SARS-CoV-2 genome and antibodies in breastmilk: a systematic review and meta-analysis

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ABSTRACT

Objective To systematically review and meta-analyse the rate of SARS-CoV-2 genome identification and the presence of SARS-CoV-2 antibodies in breastmilk of mothers with COVID-19.

Design A systematic review of studies published between January 2019 and October 2020 without study design or language restrictions.


Patients Mothers with confirmed COVID-19 and breastmilk tested for SARS-CoV-2 by RT-PCR or for anti-SARS-CoV-2 antibodies.

Main outcome measures Presence of SARS-CoV-2 genome and antibodies in breastmilk.

Results We included 50 articles. Twelve out of 183 women from 48 studies were positive for SARS-CoV-2 genome in their breastmilk (pooled proportion 5% (95% CI 2% to 15%; I²=48%)). Six infants (50%) of these 12 mothers tested positive for SARS-CoV-2, with one requiring respiratory support. Sixty-one out of 89 women from 10 studies had anti-SARS-CoV-2 antibody in their breastmilk (pooled proportion 83% (95% CI 32% to 98%; I²=88%)). The predominant antibody detected was IgA.

Conclusions SARS-CoV-2 genome presence in breastmilk is uncommon and is associated with mild symptoms in infants. Anti-SARS-CoV-2 antibodies may be a more common finding. Considering the low proportion of SARS-CoV-2 genome detected in breastmilk and its lower virulence, mothers with COVID-19 should be supported to breastfeed.

What is already known on this topic?

► Breast feeding is the optimal nutrition for infants.
► Evidence is limited on whether SARS-CoV-2 is transmitted via breastmilk, but some guidelines recommend women with COVID-19 refraining from breast feeding.
► Transmission of anti-SARS-CoV-2 antibodies in breastmilk may be beneficial.

What this study adds?

► The presence of SARS-CoV-2 genome in breastmilk is uncommon (5%), and when it occurs, it is associated with mild symptoms in infants.
► Anti-SARS-CoV-2 antibodies are more prevalent in breastmilk of COVID-19 positive women (83%).
► Breast feeding should be recommended and encouraged for women with COVID-19.

INTRODUCTION

SARS-CoV-2 is transmitted by respiratory droplets from close contact between individuals and is the cause of the current COVID-19 pandemic. The possibility of maternal–neonatal transmission via breast feeding or breastmilk consumption is uncertain. Current guidance on breast feeding for neonates born to women with suspected or confirmed COVID-19 remains controversial, and international recommendations vary. The WHO, UNICEF, Canadian Pediatric Society and UK Royal College of Paediatrics and Child Health recommend that mothers with suspected or proven COVID-19 can safely continue breast feeding.1-4 However, the European Union of Neonatal and Perinatal Societies supports the separation of symptomatic mothers from their newborns and interruption of breast feeding, and the Association of Chinese Neonatologists advises against the use of breastmilk or breast feeding.5 6 Up until 22 July 2020, the American Academy of Pediatrics recommended separating baby from mother, but new guidance now supports rooming-in and the use of breastmilk.7 Meanwhile, the Centers for Disease Control and Prevention supports the use of expressed breastmilk but advises further discussion with the mother and families to determine whether breast feeding should be initiated or continued.8 9 These divisive recommendations are the result of initial reactions based on a lack of evidence regarding transmission of SARS-CoV-2 via breastmilk and breast feeding. Given the increasing concerns relating to maternal depression and anxiety during the current pandemic, the decision to separate mothers from babies should not be taken lightly.9-11 Concerns regarding the potential presence of SARS-CoV-2 in breastmilk affect the postnatal health and well-being of both mother and baby and the potential availability of donor breastmilk for preterm neonates in the neonatal intensive care unit.10

Reports of SARS-CoV-2 in breastmilk have caused families and healthcare professionals to be concerned about the potential for transmission.11 Conversely, anti-SARS-CoV-2 antibodies in breastmilk may be beneficial.5 6 8 However, the European Union of Neonatal and Perinatal Societies supports the separation of symptomatic mothers from their newborns and interruption of breast feeding.
breastmilk may confer potential benefits to infants. Hence, a detailed examination of the literature is needed. Our primary objective was to systematically review and meta-analyse the available evidence for the presence of SARS-CoV-2 genome in the breastmilk of mothers who tested positive for COVID-19. Our secondary objective was to review the literature reporting on the presence of antibodies to SARS-CoV-2 in breastmilk.

