ABSTRACT

Objective. To describe perinatal and neonatal outcomes in newborns exposed to SARS-CoV-2.

Methods. A systematic review was conducted by searching PubMed Central, LILACS, and Google Scholar using the keywords ‘covid’ AND ‘newborn’ OR ‘child’ OR ‘infant,’ on 18 March 2020, and again on 17 April 2020. One researcher conducted the search and extracted data on demographics, maternal outcomes, diagnostic tests, imaging, and neonatal outcomes.

Results. Of 256 publications identified, 20 met inclusion criteria and comprised neonatal outcome data for 222 newborns whose mothers were suspected or confirmed to be SARS-CoV-2 positive perinatally (17 studies) or of newborns referred to hospital with infection/pneumonia (3 studies). Most (12 studies) were case-series reports; all were from China, except three (Australia, Iran, and Spain). Of the 222 newborns, 13 were reported as positive for SARS-CoV-2; most of the studies reported no or mild symptoms and no adverse perinatal outcomes. Two papers among those from newborns who tested positive reported moderate or severe clinical characteristics. Five studies using data on umbilical cord blood, placenta, and/or amniotic fluid reported no positive results. Nine studies reported radiographic imaging, including 5 with images of pneumonia, increased lung marking, thickened texture, or high-density nodular shadow. Minor, non-specific changes in biochemical variables were reported. Studies that tested breast milk reported negative SARS-CoV-2 results.

Conclusions. Given the paucity of studies at this time, vertical transmission cannot be confirmed or denied. Current literature does not support abstaining from breastfeeding nor separating mothers and newborns. Further evidence and data collection networks, particularly in the Americas, are needed for establishing definitive guidelines and recommendations.

Keywords Coronavirus infection; virus diseases; pandemics; SARS virus; congenital, hereditary, and neonatal diseases and abnormalities; infectious disease transmission, vertical
The human coronaviruses—MERS-CoV, SARS-CoV, and SARS-CoV-2—have been the cause of serious infections, including the Middle East Respiratory Syndrome (MERS), the Severe Acute Respiratory Syndrome (SARS), and Coronavirus Infectious Disease 2019 (COVID-19), respectively (1). The latter is responsible for an outbreak that began in Wuhan City, China, in December 2019. The World Health Organization (WHO) declared it a Public Health Emergency of International Concern on 30 January 2020 (2), and subsequently, a pandemic on 11 March 2020 (3). As of 26 March 2020, the number of confirmed cases of COVID-19 reported to the WHO had topped 2 million worldwide (4).

SARS-CoV-2 is a novel virus requiring a rapid response from health services, while ongoing, critical scientific evidence is being gathered and ascertained. Although the primary focus has been on vulnerable groups, particularly the elderly and individuals with underlying medical conditions, it is possible that pregnant women and newborns are also at higher risk. To date, there have been limited case-series and case reports regarding COVID-19 during pregnancy, possible maternal-fetal transmission, and newborn and infant infection. COVID-19 in newborns has been described as mild disease (5). However, there is concern about the infection’s implications in newborns, both in terms of impact, as well as appropriate care. Understanding the issues related to perinatal concerns is critical when developing recommendations for these population groups.

This review aims to consolidate the currently available scientific evidence describing perinatal and neonatal outcomes in newborns exposed to SARS-CoV-2 in order to guide prevention of COVID-19 in newborns and manage the care of mothers and newborns.
MATERIALS AND METHODS

A systematic review was conducted on 18 March 2020, and updated on 17 April 2020, by searching for the keywords ‘covid’ AND ‘newborn’ OR ‘child’ OR ‘infant’ on Google Scholar (Google Inc., Mountain View, California, United States), LILACS (Latin American and Caribbean Center on Health Sciences Information, PAHO/WHO, São Paulo, Brazil), and PubMed Central (U.S. National Library of Medicine, Bethesda, Maryland, United States). The search results included primary case reports, case series, and randomized controlled trials of pregnant women and newborns and infants affected by COVID-19. No date or language restrictions were applied. Additional relevant studies were accessed by manual searches of reference lists.

