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Mini Review

Management of Neonates Born to Mothers with COVID-19

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Abstract

The coronavirus disease 2019 (COVID-19) has spread rapidly across the world. With the sharp increase in the number of infections, the number of pregnant women and children with COVID-19 is also on the rise. Limited data are available for pregnant women and newborns with COVID-19. A few small case series suggest that congenital and perinatal transmission to newborns from infected women may occur. Pediatric data demonstrate that children of all ages are susceptible to SARS-CoV-2, and that infants under 1 year of age are at risk for severe disease although this still is a relatively rare outcome. This manuscript outlines the precautions and steps to be taken before, during, and after resuscitation of a newborn born to a COVID-19 suspected or/confirmed mother, including resuscitation of the newborn, disposition, nutrition, and post discharge care. Our aim is to conduct a rapid review to guide the health care practitioners to the practical approaches to ensure the best care for the newborn. In conclusion: neonates born to women with COVID-19 – as well as neonates born to women with testing for COVID-19 pending at the time of delivery- should be considered as persons under investigation (PUIs) for infection

Keywords: Corona virus disease 2019 (COVID-19), antenatal steroids (ANS), personal protective equipment (PPE), aerosol generating procedures (AGP)

Introduction

Novel coronavirus (SARS-COV-2) is a new strain of coronavirus causing COVID-19, first identified in Wuhan City, China. Current evidence is consistent with low rates of peripartum transmission and is inconclusive about in utero transmission of SARS-CoV-2 from mothers with COVID-19 to their newborns, based on negative samples from amniotic fluid, cord blood, vaginal discharge, neonatal throat swabs or breastmilk. Similarly, evidence of increased severe maternal or neonatal outcomes is uncertain, and limited to infection in the third trimester, with some cases of premature rupture of membranes, fetal distress, and preterm birth reported **[1].**

Perinatal T**ransmission**

Considerable uncertainty exists regarding the potential for vertical transmission (prenatal/congenital or perinatal) of SARS-CoV-2 from infected pregnant women to their newborns. Respiratory secretions and saliva are the primary infectious fluids for human-to-human transmission of SARS-CoV-2. One study of non-pregnant patients with severe illness also detected virus in blood and stool **[2].** Viremia correlated with progression to severe illness. Data from a total of 11 women in China failed to detect virus in maternal whole blood, serum, vaginal mucus, amniotic fluid, and/or breast milk when virus was detectable in maternal nasopharyngeal specimens **[3].** One study detected virus in maternal feces **[4].** Four reports from China with a total of 17 tested newborns found no evidence for mother-to-newborn transmission. In contrast, two additional reports together document detection of SARS-CoV-2 in 4/34 tested newborns. Pneumonia was clinically and radiographically diagnosed in these 4 infants and abnormalities in neonatal inflammatory markers and transaminase levels were variably documented **[4].**

Antenatal

The mode of birth should be individualized based on obstetric

indications and the woman's preferences. WHO **[1]**, Royal College of Obstetricians and Gynaecologists (RCOG) **[5]** and American College of Obstetricians and Gynaecologists (ACOG) **[6]** recommended that caesarean section should ideally be undertaken only when medically justified (COVID-19) is not an indication for C-Section.

There are different opinions around usage of antenatal steroids (ANS), they are known to accelerate the development of type-2 alveolar cells in the lung, cells that are rich in angiotensin-converting enzyme 2, a co receptor for SARS CoV-2 viral entry (ACE_2 is a functional SARS-CoV receptor in vitro and in vivo). However, this theoretical risk is countered by a significant decrease in mortality and morbidity in preterm infants following ANS. There is currently no evidence to support or refute ANS in mothers with COVID-19 with impending preterm delivery **[7].** Queensland recommendations **[8, 9]** stated that there were no current evidence sufficient to alter usual indications/recommendations for antenatal corticosteroids. On the other hand the Centers for Disease Control and Prevention (CDC) **[10]** recommend avoiding glucocorticoids in COVID-19-positive persons because they have been associated with an increased risk for mortality. However, the CDC **[10]** has not addressed use of antenatal glucocorticoids to reduce neonatal morbidity and mortality from preterm birth in pregnant COVID-19-positive patients. Because of the clear benefits of antenatal **steroid** administration between 24+0 and 33+6 weeks of gestation in patients at high risk of preterm birth within seven days, American College of Obstetricians and Gynecologists (ACOG) **[6]** continues to recommend its use for standard indications to pregnant patients with suspected or confirmed COVID-19.

