Breastfeeding/Breast Milk Safety in Infants of Mothers with Suspected or Confirmed COVID-19 Infection

Nursan Cinar¹, Ozge Karakaya Suzan¹, Sinem Ozturkler², Vedat Cinar² and Pinar Tabakoglu²

¹Department of Nursing, Faculty of Health Sciences, Sakarya University, Sakarya, Turkey
²Department of Nursing, Sakarya University, Institute of Health Sciences, Sakarya, Turkey

ABSTRACT

The purpose of this systematic review was to determine whether suspected or confirmed COVID-19 infected mothers in the lactation period can breastfeed their infants; and whether suspected or confirmed COVID-19 infected mothers can breastfeed their infants by taking some precautions. The study also aimed to present the measures that can be taken in line with the evidence. The studies conducted after November 2019 and including infants of suspected or confirmed COVID-19 infected mothers were reviewed between 2019 and 2020. A literature review was conducted in five electronic databases (MEDLINE, PubMed, ScienceDirect, Web of Science, and Scopus) to reach original quantitative studies in English. The present authors retrieved 46 of the 1,229 studies included after screening. Three studies were cross-sectional studies, 30 were case studies, and 13 were cohorts. In most of the sources examined, it was concluded that most of the breastfed infants had negative findings for SARS-Cov-2 infection in PCR. In line with the limited data available, it was concluded that most of the breastfed infants had negative findings for SARS-Cov-2 infection in PCR; and breastfeeding mothers should initiate breastfeeding by taking protective measures.

Key Words: Breastfeeding, COVID-19, Suspected COVID-19 infected mothers, Confirmed COVID-19 infected mothers.


INTRODUCTION

Coronavirus disease 2019 (COVID-19), also named SARS-CoV-2, is a respiratory tract infection caused by a newly emerging coronavirus in Wuhan, China, in December 2019. SARS-CoV-2 or COVID-19 infection was most commonly observed in the 30-79 years age range. While the epidemic was taken under control in China as a result of taking strict isolation and quarantine measures at the end of three months, the number of COVID-19 cases increased in many countries. In March 2020, the World Health Organization declared it a pandemic. According to COVID-19 data, it caused 167,252,150 cases of infection and 3,467,663 deaths worldwide as of May 25, 2021. A study by Huang et al. reported epidemiological, clinical, laboratory, and radiological features and treatment and clinical outcomes of patients with COVID-19 pneumonia. However, it primarily covered non-pregnant adults.

Correspondence to: Dr. Nursan Cinar, Department of Nursing, Faculty of Health Sciences, Sakarya University, Sakarya, Turkey
E-mail: ndede@sakarya.edu.tr

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The clinical features of COVID-19 pneumonia in pregnant women, neonates, and children were not reported. The number of pregnant women and neonates with COVID-19 is also increasing, which leaves many question marks about feeding and breastfeeding newborns during pregnancy and the postpartum period. At the same time, the epidemic started, mothers who continued breastfeeding experienced uneasiness and needed reliable advice in this regard. It is very important to protect and maintain breastfeeding during the outbreak because breast milk has unique nutritional properties and immune-boosting and infection-protecting properties. Bioactive immunological factors in breast milk are important for the development of the neonate’s immune system. It has been proven that these biologically active elements protect the neonate from infections and play a significant role in the maturing of the immune system. They have an especially strong protective impact against infectious diseases prevented through the direct transfer of antibodies and other anti-infective factors; and the long-term transfer of immunological sufficiency and memory. At the same time, if a mother or infant is infected, the immunoreactive biochemical factors of breast milk change. The breast milk has more active immune milk content.

Transmission through breast milk has not been reported in infants. In the study performed by a group of Chinese experts at the beginning of February 2020, the infant of a suspected or confirmed COVID-19 infected mother was not breastfed. Wang
et al. reported that COVID-19 suspected or diagnosed mothers’ infants should be fed with breast milk if their breast milk tests are negative. On the contrary, no concrete data support this suggestion and show that COVID-19 is transmitted through breast milk. In a recent study carried out by Chen et al., six of nine pregnant women diagnosed with COVID-19 in the laboratory in the last trimester, had negative breast milk, throat swabs, amniotic fluid and cord blood samples taken after cesarean delivery and the results of tests for SARS-CoV-2, and three mothers reported that testing could not be performed because no sample could be taken.

It is important whether suspected or confirmed COVID-19 infected mothers during the lactation period can breastfeeding their infants and whether suspected or confirmed COVID-19 infected mothers can breastfeed their infants by taking some precautions. The measures that can be taken also need to be evidence-based.

The aim of this systematic review was to examine the safety of breastfeeding or feeding infants with breast milk by suspected or confirmed COVID-19 infected mothers.

**METHODOLOGY**

A review protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42020179512; http://www.crd.york.ac.uk/prospero/display_record.php?RecordID=179512). The PRISMA and flow diagram was created. The studies conducted after November 2019 and investigating breastfeeding/breastfeeding safety in infants of suspected or confirmed COVID-19 infected mothers were reviewed from March to November 2020.