Due to time constraints, Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were considered, but not entirely adhered to and one researcher conducted the search, reviewed the full texts, and extracted data on demographics, maternal outcomes, diagnostic tests, imaging, perinatal and neonatal outcomes, and neonatal diagnostic tests.

RESULTS

The initial search identified 256 publications. Following a review of the abstracts, 201 were excluded because they were letters, recommendations, or reviews that did not analyze primary data. A full-text review of the remaining 55 articles excluded an additional 35 because they were either written in Chinese, did not provide a full text version, did not include data on newborns, or were not based on primary data. The remaining 20 studies were deemed to warrant a full-text review (Figure 1). Data was consolidated into the following categories: infection confirmation, clinical characterization, laboratory, imaging features, and care provided to newborns. Table 1 describes the papers selected and the perinatal and neonatal outcomes they report.

The 20 selected studies comprise neonatal outcomes for 222 newborns whose mothers were suspected or confirmed to be SARS-CoV-2 positive perinatally (6, 7, 9–16, 18–25), or of newborns referred to hospital with infection or pneumonia (8, 14, 17). The articles were
composed of case reports (6 – 11), case-series reports (12 – 23), a case-control study (24), and a cohort study (25). Cases reported were mostly from China, except for one report from Iran (8), one from Spain (9), and one from Australia (11). They referred mostly to pregnant women and their newborns, except for 3 case reports of only newborns.

Six studies (6, 8, 9, 17, 22, 25) examined cases of newborns who tested positive for SARS CoV-2 by reverse transcription polymerase chain reaction (RT-PCR) performed on samples taken 36 hr – 17 days after birth (10 newborns in all). One newborn was initially reported to be positive for COVID-19, but upon a second testing of the same sample, the authors changed the result to a false positive (22). Two additional papers (10, 20) reported newborns who tested negative for SARS CoV-2 by PCR but showed high levels of IgM and IgG. Dong and colleagues (10) reported a newborn who tested negative for SARS CoV-2, with IgM and IgG values > 10 AU/ml on the day of birth and 14 days later. Zeng and colleagues (20) reported a series of 6 newborns who were PCR negative for SARS CoV-2, with 5 having IgG values > 10 AU/ml and 2 also having IgM > 10AU/ml.

Five of the 20 studies (6, 7, 12, 22, 23) reported data on umbilical cord blood, placenta, and/or amniotic fluid, all with no positive results.

Most of the reports informed no or mild perinatal outcomes and clinical characteristics linked to COVID 19 (Table 1). Two papers among those from newborns who tested positive reported moderate or severe clinical characteristics. One reported a newborn with transient respiratory distress, low birth weight and Apgar score of 7 and 9 at 1 and 5 minutes, respectively (9). Another study (25) reported 3 newborns with pneumonia, 2 of whom presented fever and one (preterm) presented asphyxia at birth and respiratory distress syndrome.

Five reports among those in which newborns tested negative informed about newborns presenting moderate clinical conditions. Liu and colleagues (15) reported one newborn with chronic fetal distress in utero, chorioamnionitis and meconium stained amniotic fluid. Zhu and colleagues (16) reported 6 preterm births, out of 10 newborns included, who showed shortness of breath (n=6), fever (n=2) and Pediatric Critical Illness Score (PCIS) of less than 90. One case series (21) reported 3 cases with neonatal respiratory distress syndrome after birth, among
which 2 were preterm babies. Kahn and colleagues (23) reported 5 neonates with pneumonia. Li and colleagues (24) reported significantly higher prevalence of preterm birth and low birth-weight among newborns from suspected or confirmed COVID-19 mothers and pregnant women with non-COVID-19 pneumonia, but no significant differences in key neonatal indicators between groups. The same series reported 3 newborns with intrauterine fetal distress, two of them from COVID-19 confirmed mothers and no other comorbidity. No severe neonatal asphyxia or deaths were reported.

