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.

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 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

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 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/).

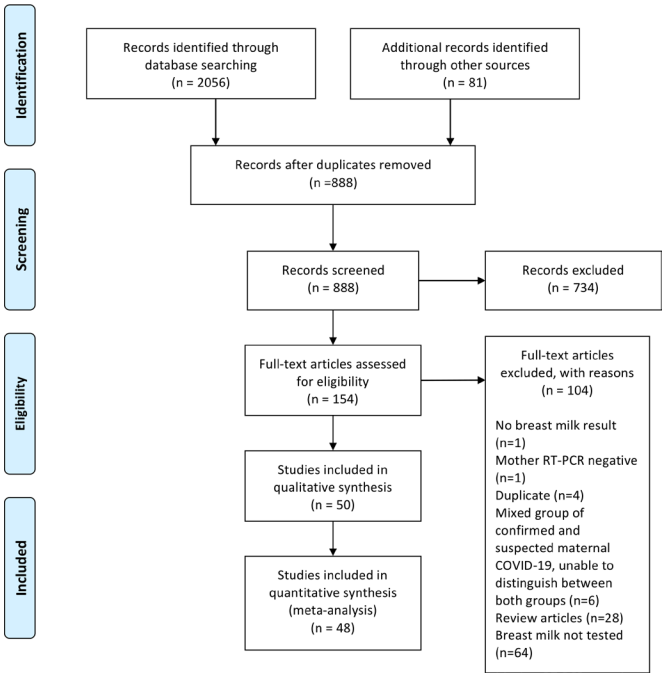

Figure 1 PRISMA flow diagram depicting search results. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

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.

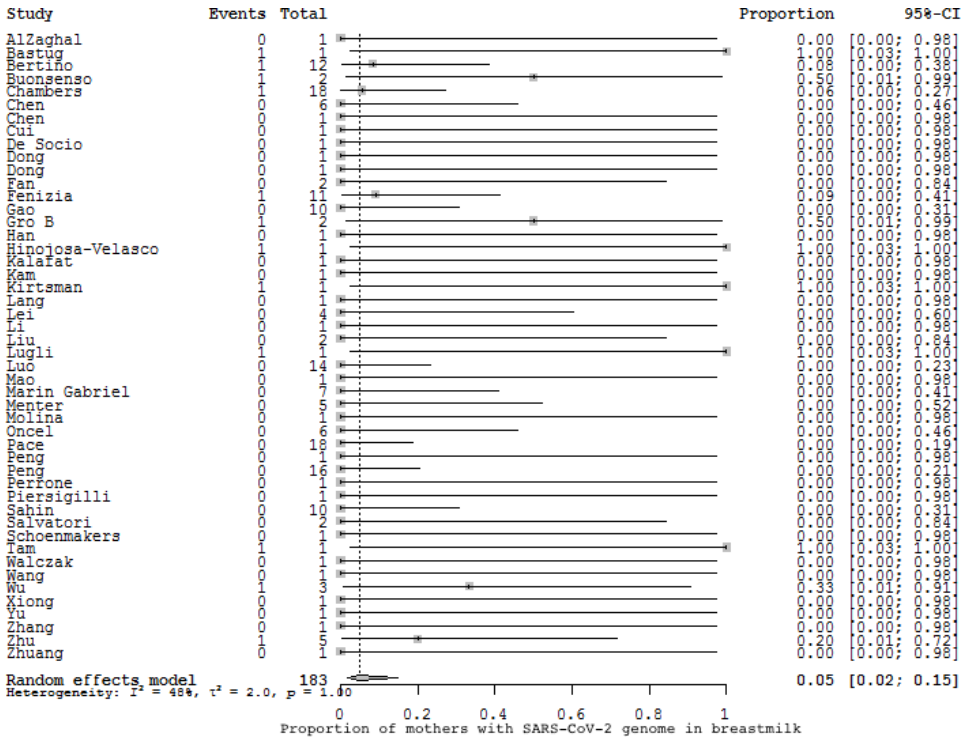

Figure 2 Meta-analysis of proportion of SARS-CoV-2 genome detection in breastmilk. Chen 1 (reference #7); Chen 2 (reference #8); Dong 1 (reference #11); Dong 2 (reference #12); Peng 1 (reference #34); Peng 2 (reference #35). All reference numbers are from the supplemental references in the online supplemental 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

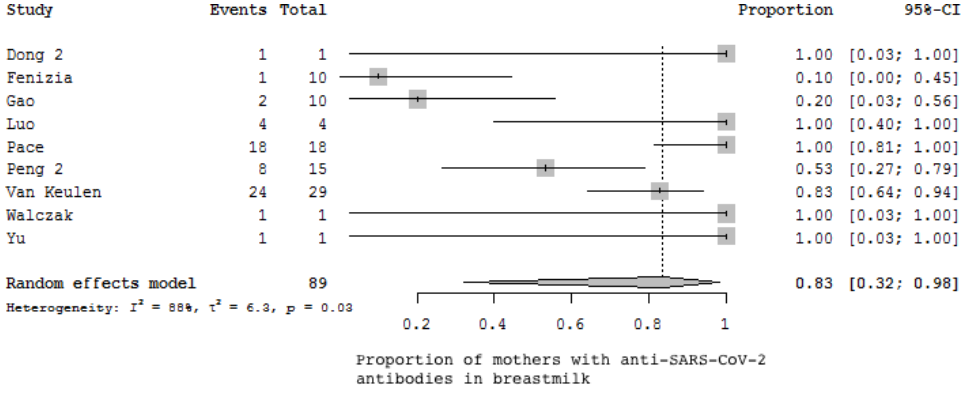

Figure 3 Meta-analysis of proportion of anti-SARS-CoV-2 genome detection in breastmilk. Dong 2 (reference #12); Peng 2 (reference #35). All reference numbers are from the supplemental references in the online supplemental material.

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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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. PSS conceptualised and designed the study, interpreted the data, oversaw the meta-analysis and revised the final draft of the manuscript.

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

Faith Zhu, Carlos Zozaya, Qi Zhou, Charmaine De Castro, Prakesh S. Shah

Supplemental Material

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eTable 1. Detailed Search Strategies

Database Searched	Search Strategy	
Ovid Medline(R) ALL	1	exp Coronavirus/
	2	exp Coronavirus Infections/
	3	(coronavirus* or corona virus* or corona virinae* or coronavirinae* or OC43 or NL63 or 229E or HKU1 or HCoV* or covid* or ncov* or coV or sars-cov* or sarscov* or Sars-coronavirus* or Severe Acute Respiratory Syndrome Coronavirus* or 2019-ncov or 2019-novel CoV or SARS-like coronavirus*).mp.
	4	((novel or new or nouveau) adj2 pandemi*).mp.
	5	((pneumonia or sars*).mp. or exp pneumonia/) and Wuhan.mp.
	6	(COVID-19 or severe acute respiratory syndrome coronavirus 2).os,ps,rs,ox,px,rx,nm.
	7	or/1-6
	8	exp Pregnancy/
	9	exp Pregnancy Complications/
	10	exp Pregnancy Outcome/
	11	exp Obstetrics/
	12	exp Breast Feeding/
	13	exp Maternal Health Services/
	14	exp Fetus/
	15	exp Fetal Therapies/
	16	exp Fetal Monitoring/
	17	exp Prenatal Diagnosis/
	18	exp Infant, Newborn/
	19	Pregnant Women/
	20	Infectious Disease Transmission, Vertical/
	21	Intensive Care Units, Neonatal/
	22	Intensive Care, Neonatal/
	23	(pregnan* or gestation* or parturition or neonatal* or neo natal* or neonate* or ante natal* or antenatal* or pre natal* or prenatal* or puerper* or postnatal* or postpartum or post partum or post natal* or peripartum or peri partum or intrapartum or intra partum or prepregnancy or pre pregnancy or preconception* or pre conception* or periconception* or peri conception* or preterm or premature or labo?r or eclamp* or preeclamp* or pre eclamp* or amniocentes* or chorion* vill* or breastfe* or breast fe* or lactation* or cesarean or caesarean or cesarian or caesarian or cesarien or caesarien or newborn* or new born* or tocoly* or fetal or foetal or fetus or foetus or miscarriage* or obstetric*).tw,kf,kw.
	24	((Vertical or Fetomaternal or Foetomaternal or Maternal-Fetal or Maternal Fetal or Maternal-Foetal or Maternal Foetal or Mother-To-Child or Mother to child) adj2 transmission*).tw,kf,kw.
	25	or/8-24
	26	antibodies/ or antibodies, viral/
	27	immunoglobulins/ or Immunoglobulin G/ or Immunoglobulin M/
	28	Oligosaccharides/
	29	Reverse Transcriptase Polymerase Chain Reaction/
	30	(antibod* or immunoglobulin* or oligosaccharide* or reverse transcription-polymerase chain reaction or RT-PCR).tw,kf,kw.
	31	or/26-30
	32	7 and 25 and 31
	33	breast feeding/ or breast milk expression/ or Milk, Human/
	34	(breastfe* or breast fe* or lactation* or breastmilk or milk).tw,kf,kw.
	35	33 or 34
	36	7 and 35
	37	32 or 36

