries across the country.⁸⁷ In a center where universal screening of neonates, parents, and staff was practiced, no SARS-CoV-2 infection among the neonates admitted to the NICU was noted in an area with a high incidence of SARS-CoV-2.⁸⁸ If parental visitation is restricted, the NICU should provide numerous ways to best support infants and their families to cope within this stressful environment.⁸⁹ As the literature on SARS-CoV-2 in neonates accumulates, evidence-based policies should be formulated to prevent horizontal spread of SARS-CoV-2 in the NICU that can be applicable universally.⁹⁰

DISCHARGE PLANNING AND FOLLOW-UP

Routine newborn care including physical examination, vitamin K injection, administration of erythromycin eye ointment, performing hearing and critical congenital heart disease screens, and administering hepatitis B vaccine per the institutional policies should be completed before discharge, regardless of SARS-CoV-2 testing. If the newborn tests positive, remains positive on repeat testing, and is asymptomatic, then the newborn can be discharged with home quarantine for 10 days from the first positive test.⁴⁵ Care should be taken to prevent spread from the newborn to other members at home. Newborn visits can be arranged by telemedicine or phone. In-office visits should be avoided as far as possible to prevent spread. Some hospital centers, through charitable organizations, have been arranging and distributing electronic scales at discharge for assessing weight gain at home.⁴⁰ This practice may decrease the need for newborn in-office visits. If an in-office visit is necessary, parents should inform the clinic about the COVID-19 status of the newborn and the accompanying parent before arrival so that necessary precautions can be in place at the pediatrician's office. If the newborn is tested negative at discharge, then thorough parental counseling and additional infection prevention education should be provided to all the possible caregivers and household members after discharge. Other household members who may have been exposed to COVID-19 should maintain 6 or more feet of distance with the use of facemasks and adequate hand hygiene.⁴⁵ In a cohort analysis of 101 neonates born to mothers with perinatal SARS-CoV-2 infections at a single institution in New York, 55 who were seen at the newborn COVID-19 follow-up clinic remained healthy at 2 weeks of life. The appropriate duration of infection control practiced by the breastfeeding mother is unknown because a varying duration of viral

shedding has been shown from different sites.³⁰ However, the AAP recommends that infection control be practiced for at least 10 days from the onset of symptoms and at least 24 hours from being afebrile without antipyretics.⁷ Other precautionary measures as mentioned elsewhere in this article should be followed by mothers while breast-feeding. Parents should be educated regarding normal newborn care and common red flags concerning illness in newborns.⁴⁵

CLINICS CARE POINTS

- While extensive research suggest horizontal transmission of COVID-19 from caregivers to neonates, there are few case reports demonstrating the rare possibility of vertical transmission.
- Although most of the neonates with SARS-CoV2 are asymptomatic or have a mild clinical course, there are rare case reports of severe disease manifestation in this age group.
- Most governing agencies have recommended mothers with COVID-19 to continue breast feeding, considering its long-term benefits.

DISCLOSURE

The authors have nothing to disclose.

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