However, for pregnant patients with suspected or confirmed COVID-19 at 34+0 to 36+6 weeks of gestation and at

risk of preterm birth within seven days, the benefits to the neonate are less clear, and American College of Obstetricians and Gynecologists (ACOG) **[9]** has advised not administering a course of betamethasone to such patients. However, these decisions may need to be individualized, weighing the neonatal benefits with the risks of potential harm to the pregnant patient.

Furthermore, Royal College of Obstetricians and Gynaecologists (RCOG) stated that steroids should be given to mothers anticipating preterm delivery where indicated and urgent delivery should not be delayed for their administration (as normal practice).

As regard, MgSO4 should be given for neuroprotection of infants < 30 weeks' gestation as per current guidance **[5, 6, 9].**

Canadian Pediatric Society **[11]** Attendance at delivery for babies of COVID-positive mothers is not routinely indicated if there are no other indications of fetal distress and/or anticipated need for advanced resuscitation. If a neonatal resuscitation team is required, only essential and experienced personnel should attend. They should maintain a distance of 2 meters from the mother.

At the Delivery Room

Aaccording to Queensland Clinical Guidelines **[5]** recommendations: delivery shall take place in a dedicated isolation room. All infant resuscitation/ assessment will occur in the location where the infant is born – AVOID TRANSFER.

Resuscitation will be carried out as per NRP protocol **[9].** Clinical staff should use Droplet and Contact Precautions. Don PPE: Gown, procedure mask, eye protection, gloves and N95, are needed when performing newborn resuscitation that can generate aerosols (bag-mask ventilation, intubation, suctioning, oxygen at a flow >2 LPM/kg, continuous positive airway pressure and/or positive pressure ventilation). Only essential staff should be present in the delivery room/theatre **[5].**

According to the recommendation of Royal College of Obstetricians and Gynaecologists (RCOG) **[5]** that once baby is stable, should be bathed by water and soap after birth to remove virus potentially present on skin surfaces before transfer to ICU. Also RCOG have made recommendations for the care of women with COVID-19 at the stage of delivery and emphasized that a delay in cord closure (DCC) is not recommended (especially for those of unwell mothers) and should be discussed with the mother, no skin-to-skin contact between mother and infant, baby's nasal suction before the first breath, isolating the infant immediately after birth, and performing a coronavirus test for the infant **[12].** In case of preterm baby, standard thermoregulatory measures including the use of a plastic bag. NO SWABS to be completed in any Operating Room **[5].**

Stabiliation and Resuscitation of the Neonates: according to Chandrasekharan et al 2020 recommendation **[7], i**t can be conducted in an adjacent room or the same place at least 6 feet or 2 meters away from the mother with a physical barrier such as a curtain in between is important. Alternatively, infant may be resuscitated in a separate room **[7].**

Advanced Resuscitation and Airway Management: it remains unclear if use of a T-piece resuscitation device to provide CPAP/PPV via facemask could generate aerosols. It is reported that 50 to 60% leakage occurred during mask ventilation in the delivery room, especially with premature neonate. It is considered that laryngeal mask airway (LMA) reduces aerosol generation and could be an alternative to face mask ventilation. Open suction of endotracheal tube while administering surfactant or clearing secretions could generate aerosols, and a provider should anticipate such situations and be prepared **[7].** An infant born to a mother with COVID-19 severe acute respiratory distress under general anesthesia could be depressed and may require resuscitation either as a consequence of maternal respiratory

disease or anesthesia. As with non-COVID-19 resuscitations, fluid boluses and blood products are needed in special circumstances with precautions recommended by CDC **[10].**