METHODS
The study was conducted according to the Meta-analysis of Observational Studies in Epidemiology guidelines and reported using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Our institution did not require ethics approval for systematic reviews, and this study was not registered on PROSPERO as their operations during this pandemic were halted.

Search strategy
We searched bibliographic databases of Ovid Medline, Ovid Embase Classic+Embase, PubMed, Web of Science and Scopus for articles published between 1 January 2019 and 7 October 2020 using a search developed by an information specialist (CDC). No limits on language were imposed. The detailed search strategy is reported in the online supplemental eTable 1. An additional search from bibliographies of relevant articles and the John Hopkins University COVID-19 database was conducted. Two reviewers (FZ and CZ) screened the search results independently and selected articles for full-text review, and conflicts were resolved by a third reviewer (PSS).

Eligibility criteria
All study designs were included in the systematic review. Studies were included if they met the following criteria: (1) mother with confirmed SARS-CoV-2 genome detected by RT-PCR in any sample and (2) breastmilk was tested either for the presence of SARS-CoV-2 RNA using RT-PCR or for the presence of antibodies to SARS-CoV-2. Studies were excluded if information on maternal infection during pregnancy was not confirmed. ‘Case series’ was defined as a report of more than one mother.

Data collection
Data on maternal characteristics, infant characteristics, test characteristics, results and any other relevant information on the follow-up of the child were extracted. An infant’s day of birth was considered day of life 1, and the day of maternal symptom onset was considered day 1 of infection.

Risk of bias assessment
The risk of bias within each included study was evaluated using the Joanna Briggs Institute Critical Appraisal Tool for case reports and case series. Studies were assessed for their inclusion criteria, methods, reporting of demographics, clinical history and follow-up. For case series, an additional assessment of consecutive or complete inclusion of cases was performed. Studies were deemed ‘low risk’ if they fulfilled all the available criteria, and ‘intermediate risk’ or ‘high risk’ when 1 or ≥2 criteria, respectively, were unmet.

Statistical analysis
We summarised data from all included studies in a table format to provide the complete context of the available evidence, types of studies, locations of studies, methods of detection and results. Meta-analyses of the proportion of mothers with breastmilk positivity for SARS-CoV-2 genome and presence of antibodies were performed, and the pooled proportions were reported as effect size with 95% CI. A generalised mixed linear model was used to derive the pooled proportion as we expected a high number of reports of zero cases of positivity. Statistical heterogeneity was calculated as I² values, and an a priori decision was made to use a random effects model. Analyses were conducted using the ‘metaprop’ command in the programme R (V4.0.2; available at https://www.r-project.org/).

RESULTS
Detailed search results are reported in figure 1. One hundred and four articles were excluded (28 were review articles, 64 studies did not test breastmilk, 6 studies included a mix of confirmed and suspected COVID-19 mothers, with no clear distinction between the groups, 4 were duplicate articles, 1 study did not provide breastmilk results and 1 study considered a mother positive based on SARS-CoV-2 antibodies, but she was negative on RT-PCR testing). A total of 50 studies (nine preprints) from 15 countries were included in the qualitative synthesis, which comprised 27 case reports, 18 case series, 4 cohort studies and 1 case control study (figure 1). There were 46 articles published in English and 4 in Chinese language. A total of 183 mothers had SARS-CoV-2 genome testing of their breastmilk, and 89 mothers had antibody testing of their breastmilk. Thirty mothers had antibody testing without SARS-CoV-2 genome testing of their breastmilk. The maternal and infant characteristics are summarised in online supplemental eTable 2. Fifteen studies had low risk of bias, 19 had intermediate risk of bias and 16 had high risk of bias (online supplemental eTable 3).

