

LEADING ARTICLE

COVID-19 Pandemic and Neonate

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Introduction

Novel coronavirus (SARS-CoV-2) is a new strain of coronavirus causing pneumonia, first was reported in Wuhan, Hubei Province, China, in December 2019.¹ On January 7, 2020 World Health Organization (WHO) named it as Corona Virus Disease 2019 (COVID-19).² COVID-19 emerged as an epidemic in China and spread rapidly to almost all countries over the globe.³ So, WHO declared COVID 19 as a pandemic on 11 March 2020.⁴

The COVID-19 pandemic has predominantly affected adults of older age groups. The effect of SARS-CoV-2 on children including neonates appears to be trivial. The knowledge on COVID-19 in neonates is only based on a recent experience over the past few months. Moreover, there is limited information regarding impact of corona virus on neonatal care in relation to newborns with confirmed or suspected COVID-19.^{5,6} Here, we discuss the basic aspects of the infection, the likely presentation in newborns and the approach of management of neonates with infection or at risk of the infection with SARS-CoV-2.

Novel coronavirus infection

The novel coronavirus (SARS-CoV-2), is belong to beta coronavirus family, a single-stranded RNA virus with a helical capsid with radiating spikes (hence the name corona), and the disease is referred to as coronavirus disease 2019 (COVID-19).⁷

The virus is highly infectious and the entire population is generally susceptible. Usually spreads by aerosol and droplet generation by atomization while coughing, sneezing, or even talking and droplet contact spread.^{8,9} SARS-CoV-2 RNA has been detected in stool specimens, but fecal-oral transmission has not been clinically described.¹⁰ The incubation period is between 3-7 days on average, with 2 days as the shortest and 14 days longest.¹¹

How do neonates get infected?

Postnatal transmission from mothers, other caregivers, visitors, or healthcare personnel who have the infection (or are asymptomatic carriers) through respiratory droplets is the commonest way a baby may get infected.⁹

Early Chinese reports suggested that vertical transmission of SARS-CoV-2 does not occur, as amniotic fluid, vaginal mucus, placenta, umbilical cord, cord blood, and neonatal stool specimens tested negative for the virus.^{12,13} Limited reports have raised concern of possible intrapartum or peripartum transmission, but the extent and clinical significance of vertical transmission by these routes is unclear.^{14,15}

The role of breast milk in spreading is not yet identified as till date no evidence of presence of SARS-CoV-2 in breast milk of pregnant women with COVID-19 is found.¹⁶

Clinical presentation

Information on clinical presentation and disease severity among neonates is limited and based on case reports and small case series. The extent to which SARS-CoV-2 infection contributed to the reported signs of infection and complications in neonates is unclear. Neonates presented with symptoms usually milder than other age groups. No severe case or death was reported till now.¹⁷⁻¹⁹ The severe disease in adults is a consequence of a cytokine storm,²⁰ and fortunately, this is less pronounced in children including neonates and that could be a factor behind the milder manifestations in neonates. The Kawasaki like inflammatory syndrome described in older children has not been noted in newborns.

In case of neonates with COVID-19, clinical presentation is nonspecific. Commonly observed

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Received: 18 May 2020;

Accepted: 28 May 2020

symptoms are depicted in Table I.^{11,21} So suspected neonates should be closely monitored for vitals, respiratory and gastrointestinal symptoms.

Table I
Clinical presentations of neonates with COVID-19

System	Manifestations
Neurological	Temperature instability Lethargy
Respiratory	Grunting Nasal flaring Tachypnea Chest retractions Central cyanosis/pallor Apnea Cough
Gastrointestinal	Abdominal distension Feeding intolerance Diarrhea/watery stools Emesis

Diagnosis

Reverse transcription polymerase chain reaction (RT-PCR) in the swab sample taken from deep intranasal and oropharyngeal swabs is currently the only test being used to confirm cases of COVID-19 infection.²¹⁻²³

Laboratory tests including CBC: leukopenia, leukocytosis, and lymphopenia (most common) and mild thrombocytopenia. Various enzymes level is found to be elevated, including creatine kinase, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, and lactate dehydrogenase.²¹

Chest X-ray and computed tomography (CT) and abdominal radiography are not recommended for initial evaluation; should reserve for hospitalized patients or symptomatic patients with specific clinical indications. The likely findings in CXR/Chest CT are ground-glass opacities (GGOs), multiple areas of consolidation, “crazy paving appearance” (GGOs + inter-/intra-lobular septal thickening), and bronchovascular thickening. Lesions usually have a bilateral, peripheral, and lower lobe distribution. Abdominal radiography may show intestinal ileus.²¹

Case definition²¹

Suspect case: A neonate born to the mother with a history of SARS-CoV-2 infection between 14 days before delivery and 28 days after delivery, or the neonate directly exposed to those infected with SARS-CoV-2 (including parents, family members, caregivers, medical staff, and visitors).

