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.

Setting Data sourced from Ovid Embase Classic+Embase, PubMed, Web of Science, Scopus, relevant bibliographies and the John Hopkins University COVID-19 database.

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%; I^2=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%; I^2=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.

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 Union of European 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] 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] 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

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.

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.[12] 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.[13] 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
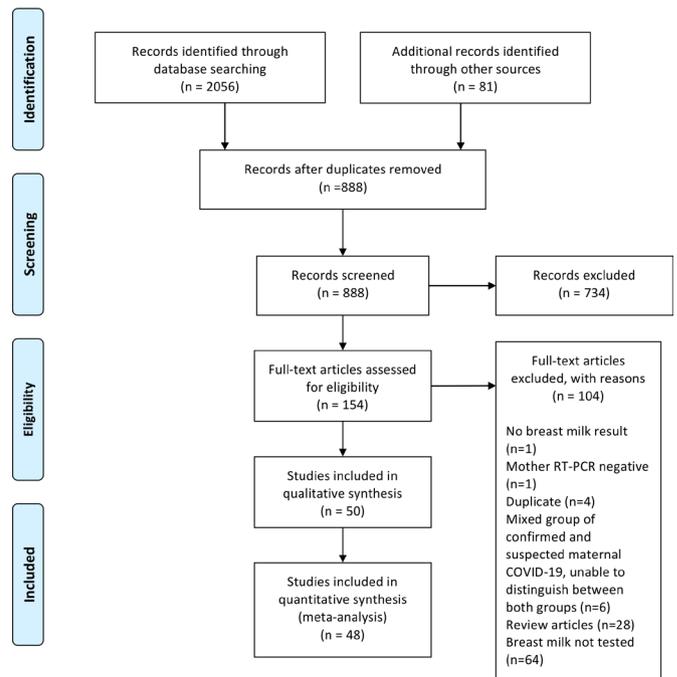

Figure 1 PRISMA flow diagram depicting search results. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

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 I^2 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 (V.4.0.2; 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.[14 15] 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.[11 16–26] 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%; I^2=48%;