A total of 12 mothers’ breastmilk samples were identified to contain SARS-CoV-2 genome. Further details of these studies are summarised in table 1. These studies reported testing of different genes, including surface glycoprotein gene (table 1). Meta-analyses identified that the pooled breastmilk positivity rate for SARS-CoV-2 was 5% (95% CI 2% to 15%; I²=48%;
<table>
<thead>
<tr>
<th>Author</th>
<th>Maternal characteristics</th>
<th>Time interval between maternal symptoms onset and BM positive</th>
<th>Time interval between maternal symptoms onset and BM negative</th>
<th>Infants of mothers with BM-positive characteristics</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bactug et al&lt;sup&gt;16&lt;/sup&gt;</td>
<td># mothers BM RT-PCR positive: 1, # BM samples tested: 3, # positive samples: 3.</td>
<td>0 days (asymptomatic)</td>
<td>Asymptomatic/no negative samples</td>
<td>Genes tested: S-gene. Cycle threshold: 28.65–32.28.</td>
<td>Type of feeding: EBM. Symptoms: no. Infant positive: yes. If yes, for how long: NK.</td>
</tr>
<tr>
<td>Bertino et al&lt;sup&gt;17&lt;/sup&gt;</td>
<td># mothers BM RT-PCR positive: 1, # BM samples tested: 6, # positive samples: 3.</td>
<td>3 days</td>
<td>28 days</td>
<td>Genes tested: ORF1ab, E-gene, N-gene and RdRp. Cycle threshold: NK.</td>
<td>Type of feeding: BF. Symptoms: no. Infant positive: yes. If yes, for how long: ≤14 days.</td>
</tr>
<tr>
<td>Buonsenso et al&lt;sup&gt;*18&lt;/sup&gt;</td>
<td># mothers BM RT-PCR positive: 1, # BM samples tested: 10.</td>
<td>9 days</td>
<td>13 days</td>
<td>Genes tested: E-gene, N-gene and RdRp. Cycle threshold: 34.3–38.3.</td>
<td>Type of feeding: EBM. Symptoms: no. Infant positive: no.</td>
</tr>
<tr>
<td>Chambers et al&lt;sup&gt;19&lt;/sup&gt;</td>
<td># mothers BM RT-PCR positive: 1, # BM samples tested: 4, # positive samples: 1.</td>
<td>1 day (collected at the day of symptoms onset)</td>
<td>12 days</td>
<td>Genes tested: RdRp and N-genes. Cycle threshold: NK.</td>
<td>Type of feeding: NK. Symptoms: yes. Infant positive: test not performed.</td>
</tr>
<tr>
<td>Fenizia et al&lt;sup&gt;20&lt;/sup&gt;</td>
<td># mothers BM RT-PCR positive: 1, # BM samples tested: 1, # positive samples: 1.</td>
<td>NK</td>
<td>NK</td>
<td>Genes tested: RdRp, E-gene and N-gene. Cycle threshold: NK.</td>
<td>Type of feeding: NK. Symptoms: no. Infant positive: no.</td>
</tr>
<tr>
<td>Groši et al&lt;sup&gt;21&lt;/sup&gt;</td>
<td># mothers BM RT-PCR positive: 1, # BM samples tested: 7, # positive samples: 4.</td>
<td>5 days</td>
<td>9 days</td>
<td>Genes tested: N-gene and ORF1b-nsp14. Cycle threshold: 29.8 (peak, whole milk), 30.4 (peak, skimmed milk).</td>
<td>Type of feeding: BF. Symptoms: yes. Infant positive: yes. If yes, for how long: 15 days.</td>
</tr>
<tr>
<td>Hinojosa-Velasco et al&lt;sup&gt;22&lt;/sup&gt;</td>
<td># mothers BM RT-PCR positive: 3, # BM samples tested: 2, # positive samples: 1.</td>
<td>6 days</td>
<td>15 days</td>
<td>Genes tested: N-gene and ORF1ab NK.</td>
<td>Type of feeding: BMS and BF. Symptoms: no. Infant positive: yes. If yes, for how long: 13 days.</td>
</tr>
<tr>
<td>Kirtzman et al&lt;sup&gt;23&lt;/sup&gt;</td>
<td># mothers BM RT-PCR positive: 1, # BM samples tested: 2, # positive samples: 1.</td>
<td>4 days</td>
<td>9 days</td>
<td>Genes tested: E-gene, N-gene and RdRp. Cycle threshold: 30.58–32.56.</td>
<td>Type of feeding: BF. Symptoms: yes. Infant positive: yes. If yes, for how long remained positive: 7 days.</td>
</tr>
<tr>
<td>Lugli et al&lt;sup&gt;24&lt;/sup&gt;</td>
<td># mothers BM RT-PCR positive: 1, # BM samples tested: 2, # positive samples: 2.</td>
<td>6 days</td>
<td>NK</td>
<td>Genes tested: E-gene, N-gene and RdRp. Cycle threshold: 37–38.</td>
<td>Type of feeding: EBM. Symptoms: no. Infant positive: no.</td>
</tr>
<tr>
<td>Tam et al&lt;sup&gt;25&lt;/sup&gt;</td>
<td># mothers BM RT-PCR positive: 1, # BM samples tested: 7, # positive samples: 2.</td>
<td>5 days</td>
<td>9 days (became positive again at 15 days)</td>
<td>Genes tested: E-gene. Cycle threshold: 20–35.1</td>
<td>Type of feeding: BF. Symptoms: yes. Infant positive: yes. If yes, for how long: 11 days.</td>
</tr>
<tr>
<td>Wu et al&lt;sup&gt;26&lt;/sup&gt;</td>
<td># mothers BM RT-PCR positive: 1 # BM samples tested: 2 # positive samples: 1</td>
<td>NK</td>
<td>NK</td>
<td>Genes tested: NK. Cycle threshold: NK.</td>
<td>Type of feeding: NK. Symptoms: no. Infant positive: no.</td>
</tr>
<tr>
<td>Zhu et al&lt;sup&gt;27&lt;/sup&gt;</td>
<td># mothers BM RT-PCR positive: 1 # BM samples tested: 2 # positive samples: 2.</td>
<td>3 days</td>
<td>NK</td>
<td>Genes tested: ORF1ab and N-gene. Cycle threshold: 38.2–38.5.</td>
<td>Type of feeding: NK. Symptoms: no. Infant positive: NK.</td>
</tr>
</tbody>
</table>