Confirm case: Neonate with positive RT-PCR test for SARS-CoV-2 infection from respiratory tract sample; or virus gene sequencing of the respiratory tract specimen is highly homologous to that of the known SARS-CoV-2 specimen.

When to test the baby²⁴

1. Approximately at 24 hours of age if the baby born to a mother with history of SARS-CoV-2 infection. If initial test results are negative, or not available, testing should be repeated at 48 hours of age.
2. As early as possible after admission if the neonates have signs suggestive of COVID-19 or neonates with history of COVID-19 exposure requiring higher levels of care.

Management of neonates born to mothers with COVID-19²⁴⁻²⁷

1. Suspected and confirmed COVID positive mothers should be delivered in separate delivery rooms or operation theaters. Stabilization and resuscitation of the neonates should be done 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. Minimum number of skilled neonatal team members (preferably 2 members) should attend to manage the newborn and wear a full set of PPE including N95 mask. Mother should perform hand hygiene and wear triple layer mask. Delayed cord clamping practices and skin-to-skin care in the delivery room should continue per usual center practice. Mothers with COVID-19 should use a mask while holding their baby. Resuscitation will be carried out as per NRP protocol and in case of any positive pressure ventilation requirement, self-inflating bag with mask should be preferred to T-piece resuscitator.
2. Stable neonates born to COVID-19 positive mothers should be roomed-in with their mothers and be exclusively breastfed. For supporting lactation, nurses trained in essential newborn

care and lactation management should be provided. A healthy asymptomatic willing family member who is not positive for COVID-19, and has not been in direct contact with suspected or confirmed COVID-19 person may be allowed to provide support for mother and neonate. Mother should wash hands frequently including before breastfeeding and wear mask. The mother-baby dyad must be isolated from other suspected and infected cases.

3. Symptomatic/ sick neonates born to a mother with suspected or confirmed COVID19 should be managed in separate isolation facility, as like as sick neonates with COVID-19.
4. Newborn should be monitored regularly for vitals and routine examination by health care personnel with adequate PPE.

Management of sick neonates with COVID-19^{25,27-30}

1. Treat suspected, or confirmed cases and symptomatic/sick neonates born to a mother with suspected or confirmed COVID19 in separate room(s) preferably negative pressure room if available. If single rooms are not available, placed them in a common isolation ward for neonates with >6 feet / 2 meters distance should be maintained between the cohorts. It is preferred to use closed incubator for affected neonate. Separate essential instruments including dedicated respiratory support devices.
2. Babies are unlikely to be infectious unless aerosol generating events like crying or sneezing, but healthcare workers should wear full PPE while handling them. Stool may be infective as well, and precautions are essential while handling stools.
3. For infants with suspected/confirmed COVID-19 needing respiratory support, CPAP should be preferred over NIPPV and high flow nasal cannulas (HFNC) and ensure optimal fitting of interface.
4. Intubation should be only for usual indications and should be performed by the most experienced person. Video laryngoscope should be preferred for intubation. For infants on mechanical ventilation, use appropriate size endotracheal tube, in-line suctioning, adequate PPE and small hydrophobic filter at exhalation port.

5. For infants with severe acute respiratory distress syndrome, high-dose surfactant, inhaled nitric oxide, and high-frequency oscillatory ventilation (HFOV) may be effective. In more severe cases, continuous renal replacement therapy and extracorporeal membrane oxygenation (ECMO) may be necessary.
6. Some babies present like acute bronchiolitis and may need a period of respiratory support.
7. As high flow nasal cannula therapy and nasal continuous positive airway pressure (CPAP) are aerosol generating procedures, such babies should be in incubators, with expiratory flow tubing preferably within the incubator.
8. The area providing respiratory support should be a negative air pressure area. Healthcare providers should practice contact and droplet isolation and wear N95 mask while providing care in that area.
9. In babies presenting with gastrointestinal concerns, a period on intravenous (IV) fluids may be needed, but most of these symptoms appear to resolve over 2-3 days.
10. Specific anti-COVID-19 treatment is not recommended in symptomatic neonates. Use of adjunctive therapy such as systemic corticosteroids, intravenous gamma globulin and convalescent plasma is not recommended in symptomatic neonates with suspected or confirmed COVID-19. Symptomatic and supportive therapy are the main principles of management. Antipyretics like paracetamol can be used as normally indicated. If the baby is unwell with respiratory distress, antibiotic cover as per unit policy would be indicated.
11. If mother is not infected and staying with the baby can directly breastfeed her infant if baby is clinically able to suck after taking appropriate precautions (hand and torso washing prior to feeding, clean linens/gown, wearing a mask). A sick baby may receive expressed breastmilk. It can be fed to infant by mother/staff or care giver.
12. Neonatal BCG vaccination can be continued in countries or settings with a high incidence of tuberculosis as per existing practice [61].