The question of this systematic review was formed using the PICO criteria.

- **P** Stood for population, which included suspected or confirmed COVID-19 infected mothers in the lactation period and their infants. There were no restrictions on age or ethnicity.
- **I** Intervention - “Breastfeeding,” “feeding with breast milk,” and “preventive measures while breastfeeding” in suspected or confirmed COVID-19 infected mothers.
- **C** Comparison - There will be no limitation on the type of comparator.
- **O** Outcome - Breast milk intake/breastfeeding safety.

The primary outcome criterion was an infant with confirmed SARS-CoV-2 infection during breastfeeding or receiving expressed breast milk from a woman with suspected or confirmed SARS-CoV-2 infection. The secondary outcome criterion was infection outcomes of the infants receiving breast milk analysed for SARS-CoV-2 infection. The selection criteria are summarised in Table I.

Medical Subjects Headings (MeSH) for English keywords and the content of Türkiye Bilim Terimleri (TBT, http://www.bilimterimleri.com/) were used to create Turkish equivalents of the English keywords. A review was made according to the keywords specified for screening in MEDLINE, Web of Science, PubMed, ScienceDirect, and Scopus databases and the keywords of “Breastfeeding” (Breastmilk OR Human milk OR Lactation) and “COVID-19” (suspected with COVID-19 infected mothers OR confirmed, COVID-19 infected mothers OR infected mother with COVID-19, Coronavirus OR Sars-Cov2).

The process of study selection was conducted following the PRISMA flow diagram in three steps. These steps include the evaluation of the title, summary, and full texts of the studies. First of all, the studies were evaluated in terms of title convenience by the researchers (OKS, SO, VC, PT), who also scanned the databases. The studies that did not meet the criteria for title inclusion were eliminated at that stage. Afterward, the five independent researchers evaluated the summaries in terms of inclusion criteria. As a result of the evaluation, a consensus was reached between the five researchers (NC, OKS, SO, VC, PT). The studies that met the inclusion criteria for abstract were recorded using the EndNote X9 program, and their full texts were downloaded. The screening process was recorded in the PRISMA flow diagram (Figure 1).

The first and second researchers (NC, OKS) performed the extraction of data on trial features, methodology, participant features, intervention features, outcome measures, and outcome data independently, and the other researchers checked them. The studies that were decided to be included in the study by both researchers were included in the review. The studies on which no consensus could be reached were reviewed by both researchers again (NC, OKS). The studies that were considered not meeting the inclusion criteria by the two researchers (NC, OKS) were excluded. The data, including data on authors, year of publication, definition of participants, research methods, and results, were extracted.

The coding table of the studies included in the systematic review contains information on the study type, design/sample size, the...
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The purpose of the study, data collection tool, study findings, and recommendations.

Two independent researchers performed quality assessments for every study. The QATQS was utilised for quantitative research. The QATQS was employed to assess the selection bias of the studies, study design, confounders, blinding, data collection method, and exclusion/abandonment. Thomas et al. performed the validity and reliability studies of the original scale, while Ergin and Akın carried out the validity and reliability studies of the Turkish version of the tool (T-QATQS). Using the said tool, it is possible to classify the methodological quality of the studies as weak, medium, and strong.

To use QATQS in the research, written permission was obtained for performing the validity and reliability studies of the tool in Turkish. No funding sources were utilised in the current study.

RESULTS

One thousand two hundred and twenty-nine studies were acquired in the screening performed in five databases. Six hundred forty-four were excluded due to duplication. After excluding the duplications, a further 538 studies were excluded since they were published in a language besides English and Turkish, were unrelated to the subject (n = 234), or were inappropriate for the study design. Two independent researchers reviewed the full texts of the remaining forty-seven studies in terms of suitability and quality. A study was excluded since it obtained a low score. Thirty of the remaining 46 studies were case reports and were directly submitted to the study. The remaining 16 studies were assessed using QATQS. In the assessment, 16 studies of medium quality were included in the systematic review. Figure 1 presents the flow diagram for the selection of studies.

Sixteen of the 46 studies, included in the present systematic review, were research articles. The populations of the assessed studies consisted of suspected or confirmed COVID-19 infected mothers during the lactation period. The sample size varied between one and 101. Studies were cross-sectional case studies, retrospective studies, and cohort studies. The mentioned report articles were included to conduct narrative analysis.

The score distribution of the 16 studies in the systematic review, according to the QATQS, is presented in Figure 2. Among case report studies, studies with laboratory findings were taken directly (30 studies).

Table II demonstrates an outline of the outcomes in every study reviewed. The said outcomes were analysed and reviewed thematically.

