

Neonatal Intensive Care Unit Care of Newborn Infants born to Mothers with Suspected or Confirmed COVID-19 Infection

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ABSTRACT

The virus severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2), which was later termed Coronavirus disease-19 (COVID-19), was first identified as a cause of atypical respiratory diseases in the Hubei Province of Wuhan, China, December 2019, and was then officially declared a pandemic by the World Health Organization (WHO) on March 11, 2020. Severe acute respiratory syndrome coronavirus 2 contains a single-stranded, positive-sense ribonucleic acid (RNA) genome surrounded by an extracellular membrane containing a series of spike glycoproteins resembling a crown. In this article, we have reviewed the perinatal clinical implications of SARS-CoV-2 infections and their management in birthing and neonatal intensive care units (NICUs). Increasing evidence suggest that strict hospital protocols are needed, but we may not need to separate the mothers and their infants or discourage breastfeeding. We have included information from our infection-control protocols in our hospitals and from an extensive literature search in the databases PubMed, EMBASE, and Scopus. To avoid bias in the identification of studies, keywords were shortlisted *a priori* from anecdotal experience and PubMed's Medical Subject Heading (MeSH) thesaurus.

Keywords: Acute respiratory syndrome-coronavirus 2, Coronavirus disease-19, Neonatal intensive care unit, Personal protection equipment, Ribonucleic acid reverse transcription-polymerase chain reaction, Reverse transcription-polymerase chain reaction, Severe acute respiratory syndrome-coronavirus 2.

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INTRODUCTION

At the end of 2019, the city of Wuhan, Hubei province, China had been challenged by patients who presented with a cluster of a pneumonia-like picture with a mysterious underlying etiology. The new challenging medical problem spread rapidly through China, followed by throughout the globe. The WHO called the COVID-19 by February 20, 2020.¹ Coronavirus disease-19 caused by SARS-CoV-2.¹

The SARS-CoV-2 is a β -coronavirus of the same subpopulation of severe acute respiratory syndrome (SARS) and many bat-related coronaviruses. It is enveloped, positive-sense, single-stranded RNA viruses of zoonotic origin (Fig. 1). All these viruses used the same angiotensin-converting enzyme 2 to enter the victim cell.² The number of confirmed infections pluming up to date with the updated numbers can be found here.

Transmission of the virus started in Wuhan was linked to the seafood market selling live animals. Later on, person-to-person transmission has evolved but was not clearly understood. However, it might be mainly through the respiratory system same as influenza does by respiratory droplets generated by talking, sneezing, and coughing. The infection either occurs directly when the droplets landed at the mucus surfaces or indirectly by coughing producing droplets that landed over surfaces. Touching the infected surfaces followed by mouth, nose, or eye touching can also cause viral transmission.³ Air-borne transmission has not been shown conclusively as of yet. Coronavirus disease-19 virus can stay alive for various periods on different surfaces.⁴ The virus has not been found in the respiratory system only but found in the blood, eyes, and stool. Despite, as of yet, we are not sure what the virus exactly does in these areas but as the disease knowledge

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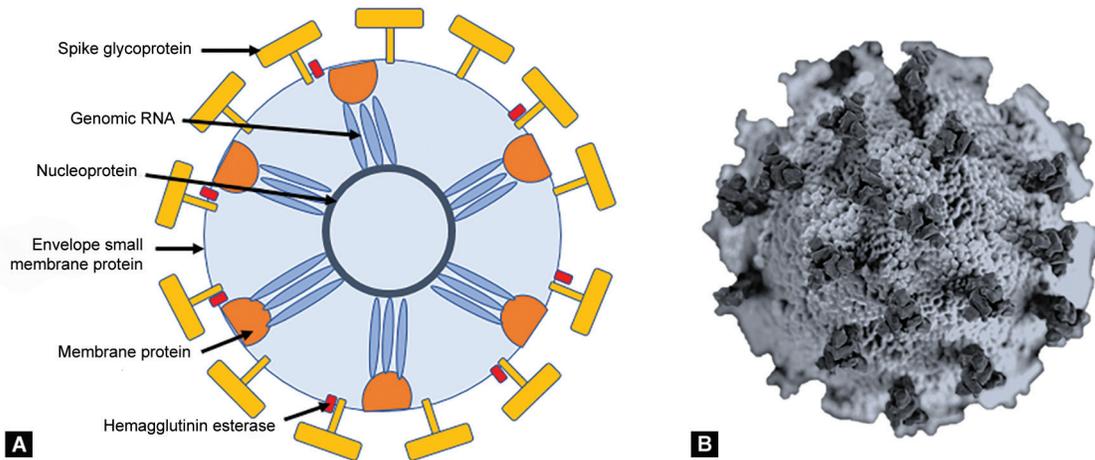
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is evolving, a new clinical presentation is being recognized. The infectivity period is not defined as the infected person can transfer the infection before and at the symptoms' appearance. The viral



