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Should we continue breastfeeding after SARS-CoV-2 infection or mRNA vaccination?

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Abstract: The coronavirus disease 2019 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has posed a potential threat to infant health. The World Health Organization recommended that the benefits of breastfeeding far outweigh the potential risk of transmission, but there is no denying that the current evidence is insufficient. Moreover, although the COVID-19 mRNA vaccine has played an effective role in protection against infection, individuals have increasing concerns about the safety of breastfeeding after vaccination, and which have caused some breastfeeding women to postpone vaccination or stop breastfeeding early. Thus, in this review, we provide an in-depth discussion of whether SARS-CoV-2 and the vaccine will affect babies through breast milk. On one hand, only a very small number of milk samples were identified positive for viral RNA and almost impossible to be live virus particles. The milk of most lactating women after vaccination did not contain vaccine-related mRNA and polyethylene glycol. On the other hand, the antibodies and biologically active molecules like lactoferrin are abundant in the milk of lactating women who have been infected or vaccinated, which can provide potential protection against infants' respiratory and gastrointestinal infections. Therefore, in terms of implications for clinical practice, the results of our study support that lactating women who have been infected or vaccinated should be encouraged to breastfeed their infants under the premise of taking appropriate sanitary measures.

Introduction

At present, the ongoing coronavirus disease 2019 (COVID-19) outbreak, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has brought severe adverse effects on global public health, society and economy. As of 18 October 2021, there are more than 230 million confirmed cases worldwide, including some 4.8 million deaths, and the number is rising sharply every day (World Health Organization, 2021). Although pediatric COVID-19 was typically mild in most cases, there were still about 10% of infants under one year of age suffering from severe COVID-19 that requires advanced care (Dong *et al.*, 2020). More seriously, a growing number of infants seemed to exhibit signs of "multisystem inflammatory syndrome in children", which is a rare but potentially deadly inflammatory condition (Riphagen *et al.*, 2020; Verdoni *et al.*, 2020). Besides, infected infants can transmit SARS-CoV-2 to others (Tang *et al.*, 2020). For these reasons, protecting these populations from infection is essential.

Unfortunately, none of the COVID-19 vaccines that have been vaccinated on a large scale are currently authorized or under investigation for use in infants (Pieri *et al.*, 2021), so the protection provided by breastfeeding is particularly important for infants. However, whether the SARS-CoV-2 is present in breast milk after infection has caused widespread controversy, and people are worried that the virus may infect infants through breastfeeding. In addition, the potential transfer of the mRNA from the COVID-19 mRNA vaccine to breast milk may result in the initiation of infant immune responses and thereby alter immunocompetence. Similarly, the polyethylene glycol (PEG), which presents in the lipid film of mRNA-based vaccines, has been reported to cause an allergic reaction in rare cases (Garvey and Nasser, 2021; Sellaturay *et al.*, 2021). These results lead to fear among lactating women, and some of them chose to stop breastfeeding. Thus, there is an urgent need to review the presence of SARS-COV-2 virus and potential allergenic components of the COVID-19 mRNA vaccine in breast milk.

Breast milk is a source of various nutrients (such as proteins and peptides) and bioactive components and which can promote neonatal growth and prevent viral and bacterial

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infections. In terms of antibodies (Abs), human milk contains a series of immunoglobulins (Igs), including IgM, secreted IgM (sIgM), IgA, secreted IgA (sIgA) and IgG. Among them, IgA is the most abundant Ab isotype (about 90% of the total Igs) in human milk and plays an important protective role (Hurley and Theil, 2011). Moreover, specific IgA Abs have been detected in breast milk of mothers infected with SARS-CoV, respiratory syncytial virus and human immunodeficiency virus (Palmeira and Carneiro-Sampaio, 2016; Robertson *et al.*, 2004). In addition, lactoferrin (LF), one of the biologically active molecules, has an antiviral effect on a variety of human viruses including rotavirus, hepatitis C, herpes virus, etc. (van der Strate *et al.*, 2001). Therefore, the existences and functions of these important biologically active molecules that may protect babies from COVID-19 infection in the milk from the mother infected or vaccinated are also worthy of attention.

