

# An overview of newborn care in the COVID-19 context: an integrative review

Um olhar para o recém-nascido no contexto da COVID-19: revisão integrativa  
Una mirada al recién nacido en el contexto de la COVID-19: revisión integrativa

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## ABSTRACT

**Objective:** To investigate clinical manifestations, risk factors, treatment, and prevention of newborns affected by COVID-19 reported in the scientific literature. **Method:** This was an integrative review carried out in May 2020 in the LILACS, MEDLINE, and Virtual Health Library databases, via the combination of the controlled terms newborn, COVID-19, SARS-CoV-2. **Results:** Seven studies composed the final sample, five of which were from China, where the first cases of neonatal infection were reported. **Discussion:** Evidence-based practice is essential for neonatal care in light of the current pandemic context, which requires constant updates about therapeutic approaches. **Conclusion:** Prevention measures are important, because there are gaps related to COVID-19 treatment in newborns. Clinical manifestations can vary from respiratory symptoms to gastrointestinal and cutaneous symptoms. Although the cases reported seem to have been acquired in the postnatal period, more studies and evidence are needed to clarify the risk of vertical transmission.

**DESCRIPTORS:** Newborn; Coronavirus Infections; COVID-19; Respiratory Tract Diseases; Signs and symptoms; Disease Prevention.

## RESUMO

**Objetivo:** Investigar manifestações clínicas, fatores de risco, tratamento e prevenção em recém-nascidos acometidos pela COVID-19 relatados na literatura científica. **Método:** Revisão integrativa realizada no mês de maio de 2020, nas bases de dados LILACS, MEDLINE e Biblioteca Virtual em Saúde, por meio de combinações entre os termos controlados newborn, COVID-19, SARS-CoV-2. **Resultados:** Sete estudos compuseram a amostra final, sendo cinco publicações provenientes da China, onde foram relatados os primeiros casos de infecção neonatal. **Discussão:** A prática baseada em evidências é fundamental para o cuidado ao recém-nascido diante do atual contexto pandêmico. Assim, atualizações sobre abordagens terapêuticas são necessárias. **Conclusão:** Medidas de prevenção são importantes, visto que existem lacunas relacionadas ao tratamento da COVID-19 em recém-nascidos. As manifestações clínicas podem variar desde sintomas respiratórios até gastrointestinais e cutâneos. Embora os casos relatados pareçam ser adquiridos no período pós-natal, faz-se necessário mais estudos e evidências para elucidar o risco de transmissão vertical.

**DESCRITORES:** Recém-Nascido; Infecções por Coronavírus; COVID-19; Doenças Respiratórias; Sinais e Sintomas; Prevenção.

## RESUMEN

**Objetivo:** Investigar las manifestaciones clínicas, factores de riesgo, tratamiento y prevención de recién nacidos infectados por COVID-19 informados en la literatura científica. **Método:** Revisión integrativa realizada en mayo de 2020 en bases de datos LILACS, MEDLINE y Biblioteca Virtual en Salud, utilizándose combinaciones entre los términos controlados newborn, COVID-19, SARS-CoV-2. **Resultados:** Muestra final integrada por siete estudios, cinco de ellos publicaciones de China, donde se reportaron los primeros casos de infección neonatal. **Discusión:** La práctica basada en evidencias es fundamental para el cuidado del recién nacido ante el contexto pandémico actual. Las actualizaciones sobre abordajes terapéuticos resultan necesarias. **Conclusión:** Las medidas preventivas son importantes, considerando existencia de brechas para tratamiento de la COVID-19 en recién nacidos. Las manifestaciones clínicas varían desde síntomas respiratorios hasta gastrointestinales y cutáneos. Aunque los casos reportados remiten a infección en período posnatal, son necesarios más estudios y evidencias para determinar el riesgo de transmisión vertical.

**DESCRIPTORES:** Recién Nacido; Infecciones por Coronavirus; COVID-19; Enfermedades Respiratorias; Signos y Síntomas; Prevención.