The primary outcome criterion was an infant with confirmed SARS-CoV-2 infection receiving expressed breast milk or breastfed by a woman with suspected or confirmed SARS-CoV-2 infection (Table II and Figure 3). According to the findings of the studies that performed the SARS-CoV-2 examination in neonates born to women diagnosed with COVID-19, breast milk samples were examined using a diagnostic tool such as RT-PCR and chest radiography, and laboratory findings were analysed. Among the breast milk samples examined, while SARS-CoV-2 was not detected in breast milk in the studies of, SARS-CoV-2 was detected in breast milk in the studies of

Figure 3: Presence of COVID-19 in breastfed and non-breastfed infants (n = 510).
*Babies who were definitely stated to be breastfed or not breastfed were included in the chart.

Table I: Eligibility criteria.

<table>
<thead>
<tr>
<th>clusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mothers with suspected or confirmed COVID-19 infection and their infants</td>
<td>Mothers with probable COVID-19 infection</td>
</tr>
<tr>
<td>Studies with mothers aged between 18-45 years during lactation</td>
<td>Mothers aged below 18 and above 45 years during lactation</td>
</tr>
<tr>
<td>Mothers with suspected or confirmed COVID-19 infection cared for at home or in clinics</td>
<td>Mothers with confirmed COVID-19 infection in the intensive care unit</td>
</tr>
<tr>
<td>Randomized Controlled Studies Semi-experimental studies</td>
<td>Expert opinions</td>
</tr>
<tr>
<td>Descriptive, cross-sectional, case-control and case reports</td>
<td>Qualitative studies</td>
</tr>
<tr>
<td>Studies published in Turkish and English</td>
<td>Unpublished theses</td>
</tr>
<tr>
<td></td>
<td>Summary studies</td>
</tr>
<tr>
<td></td>
<td>In vitro or animal study</td>
</tr>
<tr>
<td></td>
<td>Systematic and rapid reviews</td>
</tr>
</tbody>
</table>

*Published after 1 December 2019*
### Table II: Coding table of the studies included in the systematic review (N=46).