Figs 1A and B: COVID-19 virus. (A) Schematic showing the major structural components and (B) 3D model of the virus

load of SARS-CoV-2 of those recovered from the upper respiratory system seems higher than other RNA viruses.⁵⁻⁷ However, we do not know the effect of viral load on the duration of infectivity, which is still uncertain.

The risk of infectivity of SARS-CoV-2 is variable depending on many factors such as (1) type of exposure, (2) duration of exposure, (3) use of preventive measures, and (4) amount of virus in respiratory secretions. Most person-to-person infection is associated with (1) household contacts, (2) health-care providers with the protective equipment, (3) closed settings such as cruise ships, and (4) social or work gatherings with close contacts (<1.5 meter) for >15 minutes.⁸⁻¹⁰

While, indirect infection from items that were in contact with an infected person on the surface then to another person has not been documented and may be unlikely. The frequency and the importance of environmental transmission through surface contaminated with the viruses through touching the surfaces with hands then to the mouth, nose and, eyes are possible but not noticeably clear.¹¹ The length of virus survival on these surfaces is unclear but can last up to 6–9 days without disinfection. Despite the thinking that the first transmission of COVID-19 was from an animal, an animal-to-human transmission was unclear.¹²

CLINICAL FEATURES

Most cases show symptoms after 5 days of exposure, although the incubation period can extend up to 14 days after exposure.¹³ The symptoms range from asymptomatic to critically ill severe symptoms.¹⁴ The Center for Disease Control and Prevention of China estimated the severity of the symptoms to be as follows:¹⁵ (1) Mild (no or mild pneumonia) in 81%, (2) severe disease (respiratory distress, desaturation, the involvement of 50% of the lung by 24–48 hours of imaging) in 14%, and (3) critical disease (respiratory failure, shock, or multiorgan dysfunction) in 5%.

Risk for severe disease are:^{16,17} (1) cardiovascular disease, (2) diabetes mellitus, (3) hypertension, (4) chronic lung disease, (5) cancer (blood malignancies, lung cancer, and metastatic disease), (6) chronic kidney disease, and (7) obesity. Severe disease can occur at any age but middle-to-elder age were the most affected.¹⁸ Asymptomatic patients can quickly progress to critically severe status.¹⁹ The average case fatality is approximately 2.3%.

LABORATORY FINDINGS

Complete blood picture may show lymphopenia, liver enzyme may be elevated, high lactate dehydrogenase levels, high inflammatory markers such as ferritin, C-reactive protein, and erythrocyte sedimentation rate with abnormal coagulation profile such as high D-dimer.²⁰

IMAGING

Early in the course of the disease, chest X-ray might be normal, but the findings of abnormal changes increase over the course of the illness with a peak at 10–12 days of starting the symptoms. The later on common findings are: (1) consolidation and (2) bilateral, peripheral, and lower lung zone distributions ground glass appearance.²¹ No finding can confidently exclude COVID-19 infection, but the chest computed tomography (CT) scan is overly sensitive imaging for COVID-19 chest involvement.²² Bilateral and mainly peripheral ground-glass opacification with or without consolidative abnormalities in the form of viral pneumonia are the most common findings, but rarely there are pleural thickening, pleural effusion, and/or lymphadenopathy.^{23,24}

DIAGNOSIS

Clinical suspicion of COVID-19 infection includes: (1) new onset of fever with or without respiratory symptoms such as cough or dyspnea, (2) unclear cause of severe lower respiratory symptoms, and (3) other suggested symptoms such as diarrhea, myalgias, unusual or loss of smell, or taste, conjunctivitis, skin rash or discoloration of the fingers or toes. Travel history or close contact with confirmed or suspected COVID-19-infected person should increase the suspicion. Symptomatic hospital staff especially those without proper personal protective equipment (PPE) should be investigated.