## **INTRODUCTION**

At the beginning of 2020, the world saw the emergence of a new virus, initially called the novel coronavirus. It was later officially classified by the International Committee on Taxonomy of Viruses as the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), and the disease that it caused was called the Coronavirus Disease-2019 (COVID-19)<sup>(1)</sup>. The first case of the novel coronavirus was reported in the city of Wuhan, China, on December 31, 2019, and due to the rapid progression of cases, on March 11, 2020, it was declared a pandemic, causing profound repercussions in the health area and social and economic consequences in the world population<sup>(2-3)</sup>.

In general, SARS-CoV-2 presents low pathogenicity; however it can develop serious infections when it affects children, older adults, the immunosuppressed, and patients with comorbidities<sup>(4)</sup>.

Considering the growing and elevated number of cases, health departments and hospitals have sought to develop and implement guidelines and protocols focusing on diagnosing, treating and preventing the spread of COVID-19. However, little quality evidence is available, increasing conflicting information<sup>(5)</sup>.

In the pediatric and neonatal population, this scarcity is even greater. Children are little affected by the disease, and most are asymptomatic or present mild symptoms. In this age group, the highest reported proportion of patients with severe disease was 10.6%, in infants younger than one year old, followed by 7.3% in children between one to five years old<sup>(6)</sup>. Regarding newborns (NBs) and infections

in neonatal intensive care units (NICUs), there are still few findings about severe acute neonatal diseases due to SARS-CoV-2. However, many questions arise with regard to the transmission, treatment, clinical manifestations and prevention among this population<sup>(5)</sup>.

Due to the absence of evidence about this topic and given the current pandemic reality, the present study aimed to investigate clinical manifestations, risk factors, treatment and prevention of newborns affected by COVID-19 reported in the scientific literature.

## **METHOD**

This was an integrative literature review, with the aim to broadly gather and summarize the results of studies and critically review relevant studies about a given topic, contributing to the deepening of knowledge about the investigated matter<sup>(7-8)</sup>.

This review was developed in six stages: 1) developing the guiding hypothesis or question according to the Population Interest Context (PICo) strategy, considering the following structure: P-newborns, I-prevention, Co-novel coronavirus pandemic. The guiding question was "What clinical manifestations, possible risk factors, treatments, and prevention of newborns with COVID-19 have been reported in the scientific literature?"

2) Defining the descriptors. The following descriptors were selected from the Descriptors in Health Sciences (DeCS) and MeSH (Medical Subject Headings: newborn, COVID-19, SARS-CoV-2. The terms were combined with Boolean operators "and" and "or" to ensure a broad search.

3) sample selection: determining inclusion and exclusion criteria – a time to establish transparency to provide depth, quality and reliability of the selection. The studies were selected by five independent reviewers to ensure the reliability of the process. The inclusion criteria were studies published in full in the format of scientific articles, editorials, and recommendation manuals by institutions specialized in publications related to newborns and that answered at least one of the criteria of the guiding questions, given that the topic is extremely recent and little known, with no language or time limitations. Exclusion criteria were review articles, while duplicate articles were considered only once. Studies were extracted from the following databases: Latin American and Caribbean Health Sciences Literature (Lilacs) and Medical Literature Analysis and Retrieval System OnLine (MedLine) via PubMed (National Library of Medicine) and the Virtual Health Library (VHL). The search took place online in May 2020. The full publications were accessed via the Virtual Health Library (VHL) and PubMed portals. To select the scientific productions, the titles and abstracts were read according to the inclusion and exclusion criteria.

4) Critical analysis of the studies. In this stage, the researchers must have the necessary knowledge to observe the strong levels of evidence of the analyzed studies. To assess methodological quality, the following evidence classification was used: Level 1: Systematic review of randomized clinical trials; Level 2: randomized clinical trials; Level 3: non-randomized clinical trials; Level 4: cohort and case-control; Level 5: systematic reviews of

qualitative studies; and Level 6: expert opinions, case description<sup>(9)</sup>.