<table>
<thead>
<tr>
<th>Authors/ Year</th>
<th>Types of studies</th>
<th>Design/sample size</th>
<th>Aim of the study</th>
<th>Data collection tool</th>
<th>Where the test sample was taken</th>
<th>Study results</th>
<th>Suggestions</th>
<th>Studies Quality Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chen et al. (2020)</td>
<td>Research Article</td>
<td>Cross-sectional n=9</td>
<td>- Evaluated the clinical characteristics of COVID-19 in pregnancy and the intrauterine vertical transmission potential of COVID-19 infection.</td>
<td>qRT-PCR</td>
<td>throat swab breastmilk samples</td>
<td>&quot;Breastmilk samples from six patients were tested for SARS-CoV-2, and all samples tested negative for the virus.&quot;</td>
<td>Middle</td>
<td></td>
</tr>
<tr>
<td>Ferrazzi et al. (2020)</td>
<td>Research Article</td>
<td>Cross-sectional n=42</td>
<td>- &quot;To report mode of delivery and immediate neonatal outcome in COVID-19 infected women.&quot;</td>
<td>RT-PCR</td>
<td>nasopharyngeal swab</td>
<td>&quot;Represents the obstetric outcome of a cohort of COVID-19-affected pregnant women and the rate of SARS-CoV-2 positivity in newborns according to the mode of delivery and breastfeeding status.&quot;</td>
<td>Middle</td>
<td></td>
</tr>
<tr>
<td>Gao et al. (2020)</td>
<td>Research article</td>
<td>Retrospectively N=14</td>
<td>&quot;It was assessed the clinical and immunologic features of COVID-19–affected mother–infant pairs, specifically tested breast milk for pathogen, SARS-CoV-2 neutralizing antibodies and immunologic components; and explored the feasibility of breastfeeding and related transmission possibilities.&quot;</td>
<td>PCR (n=34)</td>
<td>oropharyngeal or nasopharyngeal swabs, breast milk sample, meconium sample</td>
<td>&quot;In the findings; SARS-CoV-2 was not detected in breast milk, and the mothers who continued breastfeeding had no breast lesions&quot; (n=12)</td>
<td>&quot;Breastfeeding has a low risk of transmitting SARS-CoV-2 or escalating maternal disease; mothers should continue to breastfeed but should take prudent precautions. Infants can additionally benefit from direct acquisition of antibodies against SARS-CoV-2 through breast milk.&quot;</td>
<td>Medium</td>
</tr>
<tr>
<td>Savasi et al. (2020)</td>
<td>Research article</td>
<td>Cohort study/N=57</td>
<td>&quot;To investigate the clinical evolution of coronavirus disease 2019 (COVID-19) in hospitalized pregnant women and potential factors associated with severe maternal outcomes.&quot;</td>
<td>PCR</td>
<td>nasopharyngeal swab</td>
<td>&quot;For all these newborns, rooming-in and breastfeeding were performed.&quot;</td>
<td>Medium</td>
<td></td>
</tr>
<tr>
<td>Sahin et al. (2020)</td>
<td>Research article</td>
<td>Cohort Study/N=29</td>
<td>&quot;To evaluate the course and effect of coronavirus disease 2019 (COVID-19) on pregnant women followed up in a Turkish institution.&quot;</td>
<td>PCR</td>
<td>nasopharyngeal and oropharyngeal breast milk samples</td>
<td>&quot;None of the neonates were positive for SARS-CoV-2.&quot;</td>
<td>Medium</td>
<td></td>
</tr>
<tr>
<td>Hirschberg et al. (2020)</td>
<td>Research Article</td>
<td>Retrospective Review/N=18</td>
<td>&quot;Records related to neonates born to COVID-19 positive women were also reviewed.&quot;</td>
<td>PCR</td>
<td>nasopharyngeal swab</td>
<td>&quot;3 infants tested negative, the remaining infant had an &quot;indeterminant&quot; test result. &quot;Breastfeeding was encouraged with hand hygiene and maternal masking.&quot;</td>
<td>Medium</td>
<td></td>
</tr>
<tr>
<td>Salvatore et al. (2020)</td>
<td>Research Article</td>
<td>Cohort Study/N=82</td>
<td>&quot;It was aimed to elucidate best practices regarding infection control in mother–newborn dyads, and identify potential risk factors associated with transmission.&quot;</td>
<td>PCR</td>
<td>nasopharyngeal swabs</td>
<td>&quot;All neonates were tested at 24 h of life and none were positive for SARS-CoV-2.&quot;</td>
<td>Medium</td>
<td></td>
</tr>
<tr>
<td>Griffin et al. (2020)</td>
<td>Research Article</td>
<td>Cohort study/ N=62</td>
<td>The objectives of the study are to describe the effects of COVID-19 on the obstetric and neonatal population in an area with a high incidence of SAR-CoV-2 infection.</td>
<td>RT-PCR</td>
<td>nasopharyngeal swab</td>
<td>&quot;Fifteen infants had their SARS-CoV-2 RT-PCR testing performed from a nasopharyngeal swab taken after 24 hours of life. Most (14.93%) were performed in neonates whose mothers were confirmed COVID-19 positive. Fourteen of the tests were negative, one was insufficient for analysis. No infant tested positive for COVID-19.&quot;</td>
<td>&quot;Human milk feeds were encouraged and mothers were provided electronic breast pumps, and lactation support to provide mother's own milk that could be fed to the infant during their period of isolation, and to allow direct breastfeeding once the infant and/or mother was cleared from isolation.&quot;</td>
<td>Medium</td>
</tr>
<tr>
<td>Coycou et al. (2020)</td>
<td>Research Article</td>
<td>Cohort study N=17</td>
<td>&quot;This quality improvement project was conducted to determine whether maternal breastfeeding is safe for neonates whose mothers tested positive for SARS-CoV-2.&quot;</td>
<td>PCR</td>
<td>oropharynx and nasopharynx swab</td>
<td>&quot;All neonatal tests for SARS-CoV-2 returned negative.&quot;</td>
<td>Medium</td>
<td></td>
</tr>
<tr>
<td>Anand et al. (2020)</td>
<td>Research Article</td>
<td>Retrospectively N=65</td>
<td>The study was conducted to describe the clinical profile of neonates born to mothers who tested positive for COVID-19 infection and to determine the association of neonatal COVID 19 status and viral load with maternal clinical status and viral load.&quot;</td>
<td>RTPCR</td>
<td>nasopharyngeal/oropharyngeal swabs</td>
<td>&quot;Of 65 tested neonates, 7 were confirmed COVID 19 positive by RTPCR.&quot;</td>
<td>&quot;The unit followed the policy of rooming in with mother and direct breastfeeding with precautions in stable neonates born to COVID-19 positive mothers.&quot;</td>
<td>Medium</td>
</tr>
<tr>
<td>Pereira et al. (2020)</td>
<td>Research Article</td>
<td>Cohort study N=23</td>
<td>&quot;The aim of study was to describe experience in the clinical management of 60 COVID-19 positive pregnant women who were admitted to our hospital during the first month of the epidemic in Spain.&quot;</td>
<td>PCR</td>
<td>nasopharyngeal swabs</td>
<td>&quot;In all of cases, neonates tested negative.&quot;</td>
<td>Medium</td>
<td></td>
</tr>
</tbody>
</table>
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Marin Gabriel et al. (2020a) | Research article | Descriptive study N=42 | PCR | nasopharyngeal swab oropharyngeal swab | "The aim was to describe the clinical features of mothers infected with COVID-19 and examine any potential vertical mother to newborn transmission." | "All other tests on the infants negative." | "19 babies were breastfed." | "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." | Medium

Farhaly et al. (2020) | Research article | Cohort study N=15 | PCR | nasopharyngeal swab | "This study aims to assess the characteristics of newborns born to SARS-CoV-2-positive women compared with those mothers who tested negative." | "It had only one newborn who tested positive for SARS-CoV-2." | "Five newborns of positive mothers directly breastfed with precautions." | Medium