MICROBIOLOGICAL DIAGNOSIS

SARS-CoV-2 RNA reverse transcription-polymerase chain reaction (RT-PCR) can diagnose COVID-19 infection.²⁵ The nasopharyngeal or oropharyngeal swabs are used to collect the samples.²⁶ Serology can be used to identify previous and current infection.²⁷

SPECIFIC FINDINGS IN INFECTED CHILDREN AND ADOLESCENTS

Children of all ages can get the infection in lower incidence than adult.²⁸ They account for 1–5% of total COVID-19 infections.²⁹ In the USA, the age distribution is (1) children <1 year old account for 15% of all infections, (2) 1–4 years for 11%, (3) 5–9 years for 15%, (4) 10–14 years for 27%, and (5) 15–17 years for 32%.³⁰ The overall proportion of cases in infants is 0.27%.³⁰ Severe and fatal cases of COVID-19 are rare in children as the majority of children are either asymptomatic or have mild-to-moderate disease with 1–2 weeks of disease recovery.

SPECIFIC FINDINGS IN THE PERINATAL AND NEONATAL PERIOD

Precautions to Prevent Fetal Infection during Pregnancy

The following precautions need to be taken to prevent fetal infection during pregnancy:

- Administration of steroids for fetal lung maturation should be as normal practice; there is no evidence it causes any harm.
- MgSO₄ should be given for neuroprotection of infants <30 weeks' gestation as per current guidelines; there is no evidence it causes any harm.

Precautions for the Suspected/Confirmed Maternal Infection in the Delivery Room

Droplet precautions should be implemented in the delivery room because COVID-19 infection is highly communicable despite the risk of vertical transmission is low, but so far it is not clear when and how the transmission occurs. Therefore, the following procedures need to be considered in the delivery room:

- A designated senior member of the neonatal team should be assigned to attend the suspected/confirmed COVID-19 deliveries.
- Personal protection equipment should be donned in an adjacent room and the team member should wait outside. The PPE should minimally include shows cover, suitable scrub, head cover, N95 mask, and face shield.
- If it is anticipated that the baby will require respiratory support, appropriately skilled neonatal team members should be present at delivery wearing PPE.
- Neonatal resuscitation/stabilization should proceed as per current neonatal resuscitation programs' standards.
- Avoid resuscitation in the mother room, if possible.
- If needed, the neonates should be transferred in a closed incubator.

Specific Findings in Infected Newborns and Infants^{31–47}

Minimal information is available regarding peripartum COVID-19. Although separate studies by Rothe et al. and Kupferschmidt showed no documented cases of intrauterine transmission.^{31,32} others reported several cases of transmission during pregnancy.^{33–35} The American College of Obstetricians and Gynecologists/Society of Maternal-Fetal Medicine has published online guidance for the evaluation and care of pregnant women with suspected COVID-19.

Transmission through Breast Milk or during Feeding

It is unclear whether breast milk can transmit SARS-CoV-2. There is one study of testing breast milk that found no virus in the maternal milk of six patients.³⁶ However, the usual droplet transmission could occur through close contact during breast or bottle feeding. Therefore, the standard precaution of transmission prevention should be in place during infancy care.

Precautions for the Asymptomatic Newborns in the Delivery Room

The following Precautions need to be taken for the asymptomatic newborns in the delivery room:

- Well-babies not requiring medical interventions can be managed depending on the local institutional guidelines and resources. They can remain with their mother in their designated room or can be temporarily separated from his/her mother and will be cared in closed incubator by a designated nurse. The mother should be counselled about the risk and benefits of temporarily separation from her baby until her transmission-based precautions are discontinued.
- The baby may be bathed as soon as reasonably possible after birth. The benefit of removal the virus potential contaminate secretions/materials from the baby's skin should be weighed against the risk of hypothermia and hypoglycemia.
- Well-babies may be tested for two reasons: (1) to ascertain any vertical transmission and (2) research purposes. To test for vertical transmission, the infant need to be tested within 2–3 hours of birth; adequate precautions need to be observed to not contaminate the sample by the maternal secretions.
- If a mother is acutely unwell, an alternative nonquarantined caregiver/relative should be identified to provide care for the baby at home or in a designated room, not in the neonatal unit and the babies should be isolated from their mothers.
- Early discharge may be preferred with clearly listed guidance for safety advice in close liaison with community health-care providers.
- All care should be consistent with the PPE guidelines.

Postnatal Care of both Newborn Infants and COVID-19-confirmed Mothers

As the rate of infection of COVID-19 is rare in newborns, other causes of respiratory distress immediately after birth are more likely than COVID-19. Therefore, health-care providers should actively consider other differential diagnoses for respiratory illness in the infants.