	38	37 and 20190101:20301231.(dt). [Create Date starting from January 2019]
Embase Classic + Embase	1	exp Coronavirinae/
	2	exp Coronavirus infection/
	3	(coronavirus* or corona virus* or corona virinae* or coronavirinae* or OC43 or NL63 or 229E or HKU1 or HCoV* or covid* or ncov* or coV or sars-cov* or sarscov* or Sars-coronavirus* or Severe Acute Respiratory Syndrome Coronavirus* or 2019-ncov or 2019-novel CoV or SARS-like coronavirus*).mp.
	4	((novel or new or nouveau) adj2 pandemi*).mp.
	5	((pneumonia or sars*).mp. or exp pneumonia/) and Wuhan.mp.
	6	(COVID-19 or severe acute respiratory syndrome coronavirus 2).os,rs,ox,px.
	7	or/1-6
	8	exp pregnancy/
	9	exp pregnancy complication/
	10	exp pregnancy outcome/
	11	exp obstetrics/
	12	exp breast feeding/
	13	exp maternal health service/
	14	fetus/
	15	fetal therapy/
	16	exp fetus monitoring/
	17	exp prenatal diagnosis/
	18	newborn/
	19	pregnant woman/
	20	vertical transmission/
	21	neonatal intensive care unit/
	22	newborn intensive care/
	23	(pregnan* or gestation* or parturition or neonatal* or neo natal* or neonate* or ante natal* or antenatal* or pre natal* or prenatal* or puerper* or postnatal* or postpartum or post partum or post natal* or peripartum or peri partum or intrapartum or intra partum or prepregnancy or pre pregnancy or preconception* or pre conception* or periconception* or peri conception* or preterm or premature or labo?r or eclamp* or preeclamp* or pre eclamp* or amniocentes* or chorion* vill* or breastfe* or breast fe* or lactation* or cesarean or caesarean or cesarian or caesarian or cesarien or caesarien or newborn* or new born* or tocoly* or fetal or foetal or fetus or foetus or miscarriage* or obstetric*).tw,kw.
	24	((Vertical or Fetomaternal or Foetomaternal or Maternal-Fetal or Maternal Fetal or Maternal-Foetal or Maternal Foetal or Mother-To-Child or Mother to child) adj2 transmission*).tw,kw.
	25	or/8-24
	26	antibody/ or virus antibody/
	27	immunoglobulin/ or immunoglobulin g/ or immunoglobulin m/
	28	oligosaccharide/
	29	reverse transcription polymerase chain reaction/
	30	(antibod* or immunoglobulin* or oligosaccharide* or reverse transcription-polymerase chain reaction or RT-PCR).tw,kw.
	31	or/26-30
	32	7 and 25 and 31

	33	breast feeding/ or breast milk expression/ or breast milk/
	34	(breastfe* or breast fe* or lactation* or breastmilk or milk).tw,kw.
	35	33 or 34
	36	7 and 35
	37	32 or 36
	38	limit 37 to dc=20190101-20301231
Pubmed (non-Medline)	coronavirus[mh] or alphacoronavirus[mh] or alphacoronavirus 1[mh] or coronavirus, canine[mh] or coronavirus, feline[mh] or transmissible gastroenteritis virus[mh] or porcine respiratory coronavirus[mh] or coronavirus 229e, human[mh] or coronavirus nl63, human[mh] or porcine epidemic diarrhea virus[mh] or betacoronavirus[mh] or betacoronavirus 1[mh] or coronavirus oc43, human[mh] or coronavirus, bovine[mh] or coronavirus, rat[mh] or middle east respiratory syndrome coronavirus[mh] or murine hepatitis virus[mh] or sars virus[mh] or gammacoronavirus[mh] or coronavirus, turkey[mh] or infectious bronchitis virus[mh] OR coronavirus infections[mh] or enteritis, transmissible, of turkeys[mh] or feline infectious peritonitis[mh] or gastroenteritis, transmissible, of swine[mh] or severe acute respiratory syndrome[mh] OR coronavirus* or corona virus* or corona virinae* or coronavirinae* or OC43 or NL63 or 229E or HKU1 or HCoV* or covid* or ncov* or coV or sars-cov* or sarscov* or Sars-coronavirus* or Severe Acute Respiratory Syndrome Coronavirus* or 2019-ncov or 2019-novel CoV or SARS-like coronavirus*OR novel pandemic or novel pandemics or new pandemic or new pandemics or nouveau pandemic or nouveau pandemics OR pneumonia or sars* AND Wuhan OR COVID-19 or severe acute respiratory syndrome coronavirus 2 AND Pregnancy[mh] OR Pregnancy Complications[mh] OR Pregnancy Outcome[mh] OR Obstetrics[mh] OR (Breast Feeding[mh] OR Maternal Health Services[mh] OR Fetus[mh] OR Fetal Therapies[mh] OR Fetal Monitoring[mh] OR Prenatal Diagnosis[mh] OR Infant, Newborn[mh] OR Pregnant Women[mh] OR Infectious Disease Transmission, Vertical[mh] OR Intensive Care Units, Neonatal[mh] OR Intensive Care, Neonatal[mh] OR pregnancy[Title/Abstract] OR gestation[Title/Abstract] OR parturition[Title/Abstract] OR neonatal[Title/Abstract] OR neo natal[Title/Abstract] OR neonate[Title/Abstract] OR ante natal[Title/Abstract] OR antenatal[Title/Abstract] OR pre natal[Title/Abstract] OR prenatal[Title/Abstract] OR puerperium[Title/Abstract] OR postnatal[Title/Abstract] OR postpartum[Title/Abstract] OR post partum[Title/Abstract] OR post natal[Title/Abstract] OR peripartum[Title/Abstract] OR peri partum[Title/Abstract] OR intrapartum[Title/Abstract] OR intra partum[Title/Abstract] OR prepregnancy[Title/Abstract] OR pre pregnancy[Title/Abstract] OR preconception[Title/Abstract] OR pre conception[Title/Abstract] OR periconception[Title/Abstract] OR peri conception[Title/Abstract] OR preterm[Title/Abstract] OR premature[Title/Abstract] OR labour[Title/Abstract] OR eclamp[Title/Abstract] OR preeclamp[Title/Abstract] OR pre eclamp[Title/Abstract] OR amniocentesis[Title/Abstract] OR chorion villi[Title/Abstract] OR breastfeeding[Title/Abstract] OR breast feeding[Title/Abstract] OR lactation[Title/Abstract] OR cesarean[Title/Abstract] OR caesarean[Title/Abstract] OR cesarian[Title/Abstract] OR caesarian[Title/Abstract] OR cesarien[Title/Abstract] OR caesarien[Title/Abstract] OR newborn[Title/Abstract] OR new born[Title/Abstract] OR tocolytic[Title/Abstract] OR fetal[Title/Abstract] OR foetal[Title/Abstract] OR fetus[Title/Abstract] OR foetus[Title/Abstract] OR miscarriage[Title/Abstract] OR obstetrics[Title/Abstract])) OR (Vertical transmission[Title/Abstract] OR Fetomaternal transmission[Title/Abstract] OR Foetomaternal transmission[Title/Abstract] OR Maternal-Fetal transmission[Title/Abstract] OR Maternal Fetal transmission[Title/Abstract] OR Maternal-Foetal transmission[Title/Abstract] OR Maternal Foetal transmission[Title/Abstract] OR Mother-To-Child transmission[Title/Abstract] OR Mother to child transmission[Title/Abstract] AND antibodies[mh] OR antibodies, viral[mh] OR Immunoglobulins[mh] OR Immunoglobulin G[mh] OR Immunoglobulin M[mh] OR Oligosaccharides[mh] OR Reverse Transcriptase Polymerase Chain Reaction[mh] OR antibody[Title/Abstract] OR antibodies[Title/Abstract] OR immunoglobulin[Title/Abstract] OR oligosaccharide[Title/Abstract] OR reverse transcription-polymerase chain reaction[Title/Abstract] OR RT-PCR[Title/Abstract] OR coronavirus[mh] or alphacoronavirus[mh] or alphacoronavirus 1[mh] or coronavirus, canine[mh] or coronavirus, feline[mh] or transmissible gastroenteritis virus[mh] or porcine respiratory coronavirus[mh] or coronavirus 229e, human[mh] or coronavirus nl63, human[mh] or porcine epidemic diarrhea virus[mh] or betacoronavirus[mh] or betacoronavirus 1[mh] or coronavirus oc43, human[mh] or coronavirus, bovine[mh] or coronavirus, rat[mh] or middle east respiratory syndrome coronavirus[mh] or murine hepatitis virus[mh] or sars virus[mh] or gammacoronavirus[mh] or coronavirus, turkey[mh] or infectious bronchitis virus[mh]) OR (coronavirus infections[mh] or enteritis, transmissible, of turkeys[mh] or feline infectious peritonitis[mh] or gastroenteritis, transmissible, of swine[mh] or severe acute respiratory syndrome[mh] OR ((coronavirus* or corona virus* or corona virinae* or coronavirinae* or OC43 or NL63 or	