*Information collated from both Buonsenso et al and Costa et al: same cases were reported in two separate papers.

†No exact cycle threshold values given.

β, number of; BF, breast feeding; BM, breast milk; DOL, day of life; EBM, expressed breast milk; E-gene, envelope protein gene; NA, not applicable; N-gene, nucleocapsid protein gene; NK, not known; ORF1b-nsp14, Open Reading Frame 1b-non-structural protein 14; RdRp, RNA dependent RNA polymerase gene; RT-PCR, real-time PCR; S-gene, surface glycoprotein gene.
Among the infants of these 12 mothers with positive breastmilk RT-PCR testing, 50% (6/12) tested positive for SARS-CoV-2 via nasopharyngeal swab and 33% (4/12) were symptomatic (three confirmed positive). Only one of these four symptomatic infants required respiratory support; this infant was found to have concurrent infection with respiratory syncytial virus. The time interval between maternal symptoms and positive test results for SARS-CoV-2 in the breastmilk was 1–9 days. In studies that performed repeat testing, the time interval between maternal symptom onset and subsequent negative RT-PCR test results in the breastmilk was 9–28 days.

A total of 214 infants (one set of twins) were born, of which 32 infants (15%) tested positive for SARS-CoV-2 viral genome in the nasopharyngeal swab and one tested positive for anti-SARS-CoV-2 antibodies in serum. Of these, 25% (8/32) were preterm (<37 weeks’ gestational age) and 41% (13/32) tested positive at ≥7 days of age. Among the 171 mothers who tested negative for SARS-CoV-2 in the breastmilk, 24 (14%) infants had a positive SARS-CoV-2 genome result. All infants survived to discharge.

Ten studies reported anti-SARS-CoV-2 antibody testing in the breastmilk of 89 mothers. Of these mothers, 61 (69%) had antibodies detected in their breastmilk (pooled proportion 83% (95% CI 32% to 98%; $I^2=88%$; figure 3). Time intervals between maternal symptom onset and antibody detection ranged from 3 to 79 days. Of the 61 mothers with anti-SARS-CoV-2 antibodies, only three (5%) infants had a positive nasopharyngeal swab confirming SARS-CoV-2 genome and two infants (one confirmed positive) were symptomatic. The characteristics of these studies including the types of antibodies are reported in table 2.

