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Multi-centre Spanish study found no incidences of viral transmission in infants born to mothers with COVID-19

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Short title: Infants born to mothers with COVID-19.

Abstract

Aim: Our aim was to describe the clinical features of mothers infected with COVID-19 and examine any potential vertical mother to newborn transmission. We also assessed how effective the discharge recommendations were in preventing transmission during the first month of life.

Methods: This multicentre descriptive study involved 16 Spanish hospitals. We reviewed the medical records of 42 pregnant women diagnosed with COVID-19 from 13 March to 29 March 2020, when they were in their third trimester of pregnancy. They and their newborn infants were monitored until the infant was one month old.

Results: Over half (52.4%) of the women had a vaginal delivery. The initial clinical symptoms were coughing (66.6%) and fever (59.5%) and one mother died due to thrombo-embolic events. We admitted 37 newborn infants to the neonatal unit (88%) and 28 were then admitted to intermediate care for organisational virus-related reasons. No infants died and no vertical transmission was detected during hospitalisation or follow up. Only six were exclusively breastfed at discharge

Conclusion: There was no evidence of COVID-19 transmission in any of the infants born to COVID-19 mothers and the post discharge advice seemed effective. The measures to avoid transmission appeared to reduce exclusive breastfeeding at discharge.

Keywords: breastfeeding, COVID-19, Caesarean delivery, newborn infant, horizontal transmission.

Key notes

- This study involved 42 women who were diagnosed with COVID-19 in 16 Spanish hospitals during their third trimester of pregnancy.
- One mother died due to thrombo-embolic events, but none of the infants died and there was no evidence of horizontal transmission of the virus from the mothers to the babies during the first month of life.
- The measures to avoid transmission appeared to reduce exclusive breastfeeding at discharge.

INTRODUCTION

Due to the physiological and immunological changes that occur during gestation, pregnant women seem to be more susceptible to viral infections and could develop more obstetric complications during the COVID-19 pandemic.

The main mode of viral transmission is through direct contact with respiratory droplets or indirect contact with fomites or secretions in surfaces in the immediate environment. Faecal-oral transmission is unclear and vertical transmission has not been completely ruled out[1-5].

We know that the severe acute respiratory syndrome (SARS-CoV) outbreak in 2003 caused a 25% of mortality rate in pregnant women, as well as an increase in premature delivery, but there was no evidence of vertical transmission[6,7]. There have been case reports of 11 pregnant women infected by Middle East respiratory syndrome, which was first reported in 2012. Of these 91% had serious complications, including premature birth and perinatal or maternal death or both. Again no vertical transmission was reported[6].

There is currently s insufficient evidence about how the SARS coronavirus 2 that causes COVID-19 affects pregnant women and their newborn infants. Chen et al described nine infected pregnant women delivered by Caesarean section (C-section) and four of them had late preterm babies. They did not detect the virus in breastmilk or in other maternal secretions[3]. In another series of nine pregnancies, including one set of twins, six were born preterm and one died. Again, no vertical transmission was noted[2].

Therefore, there is limited evidence to suggest that vertical viral transmission or breastmilk transmission are rare, if at all present. However, it is possible to that the pandemic is leading to an increase in C-section deliveries and preterm births due to maternal indications. This may imply an increase in morbidity and mortality in these babies.

We do not have precise knowledge yet on what implications our interventions have on mothers with COVID-19 and their newborn infants. Our protocols are frequently being updated during the pandemic, almost on a daily basis, and there is great disparity in how they are followed in different institutions, sometimes due to the hospitals' organisational limitations.

Since 17 March 2020, the Spanish Neonatology Society has stated that mothers with few or no symptoms and asymptomatic newborn infants should be in the same room if it is possible and that

contact should be managed using strict hygiene measures. This should be the case if the infection has been confirmed or the results are awaited. However, if the mother is symptomatic, the newborn infant must be admitted to the neonatal unit and separated from their mother, regardless of whether the infection has been confirmed or the results are awaited[8].