		229E or HKU1 or HCoV* or covid* or ncov* or coV or sars-cov* or sarscov* or Sars-coronavirus* or Severe Acute Respiratory Syndrome Coronavirus* or 2019-ncov or 2019-novel CoV or SARS-like coronavirus* OR (novel pandemic or novel pandemics or new pandemic or new pandemics or nouveau pandemic or nouveau pandemics OR pneumonia or sars* AND Wuhan OR COVID-19 or severe acute respiratory syndrome coronavirus 2 AND breast feeding[mh] OR breast milk expression[mh] OR Milk, Human[mh] OR breastfeeding or breast feeding or lactation or breastmilk or milk AND (pubstatusaheadofprint OR publisher[sb] OR in process[sb] OR pubmednotmedline[sb])) AND "2019/01/01"[CRDT] : "3000"[CRDT] OR ("2019/01/01"[EDAT] : "3000"[EDAT]) OR "2019/01/01"[MHDA] : "3000"[MHDA]
Web of Science	**Set**	
	# 18	#16 OR #12 **Refined by: PUBLICATION YEARS:** (2020 OR 2019) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*
	# 17	#16 OR #12 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*
	# 16	#15 AND #6 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*
	# 15	#14 OR #13 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*
	# 14	TS=(breastfe* or breast feed* or breast fed or lactation* or breastmilk or milk) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*
	# 13	TS=("breast feeding" OR "breast milk expression" OR "Human Milk") *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*
	# 12	#11 AND #10 AND #6 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*
	# 11	TS=(Antibod* OR Immunoglobulin* OR Oligosaccharide* OR "Reverse Transcriptase Polymerase Chain Reaction") *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*
	# 10	#9 OR #8 OR #7 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*
	# 9	TS=((Vertical or Fetomaternal or Foetomaternal or Maternal-Fetal or "Maternal Fetal" or Maternal-Foetal or "Maternal Foetal" or Mother-To-Child or "Mother to child") NEAR/1 transmission*) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*
	# 8	TS=(pregnan* or gestation* or parturition or neonatal* or neonate* or antenatal* or prenatal* or puerper* or postnatal* or postpartum or post partum or post natal* or peripartum or peri partum or intrapartum or intra partum or prepregnancy or pre pregnancy or preconception* or periconception* or peri conception* or preterm or premature or labo?r or eclamp* or preeclamp* or amniocentes* or chorion* vill* or breastfe* or breast fed or lactation* or cesarean or caesarean or cesarian or caesarian or cesarien or caesarien or newborn* or tocoly* or fetal or foetal or fetus or foetus or miscarriage* or obstetric*) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*
	# 7	TS=(Pregnancy OR "Pregnancy Complications" OR "Pregnancy Outcome" OR Obstetrics OR "Breast Feeding" OR "Maternal Health Services" OR Fetus OR "Fetal Therapies" OR "Fetal Monitoring" OR "Prenatal Diagnosis" OR Newborn OR Pregnant Women OR "Vertical Transmission") *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*
	# 6	#5 OR #4 OR #3 OR #2 OR #1

		Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years
	# 5	TS=((pneumonia or sars*) AND Wuhan) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*
	# 4	TS=((novel or new or nouveau) NEAR/1 pandemi*) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*
	# 3	TS=(coronavirus* or corona virus* or corona virinae* or coronavirinae* or OC43 or NL63 or 229E or HKU1 or HCoV* or covid* or ncov* or coV or sars-cov* or sarscov* or Sars-coronavirus* or "Severe Acute Respiratory Syndrome Coronavirus*" or "2019-ncov" or "2019-novel CoV" or "SARS-like coronavirus*") *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*
	# 2	TS=Coronavirus Infections *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*
	# 1	TS=Coronavirus *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*
Scopus	coronavirus* OR "corona virus*" OR "corona virinae*" OR coronavirinae* OR oc43 OR nl63 OR 229e OR hku1 OR hcov* OR covid* OR ncov* OR cov OR sars-cov* OR sarscov* OR sars-coronavirus* OR "Severe Acute Respiratory Syndrome Coronavirus*" OR 2019-ncov OR "2019-novel cov" OR "SARS-like coronavirus*" OR novel OR new OR nouveau W/1 pandemi* OR pneumonia OR sars* AND wuhan AND pregnan* or gestation* or parturition or neonatal* or "neo natal*" or neonate* or "ante natal*" or antenatal* or "pre natal*" or prenatal* or puerper* or postnatal* or postpartum or "post partum" or "post natal*" or peripartum or "peri partum" or intrapartum or "intra partum" or prepregnancy or "pre pregnancy" or preconception* or "pre conception*" or periconception* or peri conception* or preterm or premature or labo?r or eclamp* or preeclamp* or "pre eclamp*" or amniocentes* or "chorion* vill*" or breastfe* or "breast fe*" or lactation* or cesarean or caesarean or cesarian or caesarian or cesarien or caesarien or newborn* or "new born*" or tocoly* or fetal or foetal or fetus or foetus or miscarriage* or obstetric* OR Vertical or F?etomaternal or Maternal-F?etal or "Maternal F?etal" or Mother-To-Child or "Mother to child" W/1 transmission* AND antibod* OR immunoglobulin* or oligosaccharide* or "reverse transcription-polymerase chain reaction" or RT-PCR OR coronavirus* OR "corona virus*" OR "corona virinae*" OR coronavirinae* OR oc43 OR nl63 OR 229e OR hku1 OR hcov* OR covid* OR ncov* OR cov OR sars-cov* OR sarscov* OR sars-coronavirus* OR "Severe Acute Respiratory Syndrome Coronavirus*" OR 2019-ncov OR "2019-novel cov" OR "SARS-like coronavirus*" OR novel OR new OR nouveau W/1 pandemi* OR pneumonia OR sars* AND wuhan AND breastfe* or "breast fe*" or lactation* or breastmilk or milk AND (LIMIT-TO (PUBYEAR,2020) OR LIMIT-TO (PUBYEAR,2019)	