**DISCUSSION**

**Main findings**

In this systematic review and meta-analysis of 50 studies and 213 mothers, we identified that 1 in 20 mothers who had...
Table 2 Characteristics of studies with anti-SARS-CoV-2 antibodies detected in breastmilk

<table>
<thead>
<tr>
<th>Author</th>
<th>Maternal characteristics</th>
<th>Time interval between maternal symptoms onset and Ig positive</th>
<th>Assay and immunoglobulin characteristics</th>
<th>Infant characteristics</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dong et al²⁸</td>
<td># mothers BM Ig positive: 1. # BM samples tested: 6. # positive samples: 6.</td>
<td>26 days</td>
<td>Assay method: ELISA. Antigen used: S-protein. Type of Ig: IgA and IgG.</td>
<td>Type of feeding: NK. Symptoms: no. Infant RT-PCR positive: no.</td>
<td>BM IgG remained positive for 58 days after symptom onset. Maternal serum IgG positive at 26 days and remained positive 58 days after symptom onset. Infant serum IgG positive at DoL 25 but negative at DoL 44.</td>
</tr>
<tr>
<td>Fenizia et al²⁹</td>
<td># mothers BM Ig positive: 1. # BM samples tested: 1. # positive samples: 1.</td>
<td>NK</td>
<td>Assay method: chemiluminescence immunoassay. Antigen used: nucleocapsid and S-protein. Type of Ig: IgG and IgM.</td>
<td>Type of feeding: NK. Symptoms: NK. Infant RT-PCR positive: no.</td>
<td>BM positive for both virus RNA and antibodies.</td>
</tr>
<tr>
<td>Gao et al²⁹</td>
<td># mothers BM Ig positive: 2. # BM samples tested: 2. # positive samples: 2.</td>
<td>17–22 days</td>
<td>Assay method: chemiluminescence immunoassay. Antigen used: NK. Type of Ig: IgG and IgM.</td>
<td>Type of feeding: BMS¹ and EBM.¹ Symptoms: NK. Infant RT-PCR positive: no.</td>
<td>Both infants had positive serum IgM, one also had positive serum IgM. (Third mother with positive IgM in BM not included, had negative RT-PCR in throat swab but positive serum IgM!)</td>
</tr>
</tbody>
</table>
| Luo et al³⁰      | # mothers BM Ig positive: 4. # BM samples tested: 4. # positive samples: 4. | 13–45 days                                                  | Assay method: ELISA. Antigen used: NK. Type of Ig: IgM. | Type of feeding: BMS. Symptoms: no. Infant RT-PCR positive: no. | BM RT-PCR negative
All four mothers had serum IgG and IgM positive after delivery. All four mothers had negative PCR at time of BM sampling. |
| Pace et al³¹     | # mothers BM Ig positive: 18. # BM samples tested: 37. # positive samples: 37. | 0–20 days (three asymptomatic)                              | Assay method: ELISA. Antigen used: spike (S₂ and RBD) and nucleocapsid. Type of Ig: IgA and IgG. | Type of feeding: BF² and ME.¹³ Symptoms: NK. Infant RT-PCR positive: yes.² | BM-RT-PCR negative, one breast swab RT-PCR positive. Serum Ig not tested.
All mothers had positive PCR before first BM sample, two had negative PCR before second sample and one had negative PCR before third sample. |
| Peng et al³²     | # mothers BM Ig positive: 8. # BM samples tested: 27. # positive samples: 21. | 3–79 days                                                   | Assay method: ELISA. Antigen used: NK. Type of Ig: IgM. | Type of feeding: NK. * Symptoms: NK. Infant RT-PCR: NK. | BM RT-PCR negative.
Serum Ig not tested. Three mothers had IgG negative at 47–72 days. IgM positive samples collected at 31±19 days and IgM negative samples at 43±21 days after symptom onset.¹ |
| Van Keulen et al³¹ | # mothers BM Ig positive: 24. # BM samples tested: 24. # positive samples: 24. | Mean 5.9 (SD 2.6 weeks)                                      | Assay method: ELISA and bridging ELISA. Antigen used: S-protein, RBD and N protein. Type of Ig: IgA (S-protein) and total Ig (RBD and N protein). | Type of feeding: NK. Symptoms: yes. Infant RT-PCR: NK. | BM RT-PCR not tested. IgA present for at least 13 weeks from symptom onset. |
| Walczak et al³⁴  | # mothers BM Ig positive: 1. # BM samples tested: 1. # positive samples: 1. | NK                                                         | Assay method: microsphere immunoassay. Antigen used: NK. Type of Ig: IgA, IgG and IgM. | Type of feeding: NK. Symptoms: IgA. Infant RT-PCR: no. | Author states immunoassay not validated, parent serum immunoglobulin IgG and IgM positive. |
| Yu et al³⁵       | # mothers BM Ig positive: 1. # BM samples tested: 2. # positive samples: 2 (for IgG, negative for IgM). | 10 days                                                    | Assay method: NK. Antigen used: NK. Type of Ig: IgG and IgM. | Type of feeding: BF. Symptoms: yes. Infant RT-PCR positive: yes. If yes: for how long: 13 days. | BM-RT-PCR negative.
Repeat BM IgG remained positive on day 26 postsymptom onset. Maternal serum IgG positive on days 15 and 19. Infant serum IgG and IgM positive on day 13. |