In the report by Xia and colleagues (14), the inclusion criterion was children testing positive for SARS-CoV-2; patients ranged in age from 1 day – 14 years 7 months and data were not disaggregated by age. Symptoms most frequently mentioned were fever (> 37.3 °C) in 12 of 20 cases (60%) and cough in 13 (65%). One neonatal death was reported (multiorgan failure, preterm) in a non-positive SARS-CoV-2 newborn (16).

Nine articles (6, 8–10, 14, 16, 17, 22, 25) reported information on imaging in newborns. Five out of 6 papers reporting SARS-CoV-2 positive newborns referred radiographic images of pneumonia, increased lung marking, thickened texture, or high-density nodular shadow.

A few studies (6, 10, 12, 14, 15, 16, 25) described non-specific changes in the biochemical variables as non-specific. However, there were some reports of abnormal liver function (6, 10, 14 – 16).

Five of the studies (6, 7, 10, 12, 22) tested for SARS CoV-2 in breast milk and all were negative, but not all newborns were breastfed. Five studies (6, 15, 18, 19, 20) recommended abstaining from breastfeeding, while Lowe and colleagues (11) reported that breastfeeding should be allowed. In this report, both parents tested positive and the newborn negative for SARS-CoV-2; breastfeeding was allowed and no maternal-neonatal separation was indicated. Strict viral precautions of hand washing and use of surgical masks around the baby were observed and no further neonatal follow-up testing was done given the symptom-free clinical condition. One newborn was reported to be breastfeed until onset of symptoms (17).
DISCUSSION

There is only limited data on the impact of the current COVID-19 outbreak on women affected during pregnancy, their newborns, and the pediatric population. However, the reports available and analyzed by this review show similar results.

There is still no evidence supporting vertical transmission of COVID-19. Only 6 studies (6, 8, 9, 14, 17, 25) reported COVID-19-positive newborns (confirmed within 36 hours – 17 days after delivery) and those found only 13 newborns positive of 222 exposed to SARS-CoV-2. Seventeen studies included results from suspected or confirmed pregnant women and their newborns at the time of birth (8, 14 and 17 included only newborns readmitted testing positive for SARS-CoV-2). From these studies, two cases reports (6, 9) and two case series reports (22, 25) reported newborns tested positive at 36 hours (6), 8 days (9), 2 and 4 days (25) after birth; one newborn reported by Liu and colleagues (22) was classified as false positive. Two papers (10, 20) that reported elevated values of IgM and IgG were not consistent enough to support in-utero transmission; they lacked confirmatory results from maternal or newborn samples, e.g., amniotic fluid or infant’s PCR. Even when one study (10) may contribute to suspecting mother-to-child transmission, the evidence is not conclusive (26). Some newborns were positive for COVID-19 in spite of the reported use of preventive measures during and after delivery (6, 8, 9, 22, 25), but even in these cases there was no evidence supporting vertical transmission.

The Chinese Expert Consensus on the Perinatal and Neonatal Management for the Prevention and Control of the 2019 Novel Coronavirus Infection (27) has recommended that symptomatic pregnant women be isolated in the intensive care unit (or critical care unit) in a negative pressure room, with oxygen supplementation and lateral decubitus position, regardless of respiratory status; also, vaginal birth should be protected, according to obstetric indications and the woman’s preferences. Likewise, the WHO is recommending (28) that caesarean section be undertaken only when medically justified, based on gestational age, severity of maternal condition, and fetal viability and well-being.

Delayed cord clamping, skin-to-skin contact, and initiation of breastfeeding are also causing concern during this pandemic, as they impact health and early child development, as well as comprehensive care. The WHO (28) recommends that infants born to mothers with...
suspected, probable or confirmed COVID-19 infection should be fed according to standard infant feeding guidelines, while applying necessary precautions for infection prevention control. The results of this review do not discourage delayed cord clamping when the newborn’s clinical condition would allow it. The WHO states that whenever a mother is seriously ill due to COVID-19, or when other complications prevent her from caring for and/or breastfeeding her baby, she should be encouraged to safely express breast milk and offer it her baby (28).