This table outlines the literature search strategy we used in our systematic review to assess the presence of SARS-CoV-2 virus and antibodies in breast milk.
Search strategies are listed.
There were no restrictions to publication status or language.
All searches were run from inception to October 7, 2020, and filtered to articles since January 2019.

eTable 2. Characteristics of Included Studies

Author Type of Publication Country	Maternal Characteristics	Infant Characteristics	Type of Feed Given	Testing of Breast Milk	Comments
AlZaghal et al(1) Case report Jordan	Number of confirmed mothers: 1 Trimester of infection: 3rd Symptomatic at birth: Yes Detected by: RT-PCR Mode of birth: CS Antiviral medication: No	Number of infants: 1 BW: 2500g GA: 36^{+3} Symptomatic: No RT-PCR: Negative Immunoglobulin: ND	BMS & BM	Number of mothers tested: 1 Number of milk samples tested: 1 DoL at test: NK Type of test: RT-PCR Results: Negative	Infant received BMS until breast milk RT-PCR was negative.
Bastug et al(2) Case report Turkey	Number of confirmed mothers: 1 Trimester of infection: 3rd Symptomatic at birth: No Detected by: RT-PCR Mode of birth: VB Antiviral medication: No	Number of infants: 1 BW: 2980g GA: 39 weeks Symptomatic: No RT-PCR: Positive Immunoglobulin: ND	EBM & BF as of DoL 6	Number of mothers tested: 1 Number of milk samples tested: 3 DoL at test: 1 (8 hours), 4 & 5 Type of test: RT-PCR Results: All 3 samples positive	Asymptomatic mother. Infant tested negative at 8 hours of age, separated from mother at birth, but received EBM until DoL 2. Infant repeat test on DoL 4 positive. See table 1 for more details
Bertino et al(3) Case series (Preprint) Italy	Number of confirmed mothers: 12 Trimester of infection: 3rd trimester (9), PN (3) Symptomatic at birth: Yes in 10 Detected by: RT-PCR Mode of birth: CS (7), VB (5) Antiviral medication NK	Number of infants: 12 BW: NK GA: 30-41 weeks Symptomatic: No RT-PCR: Positive in 4 Immunoglobulin: ND	BF (11), BMS (1)	Number of mothers tested: 12 (1 mother tested positive) Number of milk samples tested: NK DoL at test: NK Type of test: RT-PCR Results: Positive (3/6 samples)	See table 1 for more details

Author Type of Publication Country	**Maternal Characteristics**	**Infant Characteristics**	**Type of Feed Given**	**Testing of Breast Milk**	**Comments**
Buonsenso et al[a] (4, 5) Case series Italy	Number of confirmed mothers: 7 Trimester of infection: 3rd trimester (2) Symptomatic at birth: NK Detected by: RT-PCR Mode of birth: CS Antiviral medication: Yes	Number of infants: 2 BW: 2300-3390g GA: 35^{+5} – 38^{+3} weeks Symptomatic: No RT-PCR: Positive in 1 Immunoglobulin: ND	Both BMS in hospital, BF (1), EBM (1) at home	Number of mothers tested: 2 (1 mother tested positive) Number of milk samples tested: 20 DoL at test: 1-17 Type of test: RT-PCR Results: Positive (3/20 samples)	Only 2/7 mothers delivered during study period, one spontaneous abortion at 8 weeks. Both infants tested negative at birth. Infant 1 received BMS in hospital and BF at home had positive test on DoL 15. BM for this infant tested negative. Infant 2 tested negative throughout, received BMS in hospital and after discharge home, EBM was given. BM initially tested positive but negative from DoL 5. EBM given after negative tests.
Chambers et al(6) Case series USA	Number of confirmed mothers: 18 Trimester of infection: NK Symptomatic at birth: NK Detected by: RT-PCR Mode of birth: NK Antiviral medication: NK	Number of infants: 18 BW: NK GA: NK Symptomatic: Yes in 13 RT-PCR: Positive in 2 Immunoglobulin: ND	NK	Number of mothers tested: 18 (1 mother tested positive) Number of milk samples tested: 64 DoL at test: NA Type of test: RT-PCR Results of test: Positive (1/64 samples)	Infants' age at sample collection between <1 and 25 months. BM tested negative for infants who tested positive. BM RT-PCR positive before maternal test confirmed. Viral cultures (26 samples from 9 mothers) all negative.

Author Type of Publication Country	**Maternal Characteristics**	**Infant Characteristics**	**Type of Feed Given**	**Testing of Breast Milk**	**Comments**
Chen et al(7) Case series China	Number of confirmed mothers: 9 Trimester of infection: 3rd Symptomatic at birth: Yes Detected by: RT-PCR Mode of birth: CS Antiviral medication: NK	Number of infants: 9 BW: 1880-3730g GA: 36^{+0}- 39^{+4} weeks Symptomatic: No RT-PCR: All negative Immunoglobulin: ND	NK	Number of mothers tested: 6 Number of milk samples tested: NK DoL at test: NK Type of test: RT-PCR Results: All Negative	One infant had elevated myocardial enzymes on day of birth but remained asymptomatic
Chen et al(8) Case series China	Number of confirmed mothers: 3 Trimester of infection: 3rd (1) Symptomatic at birth: No Detected by: RT-PCR Mode of birth: CS Antiviral medication: Yes	Number of infants: 1 BW: 2670g GA: 35^{+4} Symptomatic: NK RT-PCR: Negative Immunoglobulin: ND	NK	Number of mothers tested: 1 Number of milk samples tested: NK DoL at test: 2 Type of test: RT-PCR Results: Negative	
Cui et al(9) Case report China	Number of confirmed mothers: 1 Trimester of infection: PN Symptomatic at birth: NA Detected by: RT-PCR Mode of birth: NK Antiviral medication: NA	Number of infants: 1 BW: NA GA: NA Symptomatic: Yes RT-PCR: Positive Immunoglobulin: Positive	MF	Number of mothers tested: 1 Number of milk samples tested: 3 DoL at test: 61-63 days Type of test: RT-PCR Results: Negative	Infant unwell at DoL 55 with pneumonia requiring nasal oxygen in hospital. Serum IgM mildly elevated. Also had elevated cardiac and liver enzymes.
De Socio et al(10) Case report Italy	Number of confirmed mothers: 1 Trimester of infection: 3rd Symptomatic at birth: No	Number of infants: 1 BW: NK GA: NK Symptomatic: No	NK	Number of mothers tested: 1 Number of milk samples tested: 1 DoL at test: 2 Type of test: RT-PCR	Mother had positive serum IgG and weakly positive IgM after delivery.

Author Type of Publication Country	**Maternal Characteristics**	**Infant Characteristics**	**Type of Feed Given**	**Testing of Breast Milk**	**Comments**
	Detected by: RT-PCR Mode of birth: VB Antiviral medication: No	RT-PCR: Negative Immunoglobulin: ND		Results: Negative	
Dong et al(11) Case report China	Number of confirmed mothers: 1 Trimester of infection: 3rd Symptomatic at birth: NK Detected by: RT-PCR Mode of birth: CS Antiviral medication: Yes	Number of infants: 1 BW: 3120g GA: 37^{+6} weeks Symptomatic: No RT-PCR: Negative Immunoglobulin: Positive	NK	Number of mothers tested: 1 Number of milk samples tested: 1 DoL at test: 7 Type of test: RT-PCR Results: Negative	Mother tested positive 23 days before delivery. Infant IgG and IgM levels positive at 2 hours of age, with negative PCR.
Dong et al(12) Case report China	Number of confirmed mothers: 1 Trimester of infection: 3rd Symptomatic at birth: NK Detected by: RT-PCR Mode of birth: VB Antiviral medication: No	Number of infants: 1 BW: 2950g GA: 38+2 weeks Symptomatic: No RT-PCR: Negative Immunoglobulin: Yes	NK	Number of mothers tested: 1 Number of milk samples tested: 6 DoL at test: 12 Type of test: RT-PCR and antibody assay Results of test: PCR negative, Positive IgG (6/6), Positive IgA (4/6)	Infant serum IgG antibody positive. See table 2 for more details
Fan et al(13) Case series China	Number of confirmed mothers: 2 Trimester of infection: 3rd Symptomatic at birth: 1 Detected by: RT-PCR Mode of birth: CS	Number of infants: 2 BW: 2890-3400g GA: 36^{+5}-38^{+1} weeks Symptomatic: Yes RT-PCR: All negative Immunoglobulin: ND	NK	Number of mothers tested: 2 Number of milk samples tested: NK DoL at test: 2 Type of test: RT-PCR Results: All negative	Both infants had respiratory symptoms and lymphopenia, one had low-grade fever.