Management Post-Delivery

Maintain high index of suspicion for signs of sepsis/unwell baby, both stable and unstable infants will be moved immediately after resuscitation to a dedicated Isolation Room in the NICU. According to Queensland guidline recommendations **[8, 9]** COVID-19 test is not routinely recommended except if other clinical indications identified (e.g. the baby becomes unwell), hile AAP **[13]** guidance recommendations stated that babies born to suspected/confirmed mothers with COVID-19 should have a nasopharyngeal swab for COVID-19 PCR at 24 hours of age and repeat after 48 hours by special procedure* if the baby is unwell. Clinicians may consider additional rectal swab testing (if available), particularly for sick infants requiring prolonged hospital care **[8].** However, Centers for Disease Control and Prevention (CDC) **[10]** and Canadian Pediatric Society **[11]** do not recommend separation of relatively well mother and baby. Fortunately, all reports regarding newborns have shown that even neonates who had positive surface swabs recovered completely and no mortality is reported **[10].**

Rooming-in for mothers and well newborns: temporary separation minimizes the risk of postnatal infant infection from maternal respiratory secretions. The benefits of separation may be greater in mothers with more serious illness. The likely benefits of temporary maternal and newborn separation at birth for decreasing the risk of newborn infection should be discussed with the mother, optimally prior to delivery **[13].**

If possible, admit the infant to an area separate from unaffected infants, and wear gowns, gloves, eye protection goggles and standard procedural masks for newborn care. If the center cannot

place the infant in a separate area — or the mother chooses rooming-in despite recommendations, ensure the infant is at least 6 feet from the mother. A curtain or an isolette can help facilitate separation [13].

Feeding (Breastfeeding)

Because studies to date have not detected the virus in breast milk, mothers may express breast milk after appropriate breast and hand hygiene. Caregivers who are not infected may feed the breast milk to the infant. Mothers who request direct breastfeeding should comply with strict preventive precautions that include use of a mask and meticulous breast and hand hygiene **[9,** 13]. Parents should understand that the risk of transmission. If mother and baby are asymptomatic, they are discharged home with further testing only if baby becomes symptomatic **[10].**

The safety of breastfeeding when mother is on drugs/antiviral: according to Chandrasekharan et al., 2020 **[7]** recommendations, there are no ill effects reported in infants from maternal hydroxychloroquine while breastfeeding. Therapy remains unknown. There are ongoing trials of remdesivir among patients with COVID-19. Nothing is known about the passage of remdesivir into breastmilk. Investigational drug sarilumab (an interleukin-6 IgG1 monoclonal antibody), there is no data available on its safety during pregnancy or breastfeeding **[7].**

Location

COVID-19 positive mother alone (i.e. no other neonatal criteria), is not itself an indication for admission to a neonatal nursery, perform clinical assessment after birth as per usual protocols and assess if required care can safely be provided during co-location with mother **[8].**

In-Hospital Neonatal Transport: Institutions must develop pathways for transport to the post-partum wards and the NICU if an infant born to a COVID-positive mother is symptomatic. An infant on respiratory support should be transported to the NICU using a

designated route in a closed isolette to minimize the possibility of unfiltered expiratory gases exposing anyone not wearing airborne precautions. When infants are asymptomatic at birth, routine transfer with the mother to a post-partum hospital room in an open bassinet should be sufficient **[6].**

Outborn transport of infant born to COVID-positive mother: there is currently no data to guide the practice of outborn transport of an infant born to a COVID-positive mother. The earliest documented COVID-19 positive test result for a newborn was at 36 hours of age. Given this, when transporting an infant born to a mother with suspected or confirmed COVID-19, Canadian pediatric society **[11]** recommend that:

- *An infant with respiratory distress **in the first 24 hours of life,** and who requires positive pressure ventilation, should be transported using droplet precautions with the infant in a closed isolette* [11].
- *When transporting an infant who was initially well but subsequently developed respiratory distress **after 24 hours of age**, personnel should be provided with an N95 respirator* [11].
- *However, in centers where staff who perform aerosol generating medical procedures (AGMP) use N95 respirators regardless of time after birth, to be consistent, all transport team members should have access to the same precautions* [11].