The possible presence of SARS-CoV-2 RNA and vaccine-related mRNA in breast milk

To obtain definitive information regarding the transmission risks of SARS-CoV-2 through breast milk, we summarized the detection results of human breast milk and infants in Table 1 (Chambers *et al.*, 2020; Fenizia *et al.*, 2020; Gao *et al.*, 2020; Sahin *et al.*, 2020; Bertino *et al.*, 2020; Liu *et al.*, 2020; Sahin *et al.*, 2021; Chen *et al.*, 2020; Kunjumon *et al.*, 2021; Kilic *et al.*, 2021). Among the 285 breast milk samples from SARS-CoV-2 positive mothers, only 9 had SARS-CoV-2 RNA detected. Importantly, the virus culture in one of the RT-PCR positive samples was negative, indicating that it might not be replication-competent live virus that being discovered. Moreover, 279 nasopharyngeal swabs were performed in infants, with only 15 positive results for SARS-CoV-2 (Table 1). Therefore, we speculate that the virus was primarily transmitted through respiratory droplets and contact routes. Therefore, breastfeeding has a low risk of transmitting SARS-CoV-2 and it can be continued under prudent precautions.

Low *et al.* (2021a) detected a very low level of vaccine mRNA using phenol-chloroform extraction, the gold standard for RNA extraction and double quencher qPCR probes (Low *et al.*, 2021a). However, the discrepancies in the sensitivity of the detection method would lead to different test results. In most cases, vaccine mRNA was not detected in milk samples after vaccination (Golan *et al.*, 2021a; Golan *et al.*, 2021b). Notably, even if a low level of vaccine mRNA was detected, it was expected to be easily destroyed by enzymes in the infant's gut. At the same time, although allergic reactions have been reported in a few cases, no significant levels of PEG were found in breast milk after vaccination (Golan *et al.*, 2021c). Nevertheless, lots of people are panicking about the lack of data on adverse effects of breastfeeding mothers and infants.

To explore the safety of vaccination during breastfeeding, we conducted literature review using keywords "SARS-CoV-2, lactation, breast milk, breastfed, breastfeeding, mRNA vaccine" in Pubmed, Science Direct and Google Scholar database, and made Table 2 to summarize the symptoms of breastfeeding women who received the COVID-19 mRNA vaccine (Pfizer or Moderna) and adverse events in their children (Perl *et al.*, 2021; McLaurin-Jiang *et al.*, 2021; Low *et al.*, 2021a; Golan *et al.*, 2021c; Gray *et al.*, 2021; Jakuszko *et al.*, 2021; Low *et al.*, 2021b; Selma-Royo *et al.*, 2021; Lechosa-Muñiz *et al.*, 2021; Low *et al.*, 2021c). In terms of the symptoms in mothers after vaccination, following Dose 1, the frequency of specific symptoms such as pain, redness, joint or muscle pain at the injection site was not differed by vaccine brands. Following Dose 2, women who received the Moderna brand vaccines were significantly more prone to experience chills, muscle/body pain, fever, and vomiting than received the Pfizer vaccine brand. Meanwhile, allergic reactions were less common in patients treated with the second dose of any COVID-19 vaccine, which is likely because an allergic reaction to the first dose led to a contraindication to receiving a subsequent dose. Furthermore, the incidences of mastitis after the first and second doses of vaccination were lower than or close to the 2.5% to 20% estimated by global mastitis epidemiology (Table 2). It was

TABLE 1

Characteristics of breast milk and infants of women infected with SARS-CoV-2

Human milk			Infants	Reference
RT-PCR positive rate	**Viral culture**	**Anti-SARS-CoV-2 IgM and IgG antibodies**	**RT-PCR positive rate of nasopharyngeal swab**	
5.6% (1/18)	Negative	NP	NP	Chambers *et al.* (2020)
3.2% (1/31)	NP	3.2% (1/31)	6.5% (2/31)	Fenizia *et al.* (2020)
0% (0/12)	NP	75.0% (3/4)	0% (0/12)	Gao *et al.* (2020)
0% (0/29)	NP	NP	0% (0/29)	Sahin *et al.* (2020)
7.1% (1/14)	NP	NP	28.6% (4/14)	Bertino *et al.* (2020)
0% (0/10)	NP	NP	0% (0/19)	Liu *et al.* (2020)
0.76% (1/131)	NP	NP	0% (0/133)	Sahin *et al.* (2021)
0% (0/6)	NP	NP	0% (0/6)	Chen *et al.* (2020)
5.3% (1/19)	NP	NP	0% (0/19)	Kunjumon *et al.* (2021)
26.7% (4/15)	NP	NP	56.3% (9/16)	Kilic *et al.* (2021)

Note: RT-PCR, Real-Time reverse-transcriptase-Polymerase-Chain-Reaction; NP, not provided.