5) Discussion of the results. In this phase, the studies were discussed in order to understand the topic under investigation. 6) Presentation of the integrative review. For purposes of clarity and organization, the information was presented in tables containing the most relevant information extracted from the article<sup>(10-11)</sup>. In each table, the articles included in this review were identified with the letter A (article), followed by the numeral in the order in which they were described in Table 1.

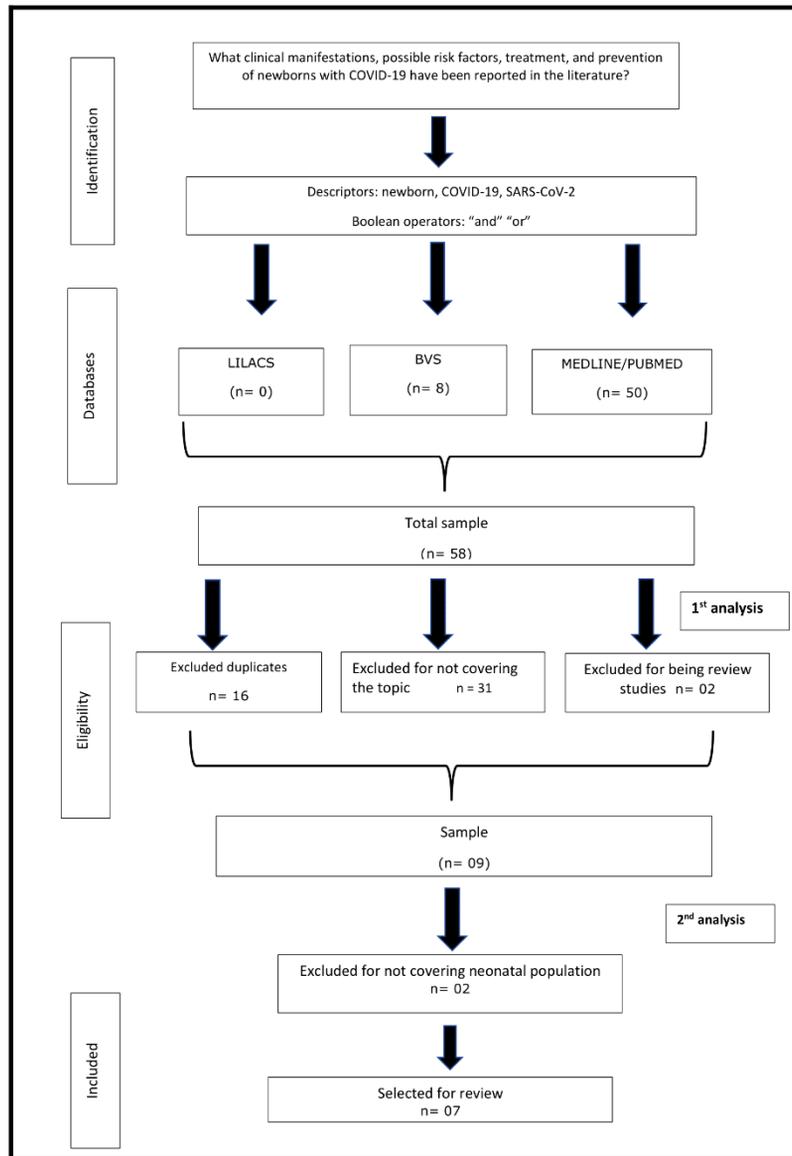
## **RESULTS**

The search for studies was carried out considering studies between January and May 2020 in the following databases: the National Library of Medicine (MEDLINE/PubMed), the Virtual Health Library and LILACS. The descriptors registered in DeCS (Descriptors in Health Science) and MeSH (Medical Subject Headings) as well as keywords not located as controlled descriptors were combined as follows to create search strategies: COVID-19 or Coronavirus or SARS-CoV-2 and newborn. Therefore, the search identified a total of 58 studies, eight in VHL and 50 in MEDLINE/PUBMED. A first analysis was performed, based on an initial reading of the title and abstracts. Those that did not answer the guiding question, did not meet the previously established inclusion criteria, were review articles or were duplicates were excluded (n=49) resulting in 9 studies selected for full reading and analysis. After reading the 9 selected articles in full, two were excluded because the population was not NBs. Thus,

seven studies composed the final sample of this integrative review. The flowchart regarding the

selection of the studies is presented in Figure 1.