Breastfeeding could be a potential route for antibody transfer from the mother to her newborn infant. Although there is not enough evidence for firm recommendations, the current suggestion is to maintain breastfeeding, due to all of its potential benefits[8-10]. This may not always be feasible, because mothers are frequently admitted to COVID-19 patient areas of hospitals and, therefore, obtaining extracted breastmilk may be difficult. This means that the newborn infants would be deprived of their mother´s milk and would not be in contact with their parents if their mothers have COVID-19 symptoms or a confirmed diagnosis.

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The Spanish Neonatology Society has established a number of recommendations on how to proceed after discharge. These are: frequent hand hygiene with soap and water for at least for 20 seconds, using a surgical or cloth mask during breastfeeding or whenever the distance between the mother and child is less than two metres and adequate breast and breast pump hygiene. Before we carried out this study, we did not know if these recommendations had been fully effective in preventing transmission during the neonatal period.

Our clinical experience in handling this pandemic has been very limited. The aim of this study was to improve our knowledge of COVID-19, by describing the clinical features and the potential vertical mother to newborn transmission from mothers who tested possible for the virus. We also wanted to assess if the post-discharge recommendations that were given were effective in preventing neonates from being infected by the virus during the first month of life.

PATIENTS AND METHODS

Study and patients

We designed a multicentre, descriptive study that comprised 16 Spanish University hospitals who were members of the newly formed Neo-COVID-19 Research Group. This was established on 19 March 2020 to study the impact that COVID-19 could have on newborn infants in Spain . The hospitals who took part were: 12 de Octubre, Clínico San Carlos, Fuenlabrada, Fundación Jiménez

Díaz, Getafe, Josep Trueta, La Paz, Hospitales-Madrid Group, Príncipe de Asturias, Puerta de Hierro-Majadahonda, Rey Juan Carlos, Río Hortega, Santiago de Compostela, Sant Joan, Severo Ochoa Leganés, Vall d'Hebrón and the European Institute of Perinatal Mental Health.

The study had two parts. First we reviewed the initial clinical data on both the mothers and the newborn infants and then we described the newborn infants´ follow up during their first month of life.

We reviewed the medical records of 42 pregnant women diagnosed with COVID-19 from 13 March to 29 March 2020, when they were in the third trimester of their pregnancy. They and their newborn infants were monitored throughout their hospital stay and until the infants were one month of age. The inclusion criteria were: neonates born to mothers diagnosed with COVID-19, after reverse transcriptase polymerase chain reaction tests (RT-PCR) detected the virus, and informed consent. Women with negative RT-PCR results, despite compatible symptoms, were excluded from the study.

A positive diagnosis was established according to official indications in the 17 March 2020 version of the technical document for the management of pregnant women and newborn infants with COVID-19 issued by the Spanish Government[11]. SARS-CoV-2 RT-PCR were obtained using nasopharyngeal and, or, oropharyngeal swab samples from the mothers and newborn infants.

This study was reviewed and approved by the Medical Ethical Committee of Puerta de Hierro-Majadahonda University Hospital, Madrid, Spain (approval number CP 01.20). All aspects of this study were performed in accordance with the ethical standards of the Declaration of Helsinki. Informed consent was obtained after delivery.

Data collection

The clinical information obtained from the mothers included: demographic data, disease history during the perinatal period, the number of days from the first COVID-19 symptoms to delivery, maternal treatment during gestation and specific details about the delivery.

The information collected on the newborn infants included: demographic information, gestational age, birth weight, Apgar test, type of resuscitation required and any respiratory assistance needed. We also looked at any antiviral treatment, the length of the hospital stay, the age when viral tests

were obtained, and their results, the infants' diagnosis at discharge and whether they received breastmilk, donor milk or formula.

All newborn infants were discharged to their parents, who were informed of the Spanish Neonatology Society standards for avoiding transmission.

The follow up was performed when the baby was one month of age. We spoke to the parents to determine whether the baby had required attention from a hospital emergency department or had been admitted to a hospital ward since discharge and for what reason.

Statistical analysis

Numerical variables were expressed as means and standard deviations or medians and interquartile ranges, according to their distribution. Qualitative variables were expressed as absolute frequencies and percentages. We estimated the 95% confidence intervals and assessed normal distribution by using Kolmogorov´s test. Statistical analyses were performed using Stata, version 15 software (StataCorp LLC, Texas, USA).