Discharge policy^{21,24,25,30,31}

Stable neonates born to mothers with suspected or confirmed COVID19 and being roomed-in with their

mothers may be discharged together at the same time. Stable neonates in whom rooming-in is not possible because of the sickness in the mother and are being cared by a trained family member may be discharged from the facility by 24-48 hours of age.

Asymptomatic COVID-19 positive neonates or those with mild to moderate clinical course whose symptoms and need of oxygen abate within 3 days can be discharged from the hospital after 10 days without repeating RT-PCR test. In severe cases, discharge can be done when neonate becomes symptoms free and after 2 consecutive negative tests for COVID-19.

Conclusion

The COVID-19 pandemic has become the most serious public health emergency, we are facing now. Though adults of older age group are the majority, children including newborns are not exempted from this infection, fortunately, disease condition of the neonates is minor. Till date little information about COVID-19 in neonates is unfolded and evidence available is updating day by day. So, emphasis should be to formulate guidelines suitable to handle the neonates on that changed situation.

References

- Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med* 2020;**382**:727-33.
- WHO. Naming the coronavirus disease (COVID-19) and the virus that causes it [Internet]; [cited 2020 Apr 12]. Available from: [https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-\(covid-2019\)-and-the-virus-that-causes-it](https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-(covid-2019)-and-the-virus-that-causes-it).
- WHO. Coronavirus disease 2019 (COVID-19) Situation Report - 82 [Internet]; [cited 2020 Apr 18]. Available from: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200411-sitrep-82-covid19.pdf?sfvrsn=74a5d15_2.
- WHO. Director-General's opening remarks at the media briefing on COVID-19; [Internet]; 11 March 2020 [cited 2020 Apr 18]. Available from: <https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19-11-march-2020>.
- Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. *Acta Paediatr* 2020;**109**:1088-95.
- Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, et al. Epidemiological characteristics of 2143 pediatric patients with 2019 coronavirus disease in China. *Pediatrics* 2020;**16**:16.
- Gorbalenya AE, Baker SC, Baric RS, de Groot RJ, Drosten C, Gulyaeva AA, et al. Severe acute respiratory syndrome-related coronavirus – the species and its viruses, a statement of the Coronavirus Study Group. *bioRxiv* 2020. [Epub February 11, 2020].
- World Health Organization. Coronavirus disease (COVID-2019) situation reports. Available at: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports/>. Accessed 15 April 2020.
- Kutter JS, Spronken MI, Fraaij PL, Fouchier RA, Herfst S. Transmission routes of respiratory viruses among humans. *Curr Opin Virol* 2018;**28**:142-51.
- Zhang W, Du R-H, Li B, Zheng X, Yang XL, Hua B, et al. Molecular and serological investigation of 2019-nCoV infected patients: Implication of multiple shedding routes. *Emerg Microbes Infect* 2020; **9**:386-89.
- Chen ZM, Fu JF, Shu Q, Chen YH, Hua CZ, Li FB, et al. Diagnosis and treatment recommendations for pediatric respiratory infection caused by the 2019 novel coronavirus. *World J Pediatr* 2020;**16**:240-46.
- Chen H, Guo J, Wang C, Luo F, Yu X, Zhang W, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *Lancet* 2020;**395**:809-15.
- Fan C, Lei D, Fang C, Li C, Wang M, Liu Y, et al. Perinatal transmission of COVID-19 associated SARS-CoV-2: should we worry? *Clin Infect Dis* ciae226.
- Dashraath P, Wong JLJ, Lim MXK, Lim LM, Li S, Biswas A, et al. Coronavirus disease 2019 (COVID-19) pandemic and pregnancy. *AJOG* 2020;**222**: 521-31.
- Kirtsman M, Diambomba Y, Poutanen SM, Malinowski AK, Vlachodimitropoulou E, Parkset ET, al. Probable congenital SARS-CoV-2 infection in a neonate born to a woman with active SARS-CoV-2 infection. *CMAJ* 2020;**192**(24):E647-E650. [published online ahead of print, 2020 May 14].
- Martins-Filho PR, Santos VS, Santos Jr HP. To breastfeed or not to breastfeed? Lack of evidence on the presence of SARS-CoV-2 in breastmilk of pregnant women with COVID-19. *Rev Panam Salud Publica* 2020;**44**:e59. Doi: 10.26633/RPSP.2020.59.

