



EDITORIAL

Neonatal COVID-19: little evidence and the need for more information[☆]



COVID-19 neonatal: poucas evidências e necessidade de mais informações

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Based on available reports (up to the writing of this editorial) and on scientific data reported by China, Italy, and the United States, newborn infants appear to be significantly less affected by COVID-19 than adults.¹⁻³ However, the lack of high-quality evidence for this situation and the steadfast pace of new and conflicting information has been an overall challenge to all medical specialties, including neonatal intensive care. In reality, the current knowledge on neonatal severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is limited. Therefore, several questions remain unanswered, while at the same time the neonatal community needs to take action. Not surprisingly, this has caused significant stress amongst neonatal health care providers.

All over the world, a number of important groups have been diligently working on the development of protocols and guidelines for the neonatal COVID-19 outbreak.⁴⁻⁷ In

Brazil, a significant number of documents on this subject have been rapidly produced by national entities such as the Brazilian Society of Pediatrics, the Ministry of Health, and the Neonatal Resuscitation Program.⁸⁻¹¹ Undoubtedly, these are critical and paramount steps in the fight against the outbreak, but given the constant updating and some conflicting information, health care providers are facing difficulties in determining best local guidelines. To make things even more challenging, daily (and often non-scientific) news is released by the press.

What's known about neonatal COVID-19 infection? It is not yet established whether COVID-19 has transplacental or vertical transmission. Recently, a report from China described three infants with elevated serum levels of IgG and IgM antibodies for SARS-CoV-2 after birth.^{12,13} The postnatal courses were benign and quantitative reverse transcriptase-polymerase chain reaction (RT-PCR) from nasopharyngeal swabs, serum, vaginal secretions, and maternal breast milk were negative. Thus, in the light of negative RT-PCR results and given that IgM false positives results are not uncommon, and that the decline of IGM levels were very unusual in comparison with other congenital infections, the possibility of maternal-infant transmission is

[☆] Please cite this article as: Procianoy RS, Silveira RC, Manzoni P, Sant'Anna G. Neonatal COVID-19: little evidence and the need for more information. *J Pediatr (Rio J)*. 2020;96:269–72.

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difficult to ascertain.¹⁴ Fetal outcomes may depend more on the severity of the maternal infection and/or concomitant obstetric diseases, rather than on a putative transmission of the COVID-19 from the pregnant mother to the fetus.¹⁵ At this point, very few positive confirmed neonatal COVID-19 cases have been reported in scientific journals, and all of them had no symptoms or very mild to moderate symptoms, with no fatal cases reported in infants <28 days.^{1-3,16-19} Acquisition of COVID-19 has been so far attributed to horizontal transmission from an infected mother or health care provider, rather than vertical. Based on this limited evidence, no specific clinical picture for neonatal COVID-19 infection has consistently emerged. Indeed, a few positive cases of neonatal COVID-19 in Brazil have been very recently reported by the news or personal communications, and clinical presentations and neonatal courses were reassuringly similar to the reported cases. Nevertheless, as the disease continues to spread throughout the world, we must remain vigilant.

What should neonatal health care providers do about COVID-19? First, all aspects involved in neonatal care (intensive or not) must be re-evaluated in the context of the pandemic. Normal newborn nurseries, neonatal units of intermediate-level care, and neonatal intensive care units (NICUs) must be prepared and adopt practices that follow the best available evidence for the outbreak. This effort involves guidelines for the following: organization of unit space and/or isolation rooms or special areas for suspected or confirmed cases, policies for visitation by parents and family, and adoption of personal protective equipment (PPE) during delivery of a suspected or positive COVID-19 mother or during neonatal care. Moreover, clear guidelines are needed for all types of procedures in the delivery room or during the hospital stay, such as cord clamping, cleaning of secretions, suction of airways and stomach, use of all the different types of respiratory support, breastfeeding, operational protocols for in-hospital transport (to radiology or operating rooms), transport of outborn neonates, and selection/scheduling of cases that should be tested.

What should be done for the overall care after birth? Clinical conditions of mother and newborn will determine the care after birth. If the mother has suspected or confirmed COVID-19, both are stable, and the infant is not preterm, neonatal health care providers must offer orientations regarding precautions to avoid spreading the virus, including washing of the mother's hands before touching the infant, using a face mask while breastfeeding, and staying in isolated rooming-in. However, if the mother or the newborn are sick they should stay separated, while considering the mother's intention to breastfeed by expressing breast milk, limiting visits, and maintaining adequate isolation measures during the hospital stay.²⁰ Neonates positive for COVID-19 must be isolated and clinically monitored, in order to prevent outbreaks in the NICU. Owing to the absence of evidence for vertical transmission, as well as for transmission through breast milk, most scientific organizations are recommending not to separate mothers and neonates, with the aim of promoting breastfeeding and neonatal bonding, with the exception of cases with severely symptomatic mothers – in such cases, barrier measures are suggested, as well as administration of expressed maternal milk.²¹

What to do when neonatal respiratory care is needed? Important questions related to respiratory management during the immediate postpartum period of infants born from suspected or positive COVID-19 mothers, and the necessary protection that health care providers should use, have been addressed.²² Also, questions have been raised about what forms of respiratory support can be safely used in the NICU in infants admitted with suspected or confirmed COVID-19, or who became positive during hospitalization.