Figure 1. Flowchart of the study selection process. 2020. Londrina, Paraná, Brazil.



Source: Created by the authors.

Of the seven studies selected, five were from China, where the virus originated from and where the first cases of neonatal infection were reported. One manuscript was published in Iran, reporting a case of neonatal infection, and another publication was from the USA. Regarding language of publication, four studies

were written in English and three in Chinese. All manuscripts were published in 2020.

The main information extracted from the selected studies was divided into: 1) general characteristics of the studies (title, year of publication, authors, journal, level of evidence and objective); 2) knowledge about the main results (clinical manifestations, risk factors,

treatment and prevention) and 3) conclusions and considerations of the studies, which are presented respectively in Tables 1, 2 and 3.

Table 1. Design and objectives of the selected studies. 2020. Londrina, Paraná, Brazil.

<b>Title/ Year of publication</b>	<b>Authors</b>	<b>Journal</b>	<b>Level of evidence</b>	<b>Objective</b>
(A1) Emergency plan for inter-hospital transfer of newborns with SARS-CoV-2 infection. (2020)	Chen Z, DU Li-Z, FU Jun-Fen et al. <sup>(12)</sup>	<i>J Contemp Pediatr</i>	VII	To manage the transfer plan of newborns with suspected or confirmed COVID-19.
(A2) Managing neonates with respiratory failure due to SARS-CoV-2. (2020)	Wang J; Shi Y. <sup>(13)</sup>	<i>The Lancet Child &amp; Adolescent Health</i>	VII	Editorial on clinical manifestations, diagnostic criteria and treatment of SARS-CoV-2 in NBs.
(A3) An interpretation on perinatal and neonatal management plan for prevention and control of SARS-CoV-2 infection. (2020)	Wang LS, Hu XJ, Zhou WH. <sup>(14)</sup>	<i>J Contemp Pediatr</i>	VII	To interpret a neonatal management plan for preventing and controlling SARS-CoV2 infection.
(A4) Experience of Clinical Management for Pregnant Women and Newborns with Novel Coronavirus Pneumonia in Tongji Hospital, China. (2020)	Wang, S., Zhou, X., Lin, X. et al. <sup>(15)</sup>	<i>Current Medical Science</i>	VI	To provide valuable experience for better management of SARS-CoV-2 infection in pregnant women and newborns.
(A5) Novel coronavirus in a 15-day-old neonate with clinical signs of sepsis, a case report. (2020)	Kamali AM, Jafari N, Eftekhari K. <sup>(16)</sup>	<i>Infectious diseases</i>	VII	To report a case of a neonate positive for SARS-CoV-2.

(A6) Potential Maternal and Infant Outcomes from Coronavirus 2019-nCoV (SARS-CoV-2) Infecting Pregnant Women: Lessons from SARS, MERS, and Other Human Coronavirus Infections. (2020)	Schwartz DA, Graham AL. <sup>(17)</sup>	<i>Viruses</i>	VI	Analyze published data addressing the epidemiological and clinical effects of SARS, MERS (Middle East Respiratory Syndrome) and other coronavirus infections in pregnant women and their children.
(A7) Perinatal and neonatal management plan for prevention and control of SARS-CoV-2 infection (2nd Edition). (2020)	Zhou WH, et al. <sup>(18)</sup>	<i>J Contemp Pediatr.</i>	VII	To guide the clinical care of newborns and pregnant women with a management plan for SARS-CoV-2 infection.

Source: Created by the authors.

As for the information found in the studies about the main clinical manifestations observed, associated risk factors, and possible

treatments and prevention, these are summarized and presented in Table 2.

Table 2. Main results related to clinical manifestations, risk factors, treatment and prevention. 2020. Londrina, Paraná, Brazil.