TABLE 2

Symptoms of breastfeeding women who received mRNA COVID-19 vaccine and their breastfed children

Type of vaccine	Subject(n1, n2)mother	Symptoms							Reference
		Breastfeeding women		Infants		Severe symptoms	Breast milk changes		
		1st dose	2nd dose	1st dose	2nd dose		Milk production	Color	
Pfizer-BioNTech BNT162b2	(84,84)	Local pain 47.6% (40/84), Fatigue 9.5% (8/84), Other 14.3% (12/84)	Local pain 40.5% (34/84), Fatigue 33.3% (28/84), Fever 11.9% (10/84), Other 26.2% (22/84)	Fever (n = 4) during the period 7, 12, 15, and 20 days		None	NP	NP	Perl *et al.* (2021)
	(10,10)	None		None		None	NP	NP	Low *et al.* (2021a)
	(88,88)	NP	Pain/redness/swelling at the injection site 64.8% (57/88), Fever/chills 43.2% (38/88), Nausea 1.1% (1/88), Headache/muscle ache/ joint pain 59.1% (52/88), Fatigue 61.4% (54/88), Lymphadenopathy (neck, axillary) 5.7% (5/88), Mastitis 3.4% (3/88), Breast engorgement 1.1% (1/88)	None		None	None	Bluish-green 1.1% (1/88)	Low *et al.* (2021c)
	(32,32)	Pain at the injection site 75% (24/32), Fatigue 28.1% (9/32), Headache 31.3% (10/32), Muscle aches 18.8% (6/32), Joint pain 15.6% (5/32), Chills 9.4% (3/32), Fever 6.3% (2/32), Swelling at the injection site 12.5% (4/32), Redness at the injection site 15.6% (5/32), Nausea 3.1% (1/32), Feeling unwell 18.8% (6/32)	Pain at the injection site 78.1% (25/32), Fatigue 53.1% (17/32), Headache 56.3% (18/32), Muscle aches 59.4% (19/32), Joint pain 31.3% (10/32), Chills 43.8% (14/32), Fever 25% (8/32), Swelling at the injection site 18.8% (6/32), Redness at the injection site 12.5% (4/32), Nausea 12.5% (4/32), Lymphadenopathy 18.8% (6/32), Feeling unwell 56.3% (18/32)	Behavior changes 3.1% (1/32), Increased tearfulness 3.1% (1/32)	Other (sleeplessness) 3.1% (1/32)	None	NP		Jakuszko *et al.* (2021)

(Continued)

Table 2 (continued)

Type of vaccine	Subject(n1, n2)mother	Symptoms							Reference
		Breastfeeding women		Infants		Severe symptoms	Breast milk changes		
		1st dose	2nd dose	1st dose	2nd dose		Milk production	Color	
	(14,14)	NP		None		None	NP		(Low *et al.*, 2021b)
	(70,70)	NP	General malaise 12.9% (9/70), Adenopathy 14.3% (10/70), Headache 5.7% (4/70), Fever 7.1% (5/70), Local pain 2.9% (2/70), Nausea 1.4% (1/70), Other 12.9% (9/70)	NP		None	NP		Lechosa-Muñiz *et al.* (2021)
	(30,30)	NP		NP		None	NP		Selma-Royo *et al.* (2021)
	(27,27)	Pain 78% (21/27), Swelling at the injection site 7% (2/27), Itching 4% (1/27), Fever 19% (5/27), Chills 11% (3/27), Headache 11% (3/27), Joint pain 7% (2/27), Muscle/body pain 30% (8/27)	Pain 78% (21/27), Redness at the injection site 4% (1/27), Swelling at the injection site 11% (3/27), Itching 4% (1/27), Fever 52% (14/27), Chills 37% (10/27), Headache 56% (15/27), Joint pain 30% (8/27), Muscle/body pain 59% (16/27)	Tiredness 2% (1/48), Diarrhea 2% (1/48), Insomnia 2% (1/48), Rash 2% (1/48)	None	None		Decrease 4.2% (2/48)	NP	Golan *et al.* (2021c)
Moderna messenger RNA (mRNA)-1273	(21,21)	Pain 100% (21/21), Redness 10% (2/21), Swelling 29% (6/21), Itching 5% (1/21), Rash around injection 5% (1/21), Fever 5% (1/21), Chills 5% (1/21), Headache 33% (7/21), Joint pain 10% (2/21), Muscle/body aches 10% (2/21)	Pain 95% (20/21), Redness 19% (4/21), Swelling 24% (5/21), Itching 5% (1/21), Rash around injection 10% (2/21), Fever 76% (16/21), Chills 62% (13/21), Headache 81% (17/21), Joint pain 33% (7/21), Muscle/body aches 81% (17/21)	Rash on the face/worsening of baby acne 2% (1/48), Sleep interruption 2% (1/48)	None				
	(21,21)	NP		NP		None	NP		Selma-Royo *et al.* (2021)
	(20,20)	NP	General malaise 35% (7/20), Adenopathy 15% (3/20), Headache 20% (4/20), Fever 10% (2/20), Other 10% (2/20)	NP		None	NP		Lechosa-Muñiz *et al.* (2021)