Can we continue to use current respiratory strategies? Yes, with a few suggested modifications to address the possibility of aerosol generation and exhaled air dispersion during oxygen administration and ventilatory support.^{23,24} Of note, a systematic review published in 2014 by the World Health Organization (WHO) graded the evidence for using precautions against aerosol generation and exhaled air dispersion as **very low**, with no studies evaluating neonates.²⁵ Based on engineering data using adult models, the likelihood of significant aerosol generation and air dispersion during bag and mask ventilation, continuous positive airway pressure, nasal intermittent positive pressure ventilation, high flow nasal cannula therapy, endotracheal intubation, and invasive mechanical ventilation is quite low, but not negligible.²⁶⁻²⁸ Given the lack of strong and clear scientific evidence during this pandemic, and until more information becomes available, health care providers should use full PPE during respiratory care of infants with suspected or confirmed cases. This should include gloves, a long-sleeved gown, eye protection, and a N95 mask or the equivalent. Also, it is recommended that infants with suspected or positive COVID-19 infection should be treated in negative pressure rooms or isolated using a 2-m distance between incubators in open plan NICUs.

Two final points deserve special attention: immediate endotracheal intubation and use of bacterial/viral filters. There is no evidence that neonates need to be immediately intubated in case of respiratory deterioration solely because of COVID-19 infection. First, because the pathophysiology of the disease is different, no cases of neonatal SARS-CoV-2 infection have been documented. Second, mechanical ventilation-associated lung injury is clearly an issue when dealing with neonatal lungs.²⁹ Third, data coming from adults suggests that endotracheal intubation is the major aerosol generating procedure and should not be performed prophylactically.^{23,24} Fourth, during previous viral epidemics a number of adults were successfully treated with non-invasive respiratory support without any evidence of increased contamination or aerosol dispersion.²³ Thus, the only recommended modification for contemporary respiratory care is the use of bacterial/viral hydrophobic filters located at the expiratory part of the systems. Any strategy in such neonates should be tailored to the individual patient, rather than to the disease. This has already been clearly outlined by the Brazilian Pediatric Society and the national Neonatal Resuscitation Program.^{8,9} It is important to highlight that the addition of a filter, although effective in decreasing viral dispersion, adds dead space and increases system resistance, which could be harmful to preterm infants if left in place for long periods. Therefore, when using these filters, health care providers should be mindful of the potential complications and monitor the infants closely. Also, in infants receiving bubble continuous

positive airway pressure (CPAP), filters may also increase system resistance, and spot checks of the pressure can guarantee safe application.

This editorial reflects the current knowledge on neonatal COVID-19, but as the outbreak and information are changing rapidly, continuing to watch for updates is highly recommended.

Conflicts of interest

The authors declare no conflicts of interest.