*Unable to distinguish feeding practices of those who tested IgG positive and IgM negative.
†No statistical difference found (Mann-Whitney U test, p=0.052).
²number of; BF, breast feeding; BM, breastmilk; BMS, breastmilk substitute; DoL, day of life; Ig, immunoglobulin; NK, not known; RT-PCR, real time polymerase chain reaction; PCR, S-protein, spike protein.
SARS-CoV-2 infection had a positive test for SARS-CoV-2 genome in the breastmilk. Meta-analyses revealed that this proportion could be as low as 1 in 50 and as high as 1 in 7. Although the presence of antibodies against SARS-CoV-2 was assessed in few studies, they were identified in the majority of mothers who were tested. Our results may be explained by the timing of tests performed, as the majority of mothers with positive SARS-CoV-2 antibodies detected in breastmilk were tested after the first week of symptom onset compared with those with positive genome detected who were tested within the first week. Infants of mothers with positive viral genome testing in the breastmilk were mostly asymptomatic; only one infant who had another concurrent viral infection required respiratory support.

Well-established examples of infection transmitted through breastmilk include HIV, cytomegalovirus (CMV), human T cell lymphotropic virus type 1 (HTLV-1) and Ebola virus. Although there have been no studies of HIV and HTLV-1, breastmilk viral levels correlate with systemic viral load. Although there have been no studies demonstrating maternal SARS-CoV-2 systemic viral load and shedding patterns in breastmilk, it is interesting to note that 4 out of 12 (33%) mothers in our study were reported to be symptomatic during the time their breastmilk tested positive for SARS-CoV-2. For primary HIV infection, elevated viral load in plasma, and presumably in breastmilk, were mostly asymptomatic; only one infant who had symptomatic during the time their breastmilk tested positive for SARS-CoV-2. Antibodies may play an immune-protective role in breastfeeding.

In nursing mothers, delineating the mode of transmission between intrapartum or postpartum infection through droplet or close contact proves challenging. Bastug et al reported a case of an infant who was separated immediately after birth from a mother asymptomatic for COVID-19. This infant initially tested negative for SARS-CoV-2 genome on nasopharyngeal swab in the first 8 hours after birth and received expressed breastmilk for the first 2 days. However, following positive testing for SARS-CoV-2 in the breastmilk, the infant was subsequently retested and found to be positive on day 4. Possible transmission via breastmilk may be considered in this case; however, transmission through other personnel contact cannot be ruled out. Although the detection of SARS-CoV-2 RNA in the breastmilk is most commonly used to establish potential transmission of the virus via breastmilk, its significance relating to infectivity is not well understood. Chambers and colleagues evaluated the replication competency of SARS-CoV-2 in breastmilk using viral culture methods. Of all samples tested, including one that was positive on RT-PCR testing, none showed evidence of cytopathic effects in culture, suggesting that the presence of RNA may not represent replication-competent virus in breastmilk.