<b>Clinical manifestations</b>	<b>Risk factors</b>	<b>Treatment</b>	<b>Prevention</b>
(A1) Respiratory distress.	Family members or people close to the newborn with a confirmed diagnosis.	No reference	Correct diagnosis, personal protective equipment for professionals, disinfection measures, isolation, trained staff for the entire transfer process.
(A2) Flu-like symptoms, can develop into respiratory distress and multiple organ failure. Complications: impaired surfactant function and pulmonary hypertension in severe cases.	Respiratory distress syndrome.	Administration of surfactant, inhalation of nitric oxide in severe cases, ventilation, extracorporeal membrane oxygenation as rescue therapy prescription of antivirals	Screening all high-risk NBs for coronavirus according to family history, testing for SARS-CoV-2; individual isolation.

<p>(A3) In confirmed cases: transient fever, sneezing, vomiting, refusal of milk, and diarrhea, imaging tests showing inflammatory changes. In suspected cases that subsequently tested negative, the symptoms were respiratory distress.</p>	<p>Confirmed NB was from a region with COVID-19 cases and had contact with them. In the case of the NBs who tested negative, the symptoms were related to pulmonary immaturity that resembled SARS-CoV-2.</p>	<p>There are no specific drugs for antiviral therapy, treatment of severe cases with plasma therapy.</p>	<p>Isolation, home and dietary care, disinfection of utensils and hand hygiene before and after changing diapers. Care when handling NB. Keeping windows open, mask use by parents.</p>
<p>(A4) Does not mention the symptoms of an NB infected within 36 hours of life.</p>	<p>Pregnant women who tested positive (possible vertical transmission - but no evidence to confirm it); infection acquired in hospital environment, confirmed family members.</p>	<p>Confirmed NB: isolation for 14 days and treatment. Suspected NB: isolation for observation until case is excluded.</p>	<p>Positive mother: sanitize newborn right after childbirth, suspend breastfeeding. Guide systematic pumping to maintain milk production; After two negative maternal swabs, reunite mother and NB. Isolate caregivers, hand sanitization, disinfect furniture, floor, bottles and pacifiers.</p>
<p>(A5) Fever, rashes, tachycardia, tachypnea, mild subcostal retraction, oxygen saturation 93%.</p>	<p>Symptomatic parents with a fever and cough, and the mother also presented sweating, weakness and malaise.</p>	<p>Proper fluid therapy, oxygen therapy, antibiotic therapy.</p>	<p>Isolation in NICU. NB and parents quarantined for 14 days.</p>
<p>(A6) Stable vital signs, no fever or cough. Distressed breathing, abnormal chest x-rays and liver function abnormalities.</p>	<p>Infected parents or professionals.</p>	<p>No mention.</p>	<p>The NBs of positive mothers should be isolated for 10 days or for the duration of the mother's isolation. Suspend breastfeeding during this period.</p>
<p>(A7) Cough and fever, chest x-ray suggests pulmonary infiltration.</p>	<p>Contact with suspected or confirmed family members, caregivers or hospital staff.</p>	<p>Symptomatic and individualized treatment. In severe infants, use surfactant, inhalation with nitric oxide and high-frequency ventilation.</p>	<p>Contact and droplet isolation for 14 days.</p>

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Source: Created by the authors.

A brief summary of the main considerations and conclusions of the selected studies is presented in Table 3.

Table 3. Main conclusions and considerations of the selected studies. 2020. Londrina, Paraná, Brazil.

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### Conclusions/considerations

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(A1) When faced with suspected or confirmed cases of COVID-19 in NB it is necessary to ensure safe transfer and prevent the spread of the virus.

(A2) Continuous updates on therapeutic approaches are necessary due to the small amount of evidence available for this population.

(A3) Early detection and isolation play a decisive role in controlling the disease.

(A4) Prevention measures are essential for newborns because this population has a weak immune system.

(A5) The disease's clinical course is milder than in adults. The most common symptoms include fever, fatigue, and cough; however nonspecific symptoms have also been observed such as rashes and gastrointestinal symptoms.

