



NEWBORNS OF COVID-19 MOTHERS: HOW TO MANAGE

Paediatrics

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ABSTRACT

Since December 2019, the spread of Novel coronavirus ("2019-nCoV") has emerged as a public health emergency across the world. Coronavirus Disease (COVID-19) can infect people of all age groups, among which pregnant women and neonates comprise a special vulnerable group. Few cases affecting neonates have been described in the literature. In neonates, this disease may be asymptomatic or present with non-specific symptoms like fever, lethargy, vomiting, refusal to feed or respiratory distress. Early identification of affected neonates, isolation and infection control measures are the main pillars of management. No specific therapy has been recommended so far. This article will provide an insight into the understanding of the disease among neonates and management strategies.

KEYWORDS

COVID-19, SARS-CoV-2, PPE

INTRODUCTION

Novel coronavirus ("2019-nCoV" or SARS-CoV-2) is a new strain of coronavirus causing COVID-19, first identified in Wuhan City, China in December 2019. It has emerged as a public health emergency of international concern. It was declared as a pandemic by the World Health Organization on 11 March 2020¹. As on 19th April 2020, it has reached 210 countries and territories with more than 2.3 million cases and 164,525 deaths².

Neonates born to pregnant women with suspected or confirmed COVID-19 infection is a vulnerable group that needs special attention. As the pandemic continues to spread, understanding of SARS-CoV-2 infection in neonates will guide in prevention and management strategies among newborns.

Epidemiology

Coronavirus (CoV) is an enveloped, positive-sense single-stranded RNA virus belonging to the Coronaviridae family. It is subdivided into four genera: α -, β -, γ -, and δ -coronavirus. The 2019-nCoV belongs to the β -coronavirus genus, which infects only mammals³. Other agents in the same group include SARS-CoV, MERS-CoV, bat-SARS-like (SL)-CoVZC45, bat-SL-CoVZXC21, etc.

This virus enters the host cells via the SARS coronavirus receptor, angiotensin converting enzyme 2 (ACE 2). ACE 2 is a surface molecule that is highly expressed in AT2 cells of the lung, esophageal upper epithelial cells, absorptive enterocytes from ileum and colon. This indicates the respiratory system and digestive system are the potential routes for SARS CoV 2 infection^{4,5}. SARS-CoV-2 has weak resistance and can be inactivated at 56°C for 30 minutes, 75% ethanol, chlorine-containing disinfectants, and peracetic acid. This virus can remain viable in aerosols for hours and on the surfaces (like plastic, aerosols, stainless steel, etc) for days depending upon viral inoculum load.

It can infect people of all age groups including neonates and children. Human-Human transmission via respiratory droplets, close contact and fomites are the main sources of infection. The feco-oral route has also been hypothesized as a possible mode of transmission as SARS-CoV-2 RNA was detected in feces of COVID-19 patients^{6,7}. It must be emphasized that even asymptomatic carriers are important sources for the spread of infection. Neonates may acquire the infection from infected mother or household contacts.

Vertical transmission

There are no studies in the literature addressing the transmission of nCoV-19 in the first and second trimester of the pregnancy. As suggested from limited evidence in the literature, the possibility of vertical transmission from infected mothers to neonates in the third trimester is unlikely but can not be ruled out completely. Schwartz found no evidence of intrauterine transfer in a retrospective analysis of 38 pregnant women with confirmed COVID-19. In his analysis, all neonatal specimens including umbilical cord blood, urine, stools, and placenta were negative for SARS-CoV-2 by RT-PCR despite the existence of perinatal complications in some of the infants⁸. Contrary

to this, SARS-CoV-2 specific IgM&IgG was detected in 3 newborns of infected mothers suggesting the probability of intrauterine transmission. Due to the possibility of false positive IgM antibodies, a clear interpretation from these studies can not be made^{9,10}. Further studies are needed to make a definite conclusion regarding vertical transmission.

Clinical presentation

The incubation period of the COVID -19 varies from 1 to 14 days, mostly ranging from 3-7 days. In neonates, the clinical presentation can vary from asymptomatic infection to severe respiratory distress. Apart from this, gastrointestinal symptoms like vomiting, refusal to feed, abdominal discomfort and diarrhea may be the first manifestation of the disease in neonates¹¹.