Patil et al. (2020) | Research article | Retrospective Cross-Sectional Study N=45 | PCR | oropharyngeal and nasopharyngeal swab | "A total of 33 newborns colected with their mothers and 3 of the 33 were breastfed with the initiation of breastfeeding within 1 h of birth." | "A total of 42 newborns tested negative and 3 tested positive." | Medium

Dumitru et al. (2020) | Research article | Cohort Study N=101 | PCR | nasopharyngeal swab | "Most mothers 91 breastfed at least partially." | "101 newborns born to mothers with perinatal SARS-CoV-2 infections, 2 (2.0%) had positive test results for SARS-CoV-2." | Medium

Wu et al. (2020) | Research article | Cohort Study N=5 | PCR | neonatal throat and anal swabs breast milk sample | "SARS-CoV-2 nucleic acid tests of neonatal throat and anal swabs were all negative on the 1st and 3rd days after birth." | "It is assessed breast milk in three women; the breast-milk sample of one woman (patient 5), collected on the 1st day after delivery, was positive using the PCR." | Mothers with COVID-19 should not breastfeed until after full recovery, when breast milk tests negative for the virus." | Effective implementation of protection measures during delivery, including a negative-pressure delivery room, may help prevent the infant from acquiring SARS-CoV-2 infection.

Li et al. (2020) | Case Study | N=1 | - | a sputum sample oropharyngeal swab specimen breast milk sample | "Breast milk samples were negative. Mother-to-child transmission is unlikely for this virus." | "19 babies were breastfed." | "That it is possible to consider rooming in post delivery for COVID-19 positive parents. Encouragement of breastfeeding appears possible and safe when viral precautions are observed." | Medium

Lowe & Bopp (2020) | Case Report | N=1 | PCR | nasopharyngeal (NP) swabs | "Describing an uncomplexed vaginal birth in a SARS-CoV-2 positive mother." | "Breast milk tests negative for the virus." | "Medium"

Yu et al. (2020) | Case Report | N=1 | PCR | maternal serum, breast milk, nasopharyngeal (NP) swabs and feces, and in the infant's serum, NP swabs and feces | "the patient's milk was positive for SARS-CoV-2 IgG and negative for IgM. On hospital day 14, the child's serum was positive for both SARS-CoV-2 IgG and IgM, suggesting either breastmilk transfer to the infant or infant de novo production of the IgG and/or IgM, or both mechanisms. A protective antibody can be passed by breastfeeding from the mother to the offspring, preventing or decreasing the severity the children's diseases." | "Observational studies suggest that breast milk is safe. Future studies should address the issue of detecting the level of SARS-CoV-2 IgG to assess the best time window for breastfeeding, and the risks vs benefits of direct breastfeeding." | Medium

Kam et al. (2020) | Case report | N=1 | PCR | nasopharyngeal swabs, breast milk samples | "nasopharyngeal swabs continued to be positive for SARS-CoV-2." | "Breast milk samples on day 11 of illness were negative for SARS-CoV-2." | Medium

Wang et al. (2020) | Case report | N=1 | PCR | pharyngeal swab breast milk sample | "The result of pharyngeal swab for SARS-CoV-2 was positive at 36 hours after birth." | "The mother’s breast milk sample was negative for SARS-CoV-2 as well." | "It was recommended the mother not to breastfeed and to empty the breast milk to avoid mastitis." | Medium

Lebrás et al. (2020) | Case report | N=1 | PCR | nasopharyngeal swab | "The participant newborn tested negative in one nasopharyngeal swab RT-PCR performed within 48 hr of life." | "The participant was instructed by the nursing team to wear surgical masks, especially when she was in contact with her newborn infant, and to wash her hands or use hand sanitizer before and after touching her baby or directly breastfeeding." | Medium

Perrone et al. (2020b) | Case report | N=4 | PCR | nasopharyngeal swab | "The participant newborn tested negative in one nasopharyngeal swab RT-PCR performed after full recovery, when breast milk tests negative for the virus." | "The participants breastfed the neonates." | "More importantly, the IgG and IgM antibodies were detected in breast milk indicate the potential immune protection for the neonates." | Medium