The rate of infection in infants less than one year is exceptionally low. The primary presentations of infants confirmed to have COVID-19 infections were cough and fever. Hence, it remains difficult to describe a specific pattern of presentation of COVID-19 infection in newborns.³⁷

NICU Precautions for the Symptomatic Newborn Infants born to Mothers with Suspected or Confirmed COVID-19 Infections

The need for admission to the NICU requires careful evaluation. The following precautions need to be considered while giving invasive or no invasive respiratory support:

- All the procedures and investigations should be carried out in a single isolated room with a minimal number of staff. Ideally,

this room should have negative pressure. If an isolation room is not available, these infants should be cohorted in a designated area (corner) of the NICU.

- The cessation of isolation precautions need careful consideration. We have noted some variation in the management policies in different hospitals. We obtain nasopharyngeal swab(s) or endotracheal tube secretions on the postnatal day 10. If the test result is negative, then we repeat the swab after 24 hours. For positive results, we repeat the tests after 48–72 hours; the availability of test results varies with individual laboratories. We continue to take all precautions until we have two successive negative swabs.
- Incubators, ventilators, intubation tools, intravenous catheters, and central arterial or venous lines should be removed carefully, preferably inside a negative pressure isolation room.
- Intubation, suctioning, and other procedures with increased risk of exposure to respiratory sections should be performed with full PPE, including gloves, eye goggles, face shield, and N95 masks.
- The additional care such as intravenous antibiotics and phototherapy needs to be evaluated for the site, as to whether additional care can safely be provided at the mother's bedside (postnatal care) or not.
- NICU admissions should be avoided if at all possible and safe. Infants who require NICU care should be assessed in a designated area in the labor room or ward by a skilled neonatal team member wearing appropriate PPE.
- Incubators may serve as a useful isolation device, even when these are not otherwise indicated. This might be safer than open bed management.
- The need for all clinical investigations should be carefully evaluated if those are needed to meet the standards of care. In many situations, point-of-care testing may be a safer alternative.
- Intubation should only be undertaken by staff with appropriate competencies. Videolaryngoscope intubation may be useful when possible to reduce the proximity to the baby's airway and the risk of transmission. Noninvasive respiratory support should be carefully considered for the risk of associated aerosolization and higher risk.
- All babies requiring respiratory support should be nursed in an incubator.
- All equipment coming out of the isolation room should be cleaned as per predetermined cleaning policies.
- We maintain a logbook for staff entering or dealing with the patient.

NICU Precautions for Asymptomatic Newborn Infants born to Mothers with Suspected or Confirmed COVID-19 Infections

Well-babies of COVID-19 suspected or confirmed mothers should be isolated with their mothers; these infants are considered potentially infectious for at least 14 days. We discharge these infants to be sent home as early as possible.

For infants who need observation without needs for respiratory support, only droplet/contact precautions are appropriate. If available, we treat these infants in an isolation room with negative pressure.

When the respiratory symptoms have resolved, the infants may be relocated to other rooms to free up the negative pressure rooms for other patients. We have had to use these policies during

the period when the admission rates of newborns of COVID-19-suspected or -confirmed mothers were higher than the capacity of the local unit. For extra precautions, these asymptomatic infants were cohorted in an isolation area.

If the mother is a confirmed COVID-19 positive case, then her baby should be admitted to NICU. As well, if the baby showed any symptoms, then to be tested as early as possible.

Hospital Transport of Newborns at Risk of COVID-19 Infection

Hospitals should develop clear guidelines for transport between the delivery room, postpartum care, and NICU. Transportation of these infants to another ward/bed should be limited, if possible. These infants should be transferred in a closed incubator with full PPE.

Outborn Transport of Newborn Infants born to Mothers with Suspected or Confirmed COVID-19 Infections

We currently have limited data to establish guidelines to transfer outborn neonatal transport of newborns of COVID-19-confirmed or -suspected mothers. During air or ground transport, the personnel are in close contact with each other and with the baby. The infant might need interventions during transport. The possibility of transmission from COVID-19-suspected or -confirmed mothers may be influenced by gestational and postnatal ages, duration of transport, absence or presence of symptoms, and the need for invasive or noninvasive respiratory support. However, even if a nasopharyngeal swab is done at birth, the earliest result would be available after 24–48 hours. Therefore, it is advisable to assume all infants born to COVID-19-confirmed or -suspected mothers to be positive and implement all droplet/contact precautions.