Based on literature review^{12,13}, neonates usually present non-specific symptoms like fever, lethargy, vomiting, refusal to feed or may present as sepsis. Physical examination may be unremarkable or suggestive of pneumonia. Common laboratory findings include normal/decreased leucocyte count, lymphocytopenia, thrombocytopenia, deranged liver function tests and/or an elevated creatine kinase-MB fraction. Chest radiographic image suggesting pneumonia was the most consistent finding. Confirmation of the diagnosis is based on SARS-CoV-2 virus RNA detection in a nasopharyngeal throat swab. The clinical outcome among neonates has been favorable so far with isolation and good supportive care. We should keep suspicion of COVID-19 infection in neonates presenting with non-specific symptoms and history of any close contact.

Common differentials among neonates include bacterial/viral pneumonia, neonatal sepsis, respiratory distress syndrome, congestive heart failure, etc

COVID Testing of Newborn

Table 1 summarizes the testing protocol for newborns born to mothers with suspected/ confirmed COVID-19 infection^{14,15,16,17}

Table 1: COVID TESTING OF NEWBORN

Whom to test	All neonates irrespective of symptoms born to mothers with COVID-19 infection within 14 days of delivery or up to 28 days after birth (If a mother is COVID-19 positive and baby's initial sample is negative, another sample should be repeated after 48 hours) Symptomatic neonates exposed to close contacts with COVID-19 infection
What sample to be collected	Specimen can be collected from multiple sites: Upper respiratory tract(nasopharyngeal /oropharyngeal swab; if both collected then in the same tubing) Lower respiratory tract (endotracheal aspirate, for neonates who are mechanically ventilated) Other samples: Currently not advised; stool, urine and blood specimens, since the isolation is less reliable than from respiratory specimens.

How to collect	Upper nasopharyngeal swab Use only synthetic fiber swabs with plastic shafts. Do not use calcium alginate swabs or swabs with wooden shafts, as they may contain substances that inactivate some viruses and inhibit PCR testing. Insert a swab into nostril parallel to the palate. The swab should reach depth equal to the distance from nostrils to the outer opening of the ear. Leave swab in place for several seconds to absorb secretions. Slowly remove swab while rotating it. Place swab immediately into sterile tubes containing 2-3 ml of viral transport media. Oropharyngeal swab (e.g., throat swab): Swab the posterior pharynx, avoiding the tongue. Nasopharyngeal wash/aspirate or nasal aspirate Collect 2-3 mL into a sterile, leak-proof, screw-cap sputum collection cup or sterile dry container.
How to store the sample	Samples should be collected in viral transport media procured from the microbiology laboratory and transported immediately in icepacks. One can use disposable thermocol cartons or plastic bags with ice cubes for in-house transport. If sending to another laboratory, the sample can be stored at 2-8°C for up to 72 hours after collection. Storage should be done in a refrigerator dedicated to this purpose. If a delay in testing or shipping is expected, store specimens at -70°C or below in deep freezers.
How to send the sample	If transporting by shipping, the samples need to be packed as per instructions Guidance for sample Collection, Packaging and Transportation for Novel Coronavirus.
Method of testing	Reverse-transcriptase polymerase chain reaction (RT-PCR) for 2019-nCoV nucleic acid;

The utility of serology testing to detect antibodies (IgG and IgM) against SARS-CoV-2 in neonates is being explored continuously. The major drawback of antibody testing is that it may not be useful in settings of acute illness and seroconversion may take 7-10 days. Moreover, as described above SARS-CoV-2 specific IgM&IgG was detected in 3 newborns of infected mothers suggesting the probability of intrauterine transmission. Due to the possibility of false positive IgM antibodies, a clear interpretation from these studies can not be made^{9,10}.

Management and Infection Control

Though several potential therapies are under evaluation, no definitive therapy has been discovered so far in neonates. Early identification and isolation are the main pillars of infection control. Some of the strategies which can be adopted by the paediatric team for infection control and care of neonates of suspected/confirmed COVID-19 mothers are discussed below.