(Continued)

Table 2 (continued)

Type of vaccine	Subject(n1, n2)mother	Symptoms							Reference
		Breastfeeding women		Infants		Severe symptoms	Breast milk changes		
		1st dose	2nd dose	1st dose	2nd dose		Milk production	Color	
Pfizer-BioNTech BNT162b2 Moderna messenger RNA (mRNA)-1273	(1396,1306) (1194,520)	Injection site pain 52.3% (1374/2627*), Fatigue 28.5% (749/2627), Headache 24.6% (646/2627), Muscle pain 16.4% (431/2627), Chills 7.9% (208/2627), Fever 2.3% (60/2627), Allergic reaction 0.5% (13/2627), Mastitis 0.1% (3/2627), Other 6.3% (166/2627)	Injection site pain 71.8% (1313/1828*), Fatigue 64.6% (1181/1828), Headache 54.8% (1002/1828), Muscle pain 51.5% (941/1828), Chills 44.2% (808/1828), Fever 21.1% (386/1828), Allergic reaction 0.3% (5/1828), Mastitis 0.2% (4/1828), Anaphylaxis 0.2% (4/1828), Other 7.4% (135/1828)	Fever 0.8% (21/2627), Rash 0.6% (16/2627), Diarrhea 1.2% (32/2627), Vomiting 0.4% (11/2627), Sleep more than usual 2.8% (74/2627), Sleep less than usual 0.3% (8/2627), Fed more than usual 0.7% (18/2627), Fed less than usual 0.3% (8/2627), More fussy than usual 2.8% (74/2627), Other 1.3% (34/2627)	Fever 0.8% (15/1828), Rash 0.6% (11/1828), Diarrhea 1.2% (22/1828), Vomiting 0.4% (7/1828), Sleep more than usual 2.8% (51/1828), Sleep less than usual 0.3% (5/1828), Fed more than usual 0.7% (13/1828), Fed less than usual 0.3% (5/1828), More fussy than usual 2.8% (51/1828), Other 1.3% (24/1828)	NP	Increase 3.9% (168/4445), Decrease 6.0% (258/4455), No changes 90.1% (3898/4455)	NP	McLaurin-Jiang *et al.* (2021)
Pfizer-BioNTech BNT162b2 Moderna messenger RNA (mRNA)-1273	(16,16) (15,15)	Injection site pain 67% (20/31), Headache 30% (9/31), Muscle pain 13% (4/31), Fatigue 13% (4/31), Fever/chills 3% (1/31)	Injection site pain 61% (17/31), Headache 39% (11/31), Muscle pain 57% (16/31), Fatigue 50% (15/31), Fever/chills 43% (12/31), Other 25% (7/31)	NP		NP	NP		Gray *et al.* (2021)

Note: n1, samples of breastfeeding women received first dose; n2, samples of breastfeeding women received second dose; NP, not provided.

worth mentioning that the milk production of most mothers did not change after vaccination, with only a small number of mothers experiencing a mild increase or decrease in milk supply (Table 2), and all cases returned to normal within 72 h after receiving the vaccine without any intervention. Interestingly, one mother reported that her color of breast milk turned bluish-green within 24 h after receiving the first dose of the Pfizer vaccine, but the alteration might be attributed to maternal dietary changes rather than vaccination as it did not recur after the second dose vaccination (Low *et al.*, 2021c). Additionally, the children whose mothers were vaccinated with either brand or either dose had almost no serious adverse events, and only a few cases had one or more symptoms (Table 2). Mothers who received a second vaccine dose were more likely to perceive some symptoms in their breastfed children, including irritability, lack of sleep, and restlessness. However, most of these symptoms disappeared up to 72 h after vaccination (Golan *et al.*, 2021c). Four infants had fever at 7, 12, 15, and 20 days after maternal vaccination. Except for one infant who was admitted to the hospital for neonatal fever evaluation and received antibiotic treatment, all infants recovered on their own (Perl *et al.*, 2021). Overall, no mothers or infants showed any serious adverse symptoms after vaccination. These results support the safety of vaccination during breastfeeding.