**Strengths and limitations**

To the best of our knowledge, this is the most comprehensive systematic review and meta-analysis on the detection of SARS-CoV-2 and its antibodies in breastmilk. To maximise the scope of our review, no languages were excluded, and studies published in languages other than English were all reviewed by native speakers trained in paediatrics. Although the majority of cases in our review were case reports and case series, this was due to the nature of the current pandemic situation; more robust studies require longer time to complete. Another limitation of this review could be publication bias as negative results may not be reported. Thus, our results could be an overestimation of the true positive rate.

A restrictive approach to breast feeding can significantly affect the type of feeding for infants in hospital and following discharge home. Popofsky and colleagues demonstrated increased formula feeding in hospital in separated versus unseparated mothers (81.6% vs 27.8%, respectively), which continued at home (34.7% vs 8.3%, respectively). In line with this, Patil and colleagues found rooming-in and breast feeding for infants of women with SARS-CoV-2 did not result in adverse neonatal outcomes. According to one estimate, 5%, 10%, 25% or 50% relative reductions in the prevalence of breast feeding due to the COVID-19 pandemic can result in 16,469, 32,139, 75,455 or 138,398 child deaths, respectively. Given the magnitude of the impact of withholding breast feeding and the findings of this review, breast feeding should be recommended and supported in women with SARS-CoV-2 infection after appropriate counselling and instructions regarding other measures of infection prevention.

Future longitudinal research examining the correlations between maternal viral load and the symptoms and presence of the viral genome in breastmilk can help establish the pattern of viral shedding and its relationship with maternal viral load and symptoms. Simultaneous measurements of viral culture and SARS-CoV-2 antibodies may also give a more comprehensive understanding of the benefits and risks of breast feeding in mothers with SARS-CoV-2, which could help guide clinicians in their discussions with families.
CONCLUSION
The presence of SARS-CoV-2 genome in breastmilk is uncommon in mothers with confirmed SARS-CoV-2 infection while the presence of antibodies in breastmilk is more prevalent, especially beyond the first week of maternal symptom onset. However, the role of SARS-CoV-2 antibodies in neonatal protection is unclear. With low viral prevalence and virulence, breastfeeding should be recommended in mothers with SARS-CoV-2 after counselling and education regarding safe hygiene practices.

Acknowledgements We would like to thank Drs Mehmet Cizmeci, Beate Grasse, Nadja Skravset and Maxim Kirtman for helping with translation of manuscripts in Turkish, German and Russian. We would like to thank Heather McDonald Kinkaid PhD, for editorial support in preparing this manuscript, and Philip Ye, MSc, for his help with statistical analyses. Both are from the Maternal-Infant Care Research Centre (MiCare) at Mount Sinai Hospital in Toronto, Ontario, Canada. MiCare is supported by the Canadian Institutes of Health Research and the participating hospitals.

Contributors FZ performed an independent literature search, selected studies for inclusion, extracted and interpreted the data, assessed the risk of bias of included studies and wrote the first draft of the manuscript. CZ performed an independent literature search, selected studies for inclusion, verified the extracted data, assessed risk of bias, interpreted data, translated studies in Spanish, reviewed the manuscript and provided critical feedback. QZ participated in extracting data from studies in Chinese, assessed the risk of bias of included studies and reviewed the manuscript. CDC was the information specialist who developed the search strategy, performed the database search and reviewed the manuscript. FSS conceptualised and designed the study, interpreted the data, oversaw the meta-analysis and revised the final draft of the manuscript.

Funding PSS holds an Applied Research Chair in Reproductive and Child Health Services and Policy Research and has received funding for the Canadian Perinatal Birth Network from the Canadian Institutes of Health Research (APR-126340).

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; internally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information. As this was a systematic review and meta-analysis, all included data were publicly available from published research articles. A complete reference list of included studies is provided in the supplemental references in the supplemental material.

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Original research