Table 1 Characteristics of studies with SARS-CoV-2 genome detected in breastmilk

Author	Maternal characteristics	Time interval between maternal symptoms onset and BM positive	Time interval between maternal symptoms onset and BM negative	Type of test	Infants of mothers with BM-positive characteristics	Comments
Bastug et al[16]	# mothers BM RT-PCR positive: 1. # BM samples tested: 3. # positive samples: 3.	0 days (asymptomatic)	Asymptomatic/no negative samples	Genes tested: S-gene. Cycle threshold: 28.85–32.28.	Type of feeding: EBM. Symptoms: no. Infant positive: yes. If yes, for how long: NK.	Infant separated from mother at birth and tested negative at birth. Was exposed to EBM on DoL 1. Repeat infant PCR positive at 96 hours. BM continued to test positive on DoL 4 and 5.
Bertino et al[17]	# mothers BM RT-PCR positive: 1. # BM samples tested: 6. # positive samples: 3.	3 days	28 days	Genes tested: ORF1ab, E-gene, N-gene and RdRp. Cycle threshold: NK.	Type of feeding: BF. Symptoms: no. Infant positive: yes. If yes, for how long: ≤14 days.	Mother symptomatic at time of positive BM test. Infant only retested 14 days after first test. BM negative on day 15 but positive on day 26 of maternal symptoms. BM negative from day 28 onwards.
Buonsenso et al*[18]	# mothers BM RT-PCR positive: 1. # BM samples tested: 10.	9 days	13 days	Genes tested: E-gene, N-gene and RdRp. Cycle threshold: 34.3–38.3.	Type of feeding: EBM. Symptoms: no. Infant positive: no.	BM PCR negative on day 11 but positive on day 12 of maternal symptoms. Repeat on day 13 and after remained negative.
Chambers et al[19]	# mothers BM RT-PCR positive: 1. # BM samples tested: 4. # positive samples: 1.	1 day (collected at the day of symptoms onset)	12 days	Genes tested: RdRp and N-genes. Cycle threshold: NK.	Type of feeding: NK. Symptoms: yes. Infant positive: not tested.	Mother symptomatic at time of BM testing. Infant (9 months) had fever (1 day). BM PCR was positive 14 days before maternal test. Repeat testing negative. BM also negative by infectivity assay.
Fenizia et al[20]	# mothers BM RT-PCR positive: 1. # BM samples tested: 1. # positive samples: 1.	NK	NK	Genes tested: RdRp, E-gene and N-gene. Cycle threshold: NK.	Type of feeding: NK. Symptoms: NK. Infant positive: no.	
Groβ et al[11]	# mothers BM RT-PCR positive: 1. # BM samples tested: 7. # positive samples: 4.	5 days	9 days	Genes tested: N-gene and ORF1b-nsp14. Cycle threshold: 29.8 (peak, whole milk), 30.4 (peak, skimmed milk).	Type of feeding: BF. Symptoms: yes. Infant positive: yes. If yes, for how long: 15 days.	Mother symptomatic at time of positive BM test. Repeat BM sample negative (9 days after maternal symptom). Baby was also positive for RSV.
Hinojosa-Velasco et al[21]	# mothers BM RT-PCR positive: 1. # BM samples tested: 2. # positive samples: 1.	6 days	15 days	Genes tested: N-gene and ORF1ab NK.	Type of feeding: BMS and BF. Symptoms: no. Infant positive: yes. If yes, for how long: 13 days.	
Kirtsman et al[22]	# mothers BM RT-PCR positive: 1 # BM samples tested: 2 # positive samples: 1	4 days	9 days	Genes tested: E-gene, N-gene and RdRp. Cycle threshold: 30.58–32.56.	Type of feeding: BF. Symptoms: yes Infant positive: yes If yes, for how long remained positive: 7 days.	
Lugli et al[23]	# mothers BM RT-PCR positive: 1. # BM samples tested: 2. # positive samples: 2.	6 days	NK	Genes tested: E-gene, N-gene and RdRp. Cycle threshold: 37–38.	Type of feeding: EBM. Symptoms: no. Infant positive: no.	First sample taken from EBM expressed at home without precautions, second taken under strict precautions.
Tam et al[24]	# mothers BM RT-PCR positive: 1. # BM samples tested: 7. # positive samples: 2.	5 days	9 days (became positive again at 15 days)	Genes tested: E-gene. Cycle threshold: 20-35.†	Type of feeding: BF. Symptoms: yes. Infant positive: yes. If yes, for how long: 11 days.	4 negative BM samples in between both positive samples. Last sample positive on day 15 of symptoms.
Wu et al[25]	# mothers BM RT-PCR positive: 1 # BM samples tested: 2 # positive samples: 1	NK	NK	Genes tested: NK. Cycle threshold: NK.	Type of feeding: NK. Symptoms: no. Infant positive: no.	Repeat BM sample negative (3 days postmaternal PCR test).
Zhu et al[26]	# mothers BM RT-PCR positive: 1. # BM samples tested: 2. # positive samples: 2.	3 days	NK	Genes tested: ORF1ab and N-gene. Cycle threshold: 38.2–38.5.	Type of feeding: NK. Symptoms: NK. Infant positive: NK.	Mother symptomatic at time of positive BM test.

*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.
#, number of; BF, breast feeding; BM, breastmilk; DoL, day of life; EBM, expressed breastmilk; 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.
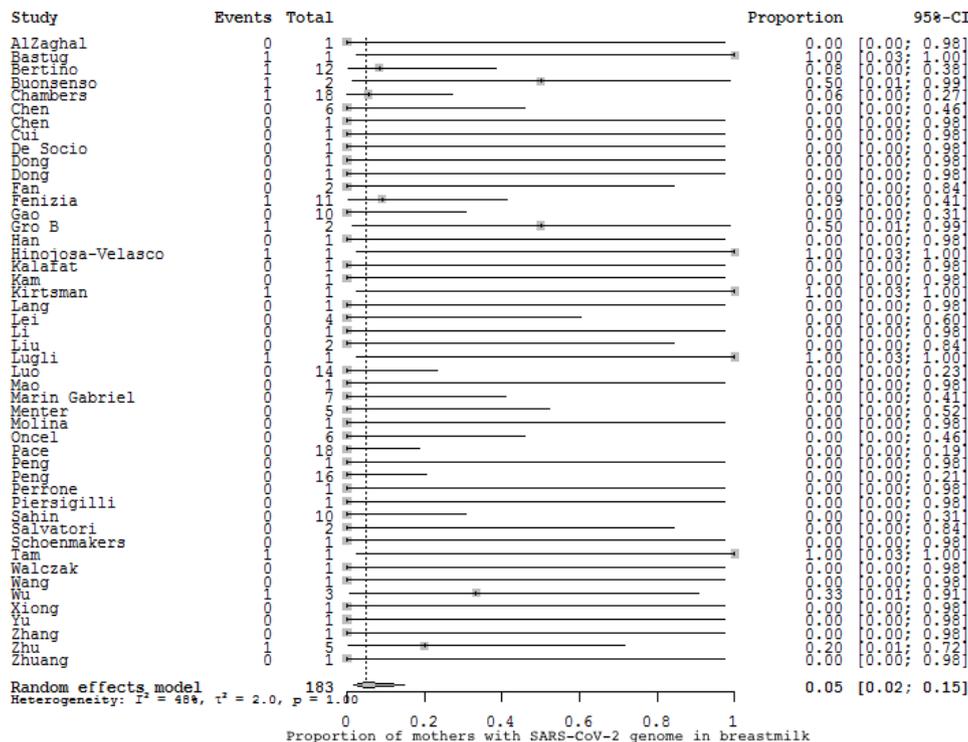
Figure 2 Meta-analysis of proportion of SARS-CoV-2 genome detection in breastmilk. Chen 1 (reference #7); Chen 2 (reference #8); Dong 1 (reference #11); Dong 2 (reference #12); Peng 1 (reference #34); Peng 2 (reference #35). All reference numbers are from the supplemental references in the online supplemental material.