Author Type of Publication Country	Maternal Characteristics	Infant Characteristics	Type of Feed Given	Testing of Breast Milk	Comments
	Antiviral medication: Yes				
Fenizia et al(14) Case series Italy	Number of confirmed mothers: 31 Trimester of infection: 3rd Symptomatic at birth: NK Detected by: RT-PCR Mode of birth: VB (25), CS (6) Antiviral medication: 8	Number of infants: 31 BW: 2180-4165g GA: NK (1 preterm) Symptomatic: RT-PCR: Positive in 2 Immunoglobulin: IgG in 12, IgM in 1 (cord blood)		Number of mothers tested: 11 for RT-PCR, 10 for IgG & IgM (1 mother positive) Number of milk samples tested: RT-PCR (11), IgG (10), IgM (10) DoL at test: 5 Type of test: RT-PCR, IgG, IgM Results: Positive both RT-PCR and IgM. Negative IgG	One mother tested positive for both RT-PCR and IgM in BM. IgG was negative. Infant tested negative. All infants reported to be healthy
Gao et al(15) Case series China	Number of confirmed mothers: 12 Trimester of infection: 3rd Symptomatic at birth: NK Detected by: RT-PCR Mode of birth: VB (2), CS (12) Antiviral medication: NK	Number of infants: 14 BW: 2700-4120g GA: 36^{+4}-41^{+1} weeks RT-PCR: All negative Immunoglobulin: IgG in 4 (1 cord blood), IgM in 1	BMS, EBM, BF	Number of mothers tested: 10 Number of milk samples tested: 10 DoL at test: NK Type of test: RT-PCR, IgG, IgM Results: RT-PCR all negative and IgG positive (2/10), IgM positive in (2/10)	Both infants had serum Ig positive (see table 2). Third mother with positive IgM in BM only did not have confirmed RT-PCR in throat swab.
Groβ et al(16) Case series Germany	Number of confirmed mothers: 2 Trimester of infection: PN Symptomatic at birth: No	Number of infants: 2 BW: NK GA: NK Symptomatic: Yes (2)	BF	Number of mothers tested: 2 (1 mother tested positive) Number of milk samples tested: 11	Infants tested positive on DoL 9 and 10. See table 1 for more details.

Author Type of Publication Country	**Maternal Characteristics**	**Infant Characteristics**	**Type of Feed Given**	**Testing of Breast Milk**	**Comments**
	Detected by: RT-PCR Mode of birth: NK Antiviral medication: No	RT-PCR: Positive (2) Immunoglobulin: ND		DoL at test: 9-25 Type of test: RT-PCR Results: 4/11 samples positive	
Han et al(17) Case report South Korea	Number of confirmed mothers: 1 Trimester of infection: PN Symptomatic at birth: NA Detected by: RT-PCR Mode of birth: VB Antiviral medication: NA	Number of infants: 1 BW: 2730g GA: 38^{+6} weeks Symptomatic: Yes RT-PCR: Positive Immunoglobulin: ND	BF	Number of mothers tested: 1 Number of milk samples tested: NK DoL at test: NA Type of test: RT-PCR Results: Negative	Infant was 27 days old, had fever, tachycardia and vomiting. No respiratory distress or need for oxygen.
Hinojosa-Velasco et al(18) Case report Mexico	Number of confirmed mothers: 1 Trimester of infection: 3^{rd} Symptomatic at birth: Yes Detected by: RT-PCR Mode of birth: CS Antiviral medication: NK	Number of infants: 1 BW: 3075g GA: 38 Symptomatic: No RT-PCR: Positive Immunoglobulin: NK	BMS, BF	Number of mothers tested: 1 Number of milk samples tested: 2 DoL at test: 4 & 13 Type of test: RT-PCR Results: Positive (on DoL 4), Negative DoL 13	Maternal BM given only after infant tested positive
Kalafat et al(19) Case report Turkey	Number of confirmed mothers: 1 Trimester of infection: 3^{rd} Symptomatic at birth: Yes Detected by: RT-PCR Mode of birth: CS Antiviral medication: NK	Number of infants: 1 BW: 2790g GA: 36+1 Symptomatic: NL RT-PCR: NK Immunoglobulin: NK	NK	Number of mothers tested: 1 Number of milk samples tested: 1 DoL at test: NK Type of test: RT-PCR Results: Negative RT-PCR	

Author Type of Publication Country	**Maternal Characteristics**	**Infant Characteristics**	**Type of Feed Given**	**Testing of Breast Milk**	**Comments**
Kam et al(20) Case report Singapore	Number of confirmed mothers: 1 Trimester of infection: PN Symptomatic at birth: NA Detected by: RT-PCR Mode of birth: NK Antiviral medication: NA	Number of infants: 1 BW: NA GA: NA Symptomatic: Yes RT-PCR: Positive Immunoglobulin: Positive	NK	Number of mothers tested: 1 Number of milk samples tested: NK DoL at test: 6 months Type of test: RT-PCR Results: Negative	6 month age infant with one episode of fever at time of positive testing. No respiratory support required.
Kirtsman et al(21) Case report Canada	Number of confirmed mothers: 1 Trimester of infection: 3rd Symptomatic at birth: Yes Detected by: RT-PCR Mode of birth: CS Antiviral medication: No	Number of infants: 1 BW: 2930g GA: 35^{+5} weeks Symptomatic: Yes RT-PCR: Positive Immunoglobulin: ND	BF	Number of mothers tested: 1 Number of milk samples tested: 1 DoL at test: 2 & 7 Type of test: RT-PCR Results: Positive (1/2 samples)	Infant was neutropenic and had mild hypothermia and feeding difficulties. Required NICU stay for management of hypoglycaemia. See table 1 for more details
Lang et al(22) Case report China	Number of confirmed mothers: 1 Trimester of infection: 3rd Symptomatic at birth: Yes Detected by: RT-PCR Mode of birth: CS Antiviral medication: Yes	Number of infants: 1 BW: NK GA: 35^{+4} weeks Symptomatic: No RT-PCR: Negative Immunoglobulin: ND	NK	Number of mothers tested: 1 Number of milk samples tested: NK DoL at test: 2 Type of test: RT-PCR Results: Negative	
Lei et al(23) Case series China	Number of confirmed mothers: 9 Trimester of infection: 2nd trimester (4), 3rd trimester	Number of infants: 4 BW: 2350-3400g GA: 34^{+2} – 37 weeks Symptomatic: No	NK	Number of mothers tested: 4 Number of milk samples tested: 4 DoL at test: NK Type of test: RT-PCR	Only 4/9 mothers delivered during the study period. One pregnancy was terminated.