RESULTS

Clinical features of the mothers with COVID-19

We included 42 women with confirmed COVID-19 in their third trimester. They were diagnosed when their babies were 37.6 ±3.2 weeks of gestation. The most common symptoms were coughing (66.6%) and fever (59.5%) (Table 1), with infrequent ageusia (4.7%), odynophagia (2.3%) and otalgia (2.3%). Only three patients required intensive care (7.1%), including one who died due to a massive thrombo-embolism. In most cases, the treatment received during pregnancy was hydroxychloroquine (28.5%). Azitromycin (4.7%), darunavir (2.3%) or cobicistat (2.3%) were only used in exceptional cases. No side effects from this medication were observed in the newborn infants.

C-sections were performed on 20 women (47.6%) and the mothers' clinical deterioration due to COVID-19 was the indication in four patients (20.0%), who represented 9.5% of all the pregnancies. This was followed by failure to progress (20.0%), abnormal presentation (15.0%), repeated C-sections (15.0%), and presumed fetal compromise (15.0%). In three cases (15%) the reason for the C-section was not recorded.

Clinical features of neonates born to COVID-19 mothers

Most of the 42 neonates were term infants. Only nine were preterm (21.4%) and six of those were late preterm babies. Five infants (11.9%) were not separated from their mothers after delivery. We admitted 37 newborn infants (88.1%) to the neonatal unit and their median stay was three (2-7) days. Of those 37 admissions, 28 (75.6%) were only admitted for intermediate care due to organisational circumstances, namely because the mother had been admitted to a dedicated COVID-19 area rather than the maternity ward. At the time of writing, two of these patients were still in the neonatal intensive care unit due to their prematurity and their clinical features are shown in Table 2.

We carried out RT-PCR tests on nasopharyngeal swab samples in 37 cases (88.1%) and oropharyngeal swab samples in 36 cases (85.7%). Re-tests were carried out on 26 of the 42 infants (61.9%) at a median age of 48 hours (range 42-48). A third test was only obtained in four cases at a median age of 41.5 hours (range 21-60). The result were positive for three newborn infants: one born by C-section and two vaginal deliveries. The newborn infants' mothers had been admitted based on the COVID-19 criteria in all cases, but with only mild to moderate symptoms, and they had all tested positive. The three infants were re-tested within the first 24 hours of life and the tests came back negative, suggesting the initial results were false positives. All other tests on the infants came back negative and this means that we did not find any evidence of any vertical transmission from mother to child.

The vast majority, 32/42 (76.2%) did not need any respiratory support and surfactant therapy was only used in three infants (7.1%) due to their prematurity. Six patients (14.2%) were diagnosed with transient tachypnoea and three of these were preterm infants. There were no cases of pneumonia, pneumothorax or hypoxic-ischaemic encephalopathy. There were two other diagnoses not related to COVID-19: one case of polimarfomation syndrome with oesophagus and duodenal atresia and one case of haemolytic disease of the newborn. There were no deaths.

In 10 cases, (23.8%) the newborn infants received their own mother's milk at birth. Formula feeding was the predominant feeding option at discharge (52.5%) and only six infants were exclusively breastfeeding at this point.

Of the 42 mothers and infants recruited, 31 (73.8%) completed the follow up when the infant was one month of age and four of the infants (12.9%) were brought to the emergency department.

There was one case each of conjunctivitis, jaundice, gastroesophageal reflux and a suspected urinary tract infection. None of them were tested for COVID-19, as they had no relevant clinical symptoms. There were no deaths reported during our follow up.

DISCUSSION

This study describes the clinical features of 42 mothers infected with COVID-19 and the clinical course of their newborn infants.

The clinical presentation in our series of pregnant women was similar to other published papers[1-3,5], namely mild to moderate symptoms. These were mainly coughing, fever and dyspnoea and, less frequently, diarrhoea, headache or anosmia. The complete absence of symptoms before labour was rare and was only noted in four cases. There were three mothers who were admitted to the intensive care unit and one mother died due to a massive thrombo-embolism. Zaigham and Andersson[12] carried out a systematic review of 18 papers published in English and Chinese, covering108 pregnant women with COVID-19, and showed similar results to ours. Most women presented with coughing and fever, followed by muscle pain and discomfort and only 3% of them had to be admitted to intensive care.