(A6) Further studies are needed to confirm all forms of transmission of COVID-19 in NBs.

(A7) Detecting suspected cases, early diagnosis of confirmed cases and proper handling of cases to reduce horizontal transmission.

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Source: Created by the authors.

## DISCUSSION

As of January 2021, more than 99 million cases of COVID-19 worldwide had been confirmed; however, the proportion of newborns with the disease has been extremely low. The studies indicated that transmission seems to occur in the postnatal period<sup>(5,13-14,18)</sup>. However, some researchers considered the risk of vertical transmission<sup>(19-20)</sup>.

Regarding diagnostic procedures, the studies recommend screening all newborns admitted to NICUs by taking family history, testing for SARS-CoV-2 and isolation<sup>(13-14,16-17)</sup>, as well as conducting computerized tomography, blood count, arterial blood gas, chest x-ray, and stool and urine cultures, because differential diagnosis is essential to exclude other common upper respiratory tract viruses that cause pneumonia<sup>(14,16)</sup>.

With the exception of one study that did not mention clinical manifestations of COVID-19 infection in NBs<sup>(12,15)</sup>, the others reported that symptoms can vary from mild respiratory symptoms to more severe evolutions with

significant respiratory impairment and multiple organ failure, and that febrile condition may or may not be associated with the other symptoms<sup>(13-15, 17)</sup>.

In relation to respiratory symptoms, NBs may have difficulty breathing, including tachypnea associated with mild subcostal retraction<sup>(16)</sup>. Despite the scarce amount of evidence available about how this disease affects this population, authors suggest that respiratory distress may be related to pulmonary surfactant dysfunction in infants with the infection<sup>(13)</sup>.

Because of their pulmonary immaturity, preterm newborns (PNB) may present surfactant dysfunction since it is a substance that begins to be produced around week 24 to 28 of gestation and reaching its peak around 35 weeks. The role of surfactant is to reduce the tension of the alveolar surface and thus avoid atelectasis and respiratory distress. However, when this does not occur, PNBs will present respiratory distress, which can be mild or even very severe depending on gestational age and

the severity of the hyaline membrane disease caused by surfactant dysfunction. This condition can cause difficulty in differentiating the diagnosis of COVID-19, when NBs present risk factors, such as when a mother is diagnosed with COVID-19<sup>(21)</sup>.

In addition to respiratory symptoms, other nonspecific symptoms were also observed. In one of the studies, a 17-day old NB presented gastrointestinal symptoms, such as vomiting, refusal of milk and diarrhea<sup>(14)</sup>. Another case of COVID-19 in NBs was reported in Iran, and in addition to respiratory symptoms, the other clinical manifestations were skin rashes<sup>(16)</sup>. These findings suggest that the clinical course of the disease in the NBs does not present similarly in all, and, because of the low prevalence of COVID-19 in this population, ongoing research is necessary to help identify suspected cases.

Of all the cases of newborns affected by COVID-19 included in this review, none evolved with severity, and, despite little evidence available about the newborn population, to date, studies have shown that the clinical course of the disease is milder than in adult patients<sup>(16)</sup>.

The provision of respiratory care for NBs should continue according to the current standards, and major changes in practice should be widely discussed to minimize possible harm<sup>(5)</sup>. Furthermore, further discussions should also highlight symptomatic and individualized treatment<sup>(18)</sup>. Some authors recommend administering surfactant and nitric oxide to NBs in severe cases<sup>(13,18)</sup>, prescribing antivirals, but with caution due to the scarcity of evidence regarding its safety and efficacy in this

population<sup>(13)</sup>, in addition to antibiotic therapy<sup>(16)</sup>.

In confirmed cases of neonatal SARS-CoV-2 infection, it is essential to implement safe respiratory practices, including adequate isolation of the NB, adequate personal protective equipment (PPE) for all professionals involved in the care of these babies and use of expiratory viral filters in any respiratory device<sup>(5)</sup>.