References

- 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:e20200702.
- Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: Summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *JAMA*. 2020;323:1239–42.
- Livingston E, Bucher K. Coronavirus disease 2019 (COVID-19) in Italy. *JAMA*. 2020;323:1335.
- Management of the newborn with suspected or confirmed SARS-CoV-2 infection. *SIN Informa*. 2020;78:1–23. Milan, Italy: Magazine of the Italian Society of Neonatology, March 2020. Available from: https://www.sin-neonatologia.it/pdf/SIN_INFORMA.n78_speciale_covid19.pdf [cited 6.4.20].
- Royal College of Obstetricians and Gynaecologists. Coronavirus (COVID-19) infection in pregnancy. Information for healthcare professionals. Version 1: published Monday 9 March, 2020. Available from: <https://www.rcog.org.uk/globalassets/documents/guidelines/coronavirus-covid-19-virus-infection-in-pregnancy-2020-03-09.pdf> [cited 6.4.20].
- American Academy of Pediatrics. Critical updates on COVID-19. Available from: <https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/> [cited 6.4.20].
- Wang L, Shi Y, Xiao T, Fu J, Feng X, Mu D, et al., on behalf of the 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.
- Sociedade Brasileira de Pediatria. Recomendações para Assistência ao Recém-Nascido na sala de parto de mãe com COVID-19 suspeita ou confirmada. Available from: https://www.sbp.com.br/fileadmin/user_upload/22422d-NAleria-Assist_RN_SalaParto.de.mae.com.COVID-19.pdf [cited 6.4.20].
- Sociedade Brasileira de Pediatria. Recomendações sobre os cuidados respiratórios do recém-nascido com COVID-19 SUSPEITA ou CONFIRMADA. Available from: https://www.sbp.com.br/fileadmin/user_upload/22428b-DC_RED_-Recom_cuidados_Respir_RN_com_COVID.pdf [cited 6.4.20].
- Sociedade Brasileira de Pediatria. Prevenção e Abordagem da Infecção por COVID-19 em mães e Recém-Nascidos, em Hospitais-Maternidades. Available from: https://www.sbp.com.br/fileadmin/user_upload/22412b-Nota_Aleria_PrevenAbordagem_infeccao_COVID19_maes-RN_em_HospMatern.pdf [cited 6.4.20].
- Brasil, Ministério da Saúde. Secretaria de Atenção Primária à Saúde. Nota Técnica N° 6/2020-COCAM/CGCIVI/DAPES/SAPS/MS. Available from: <http://189.28.128.100/dab/docs/portaldab/documentos/notatecnicaneonatal30mar2020COVID-19.pdf> [cited 6.4.20].
- Zeng H, Xu C, Fan J, Tang Y, Deng Q, Zhang W, et al. Antibodies in infants born to mothers with COVID-19 pneumonia. *JAMA*. 2020, <http://dx.doi.org/10.1001/jama.2020.4861> [Epub ahead of print].
- Dong L, Tian J, He S, Zhu C, Wang J, Liu C, et al. Possible vertical transmission of SARS-CoV-2 from an infected mother to her newborn. *JAMA*. 2020, <http://dx.doi.org/10.1001/jama.2020.4621> [Epub ahead of print].
- Kimberlin DW, Stagno S. Can SARS-CoV-2 infection be acquired *in utero*? More definite evidence is needed. *JAMA*. 2020, <http://dx.doi.org/10.1001/jama.2020.4868> [Epub ahead of print].
- Rasmussen SA, Smulian JC, Lednicky JA, Wen TS, Jamieson DJ. Coronavirus disease 2019 (COVID-19) and pregnancy: what obstetricians need to know. *Am J Obstet Gynecol*. 2020;222:415–26.
- 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].
- Wang S, Guo L, Chen L, Liu W, Cao Y, Zhang J, et al. A case report of neonatal COVID-19 infection in China. *Clin Infect Dis*. 2020, <http://dx.doi.org/10.1093/cid/ciaa225> [Epub ahead of print].
- Xia W, Shao J, Guo Y, Peng X, Li Z, Hu D. Clinical and CT features in pediatric patients with COVID-19 infection: different points from adults. *Pediatr Pulmonol*. 2020, <http://dx.doi.org/10.1002/ppul.24718> [Epub ahead of print].
- Zeng LK, Tao XW, Yuan WH, Wang J, Liu X, Liu ZS. First case of neonate infected with novel coronavirus pneumonia in China. *Zhonghua Er Ke Za Zhi*. 2020;58:E009, <http://dx.doi.org/10.3760/cma.j.issn.0578-1310.2020.0009> [Epub ahead of print].
- Australia, Government of Queensland. Queensland Health. COVID-19 guidance for maternity services statewide maternity and neonatal clinical network. Available from: http://www.cec.health.nsw.gov.au/_data/assets/pdf_file/0004/573871/COVID-19-Guidance-for-Maternity-Services.pdf [cited 6.4.20].
- American College of Obstetrics and Gynecologists. Novel coronavirus 2019 (COVID-19). Available from: <https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2020/03/novel-coronavirus-2019> [cited 6.4.20].
- Feroli N, Cisternino C, Leo V, Pisani L, Palange P, Nava S. Protecting healthcare workers from SARS-CoV-2 infection: practical indications. *Eur Respir Rev*. 2020;29:200068.
- Thompson KA, Pappachan JV, Bennett AM, Mittal H, Macken S, Dove BK, et al. Influenza aerosols in UK hospitals during the H1N1 (2009) pandemic – the risk of aerosol generation during medical procedures. *PLoS One*. 2013;8:e56278.
- Tran K, Cimon K, Severn M, Pessoa-Silva CL, Conly J. Aerosol-generating procedures and risk of transmission of acute respiratory infections: a systematic review. *PLoS One*. 2012;7:e35797.
- World Health Organization (WHO). Infection prevention and control of epidemic- and pandemic-prone acute respiratory infections in health care. Geneva, Switzerland: WHO; 2014. Available from: https://apps.who.int/iris/bitstream/handle/10665/112656/9789241507134_eng.pdf [cited 6.4.20].
- Hui DS. Non-invasive mechanical ventilation: models to assess air and particle dispersion. In: Esquinas AM, editor. Non-invasive

- ventilation in high-risk infections and mass casualty events. Vienna, Austria: Springer; 2014. p. 7–16.
27. Hui DS, Chow BK, Chu L, Ng SS, Lai ST, Gin T, et al. Exhaled air dispersion and removal is influenced by isolation room size and ventilation settings during oxygen delivery via nasal cannula. *Respirology*. 2011;16:1005–13.
 28. Simonds AK, Hanak A, Chatwin M, Morrell M, Hall A, Parker KH, et al. Evaluation of droplet dispersion during non-invasive ventilation, oxygen therapy, nebuliser treatment and chest physiotherapy in clinical practice: implications for management of pandemic influenza and other airborne infections. *Health Technol Assess*. 2010;14:131–72.
 29. Keszler M, Sant'Anna G. Mechanical ventilation and bronchopulmonary dysplasia. *Clin Perinatol*. 2015;42:781–96.