Author Type of Publication Country	Maternal Characteristics	Infant Characteristics	Type of Feed Given	Testing of Breast Milk	Comments
	(5) Symptomatic at birth: No Detected by: RT-PCR Mode of birth: CS (3), VB (1) Antiviral medication: Yes	RT-PCR: All negative Immunoglobulin: ND		Results: All negative	
Li et al(24) Case report China	Number of confirmed mothers: 1 Trimester of infection: 3rd Symptomatic at birth: No Detected by: RT-PCR Mode of birth: CS Antiviral medication: Yes	Number of infants: 1 BW: NK GA: 35^{+2} weeks Symptomatic: No RT-PCR: Negative Immunoglobulin: ND	NK	Number of mothers tested: 1 Number of milk samples tested: 3 DoL at test: 1-3 Type of test: RT-PCR Results: Negative	
Liu et al(25) Case series (Preprint) China	Number of confirmed mothers: 3 Trimester of infection: 3rd Symptomatic at birth: Yes (2), No (1) Detected by: RT-PCR Mode of birth: CS (2), VB (1) Antiviral medication: Yes (PN)	Number of infants: 3 BW: 3250-3670g GA: 38^{+4} – 40 weeks Symptomatic: No RT-PCR: All negative Immunoglobulin: ND	NK	Number of mothers tested: 2 Number of milk samples tested: 4 DoL at test: 1-11 Type of test: RT-PCR Results: All negative	Mothers received postpartum antiviral medication
Lugli et al(26) Case report	Number of confirmed mothers: 1 Trimester of infection: PN Symptomatic at birth: No	Number of infants: 1 BW: 1614g GA: 32 weeks Symptomatic: No	EBM	Number of mothers tested: 1 Number of milk samples tested: 2 DoL at test: 9 Type of test: RT-PCR	First sample taken without any precautions, second taken with strict precautions

Author Type of Publication Country	**Maternal Characteristics**	**Infant Characteristics**	**Type of Feed Given**	**Testing of Breast Milk**	**Comments**
	Detected by: RT-PCR Mode of birth: CS Antiviral medication: No	RT-PCR: Negative Immunoglobulin: Negative		Results: RT-PCR positive (both samples)	
Luo et al(27) Cohort study (Preprint) China	Number of confirmed mothers: 14 Trimester of infection: 3rd trimester (12), PN (2) Symptomatic at birth: NK Detected by: RT-PCR Mode of birth: CS (12), VB (2) Antiviral medication: Yes (6)	Number of infants: 14 BW: NK GA: NK (3 preterm) Symptomatic: No RT-PCR: All negative Immunoglobulin: ND	BF (1), AF (13)	Number of mothers tested: 14 RT-PCR, 4 antibodies Number of milk samples tested: 14 DoL at test: 1-15 days Type of test: RT-PCR and ELISA Results: PCR all Negative, IgG Negative, IgM Positive (4)	Four confirmed mothers had both serum and BM antibody testing. 3/4 had positive serum IgG and IgM before delivery and 4/4 had positive serum IgM post-delivery. See table 2 for details.
Mao et al(28) Case report China	Number of confirmed mothers: 1 Trimester of infection: PN Symptomatic at birth: NA Detected by: RT-PCR Mode of birth: NA Antiviral medication: NA	Number of infants: 1 BW: NK GA: NK Symptomatic: Yes RT-PCR: Positive Immunoglobulin: ND	BF	Number of mothers tested: 1 Number of milk samples tested: NK DoL at test: 14 months Type of test: RT-PCR Results: Negative	14 month old child with fever and coryza
Marín Gabriel et al(29) Case series Spain	Number of confirmed mothers: 7 Trimester of infection: 3rd Symptomatic at birth: Yes (1) Detected by: RT-PCR	Number of infants: 7 BW: 2866-4574g GA: 38^{+3} – 41^{+2} weeks Symptomatic: No RT-PCR: All negative Immunoglobulin: ND	NK	Number of mothers tested: 7 Number of milk samples tested: 7 DoL at test: 2 Type of test: RT-PCR Results: Negative	Samples collected were colostrum

Author Type of Publication Country	**Maternal Characteristics**	**Infant Characteristics**	**Type of Feed Given**	**Testing of Breast Milk**	**Comments**
	Mode of birth: VB (6), CS (1) Antiviral medication: No				
Menter et al(30) Case series Switzerland	Number of confirmed mothers: 5 Trimester of infection: 3rd Symptomatic at birth: Yes (1) Detected by: RT-PCR Mode of birth: VB (3), CS (2) Antiviral medication: No	Number of infants: 5 BW: 2790-3500g GA: 39^{+0} – 40^{+5} weeks Symptomatic: Yes (1) RT-PCR: NK Immunoglobulin: ND	BF (2) MF (3)	Number of mothers tested: 5 Number of milk samples tested: 5 DoL at test: NK Type of test: RT-PCR Results: Negative	One infant had hypothermia
Molina et al(31) Case report USA	Number of confirmed mothers: 1 Trimester of infection: 3rd Symptomatic at birth: No Detected by: RT-PCR Mode of birth: VB Antiviral medication: No	Number of infants: 1 BW: 3810g GA: 38^{+1} weeks Symptomatic: No RT-PCR: Negative Immunoglobulin: Yes	NK	Number of mothers tested: 1 Number of milk samples tested: NK DoL at test: NK Type of test: RT-PCR Results of test: Negative	First maternal positive PCR and symptoms at 28^{+2} weeks, and remained positive for 104 days. Cord blood positive for IgG antibodies.
Oncel et al(32) Cohort study Turkey	Number of confirmed mothers: 125 Trimester of infection: NK Symptomatic at birth: NK Detected by: RT-PCR Mode of birth: CS (89), VB	Number of infants: 125 BW: 1480-3415g GA: 26-39 weeks Symptomatic: Yes in 3 RT-PCR: Positive in 4 Immunoglobulin: ND	BF (9), EBM (45), BMS (71)	Number of mothers tested: 6 Number of milk samples tested: 6 DoL at test: NK Type of test: RT-PCR Results: Negative	Positive test on 3/4 infants on DoL 2-5, 1/4 infant positive on DoL 1.Three infants required CPAP. All 4 became negative on DoL 6-11. None of these 4 infants received BF/EBM.

Author Type of Publication Country	Maternal Characteristics	Infant Characteristics	Type of Feed Given	Testing of Breast Milk	Comments
	(36) Antiviral medication: NK				
Pace et al(33) Case series (Preprint) USA	Number of confirmed mothers: 18 Trimester of infection: NK Symptomatic at birth: NK Detected by: RT-PCR Mode of birth: CS (6), VB (12) Antiviral medication: NK	Number of infants: 18 BW: 3372 ± 560g GA: 38.6 ± 1.7 weeks Symptomatic: NK RT-PCR: Positive in 2 Immunoglobulin: ND	BF (5), MF (13)	Number of mothers tested: 18 Number of milk samples tested: 37 DoL at test: NK Type of test: RT-PCR, IgA, IgG Results: PCR Negative, IgA Positive (37/37 samples), IgM Positive (37/37 samples)	See table 2 for more details.
Peng et al(34) Case report China	Number of confirmed mothers: 1 Trimester of infection: 3rd Symptomatic at birth: NK Detected by: RT-PCR Mode of birth: CS Antiviral medication: Yes	Number of infants: 1 BW: 2600g GA: 35^{+3} weeks Symptomatic: Yes RT-PCR: Negative Immunoglobulin: ND	NK	Number of mothers tested: 1 Number of milk samples tested: 8 DoL at test: 2-14 Type of test: RT-PCR Results: Negative	Infant presented with respiratory distress after birth requiring CPAP and surfactant.
Peng et al(35) Cohort study (Preprint) China	Number of confirmed mothers: 24 Trimester of infection: 3rd trimester (2), PN (22) Symptomatic at birth: Yes in	Number of infants: 25 BW: 3000 ± 500g GA: 38.2 ± 2.1 weeks Symptomatic: No RT-PCR: NK	BF (1), BMS (10), MF (13)	Number of mothers tested: 16 RT-PCR, 15 antibodies (8 mothers tested positive) Number of milk samples tested: 44 (RT-PCR), 38 (antibodies)	Milk samples were collected from confirmed cases. Total 44 samples were tested but only 38 samples underwent both RT-PCR and ELISA tests.