figure 2). 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.[27] 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.[14 15 20 28–34] 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
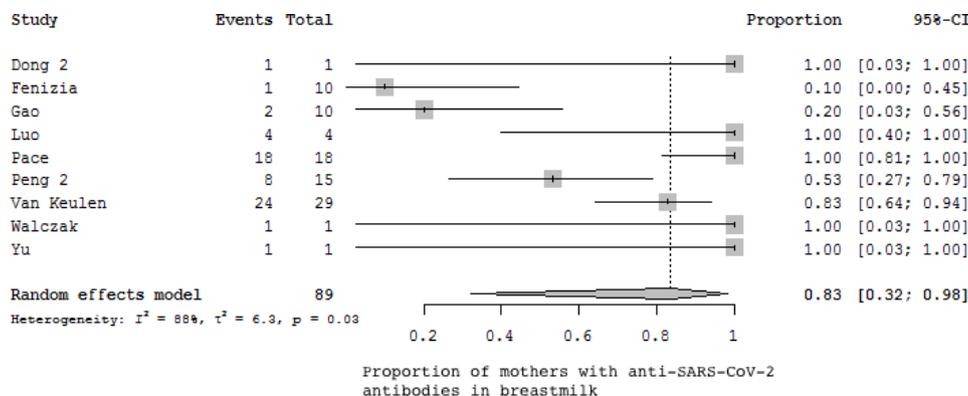

Figure 3 Meta-analysis of proportion of anti-SARS-CoV-2 genome detection in breastmilk. Dong 2 (reference #12); Peng 2 (reference #35). All reference numbers are from the supplemental references in the online supplemental material.

Table 2 Characteristics of studies with anti-SARS-CoV-2 antibodies detected in breastmilk