Most of the women did not receive any treatment for COVID-19 during pregnancy. However, when it was deemed necessary, hydroxychloroquine and antiretroviral therapy with ritonavir and lopinavir were the most commonly used drugs, in line with

current recommendations (Table 1)[13,14]. Antenatal corticoid therapy was rare and only administered according to clinical indications for pulmonary maturation in preterm deliveries.

There has been no evidence to recommend that pregnant women with COVID-19 should undergo a C-section and the indications for surgery should follow the existing obstetric guidelines[13,15,16]. Although it has been the most frequent method of delivery in COVID-19 cases, according to the data published to date, the majority of our mothers (52.4%) had a vaginal delivery. Zaigham and Anderssons' systematic review of 108 women[12] found that 92% of the pregnant women who were included in those studies had C-sections. Chen et al[3] and Zhu et al[2] studied 18 pregnant women with COVID-19 who had C-sections. In the Chen et al study, nine women with pneumonia related to COVID-19 all had C-sections. In the Zhu et al study, none of the nine C-sections were related to COVID-19. The C-sections in our study were always performed according to current obstetric

guidelines. In four cases a C-section was indicated because the mother showed clinical deterioration due to COVID-19.

To date, there has been limited evidence to support possible vertical transmission of the virus. These were mainly based on serological studies performed in the first hours of life on a limited number of newborn infants who all had negative RT-PCR tests[4,17]. In our study we only had three newborn infants who initially tested positive for the virus, but then tested negative when the tests were repeated with the same samples. We interpreted these as false positive results.

Newborn infants of mothers with COVID-19 tend to have mild symptoms if they test positive for the virus. They mainly present with fever, respiratory distress, digestive intolerance, coughing and diarrhoea[3,5,18-20], although some sepsis-like cases during the neonatal period have been reported[21]. Clinical outcomes were good in all cases, without any case of hypoxic-ischaemic encephalopathy or death during the neonatal period and minimal need for respiratory support. Our study found that that most newborn infants were asymptomatic and any mild symptoms were attributable to underlying illnesses, such as prematurity, oesophagus and duodenal atresia or haemolytic disease. We had no infant deaths in our study.

There is insufficient evidence about whether the virus that causes COVID-19 can be transmitted via breast milk[3,22]. Breastfeeding enables the mother to transfer immunoglobulins and other factors with immunological activity to her baby that could potentially help to protect them. The impact that separation has on breastfeeding and newborn infants' health has been well documented. Studies have shown that early separation decreases breastfeeding duration and this limits the protection it provides against infectious diseases. In addition, separation affects bonding, doubles the resources required during hospital stays and increases the risk of maternal stress during hospitalisation[23-25].

Various institutions related to newborn health have maintained their recommendations to provide breastfeeding when the mothers have COVID-19, as long as the correct hygiene and protection measures are taken to reduce the risk of infection in the postnatal period[10, 26,27]. If direct breastfeeding cannot occur, or donated breast milk is used, recommendations have been provided to reduce the risk of contagion through fomites and ensure that babies can receive breastmilk[28,29].

However, this is not always feasible, mainly due to organisational issues at hospitals. Information about how infected mothers feed their newborn infants with breastmilk or formula during the immediate neonatal period is scarce[1-3,12].

Our study found that newborn infants received formula more frequently than breastmilk, both at birth and at discharge. This could have been due to various factors, such as the absence of skin-to-skin contact after birth and the need to sometimes separate the mother and child. It is difficult to know what role anxiety and fear of transmission played in those decisions, both in the mother and in the healthcare providers. This aspect deserves further research. Therefore, it is essential to keep the mother and child together, when clinically possible, and promote, and guarantee, correct breastfeeding support during their hospital stay and when they are discharged.

When possible, each hospital should establish certain specific areas for COVID-19 positive mothers who have none, or only mild symptoms, so they can safely stay with their newborn infants according to current recommendations. This would contribute to promoting and maintaining breastfeeding, which is important given the potential benefits it may provide in this situation.