The determination of whether or not separate a mother with known or suspected COVID-19 and her infant should be made on a case-by-case basis using shared decision-making between the mother and the clinical team. Some reports in this review show that isolation and non-promotion of breastfeeding have been implemented, according to the recommendations of China’s experts (27). Routine separation of mother and baby is not promoted, however, by the Royal College of Obstetricians & Gynecologists (30), which provides guidance on individualized care based on a systematic review (31) of COVID-19 in pregnancy and delivery. In one case included in this review (11) no infection in a newborn of a COVID-19-positive mother was shown despite unrestricted attachment and breastfeeding along with implementation of strict prevention measures and support from the health system. As seen, widely differing guidelines are currently available, but consistent evidence is lacking.

This review provides additional evidence related to newborn care that can contribute to developing guidelines and recommendations. The knowledge gap regarding mother and newborn separation needs to be filled. According to the current evidence, it seems that skin-to-skin contact and breastfeeding can be recommended, but it is critical to screen pregnant women, implement prevention and control measures, and closely monitor newborns at risk of COVID-19. Solid evidence is needed to develop discharge instructions for newborns born to mothers with COVID-19 or newborns with COVID-19 themselves in terms of their vaccines, and postnatal follow-up, particularly for newborns with risk conditions as extreme premature babies.

This review has some limitations. All the studies included were case reports or low-quality series, case-control, or cohort studies. The outcomes, designs, and data reported varied
and were not fully comparable. A full and exhaustive search of all medical literature would have demanded more time and staff than currently available.

To date, evidence on mother-to-newborn transmission is not consistent, given the paucity of studies on COVID-19 and pregnant women. The current literature does not support a recommendation to abstain from breastfeeding—based on a lack of evidence regarding the presence of the virus in breast milk. Likewise, there is not enough evidence to recommend separating mothers and their newborns. It is crucial to screen pregnant women, to implement infection prevention and control measures, and to provide close monitoring of neonates at risk of COVID-19.

The research studies analyzed here are mostly from China. Data collection and communication of the cases is particularly important for countries in the Americas where evidence is lacking. The dynamic of the pandemic urges not only an adequate response, but the strengthening and coordination of efforts to collect and report data. In the context of a pandemic, when health services are saturated and the movement of the population is greatly restricted, it is essential to have evidence on which to base guidelines and recommendations. The dynamic of the pandemic urges not only an adequate response, but the strengthening and coordination of international data collection networks to provide evidence for consistent and accurate COVID-19 guidelines and recommendations.

**Author contributions.** All authors conceived the original idea and contributed to the analysis and interpretation of the results. All authors reviewed and approved the final version.

**Conflicts of interest.** None declared.

**Disclaimer.** Authors hold sole responsibility for the views expressed in the manuscript, which may not necessarily reflect the opinion or policy of the RPSP/PAJPH and/or PAHO.

**REFERENCES**


COVID-19 y la salud del recién nacido: revisión sistemática

RESUMEN

Objetivo. Describir los resultados perinatales y neonatales de los recién nacidos expuestos al SARS-CoV-2. Métodos. Se realizó una revisión sistemática con búsqueda bibliográfica en PubMed Central, LILACS, y Google Scholar usando las palabras clave 'covid' Y 'newborn' O 'child' O 'infant', el 18 de marzo de 2020, y de nuevo el 17 de abril de 2020. Un investigador llevó a cabo la búsqueda y extrajo datos sobre demografía, resultados maternos, pruebas de diagnóstico, imágenes y resultados neonatales. Resultados. De las 256 publicaciones identificadas, 20 cumplieron los criterios de inclusión y comprendían datos de resultados neonatales de 222 recién nacidos cuyas madres eran casos sospechosos o positivos confirmados de SARS-CoV-2 en el período perinatal (17 estudios) o bien recién nacidos internados en el hospital con infección/neumonía (3 estudios). La mayoría (12 estudios) eran informes de series de casos; todos procedían de China, excepto tres (de Australia, España e Irán). De los 222 recién nacidos, 13 tenían resultados positivos para SARS-CoV-2; en la mayoría de los estudios se informó que los recién nacidos eran asintomáticos o tenían síntomas leves y que no se habían producido resultados perinatales adversos. Entre los estudios con recién nacidos positivos, en dos se informaron características clínicas moderadas o graves. En cinco estudios se analizó la sangre del cordón umbilical, la placenta o el líquido amniótico y no se informaron resultados positivos. En nueve estudios se reportaron imágenes radiográficas, entre ellos cinco con imágenes de neumonía, aumento de la trama pulmonar, textura engrosada u opacidades nodulares de alta densidad. Se informaron alteraciones menores e inespecíficas de los parámetros bioquímicos. En los estudios en que se analizó la leche materna se informaron resultados negativos para el SARS-CoV-2.