Author	Maternal characteristics	Time interval between maternal symptoms onset and Ig positive	Assay and immunoglobulin characteristics	Infant characteristics	Comments
Dong et al[28]	# mothers BM Ig positive: 1. # BM samples tested: 6. # positive samples: 6.	26 days	Assay method: ELISA. Antigen used: S-protein. Type of Ig: IgA and IgG.	Type of feeding: NK. Symptoms: no. Infant RT-PCR positive: no.	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.
Fenizia et al[20]	# mothers BM Ig positive: 1. # BM samples tested: 1. # positive samples: 1.	NK	Assay method: chemiluminescence immunoassay. Antigen used: nucleocapsid and S-protein. Type of Ig: IgG and IgM.	Type of feeding: NK. Symptoms: NK. Infant RT-PCR positive: no.	BM positive for both virus RNA and antibodies.
Gao et al[29]	# mothers BM Ig positive: 2. # BM samples tested: 2. # positive samples: 2.	17–22 days	Assay method: chemiluminescence immunoassay. Antigen used: NK. Type of Ig: IgG and IgM.	Type of feeding: BMS[1] and EBM.[1] Symptoms: NK. Infant RT-PCR positive: no.	Both infants had positive serum IgG, 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.)
Luo et al[30]	# 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 al[31]	# 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: BF[5] and MF.[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 al[32]	# 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 IgM negative at 47–72 days. IgM positive samples collected at 31±19 days and IgM negative samples at 43±21 days after symptom onset.†
Preβler et al[14]	# mothers BM Ig positive: 1. # BM samples tested: NK. # positive samples: 1.	NK	Assay method: NK. Antigen used: nucleocapsid. Type of Ig: IgG.	Type of feeding: NK. Symptoms: yes. Infant RT-PCR: no.	Maternal serum IgG positive 4–5 weeks after symptom onset. Infant RT-PCR and serum antibodies. negative.
Van Keulen et al[15]	# 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: NK. Infant RT-PCR: NK.	BM RT-PCR not tested. IgA present for at least 13 weeks from symptom onset.
Walczak et al[33]	# mothers BM Ig positive: 1. # BM samples tested: NK. # positive samples: NK.	NK	Assay method: microsphere immunoassay. Antigen used: NK. Type of Ig: IgA, IgG and IgM.	Type of feeding: NK. Symptoms: NK. Infant RT-PCR: no.	Author states immunoassay not validated, parent serum immunoglobulin IgG and IgM positive.
Yu et al[34]	# 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 Ig positive and Ig negative.
†No statistical difference found (Mann-Whitney U test, p=0.052).
#, number of; BF, breast feeding; BM, breastmilk; BMS, breastmilk substitute; DoL, day of life; Ig, immunoglobulin; NK, not known; RT-PCR, real time polymerase chain reactionPCR; 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.[35–38] In the cases of HIV and HTLV-1, breastmilk viral levels correlate with systemic viral load.[36 39] 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.[11 17 19 21] For primary HIV infection, elevated viral load in plasma, and presumably in breastmilk, were associated with an almost 30% postnatal transmission rate.[35] The mother-to-infant transmission rate for CMV via breastmilk has been reported to be 66%–96% among CMV-IgG positive mothers, with subsequent CMV positivity in 5.7%–58.6% of the infants.[37] These transmission rates are in stark contrast to our current estimates of a very low rate of SARS-CoV-2 RNA in breastmilk.

Coronaviruses typically cause the common cold in humans.[40] However, within the last two decades, more virulent strains have emerged: initially SARS-CoV-1 in 2003, followed by Middle Eastern Respiratory Syndrome (MERS-CoV) in 2012 and SARS-CoV-2 in 2019. Although transmission of SARS-CoV-1 or MERS-CoV via breastmilk has not been reported, this is likely due to a lack of testing. There are only two reports in which breastmilk was tested for SARS-CoV-1[41 42] and two reports of breastmilk testing for SARS-CoV-1 antibodies,[41 43] with one positive SARS-CoV-1 detected[42] and one positive antibody result.[41] To the best of our knowledge, there have been no reports of MERS-CoV in human breastmilk; however, this virus has been reported in the milk of dromedary camels resulting in a case of likely direct zoonosis through consumption of unpasteurised camel milk.[44]

Oligosaccharides, lactoferrin and immunoglobulins in breastmilk are some of the known protective agents against infection.[45] Infants who are not breast fed have a threefold increase in developing severe respiratory tract illnesses requiring hospitalisation compared with those who are exclusively breast fed for 4 months.[46] Antibodies may play an immune-protective role as they are present in milk (IgA, IgG and IgM), with IgA most abundant.[45] Breastmilk IgA and secretory IgA, which acts on the mucosal surfaces, have been linked to both decreased episodes of respiratory illness in infants of mothers who receive antenatal influenza vaccine and reduced maternal-to-child transmission of HIV-1 from infected mothers.[47 48] Anti-SARS-CoV-2 IgA antibodies have also demonstrated virus-neutralising properties in vitro.[15] Thus, in our review, where the presence of anti-SARS-CoV-2 antibodies in breastmilk are more commonly identified, with a predominance of IgA, there is a likelihood of potential immune protection of infants. However, the clinical impact of anti-SARS-CoV-2 antibodies in breastmilk is yet to be determined and further studies are required.

In nursing mothers, delineating the mode of transmission between intrapartum or postpartum infection through droplet or close contact proves challenging.[49] Bastug et al[16] 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[19] 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[50] 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[51] 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, in low-income and middle-income countries in 1 year.[52] 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, breast feeding should be recommended in mothers with SARS-CoV-2 after counselling and education regarding safe hygiene practices.

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