Dong et al. (2020a) | Case report | N=1 | PCR | oropharyngeal swab breast milk sample | "The infant’s oropharyngeal swab specimen, obtained immediately after she was taken from the uterus, showed a negative result for the detection of SARS-CoV-2 RNA." | "Breast milk, collected were negative." | "Medium"
<table>
<thead>
<tr>
<th>Authors</th>
<th>Type</th>
<th>N</th>
<th>Description</th>
<th>Test(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Al-Kuraishy et al.</td>
<td>Case report</td>
<td>N=1</td>
<td>&quot;This study presents clinical feature and management of pregnant women with confirmed COVID-19 pneumonia with suspected vertical transmission to premature baby.&quot;</td>
<td>PCR Antigen-antibody reactions</td>
</tr>
<tr>
<td>Marin Gabriel et al.</td>
<td>Case report</td>
<td>N:7</td>
<td>&quot;The objective of our study was to determine whether the SARS-CoV-2-positive mothers transmit the virus to their hand-expressed colostrum.&quot;</td>
<td>PCR nasopharyngeal swab breast milk sample</td>
</tr>
<tr>
<td>Chhabra et al.</td>
<td>Case report</td>
<td>N:1</td>
<td>&quot;It describes the anaesthetic management of a mildly symptomatic, COVID-19 positive, 28-year-old second gravida with term pregnancy who was taken up for an elective caesarean section under subarachnoid block in a stand-alone maternity facility.&quot;</td>
<td>PCR nasopharyngeal swab breast milk sample</td>
</tr>
<tr>
<td>Dong et al.</td>
<td>Case report</td>
<td>N:1</td>
<td>&quot;It is reported a newborn with elevated IgM antibodies to SARS-CoV-2 born to a mother with coronavirus disease 2019 (COVID-19).&quot;</td>
<td>PCR nasopharyngeal swab breast milk sample</td>
</tr>
<tr>
<td>Perrone et al.</td>
<td>Case report</td>
<td>N:1</td>
<td>&quot;It is reported the case of a mother who presented clinical symptoms of respiratory tract infection 10 days after the spontaneous delivery of a preterm newborn.&quot;</td>
<td>PCR nasopharyngeal swab breast milk sample</td>
</tr>
<tr>
<td>Hinojosa-Velasco et al.</td>
<td>Case report</td>
<td>N:1</td>
<td>&quot;This report describes a SARS-CoV-2 infection in a 21-year-old mother-daughter duo at the time of birth, focusing on the viral RNA detection in the stool of both and the human breast milk.&quot;</td>
<td>PCR nasopharyngeal and oropharyngeal swabs stool sample human milk sample</td>
</tr>
<tr>
<td>Costa et al.</td>
<td>Case report</td>
<td>N:2</td>
<td>&quot;It is presented this case to highlight the following important issues: placental pathology, the absence of vertical transmission in the context of preterm birth and placental abruption.&quot;</td>
<td>PCR amniotic fluid, cord blood, placental tissue, neonatal throat swab, and breast milk samples</td>
</tr>
<tr>
<td>Kuhrt et al.</td>
<td>Case report</td>
<td>N:2 (twins)</td>
<td>&quot;The mother expressed breast milk. Both babies had a negative result for COVID-19 PCR test on postnatal days 3 and 5.&quot;</td>
<td>PCR throat swab</td>
</tr>
<tr>
<td>De Socio et al.</td>
<td>Case report</td>
<td>N:1</td>
<td>&quot;The newborn’s tested negative for SARS-CoV-2. The mother was assessed for SARS-CoV-2 RNA and resulted negative in the breast milk.&quot;</td>
<td>PCR Breast milk sample nasopharyngeal swab</td>
</tr>
<tr>
<td>Pereira et al.</td>
<td>Case report</td>
<td>N:22</td>
<td>&quot;It was described the management of the mothers and babies during breastfeeding, the indication of breastfeeding depending on the severity of symptoms and finally breastfeeding in preterm neonates during NICU admission.&quot;</td>
<td>PCR nasopharyngeal swab</td>
</tr>
</tbody>
</table>