Author Type of Publication Country	Maternal Characteristics	Infant Characteristics	Type of Feed Given	Testing of Breast Milk	Comments
	15 Detected by: RT-PCR Mode of birth: CS (19), VB (5) Antiviral medication: NK	Immunoglobulin: ND		DoL at test: 3-70 days Type of test: RT-PCR, ELISA Results: PCR Negative, IgG Negative, IgM Positive (21/38 samples)	See table 2 for more details
Perrone et al(36) Case report Italy	Number of confirmed mothers: 1 Trimester of infection: PN Symptomatic at birth: No Detected by: RT-PCR Mode of birth: NK Antiviral medication: NA	Number of infants: 1 BW: NK GA: 32 weeks Symptomatic: NK RT-PCR: Negative Immunoglobulin: ND	EBM & BF	Number of mothers tested: 1 Number of milk samples tested: 1 DoL at test: 13 Type of test: RT-PCR Results: Negative	Mother developed symptoms 11 days postpartum. Infant was premature and required 24 hours of CPAP at birth.
Piersigilli et al(37) Case report Belgium	Number of confirmed mothers: 1 Trimester of infection: PN Symptomatic at birth: Yes Detected by: RT-PCR Mode of birth: CS Antiviral medication: No	Number of infants: 1 BW: 960g GA: 26^{+4} weeks Symptomatic: No RT-PCR: Positive Immunoglobulin: ND	EBM	Number of mothers tested: 1 Number of milk samples tested: 1 DoL at test: NK Type of test: RT-PCR Results: Negative	First neonatal test at DoL 7, positive on repeat on DoL 14 but negative at DoL 21. Infant had leucopenia and lymphopenia.
Preβler et al(38) Case series Germany	Number of confirmed mothers: 5 Trimester of infection: PN Symptomatic at birth: NA Detected by: RT-PCR Mode of birth: NK	Number of infants: 5 BW: NK GA: NK Symptomatic: Yes in 3 RT-PCR: Positive in 2 Immunoglobulin:	NK	Number of mothers tested: NK Number of milk samples tested: NK DoL at test: NK Type of test: antibody assay Results: Positive IgG in 1 mother	Mother with BM IgG positive had symptomatic infant but negative RT-PCR test. One symptomatic infant with positive RT-PCR had positive serum IgA at 4-5 weeks. The

Author Type of Publication Country	Maternal Characteristics	Infant Characteristics	Type of Feed Given	Testing of Breast Milk	Comments
	Antiviral medication: NK	Positive in 1			other asymptomatic infant with RT-PCR positive at 4-5 weeks was negative for IgA and IgG at 4-5 weeks See table 2 for more details
Sahin et al(39) Cohort study Turkey	Number of confirmed mothers: 29 Trimester of infection: 1st trimester (6), 2nd trimester (8), 3rd trimester (15) Symptomatic at birth: NK Detected by: RT-PCR Mode of birth: CS (5), VB (5) Antiviral medication: 1	Number of infants: 10 BW: 1630-4010g GA: 31-40 weeks Symptomatic: No RT-PCR: All negative Immunoglobulin: ND	NK	Number of mothers tested: 10 Number of milk samples tested: NK DoL at test: NK Type of test: RT-PCR Results: Negative	Only 10/29 mothers delivered during study period.
Salvatori et al(40) Case series Italy	Number of confirmed mothers: 2 Trimester of infection: PN Symptomatic at birth: No Detected by: RT-PCR Mode of birth: NK Antiviral medication: NK	Number of infants: 2 BW: 3120-4440g GA: 39-41+2 weeks Symptomatic: Yes in 1 RT-PCR: Positive in both Immunoglobulin: ND	BF	Number of mothers tested: 2 Number of milk samples tested: NK DoL at test: NK Type of test: RT-PCR Results: All negative	Infants were admitted on DoL 10-18 One infant had diarrhoea and required intravenous fluids until day 5 of admission.
Schoenmakers et al(41) Case report Netherlands	Number of confirmed mothers: 1 Trimester of infection: 3rd Symptomatic at birth: No	Number of infants: 1 BW: NK GA: NK Symptomatic: Yes	NK	Number of mothers tested: 1 Number of milk samples tested: 2 DoL at test: 3 Type of test: RT-PCR	Premature infant, with multi-organ failure, PPHN, and hypotension. Suspected pediatric inflammatory

Author Type of Publication Country	Maternal Characteristics	Infant Characteristics	Type of Feed Given	Testing of Breast Milk	Comments
	Detected by: RT-PCR Mode of birth: CS Antiviral medication: No	RT-PCR: negative Immunoglobulin: ND		Results: Negative	multisystem syndrome. Tested negative on PCR or for antibodies on multiple occasions. Both fetal and maternal sides of the placenta tested positive.
Tam et al(42) Case report Australia	Number of confirmed mothers: 1 Trimester of infection: PN Symptomatic at birth: NA Detected by: RT-PCR Mode of birth: NA Antiviral medication: NA	Number of infants: 1 BW: NA GA: NA Symptomatic: Yes RT-PCR: Positive Immunoglobulin: ND	BF	Number of mothers tested: 1 Number of milk samples tested: 7 DoL at test: NA Type of test: RT-PCR Results: Positive (2/7 samples from one mother)	Postnatal infection of 8 month old with cough and coryzal symptoms. See table 1 for more details
Van Keulen et al(43) Case control (Preprint) Netherlands	Number of confirmed mothers: 29 Trimester of infection: NK Symptomatic at birth: NK Detected by: RT-PCR Mode of birth: NK Antiviral medication: NK	Number of infants: 29 BW: NK GA: 38^{+4} – 40^{+5} weeks Symptomatic: NK RT-PCR: NK Immunoglobulin: NK	NK	Number of mothers tested: 29 Number of milk samples tested: 29 DoL at test: 12 – 39 weeks Type of test: Total Ig and IgA Results: Positive (24/29 samples)	BM RT-PCR not tested. See table 2 for more details.
Walczak et al(44) Case report Australia	Number of confirmed mothers: 1 Trimester of infection: 3rd Symptomatic at birth: Yes Detected by: RT-PCR	Number of infants: 1 BW: 3770g GA: 40^{+1} weeks Symptomatic: NK RT-PCR: Negative	NK	Number of mothers tested: 1 Number of milk samples tested: NK DoL at test: NK Type of test: RT-PCR, IgA, IgG,	Authors state immunoassay not validated for sample type. Serum immunoglobulin (parent) positive for IgG and IgM

Author Type of Publication Country	**Maternal Characteristics**	**Infant Characteristics**	**Type of Feed Given**	**Testing of Breast Milk**	**Comments**
	Mode of birth: VB Antiviral medication: No	Immunoglobulin: ND		IgM Results: Negative RT-PCR; Positive IgA, IgG and IgM	
Wang et al(45) Case report China	Number of confirmed mothers: 1 Trimester of infection: 3rd Symptomatic at birth: Yes Detected by: RT-PCR Mode of birth: CS Antiviral medication: No	Number of infants: 1 BW: 3205g GA: 40^{+1} weeks Symptomatic: No RT-PCR: Positive Immunoglobulin: ND	BMS	Number of mothers tested: 1 Number of milk samples tested: 1 DoL at test: 2 Type of test: RT-PCR Results:Negative	
Wu et al(46) Case series China	Number of confirmed mothers: 13 Trimester of infection: 1st trimester (5), 2nd trimester (3), 3rd trimester (5) Symptomatic at birth: Yes in 1 Detected by: RT-PCR Mode of birth: CS (4), VB (1) Antiviral medication: Yes	Number of infants: 5 BW: 2300-3910g GA: 35^{+5} – 38^{+4} weeks Symptomatic: No RT-PCR: NK Immunoglobulin: ND	NK	Number of mothers tested: 3 (1 mother tested positive) Number of milk samples tested: 4 DoL at test: 1-27 days. Type of test: RT-PCR Results: 1/4 samples positive	Only 5/13 mothers delivered. Repeat BM test subsequently all negative. See table 1 for more details
Xiong et al(47) Case report China	Number of confirmed mothers: 1 Trimester of infection: 3rd Symptomatic at birth: No	Number of infants: 1 BW: 3070g GA: 38^{+4} weeks Symptomatic: NK	NK	Number of mothers tested: 1 Number of milk samples tested: 1 DoL at test: 1 Type of test: RT-PCR	