Neonatal Resuscitation^{17,18}

1. As the newborns of suspected or confirmed COVID-19 pregnant mothers are likely to be infectious, neonatologist must wear personal protective equipment including N 95 mask. Try to reduce the number of personnel involved in neonatal care to one in low-risk cases and two in anticipated high-risk cases.
2. If possible, resuscitation of the newborn should be done in a separate well-equipped room adjacent to the delivery point. If not feasible, the resuscitation point with the warmer should be at least 2 meters away from the delivery point.
3. Early cord clamping with no skin-to-skin contact after delivery should be practiced. There is insufficient evidence regarding whether delayed cord clamping increases the risk of infection to the newborn via direct contact. The Royal College of Obstetricians and Gynecologists of UK (RCOG) and Society of Obstetricians and Gynecologists of Canada recommend delayed cord clamping unless there are other contraindications, while American College of Obstetrics and Gynecologists (ACOG) and Chinese guidelines recommend immediate cord clamping.
4. Neonate should be handed over to neonatologists at the resuscitation area by any member of the delivery team.
5. Routine care and initial steps of neonatal resuscitation like drying, tactile stimulation, placement into a plastic bag or wrap, assessment of heart rate, placement of pulse oximetry are unlikely to be aerosol-generating.

6. Routine suctioning of the airway for uncomplicated deliveries should not be performed.
7. Such newborns should be kept in isolation. Neonates positive for the COVID-19 infection should preferably be placed in negative pressure rooms or in rooms with high-efficiency particulate air filters to exhaust room air.
8. Standard resuscitation guidelines (NRP-7th edition) to be followed. If positive-pressure ventilation is needed, self-inflating bag and mask may be preferred over a T-piece resuscitator.
9. Endotracheal instillation of medications, such as surfactant or epinephrine, are aerosol-generating procedures, especially via an uncuffed tube. Intravenous delivery of epinephrine via a low-lying umbilical venous catheter should be the preferred route of drug administration during neonatal resuscitation.

Isolation of Newborn

There are no strict recommendations regarding the isolation of the newborn. The isolation strategy for neonates of suspected/confirmed COVID19 mothers can be adopted depending upon the availability of health-care resources and a thorough discussion with parents. Table 2 describes options for isolation/rooming-in of the newborn after birth.

TABLE 2: Planning for isolation/rooming-in of Newborn

Condition	Where to keep the baby
For healthy newborns when a) Resources for isolation not available, or b) healthcare facilities are overwhelmed because of the large number of COVID -19 infection, or c) evidence of community spread is present	• The healthy neonate may be roomed-in with mother. • The mother-baby dyad must be isolated from other suspected/confirmed cases. • They should also be isolated from other uninfected mothers and neonates.
For Healthy newborns when a) resources for isolation of baby are available, or b) no evidence of community spread	• Isolate the newborn after immediate cord clamping • During isolation, the healthy neonate should preferably be cared by a family member, not in contact with the mother or other suspected/confirmed case.
Symptomatic newborn	• Should be managed in separate isolation facility by trained staff wearing PPE and following universal precautions

Feeding issues in neonates of COVID-19 infected mother

There is a paucity of literature addressing feeding issues and the safety of breastmilk for newborns born to suspected/confirmed COVID-19 mothers. Till date, eight studies in the literature have reported outcomes of 42 pregnancies with coronavirus infection. Out of these, 4 studies did not provide any details of the feeding policy; breastfeeding was not allowed in the remaining 4 studies. In a study by Chen et al, breast milk samples from six COVID-19 mothers were negative for the virus¹⁹.

The CDC also states that “we do not know whether mothers with COVID-19 can transmit the virus via breast milk”²⁰. The choice of breastfeeding can be made considering the preferences of mother and family after explaining all the risks and potential benefits of breastfeeding especially in low and middle-income countries. There is no doubt regarding the transmission of infected airborne droplets due to close contact of the infant with mother during breastfeeding. Some precautionary measures to be taken by suspected/confirmed COVID-19 mothers who are willing to breastfeed are as follows^{20,21}:

1. Proper hand-washing before and after touching the baby
2. Adequate respiratory hygiene measures to be taken by mother i.e wearing a mask and not sneezing in front of a baby during breastfeeding
3. Mothers who wish to give expressed milk should wash her hands before touching any breast pump and bottle. She should also follow the recommendations for proper pump cleaning after each use.

Role of specific treatment

Upcoming literature is available on the effect of different antivirals, other drugs like chloroquine or hydroxychloroquine or adjuvant treatment like corticosteroids and intravenous gamma globulin in

adults but no such clinical trials are available for neonates. As of now, no such specific therapy is recommended for the treatment of neonates with COVID-19 infection.

CONCLUSION

Neonates are a special vulnerable group for COVID-19 infection. Till some definitive therapy or vaccination is available, early diagnosis and infection control measures remain the cornerstones of neonatal management. As the pandemic continues, there will be more data available that could lead to significant changes in the current recommendations.

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