Our study did not detect any cases of virus transmission during the neonatal period. This suggests that correct implementation of the standard hygiene recommendations given at discharge may have been effective in preventing infections in this group of patients. Therefore, we consider that the recommendation from some authors, that newborn infants should be isolated from their mothers for 14 days after discharge, may not be necessary[30].

The limitations of our study include those specific to all retrospective studies. The sample size was small because we only included the pregnant women that had been diagnosed in the first two weeks of the pandemic in our country, when we had not reached our peak. At that point, the criteria for RT-PCR testing of pregnant women was different from one hospital to another, and changed from day to day, so we cannot rule out the possibility that asymptomatic infected mothers were not detected. This means that a number of eligible newborn infants may have been have missed. Also, the sensitivity of the diagnostic test for the virus has been shown to be limited and it is possible that we may not have obtained all the data concerning newborn infants born to virus positive mothers. This limits the external validity of the study. In addition, samples, such as amniotic fluid, placenta and cord blood, were not collected for virus testing. Finally, during the

postnatal period follow up, we had a moderate number of drop-outs, 11/42 (26.2%), which may have limited our conclusions.

CONCLUSION

We did not detect any COVID-19 transmission during labour in the newborn infants included in our study. Therefore, the delivery method should be based on regular obstetric criteria.

The measures implemented to protect the babies of infected mothers who had symptoms reduced the rates of breastfeeding at discharge. The benefits of breastfeeding have already been demonstrated and it appears to play a role in providing immunological protection for newborn infants during the pandemic. This suggests that strategies need to be implemented to help increase the number of newborn infants that receive breastmilk during their first days of life and onwards.

Correct implementation of the standard hygiene recommendations given at discharge may be effective in preventing mother to child transmission during and after birth.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare

Abbreviations: RT-PCR reverse transcriptase polymerase chain reaction tests (RT-PCR).

References

1. Schwartz DA. An Analysis of 38 Pregnant Women with COVID-19, Their Newborn Infants, and Maternal-Fetal Transmission of SARS-CoV-2: Maternal Coronavirus Infections and Pregnancy Outcomes. Arch Pathol Lab Med. 2020. doi: 10.5858/arpa.2020-0901-SA.
2. Zhu H, Wang L, Fang C, et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. Transl Pediatr 2020;9(1):51-60. doi: 10.21037/tp.2020.02.06.
3. Chen H, Guo J, Wang C, 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 Mar 7;395(10226):809-815. doi: 10.1016/S0140-6736(20)30360-3.
4. Zeng H, Xu C, Fan J, et al. Antibodies in infants born to mothers with COVID-19 pneumonia. JAMA 2020; Mar 26. doi: 10.1001/jama.2020.4861
5. Zeng H, Xia L, Yuan W, 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 Mar 26. doi: 10.1001/jamapediatrics.2020.0878.
6. Schwartz DA, Graham AL. Potential maternal and infant outcomes from Coronavirus 2019-nCoV (SARS-CoV-2) infecting pregnant women: Lessons from SARS, MERS, and other human coronavirus infections. Viruses. 2020;12:194. doi: 10.3390/v12020194.
7. Wong SF, Chow KM, Leung TN, et al. Pregnancy and perinatal outcomes of women with severe acute respiratory syndrome. Am J Obstet Gynecol. 2004;191(1):292-297.
8. Sociedad Española de Neonatología. Recomendaciones para el manejo del recién nacido en relación con la infección por SARS-Cov-2. https://www.seneo.es/images/site/noticias/home/Recomendaciones_SENeo_SARS-CoV-2Version_50.pdf (access 29 March 2020).
9. Centers for Disease Control and Prevention. Coronavirus Disease 2019 (COVID-19). https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/pregnancy-breastfeeding.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fprepare%2Fpregnancy-breastfeeding.html. (access 29 March 2020).