Author Type of Publication Country	**Maternal Characteristics**	**Infant Characteristics**	**Type of Feed Given**	**Testing of Breast Milk**	**Comments**
	Detected by: RT-PCR Mode of birth: VB Antiviral medication: Yes	RT-PCR: Negative Immunoglobulin: Negative		Results: Negative	
Yu et al(48) Case report (Preprint) China	Number of confirmed mothers: 1 Trimester of infection: PN Symptomatic at birth: NA Detected by: RT-PCR Mode of birth: NA Antiviral medication: NA	Number of infants: 1 BW: NA GA: NA Symptomatic: Yes RT-PCR: Positive Immunoglobulin: Positive	BF	Number of mothers tested: 1 Number of milk samples tested: 5 DoL at test: NA Type of test: RT-PCR and antibody Results of test: PCR Negative, IgM Negative, IgG Positive (2/2 samples)	Infant was 13 months old, weight 10kg had fever, cough and nasal congestion. See table 2 for more details
Zhang et al(49) Case report China	Number of confirmed mothers: 1 Trimester of infection: PN Symptomatic at birth: NA Detected by: RT-PCR Mode of birth: VB Antiviral medication: NA	Number of infants: 1 BW: NA GA: NA Symptomatic: Yes RT-PCR: Negative Immunoglobulin: ND	BF, EBM	Number of mothers tested: 1 Number of milk samples tested: 1 DoL at test: NA Type of test: RT-PCR Results: Negative	Infant diagnosed at 3 months old.
Zhu et al(50) Case series China	Number of confirmed mothers: 5 Trimester of infection: 3rd Symptomatic at birth: Yes in 3 Detected by: RT-PCR	Number of infants: 5 BW: NK GA: 35^{+0} – 40^{+1} Symptomatic: NK RT-PCR: NK Immunoglobulin: ND	NK	Number of mothers tested: 5 (1 mother tested positive) Number of milk samples tested: 8 DoL at test: NA Type of test: RT-PCR Results of test: Positive (2/8	See table 1 for more details

Author Type of Publication Country	Maternal Characteristics	Infant Characteristics	Type of Feed Given	Testing of Breast Milk	Comments
	Mode of birth: CS (4), VB (1) Antiviral medication: NK			samples)	
Zhuang et al(51) Case report China	Number of confirmed mothers: 1 Trimester of infection: 3rd Symptomatic at birth: Yes Detected by: RT-PCR Mode of birth: CS Antiviral medication: Yes	Number of infants: 1 BW: 2870g GA: 37^{+2} Symptomatic: No RT-PCR: Negative Immunoglobulin: ND	BMS	Number of mothers tested: 1 Number of milk samples tested: 1 DoL at test: 5 Type of test: RT-PCR Results of test: Negative	

Abbreviations: BF, breastfeeding; BM, breastmilk; BMS, breastmilk substitute; BW, birth weight; CPAP, continuous positive airway pressure; CS, caesarean section; DoL, day of life; EBM, expressed breastmilk; ELISA, enzyme linked immunosorbent assays; GA, gestational age; IQR, interquartile range; MF, mixed breastmilk and breastmilk substitute feeds; NA, not applicable; NICU, neonatal intensive care unit; NK, not done; NK, not known; PN, postnatal; PPHN, persistent pulmonary hypertension of the newborn; RT-PCR, real time polymerase chain reaction; VB, vaginal birth.

[a] Information collated from 2 papers by Buonsenso et al and Costa et al: same cases were reported in 2 separate papers.

eTable 3. Risk of Bias for Included Studies

Author	Inclusion Criteria	Condition Assessment	Method of Detection	Consecutive Cases	Complete Inclusion	Demographic Reporting	Clinical Reporting	Follow-up	Overall Judgement
AlZaghal et al(1)	Yes	Yes	Yes	NA	NA	Yes	Yes	Yes	Low risk
Bastug et al(2)	Yes	Yes	Yes	NA	NA	Yes	Yes	Yes	Low risk
Bertino et al(3)	Yes	Yes	Yes	Unclear	Unclear	No	No	Yes	High risk
Buonsenso et al[a] (4, 5)	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	High risk
Chambers et al(6)	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	No	High risk
Chen et al(7)	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	No	High risk
Chen et al(8)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk
Cui et al(9)	Yes	Yes	Yes	NA	NA	No	Yes	Yes	Intermediate risk
De Socio et al(10)	Yes	Yes	Yes	NA	NA	No	Yes	Yes	Intermediate risk
Dong et al(11)	Yes	Yes	Yes	NA	NA	Yes	Yes	Yes	Low risk
Dong et al(12)	Yes	Yes	Yes	NA	NA	Yes	Yes	Yes	Low risk
Fan et al(13)	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	No	High risk
Fenizia et al(!4)	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	No	High risk
Gao et al(15)	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	High risk
Groβ et al(16)	Yes	Yes	Yes	Unclear	Unclear	No	Yes	Yes	High risk
Han et al(17)	Yes	Yes	Yes	NA	NA	Yes	Yes	No	Intermediate risk
Hinojosa-Velasco et al(!8)	Yes	Yes	Yes	NA	NA	Yes	Yes	Yes	Low risk
Kalafat et al(19)	Yes	Yes	Yes	NA	NA	Yes	Yes	No	Intermediate risk
Kam et al(20)	Yes	Yes	Yes	NA	NA	Yes	Yes	No	Intermediate risk
Kirtsman et al(21)	Yes	Yes	Yes	NA	NA	Yes	Yes	Yes	Low risk
Lang et al(22)	Yes	Yes	Yes	NA	NA	Yes	Yes	Yes	Low risk
Lei et al(23)	Yes	Yes	Yes	NA	NA	Yes	No	No	High risk
Li et al(24)	Yes	Yes	Yes	NA	NA	Yes	Yes	Yes	Low risk
Liu et al(25)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Intermediate risk
Lugli et al(26)	Yes	Yes	Yes	NA	NA	Yes	Yes	Yes	Low risk
Luo et al(27)	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	No	High risk
Mao et al(28)	Yes	Yes	Yes	NA	NA	Yes	Yes	Yes	Low risk
Marín Gabriel et al(29)	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	No	High risk
Menter et al(30)	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	High risk

Molina et al(31)	Yes	Yes	Yes	NA	NA	Yes	Yes	Yes	Low risk
Oncel et al(32)	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	No	High risk
Pace et al(33)	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	No	High risk
Peng et al(34)	Yes	Yes	Yes	NA	NA	Yes	Yes	Yes	Low risk
Peng et al(35)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk
Perrone et al(36)	Yes	Yes	Yes	NA	NA	No	Yes	No	High risk
Piersigilli et al(37)	Yes	Yes	Yes	NA	NA	Yes	Yes	Yes	Low risk
Preβler et al(38)	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Intermediate risk
Sahin et al(39)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Intermediate risk
Salvatori et al(40)	Yes	Yes	Yes	NA	NA	Yes	Yes	No	Intermediate risk
Schoenmakers et al(41)	Yes	Yes	Yes	NA	NA	Yes	Yes	No	Intermediate risk
Tam et al(42)	Yes	Yes	Yes	NA	NA	Yes	Yes	No	Intermediate risk
Van Keulen et al(43)	Yes	Yes	Yes	Unclear	Unclear	No	Yes	No	High risk
Walczak et al(44)	Yes	Yes	Yes	NA	NA	Yes	Yes	No	Intermediate risk
Wang et al(45)	Yes	Yes	Yes	NA	NA	Yes	Yes	No	Intermediate risk
Wu et al(46)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Intermediate risk
Xiong et al(47)	Yes	Yes	Yes	NA	NA	Yes	Yes	No	Intermediate risk
Yu et al(48)	Yes	Yes	Yes	NA	NA	Yes	Yes	No	Intermediate risk
Zhang et al(49)	Yes	Yes	Yes	NA	NA	Yes	Yes	No	Intermediate risk
Zhu et al(50)	Yes	Yes	Yes	NA	NA	Yes	Yes	No	Intermediate risk
Zhuang et al(51)	Yes	Yes	Yes	NA	NA	Yes	Yes	Yes	Low risk

Abbreviation: NA, not applicable.
[a] Information collated from 2 papers by Buonsenso et al and Costa et al: same cases were reported in 2 separate papers.
Risk of bias based on Joanna Briggs Institute Critical Appraisal Tool for case reports and case series.
Refer to methods section for details of assessment.

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