Testing the Newborn

We do not currently have standard, immediately available tests to determine COVID-19 infections in neonates. Early documentation of COVID-19 infections may still take 36 hours. Given this, testing an infant born to a mother with suspected or confirmed COVID-19, it seems prudent to recommend the following:

- Testing asymptomatic neonates of COVID-19-suspected or -confirmed mothers is needed to detect vertical transmission or for research purposes. The test should be done before the possible occurrence of postnatal contamination, which is within 1–3 hours after birth.
- Testing symptomatic neonates born to suspected or confirmed COVID-19 mothers is needed per the local hospital's guidelines. However, two negative tests obtained 24 hours apart might be needed to declare a negative result. If positive, the baby will require supportive care institutional policy with full PPE and droplet/contact precautions, with the involvement of an infectious disease specialist.

Visitation

Social distancing practices have changed the hospital visiting policies and have been restricted to very necessary visits in many centers. Parents who test positive should be prevented from visiting their baby until they declared negative. A mother or a father with negative screening should be allowed to visit her/his baby. However, we have been cautious and have restricted other family visits.

Breastfeeding

Breastfeeding should be encouraged by supporting mothers who have been separated from their babies to expressed breast milk. Mothers should have a designated breast pump for exclusive use. Local infection control policies should be consulted in the cleansing.

It is not yet clear whether COVID-19 can be transferred via breast milk. Despite the low risk of COVID-19 transmission via breast milk, pasteurization of the breast milk might be beneficial. Alternatively, donor breast milk or formula milk should be considered. Evidence have showed that other coronaviruses are destroyed by pasteurization, but there are no evidence whether COVID-19 (if present in the breast milk) would be similarly destroyed. The Canadian Pediatric Society and the WHO recommend skin-to-skin contact and kangaroo care.

Newborn Screening

Clinical examination and screening for a newborn of COVID-19 positive mother should be carried out before discharge as per the standard of practice. Audiology screening of asymptomatic COVID-19-confirmed or -suspected mothers should be deferred to after discharge by 14 days.

Managing Unit Capacity

Staffing plan should be in place to manage situations due to sudden increase in NICU census or staff shortage as a result of direct or indirect COVID-19 pandemic. Patient ward and sign-in and -out rounds of the health-care providers should be organized to reduce direct contact. Virtual meetings may be used for work-related meetings, educational activities, and other meeting for formulating policies.

There is no need for staff to self-isolate after looking after a suspected or confirmed case of COVID-19 if correct PPE precautions have been taken. Any staff concerns regarding contact with a possible case should be discussed with him/her to determine the necessary steps that should be taken.

Imaging X-ray, Ultrasound, Magnetic Resonance Imaging, and Lab Tests

Imaging requests need to be discussed with the radiology department and with the senior neonatologist. Possibilities of deferral of the radiology/laboratory tests should be considered if the medical condition of the baby allowed. Otherwise, standard PPE should be the donned by the technician, and care of cleaning and sterilization between the procedures should be done.

Respiratory Support of Newborns at Risk of COVID-19

Aerosol generating medical procedures that should be performed using full PPE include (1) intubation, extubation, and surfactant administration; (2) management with continuous positive pressure ventilation (CPAP), bi-level positive airway pressure, high-flow nasal cannula, noninvasive positive pressure ventilation, invasive conventional mechanical ventilation, high-frequency oscillatory ventilation, and high-frequency jet ventilation; (c) nebulized therapy; and (d) open airway suctioning. Aerosolization, noninvasive respiratory support, surfactant administration, and airway suctioning are associated with significant aerosolization and should also be performed using full PPE. Assisted ventilation with a heat and moisture exchanger (HME) filter installed at the expiratory port of the ventilator is preferred over CPAP, biphasic CPAP, and high-flow therapy to reduce the risk of aerosolizing COVID-19 in the room.

In patients receiving positive pressure ventilation, the following procedures should be considered:

- To use disposable circuits only when transporting patients from the delivery room and in the NICU.
- To use a disposable expiratory valve.
- To connect a HME filter at the expiratory port of the ventilator. The HME filter is connected only when connecting the circuit to the patient.
- Change the HME filter every 24 hours.

To use a closed suction system, surfactant therapy, inhaled nitric oxide, high-frequency ventilation, continuous renal replacement therapy, and extracorporeal membrane oxygenation may be considered as for non-COVID-19 patients when required. All equipment coming out of the isolation room should be cleaned as per local institute policy for cleaning potentially infectious equipment.

The respiratory support equipment should be disinfected per protocol following its use on a COVID-19 patient. It is then kept aside and not used for a minimum of 14 days to a maximum of 28 days. But in case there is a shortage of machines, it can be used for the next suspected positive case. The disposable of the consumables used for respiratory support follows the same protocol as what has been followed so far for the waste management according to the CDC guidelines for COVID-19.⁴⁷

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