10. UNICEF. Coronavirus disease (COVID-19): what parents should know. https://www.unicef.org/stories/novel-coronavirus-outbreak-what-parents-should-know. (access 29 March 2020).
11. Ministerio de Sanidad, Consumo y Bienestar Social. Manejo de la mujer embarazada y el recién nacido con COVID-19. https://www.mscbs.gob.es/en/profesionales/saludPublica/ccayes/alertasActual/nCov-China/documentos/Documento_manejo_embarazo_recien_nacido.pdf (access 30 March 2020).
12. Zaigham M, Andersson O. Maternal and perinatal outcomes with COVID-19: a systematic review of 108 pregnancies. Acta Obstet Gynecol Scand 2020 Apr 7. doi: 10.1111/aogs.13867.
13. Dashraath P, Jing Lin Jeslyn W, Mei Xian Karen L, et al. Coronavirus Disease 2019 (COVID-19) Pandemic and Pregnancy. Am J Obstet Gynecol. 2020 Mar 23. pii: S0002-9378(20)30343-4. doi: 10.1016/j.ajog.2020.03.021.
14. Rasmussen SA, Smulian JC, Lednicky JA, et al. Coronavirus Disease 2019 (COVID-19) and pregnancy: what obstetricians need to know. Am J Obstet Gynecol 2020 Feb 24. doi: 10.1016/j.ajog.2020.02.017.
15. Qi H, Luo X, Zheng Y, et al. Safe Delivery for COVID-19 Infected Pregnancies. BJOG. 2020 Mar 26. doi: 10.1111/1471-0528.16231.
16. World Health Organization. Q & A on COVID-19, pregnancy, childbirth and breastfeeding. Available from https://www.who.int/news-room/q-a-detail/q-a-on-covid-19-pregnancy-childbirth-and-breastfeeding. (accessed 12 April 2020).
17. Dong L, Tian J, He S, et al. Possible Vertical Transmission of SARS-CoV-2 From an Infected Mother to Her Newborn. JAMA. 2020 Mar 26. doi: 10.1001/jama.2020.4621.
18. Zhang ZJ, Yu XJ, Fu T, et al. Novel Coronavirus Infection in Newborn Babies Under 28 Days in China. Eur Respir J. 2020 Apr 8. pii: 2000697. doi: 10.1183/13993003.00697-2020.
19. Karimi-Zarchi M, Neamatzadeh H, Dastgheib SA, et al. Vertical Transmission of Coronavirus Disease 19 (COVID-19) from Infected Pregnant Mothers to Neonates: A Review. Fetal Pediatr Pathol. 2020 Apr 2:1-5. doi: 10.1080/15513815.2020.1747120.
20. Lu Q, Shi Y. Coronavirus disease (COVID-19) and neonate: What neonatologist need to know. J Med Virol. 2020 Mar 1. doi: 10.1002/jmv.25740.

21. Kamali Aghdam M, Jafari N, Eftekhari K. Novel coronavirus in a 15-day-old neonate with clinical signs of sepsis, a case report. Infect Dis (Lond). 2020 Apr 1:1-3. doi: 10.1080/23744235.2020.1747634.
22. Buonsenso D, Costa S, Sanguinetti M, et al. Neonatal late onset infection with severe acute respiratory syndrome conoravirus 2. Am J Perinatol 2020 May 2. doi: 10.1055/s-0040-1710541
23. Tomori C, Gribble K, Palmquist AEL, et al. When separation is not the answer: breastfeeding mothers and infants affected by COVID19. Matern Child Nutr 2020 May 26;313033. doi: 10.1111/mcn.13033.
24. Stuebe A. Should infants be separated from mothers with COVID-19? First, do no harm. Breastfeed Med. 2020;15(5):351-352. doi: 10.1089/bfm.2020.29153.
25. Arnaez J, Montes MT, Herranz-Rubia N, et al. The impact of the current SARS-CoV-2 pandemic on neonatal care. Front Pediatr 2020 Apr 30;8:247. doi: 10.3389/fped.2020.00247
26. Centers for Disease Control and Prevention, National Center for Immunization and Respiratory Diseases. Interim infection prevention and control recommendations for patients with confirmed 2019 novel coronavirus (2019-nCoV) or patients under investigation for 2019-nCoV in healthcare settings. Centers for Disease Control and Prevention; 2020 Feb 28 [accessed 2020 Mar 4]. https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html.
27. World Health Organization. Clinical management of severe acute respiratory infection when novel coronavirus (nCoV) infection is suspected. Interim guidance V 1.2. https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected. (accessed 13 April 2020).
28. Marinelli KA, Lawrence RM. Safe handling of containers of expressed human milk in all settings during the SARS-CoV-2 (COVID-19) pandemic. J Hum Lact 2020 Apr 3:890334420919083. doi: 10.1177/0890334420919083.
29. Marinelli KA. International perspectives concerning donor milk banking during the SARS-CoV-2 (COVID-19) Pandemic. J Hum Lact. 2020 Mar 30:890334420917661. doi: 10.1177/0890334420917661.
30. Chen D, Yang H, Cao Y, et al. Expert consensus for managing pregnant women and neonates born to mothers with suspected or confirmed novel coronavirus (COVID-19)