Intensive Care

Infants requiring neonatal intensive care ideally should be admitted to a single-patient room with the potential for negative room pressure or other air filtration system. If unavailable, or if the center must cohort multiple COVID-exposed infants, there should be at least 6 feet between infants. In-line suction with endotracheal tubes should be used if possible. Where possible use of a video-laryngoscope should be considered for intubation (if available), and the baby kept within the incubator

Intubation/LISA are particularly high risk and must involve use of appropriate PPE, even in an emergency. Consider reduction unnecessary investigations [10].

Care of a Preterm or Symptomatic Term Infant in the NICU: if a newborn with COVID-19 exhibits respiratory symptoms, a chest X-ray is indicated. The radiographic features of neonates with lower respiratory tract infection due to SARS-CoV-2 have not been well characterized. In the NICU, these infants should be cared for in an isolette in a negative pressure room (if available). Contact and droplet precautions are recommended. Both conventional ventilators and high-frequency ventilators include some risk of aerosolization. The oxygen filters, tubing for the ventilator, face mask, and any other device as part of the respiratory management should be disposed or carefully sterilized depending upon the availability of resources **[7].**

If the preterm infant had features of respiratory distress syndrome and pneumonia with signs of sepsis and coagulopathy. Laboratory analysis revealed leukocytosis, lymphopenia, thrombocytopenia, and elevated creatinine kinase-MB fraction. There is no evidence to date that administration of immunoglobulins, antivirals, and steroids improves outcomes of neonates with severe COVID-19 **[7].**

Postnatal Workup Testing and Discharge According to American Academy of Pediatrics (AAP) [13] **if** the mother is positive for SARS-CoV-2, the infant should be tested at or beyond 24 hours after birth. A nasopharyngeal swab is preferably obtained in a negative pressure room or in isolation with adequate PPE**.** A positive RT-PCR from either the nasopharyngeal/oropharyngeal or rectal swab (if available) is sufficient for diagnosis **[7].**

Discharge and Post-hospital Care [13]

- Infants who cannot be tested should be treated as if they are positive for the virus

for the 14-day observation period. The mother should continue to maintain precautions until she meets the criteria for non-infectivity ***.

- *Positive test results:* If an infant tests positive for COVID-19 but does not display symptoms, plan for frequent outpatient follow-up (phone, telemedicine or in-office) through 14 days after birth. Follow precautions (including stools) to prevent household spread from infant to caregivers

- *Negative test results:* Discharge the infant, ideally, to the care of a designated healthy caregiver. The mother should maintain a 6-foot distance when possible and use a mask and hand hygiene when directly caring for the infant until **either** a) she meets the **criteria for non-infectivity ***.**

*** *(a) she has been afebrile for 72 hours without use of antipyretics, and*

(b) at least 7 days have passed since her symptoms first appeared;

***- OR** she has negative results of a SARS-CoV-2 test from at least two consecutive specimens collected ≥24 hours apart.* Other caregivers in the home who are persons under investigation (PUIs) for COVID-19 should use standard procedural masks and hand hygiene when they are within 6 feet of the newborn.

To date, there have been no reports of mortality reported in infants with COVID-19. A healthy caregiver may care for the newborn until mother is afebrile (without antipyretics), demonstrates improvement of symptoms and has two negative tests for SARS-CoV-2 at least 24-hour apart **[7].**

Visiting Protocol if the baby is in the NICU

Mothers with COVID-19 should not visit infants requiring neonatal intensive care until she met the criteria of non-infectivity***

- *COVID-19 positive parents should not be able to visit their baby on the NNU.*
- *No other visitors (including siblings) should be allowed to visit*

infants in NNUs (all areas), except under exceptional circumstances, to be discussed with local infection control **[13].**

Follow up

American Academy of Pediatrics (AAP) **[13]** advised to postpone the routine follow-up hospital visits of newborns except for vaccination.

*N.B ** Use one swab to sample first the throat and then the nasopharynx. Place single swab in one viral transport media tube and send it to the lab for molecular testing.*

For infants who are positive on their initial testing, follow-up testing of combined throat/nasopharynx specimens should be done at 48- to 72-hours intervals until there are two consecutive negative tests.

Conclusions: The COVID-19 pandemic is a dynamic evolving global health emergency. The limited information on the complications and outcomes of the virus in pregnancy and childbirth require refinement as more information becomes available about the nature and transmission of the disease.

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