Manuscript received on 17 March 2020. Revised version accepted for publication on 20 April 2020.
**Conclusiones.** Dada la escasez de estudios, en este momento no es posible confirmar ni descartar la transmisión vertical. La bibliografía actual no apoya la abstención de la lactancia materna ni la separación de los recién nacidos de sus madres. Se necesitan más evidencia y redes de recolección de datos, en particular en la Región de las Américas, para establecer directrices y recomendaciones definitivas.

**Palabras clave**
- Infecciones por coronavirus; virosis; pandemias; virus del SRAS; enfermedades y anomalías neonatales congénitas y hereditarias; transmisión vertical de enfermedad infecciosa

**COVID-19 e saúde do recém-nascido: revisão sistemática**

**RESUMO**

**Objetivo.** Descrever os resultados perinatais e neonatais dos recém-nascidos expostos à SARS-CoV-2.

**Métodos.** Uma revisão sistemática com pesquisa bibliográfica em PubMed Central, LILACS e Google Scholar foi realizada utilizando as palavras-chave 'covid' E ('newborn' OU 'child' OU 'infant') em 18 de março de 2020, e novamente em 17 de abril de 2020 por um pesquisador. Foram analisados dados sobre demografia, resultados maternos, testes de diagnóstico, técnicas de imagem e resultados neonatais.

**Resultados.** Das 256 publicações identificadas, 20 preenchiam os critérios de inclusão e incluíam dados de resultados neonatais de 222 recém-nascidos cujas mães eram suspeitas ou positivas para a SARS-CoV-2 no período perinatal (17 estudos) ou recém-nascidos internados no hospital com infecção/pneumonia (3 estudos). A maioria (12 estudos) eram relatos de séries de casos; todos, exceto três (Austrália, Irão e Espanha), eram provenientes da China. Dos 222 recém-nascidos, 13 eram positivos para SARS-CoV-2; a maioria dos estudos relatou que os recém-nascidos eram assintomáticos ou tinham sintomas leves e que não foram observados resultados perinatais adversos. Entre os estudos com recém-nascidos positivos, dois descreviam características clínicas moderadas ou graves. O sangue do cordão umbilical, a placenta ou o líquido amniótico foram analisados em cinco estudos, não tendo sido relatados resultados positivos. Imagens radiográficas foram descritas em nove estudos, incluindo cinco com imagens de pneumonia, aumento da trama pulmonar, espessamento da textura ou opacidades nodulares de alta densidade. Foram relatadas alterações menores e não específicas dos parâmetros bioquímicos. Estudos que analisaram leite materno mostraram resultados negativos para SARS-CoV-2.

**Conclusões.** Dada a escassez de estudos, neste momento a transmissão vertical não pode ser confirmada ou excluída. A literatura atual não apoia a abstenção da amamentação ou a separação dos recém-nascidos das suas mães. São necessárias mais provas e mais dados, especialmente na Região das Américas, para estabelecer orientações e recomendações definitivas.