infection. Int J Gynaecol Obstet. 2020;149(2):130-136. doi: 10.1002/ijgo.13146. Epub 2020 Apr 1.

Table 1. Clinical features of the 42 mothers with COVID-19

Age in years, mean (range)	33.6±4.9
Maternal symptoms	
Coughing	28 (66.6%)
Fever	25 (59.5%)
Dyspnoea	10 (23.8%)
Discomfort	7 (16.6%)
Mialgias	6 (14.2%)
Diarrhoea	3 (7.1%)
Headache	3 (7.1%)
Anosmia	3 (7.1%)
Asymptomatic	4 (9.5%)
Number of days from the start of symptoms to delivery, median (interquartile range)	4.5 (1-8)
Admitted to hospital due to COVID-19 related illness	18 (42.8%)
Admitted to intensive care due to COVID-19 related deterioration	3 (7.1%)
Maternal treatment during pregnancy	
None	29 (69%)
Hydroxichloroquine	12 (28.5%)
Lopinavir/Ritonavir	3 (7.1%)
Tocilizumab	2 (4.7%)
Corticoid administration	5 (11.9%)
Method of delivery	
Vaginal	22 (52.4%)
Caesarean section	20 (47.6%)
Time of rupture of membranes>18h	7 (16.6%)

Results are expressed as absolute values and percentages unless otherwise stated.

Table 2. Clinical features of the 42 neonates born to mother with COVID-19

Clinical features of neonates	
Gestational age in weeks, mean and SD	38±3.1
Weight in grams, mean and SD	3082±683
Head circumference (cm)	33.6±2.9
Female n (%)	24 (57.1%)
Delivery room	
Apgar score at one minute, median (IQR)	9 (9-9)
Apgar score at five minutes, median (IQR)	10 (9-10)
Advanced resuscitation*	6 (14.2%)
Skin-to-skin contact, n (%)	11 (26.1%)
Initially admitted to neonatal ward, n (%)	37 (88.1%)
Subsequently admitted to intermediate care, n (%)	28 (66.6%)
Subsequently admitted to intensive care unit, n (%)	9 (21.4%)
Age at first virus test in hours, median (IQR)	6 (1-15)
Need for respiratory support, n (%)	10 (23.8%)
Mechanical ventilation, n (%)	2 (4.7%)
Nasal continuous positive airway pressure, number (%)	7 (16.6%)
High-flow nasal cannula, number (%)	3 (7.1%)
Neonatal symptoms	
Respiratory distress, n (%)	9 (21.4%)
Jaundice, n (%)	4 (9.5%)
Digestive intolerance, n (%)	2 (4.7%)
Age to start feeding in hours, median (IQR)	2 (1-3)
Initial type of feeding	
Own mother´s milk, n (%)	10 (23.8%)
Formula, n (%)	23 (54.7%)
Donated breastmilk, n (%)	9 (21.4%)
Type of feeding at discharge (n=40)	
Exclusive breastfeeding, n (%)	6 (15%)

Breastfeeding, n (%)	13 (32.5%)
Formula, n (%)	21 (52.5%)

SD, standard deviation; IQR, interquartile range.

*Advanced resuscitation was defined as needing positive pressure ventilation or nasal continuous positive airway pressure at birth, intubation or vasoactive drug administration.