17. Zhu H, Wang L, Fang C, Peng S, Zhang L, Chang G, et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. *Transl Pediatr* 2020;**9**:51-60.
18. Chen H, Guo J, Wang C, Luo F, Yu X, Zhang W, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: A retrospective review of medical records. *Lancet* 2020;**395**:809-15.
19. Zeng L, Xia S, Yuan W, Yan K, Xiao F, Shao J, et al. Neonatal early-onset infection with SARS-CoV-2 in 33 neonates born to mothers with COVID-19 in Wuhan, China. *JAMA Pediatr*. 2020, <http://dx.doi.org/10.1001/jamapediatrics.2020.0878> [Epub ahead of print].
20. Chen L, Liu HG, Liu W, Liu J, Liu K, Shang J, et al. Analysis of clinical features of 29 patients with 2019 novel coronavirus pneumonia. *Chinese J Tuberc Respir Dis* 2020;**43**:E005.
21. Wang L, Shi Y, Xiao T, Fu J, Feng X, Mu D, et al; Working Committee on Perinatal and Neonatal Management for the Prevention and Control of the 2019 Novel Coronavirus Infection. Chinese expert consensus on the perinatal and neonatal management for the prevention and control of the 2019 novel coronavirus infection (First edition). *Ann Transl Med* 2020;**8**:47.
22. Centers for Disease Control and Prevention. Interim guidelines for collecting, handling, and testing clinical specimens from persons under investigation (PUIs) for coronavirus disease 2019 (COVID19). February 14, 2020. <https://www.cdc.gov/coronavirus/2019-nCoV/lab/guidelines-clinical-specimens.html> (Accessed on April 18, 2020).
23. World Health Organization. Laboratory testing for coronavirus disease (COVID-19) in suspected human cases: interim guidance, 19 March 2020. World Health Organization; 2020
24. Chandrasekharan P, Vento M, Trevisanuto D, Partridge E, Underwood MA, Wiedeman J, et al. Neonatal resuscitation and post resuscitation care of infants born to mothers with suspected or confirmed SARS-CoV-2 infection. *Am J Perinatol* 2020;**37**: 813-24.
25. Chawla D, Chirla D, Dalwai S, et al. Perinatal-neonatal management of COVID-19 infection [published online April 1, 2020]. *Indian Pediatr*. pii:S097475591600154. PubMed PMID: 32238615. 6. COVID-19
26. Royal College of Obstetricians and Gynaecologists. Coronavirus (COVID19) infection in pregnancy: information for healthcare professionals V4. [Internet]. 2020 April 12 [cited 2020 March 25]. Available from: <https://www.rcog.org.uk>.
27. Kallem VR, Sharma D. COVID 19 in neonates. *The Journal of Maternal-Fetal & Neonatal Medicine*
28. Paraluppi V, Pintus MC, Fanos V, Marcialis MA. COVID-19 in newborns and in children: the state of the art. *Journal of Pediatric and Neonatal Individualized Medicine* 2020;**9**:e090138. doi: 10.7363/090138.
29. Li F, Feng ZC, Shi Y. Proposal for prevention and control of the 2019 novel coronavirus disease in newborn infants. *Arch Dis Child Fetal Neonatal Ed*. 2020. Doi: 10.1136/archdischild-2020-318996 [Epub March 4, 2020].
30. Neonatal guidelines by Kerala NNF March 2020. <http://www.pedijatri.org/wp-content/uploads/2020/03/Neonatoski-vodic-iz-Kerale.pdf>. Accessed April 20, 2020.
31. Puopolo KM, Hudak ML, Kimberlin DW, Cummings J. Management of infants born to mothers with COVID-19. INITIAL GUIDANCE. American Academy of Pediatrics Committee on Fetus and Newborn, Section on Neonatal Perinatal Medicine, and Committee on Infectious Diseases, April 2, 2020.