- Hand expression measuring that a mask is used and that appropriate hygienic measures are used for the hands and the breast, when direct breastfeeding is not possible, appears to be a safe way of feeding newborns of mothers with COVID-19.
- She was instructed to keep on the N95 respirator and maintain hand hygiene.
- The adherence to hygiene measures by health workers and newborn parents, in addition to the paths implemented for the management of positive COVID-19 patients, contributes to infection control and its spreading prevention.
- Investigations of pregnant women with COVID-19 symptoms should necessarily include testing from various body sites or fluids.
- Mother direct breastfeeding is advisable, under strict measures of infection control, i.e. a face mask should be worn due to the proximity between mother and child to reduce the risk of droplet transmission.
<table>
<thead>
<tr>
<th>Authors</th>
<th>Case report</th>
<th>N:1/2/4</th>
<th>Method(s)</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kalaf et al.</td>
<td>Case report</td>
<td>N:1</td>
<td>PCR, nasopharyngeal swabs or analys swabs</td>
<td>&quot;The neonatal swabs, cord blood, breast milk sample and placental swab were negative for SARS-CoV-2.&quot;</td>
</tr>
<tr>
<td>Bastug et al.</td>
<td>Case report</td>
<td>N:1</td>
<td>PCR, breast milk sample</td>
<td>Breast milk obtained after first lactation was tested by real-time RT-PCR and was positive for SARS-CoV-2.</td>
</tr>
<tr>
<td>Buonassenso et al.</td>
<td>Case report</td>
<td>N:2</td>
<td>PCR, breast milk sample</td>
<td>At birth and 3 days of life, newborns were negative to SARS-CoV-2. The mother breastfed him at home. At 2-week follow-up, one newborn tested positive although asymptomatic.</td>
</tr>
<tr>
<td>Zhang et al.</td>
<td>Case report</td>
<td>N:4</td>
<td>PCR, breast milk sample, human milk sample</td>
<td>Four newborn babies tested positive in nucleic acid detection.</td>
</tr>
<tr>
<td>Salvatori et al.</td>
<td>Case report</td>
<td>N:2</td>
<td>PCR, nasopharyngeal swabs or analys swabs</td>
<td>It was analyzed expressed breast milk samples of both mothers, and SARS-CoV-2 was not detected by RT-PCR, as already described.</td>
</tr>
<tr>
<td>Tam et al.</td>
<td>Case report</td>
<td>N:1</td>
<td>PCR, nasopharyngeal swab, breast milk sample</td>
<td>Samples of the mother’s human milk none had detectable RNA.</td>
</tr>
<tr>
<td>Krisman et al.</td>
<td>Case report</td>
<td>N:3</td>
<td>PCR, nasopharyngeal swab, placental tissue</td>
<td>&quot;All 3 of the neonate’s nasopharyngeal swabs were positive for SARS-CoV-2 and gene targets via RT-PCR testing.&quot;</td>
</tr>
<tr>
<td>Han et al.</td>
<td>Case report</td>
<td>N:1</td>
<td>PCR, nasopharyngeal swab, breast milk sample</td>
<td>The virus was also not detected in the nasopharynx, oropharynx, stool, saliva, plasma, and urine.</td>
</tr>
<tr>
<td>Chacón-Aguilar et al.</td>
<td>Case report</td>
<td>N:1</td>
<td>PCR, nasopharyngeal swab</td>
<td>The polymerase chain reaction (PCR) test for detection of SARS-CoV-2 was positive.</td>
</tr>
<tr>
<td>Zhu et al.</td>
<td>Case report</td>
<td>N:5</td>
<td>PCR, breast milk sample</td>
<td>Four out of five (80%) patient's breastmilk samples were negative for SARS-CoV-2 RT-PCR.</td>
</tr>
<tr>
<td>Piersigilli et al.</td>
<td>Case report</td>
<td>N:1</td>
<td>PCR, nasopharyngeal swab, breast milk sample</td>
<td>Maternal milk sample was negative.</td>
</tr>
<tr>
<td>Bertinon et al.</td>
<td>Case report</td>
<td>N:14</td>
<td>PCR, nasopharyngeal swab, breast milk sample</td>
<td>Contamination of breastmilk and other bodily fluids needs to be studied further.</td>
</tr>
</tbody>
</table>

Breastfeeding/breast milk safety in infants of mothers with suspected or confirmed COVID-19 infection

It was reported a case of detectable SARS-CoV-2 RNA in a woman with mild symptoms of COVID-19.

"It was described the clinical manifestation of COVID-19 in a neonate and her mother, and further analyzed the viral load kinetics of SARS-CoV-2 in clinical specimens from different sources.

"It was presented one case of infection by coronavirus with an atypical course.

"The aim was to look for the presence of SARS-CoV-2 RNA in the milk of a group of SARS-CoV-2 positive mothers from North West Italy.

"The recommended hygiene measures for the control of airborne exposure, for direct breastfeeding, must be carefully followed.

"Whenever direct breastfeeding is not possible, the use of expressed mother’s milk should be considered and promoted to take advantage of its unquestionable benefits.

"Newborn 2, the father fed him at home with expressed milk. The newborn nasopharyngeal and rectal swabs were negative.

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"The recommended hygiene measures for the control of airborne exposure, for direct breastfeeding, must be carefully followed.

"Although the benefits of breastfeeding may outweigh the risks, this decision should be made together by the parent and the doctor.

"Contamination of breastmilk and other bodily fluids needs to be studied further, but the current policy is to allow the use of expressed breastmilk.

"Whenever direct breastfeeding is not possible, the use of expressed mother’s milk should be considered and promoted to take advantage of its unquestionable benefits.

"Newborns to mothers were negative to SARS-CoV-2.

"Newborn 2, the father fed him at home with expressed milk. The newborn nasopharyngeal and rectal swabs were negative.

"At birth and 3 days of life, newborns were negative to SARS-CoV-2. The mother breastfed him at home. At 2-week follow-up, one newborn tested positive although asymptomatic.

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The infection outcomes of breastfed neonates are summarised in Tables III and IV. Four hundred and ten breastfed neonates were identified, including 26 positive SARS-CoV-2 infection cases and 384 negative SARS-CoV-2 infection cases, based on the absence of viral RNA detection by RT-PCR tests. There were also three breastfed infants (infants older than 28 days) who were positive for SARS-CoV-2 infection.