**Palavras-chave**
- Infecções por coronavirus; virosis; pandemias; vírus da SARS; doenças e anormalidades congênitas, hereditárias e neonatais; transmissão vertical de doença infecciosa
FIGURE 1. Systematic review of literature investigating newborns exposed to SARS-CoV-2, available up to 17 April 2020

256 records identified and screened

201 records excluded
- not primary data

55 full-text articles assessed

35 articles excluded
- written in Chinese
- not within age range (newborns)
- not based on primary data

20 studies included in analysis
TABLE 1. Summary of findings in studies of newborns exposed to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), available from Google Scholar, LILACS, and PubMed Central on 18 March 2020, updated 17 April 2020

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<th>Study (Ref.)</th>
<th>Design</th>
<th>Population</th>
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Liu W et al. (22)  
Case series  
19 pregnant women with confirmed SARS-CoV-2 and 19 newborns (13 male, 6 female)  
All 19 newborns were negative for SARS CoV-2. Ten breast milk samples tested for SARS-CoV-2 RT-PCR were negative. SARS-CoV-2 RT-PCR test results in throat swab, gastric fluid right after birth, urine, and feces of all newborns were negative, except one positive SARS-CoV-2 RT-PCR in throat swab once that repeated testing showed was a false positive. Consistently, the virus was undetectable in amniotic fluid and umbilical cord blood.  
Gestational age 38.6 ± 1.5 weeks, mean birth weight 3293 ± 425 g; Apgar scores of 8 and 9 at 1 and 5 min, respectively; no fetal distress found.  
Delivery occurred in an isolated operating room. Eighteen pregnant women delivered by cesarean section and one by vaginal delivery. All newborns were isolated in Neonatal Intensive Care Unit for at least 14 days.  

Khan S et al. (23)  
Case series  
17 pregnant women positive for COVID-19 and 17 newborns  
Cord blood and neonatal throat swab samples were collected immediately after delivery. All newborns were negative for SARS-CoV-2. Three of 17 newborns were preterm; birthweight ranging 2300 g - 3750 g. Apgar scores for 16 newborns were 9 - 10. Only two newborns were suspected for COVID-19; five were reported with neonatal pneumonia. All deliveries were by cesarean section. No fetal or neonatal deaths.  

Li N et al. (24)  
Case-control study  
Four groups: A. pregnant women with suspected COVID-19 (n = 16; 17 newborns); B. pregnant women positive for COVID-19 (n= 18; 19 newborns); C. pregnant women without pneumonia during hospital stay in 2020 (n = 121); and D. pregnant women without pneumonia during hospital stay in 2019 (n = 121)  
Oropharyngeal swab samples from three newborns delivered by cesarean section (group A) at 4 and 14 days after birth were negative for SARS-CoV-2. Two singletons were born prematurely. Prevalence of prematurity was similar (23.5% and 21.1%) among group A and B and significantly higher than controls (C: 5.8% and D: 5.0%). Low birth weight more often among groups A and B (17.6% and 10.5%) than control groups (2.5%). No significant differences in key neonatal indicators between groups. Of three newborns with intrauterine fetal distress, two were from COVID-19 confirmed mothers, one also had sinus tachycardia. One case of fetal distress from group B, but no other comorbidity. No significant differences in intrauterine fetal distress.  
All COVID-19 positive mothers were immediately moved to isolation wards after delivery. Newborns were cared for by family members. No severe neonatal asphyxia or deaths.  

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33 newborns with mothers positive for COVID-19 (17 female, 16 male)  
Three of 33 newborns tested positive. Nasopharyngeal and anal swabs were positive for SARS CoV-2 on days 2 and 4 after birth. Three newborns presented pneumonia; two presented fever; and one (preterm) presented asphyxia at birth, with respiratory distress syndrome, cyanosis, feeding intolerance, and respiratory distress syndrome. Chest x-ray showed pneumonia in three cases. Procalcitonin was elevated in three cases. One newborn showed elevated procalcitonin, neutrophils decreased, lymphocytopenia, and a positive enteric bacterial culture. One newborn had elevated procalcitonin, neutrophils decreased, respiratory distress syndrome, sepsis, and suspected enteric bacterial infection. Three newborns were referred to the Neonatal Intensive Care Unit. One newborn required noninvasive ventilation, caffeine, and antibiotics. Vital signs stabilized at 7 days after birth.  

Notes: COVID-19: coronavirus disease 2019; CT: computerized tomography scan; NA: not available.  
Source: Prepared by the authors from the study results.