Regarding the prevention of COVID-19, the first step is screening all NBs according to family history, followed by individual isolation and testing for SARS-CoV-2<sup>(13-14,16,18)</sup>. In cases in which mothers have tested positive, the recommendation is to clean the NB immediately after birth, maintain isolation for 14 days<sup>(14,16,18)</sup> and, after two negative maternal swabs, keep mother and child together<sup>(15,17)</sup>.

Discontinuation of breastfeeding is indicated in some studies<sup>(15,17)</sup>. However, in Brazil, the recommendation of the Ministry of Health and the Brazilian Society of Pediatrics is that breastfeeding should be stimulated and promoted, regardless of mothers suspected or confirmed COVID-19 diagnosis; however following the guidelines of mask use and hand washing before and after feeding<sup>(22-23)</sup>. It is worth noting that to date, there is no evidence of vertical transmission through breastfeeding, so breast milk should be offered, as it is the best source of nutrients for the newborn<sup>(23-24)</sup>.

It is necessary to pay attention to home care when handling utensils used in NB care, disinfecting pacifiers and bottles at high temperatures, hand sanitization before and after diaper changes, handling NBs and bottle

preparation and mask use by parents. Other care measures related to the environment are also essential, such as keeping windows open for air circulation and frequently disinfecting floors and furniture<sup>(14-15)</sup>.

Newborns of suspected or confirmed mothers should be transferred to reference units for COVID-19 treatment, and the following measures should be taken, such as: effective communication with the reference hospital, use of PPE by professionals, transportation of the baby in an incubator with suitable equipment available for emergency care, NBs should be kept in isolation in units with negative pressure and disinfecting equipment after use<sup>(14)</sup>. Considering the importance of ensuring safe transportation for both suspected or confirmed NBs and health teams, one of the studies included in this review aimed to develop a management plan for the entire transfer process of suspected or confirmed NBs, focusing on how to manage the transfer organization, strategies for the prevention of health professionals, and measures to prevent the spread of the virus during this process<sup>(18)</sup>. It is important to emphasize that information is changing rapidly and health professionals should pay attention to updates as the state of knowledge evolves and new evidence is published<sup>(5)</sup>.

Considering that, in the present literature review, none of the studies that composed the sample presented a level of evidence I or II, further research is needed to produce results with strong levels of scientific evidence that can inform neonatal care.

Limitations of this study include the scarcity of studies about the topic, the difficulty of accessing case reports with details about clinical manifestations, as well as the interventions and number of cases of newborns with confirmed COVID-19 cases. However, the contemporaneity of the disease is a predominant factor that justifies the incipient nature of the studies and divergent findings among authors in the area.

## **CONCLUSION**

Studies indicate that prevention measures are important for this population group, since there are gaps related to treatment. The use of PPE by health professionals during neonatal care is necessary and indispensable. Since the clinical manifestation of the infection can range from respiratory symptoms and also include nonspecific symptoms, such as gastrointestinal and even cutaneous manifestations, it is of utmost importance to screen suspected NBs for diagnostic confirmation to reduce the risks of horizontal transmission. Although the reported cases appeared to have been acquired in the postnatal period, more studies and evidence are needed to clarify whether there is a risk of vertical transmission.

This study was necessary considering the pandemic situation that we are currently experiencing. Although scarce, the findings are important for newborn care, and continuous updates are necessary to guide professionals on the best management and control of COVID-19 in the neonatal population.

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<p><u>Study design</u>: Araujo JP, Zani AV <u>Data collection</u>: Zani, AV <u>Data analysis and interpretation</u>: Araujo JP, Campana KSS, Bussú KV, Sczindrowski M, Leal, LB, Zani AV, <u>Discussion of results</u>: Araujo JP, Campana KSS, Bussú KV, Sczindrowski M, Leal LB, Zani AV <u>Writing and/or critical review of content</u>: Araujo JP, Campana KSS, Bussú KV, Sczindrowski M, Leal LB, Zani AV <u>Review and final approval of the final version</u>: Araujo JP, Campana KSS, Bussú KV, Sczindrowski M, Leal LB, Zani AV</p>