Among the studies included in the systematic review, emphasised that mothers should take protective measures while breastfeeding. The use of a mask, hand hygiene, breast cleaning, taking hygienic measures, feeding by expressing breast milk, and keeping the infant away from the mother except for breastfeeding, were among the recommended protective measures. Furthermore, studies put forward that infants could additionally benefit from the direct acquisition of antibodies against SARS-CoV-2 through breast milk. It was recommended to provide mothers with their breast milk that could be given to infants during isolation and provide electronic breast pumps and breastfeeding support to allow the infant and/or mother to breastfeed directly after isolation. Wu et al. suggested that “mothers with COVID-19 should not breastfeed until after full recovery, when breast milk tests negative in terms of virus.” Pereira et al. suggested that “when mother-baby separation occurs, supplementary feeding with pasteurised donor milk or infant formula may be effective until breastfeeding is resumed.”

The infection outcomes of breastfed neonates are summarised in Table IV. In the studies analysing breast milk in the laboratory, while it was determined that 13 breastfed neonates (≤28 days old) and three infants aged 13.8 and 6 months outside the neonatal period had SARS-CoV-2 infection, SARS-CoV-2 infection was not detected in 60 neonates.

### DISCUSSION

To the best of the authors’ knowledge, this is the first systematic review that examined suspected or confirmed COVID-19 infected mothers during the lactation period; and addressed whether it was safe to breastfeed/feed infants with breast milk.

In this study, a total of 1,229 articles were examined until November 15, 2020. Forty-six of which were assessed within the scope of the study. Among the 24 studies reviewed with breast milk samples taken, RT-PCR analysis reported that breast milk samples were positive for COVID-19 in seven studies and one sample had IgG (Table II). While the nasopharyngeal test result for COVID-19 was negative in a healthy neonate with SARS-CoV-2 in breast milk samples, SARS-CoV-2 was detected in breast milk samples. However, it is very difficult to determine the SARS-CoV-2 infection as the neonate receives breast milk. In another study, a neonate was determined to be positive for SARS-CoV-2 based on viral RNA detected by RT-PCR, while being fed with maternal breast milk tested positive in terms of infection. In this specific case, the neonate was fed with synthetic milk formula instead of human milk. Therefore, it is unclear whether the neonate received the infection from its positive mother or contact with other patients with SARS-CoV-2 infection.

It is an interesting fact that there were some infants with confirmed COVID-19 infection by RT-PCR tests who received SARS-CoV-2 negative breast milk, including two exclusively breastfed neonates, one 27-day breastfed neonate, and an infant aged 8 months. Therefore, it is thought that these infants may have been exposed to SARS-CoV-2 through close contact with infected relatives.
In line with the evidence obtained in articles not analysing breast milk samples, it cannot be confirmed whether there is an increase in the risk of SARS-CoV-2 transmission through breast milk among breastfed children. According to negative RT-PCR tests, most breastfed neonates did not have evidence of SARS-CoV-2 RNA (324 out of 334).

Only one study made conclusions and suggestions to keep the mother and infant apart.²⁶ However, most of the available publications and the WHO, UNICEF, and WFO recommend that mothers with suspected or confirmed COVID-19 infection and isolated at home should continue feeding practices by taking necessary hygiene precautions during feeding.²⁷

During the pandemic process, both pregnant women and breastfeeding mothers should be informed by a correct and reliable source on how to breastfeed/feed with breast milk, if they are in contact with the disease. The persons to whom they can refer in this regard are physicians, midwives, and nurses. However, in this rapidly developing process, healthcare professionals need reliable, evidence-based information to guide mothers in the right direction. Systematic reviews on this subject are important for meeting the needs of nurses and healthcare professionals who work very hard in this process. However, it should not be overlooked that the current information should be continuously updated with new and reliable studies in this process. The relevant systematic reviews are important to ensure the standardisation of nursing practices.

The limitation of this systematic review is that it is based on very recent studies on the subject. Despite the said limitation, the present comprehensive review consolidates important data to optimise outcomes better. This systematic review will be updated by including renewed publications. It is recommended to exclusively breastfeed infants for six months with complementary foods for up to 24 months and beyond. Among the studies, there were very few reports on infants outside the neonatal period. There is a need for a high level of evidence in a wide range of populations and different cultures, remaining current. A present systematic review allows us to incorporate relevant new evidence as it becomes available, which is crucial and rapidly increasing in the international health crisis.

CONCLUSION

In line with the limited data available, it was concluded that most of the infants breastfed had negative findings for SARS-CoV-2 infection in PCR, and breastfeeding mothers should initiate breastfeeding by taking protective measures such as wearing a mask and gloves and applying breast hygiene before breastfeeding and before contact with the infant.

CONFLICT OF INTEREST:
The authors declared no conflict of interest.

AUTHORS’ CONTRIBUTION:
NC, OKS: Conceptualisation, writing original draft, writing review and editing, investigation, methodology, project administration, resources, visualisation, data curation.
SO, PT: Conceptualisation, writing original draft, writing review editing, and fund acquisition.
VC: Conceptualisation, writing original draft, writing review editing, and formal analysis.

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