Antibodies in breast milk after COVID-19 infection or mRNA vaccination

Infection or exposure to SARS-CoV-2 can cause the production of anti-SARS-CoV-2 Abs in human milk. On one hand, sIgA has been shown to be the main form of receptor-binding domain-specific IgA in milk samples obtained from COVID-19 patients and recovered donors (Fox *et al.*, 2020). It can prevent adhesion to target epithelial cells through binding to the SARS-CoV-2 nucleocapsid protein or neutralization of the spike protein, and thereby provide a potential protective effect against gastrointestinal infection in the infant. Of note is that the specificity of sIgA is determined by the maternal immune response to prior infection and this may explain the low infection rate or milder symptoms of the infants who were breastfed by SARS-CoV-2-infected mothers. On another hand, IgM and IgG are less in human milk samples collected (Table 1), but these two Abs have known immune-surveillance properties. IgG not only plays an anti-inflammatory role, but also prevents infection at the intestinal level. High-avidity IgM Abs can act as an essential part of protecting the infant's mucosal surfaces from bacteria and viruses. In addition, because the capillary bed connects gastrointestinal system with the circulatory and lymphatic systems, the lacteal lymphatic capillary located in intestinal villi of the small intestine may absorb and transport breast milk Abs to the respiratory system, thereby providing respiratory protection for newborns (Demers-Mathieu *et al.*, 2021a). By the way, it has been reported that SARS-CoV-2-spiked donor milk samples have no cytopathic activity after pasteurization (Unger *et al.*, 2020). Further, some have suggested that breast milk should be pasteurized. However, due to the heat load of milk exposure, Holder pasteurization can affect the immune protection provided by breast milk and reduce the immunological and biological value. Mothers should be supported and encouraged to offer fresh breast milk to their infants under the premise of applying appropriate hygiene measures.

After the 1st dose of COVID 19 mRNA vaccine, maternal plasma IgG and IgM Abs increased significantly, and the IgG level after the 2nd dose has been proven to increase by 6-fold (Golan *et al.*, 2021c), which indicates the importance of the 2nd dose enhancing the antibody response. Besides, the antibody response was highly synchronized between serum and breast milk (Friedman *et al.*, 2021). A large number of anti-SARS-CoV-2 IgA and IgG Abs were detected in breast milk beginning at Day 7 after the initial dose, and anti-SARS-CoV-2 IgG dominated (Baird *et al.*, 2021). As we all know, IgG in breast milk has been shown to play a critical role in neonatal immunity against several other viral pathogens, including human immunodeficiency virus, influenza and respiratory syncytial virus (Fouda *et al.*, 2011; Mazur *et al.*, 2019; Demers-Mathieu *et al.*, 2021b). By the way, the levels of Abs produced in breast milk after COVID-19 mRNA vaccination were significantly higher than those in the natural infection or convalescent period (Low *et al.*, 2021a). Thus, even for lactating women who are naturally infected with COVID-19, vaccination may be helpful to induce and promote the transfer of anti-SARS-CoV-2 Abs in breast milk, as these protective Abs acquired after infection will weaken over time. Interestingly, unlike the significant anti-SARS-CoV-2 sIgA levels detected in breast milk after previous infections (Fox *et al.*, 2020), only a few post-vaccination (mRNA-1273 and BNT162b2) milk samples contain spike-specific secretions and the titer is very low (Fox *et al.*, 2021). It is mainly because the intramuscular (IM) vaccination may not elicit a robust sIgA response. Besides, although plasma levels of anti-SARS-CoV-2 IgG, IgM and IgA were not detectable in infants after maternal vaccination during lactation, breastmilk anti-SARS-CoV-2 IgA and IgG survived gastric digestion (Pieri *et al.*, 2021), and notably, anti-SARS-CoV-2 IgG was detected in infant stool samples collected 4 and 8 weeks post maternal vaccine and were correlated with maternal milk anti-SARS-CoV-2 IgG levels (Golan *et al.*, 2021c). Thus, milk-derived Abs might persist and provide mucosal immunity in the infant gastrointestinal tract.

By the way, spike-reactive T cells were also detected in the breast milk of vaccinated mothers (Gonçalves *et al.*, 2021). The frequency seems low, but a suckling infant ingests a lot of milk daily, which implies the ingestion of quantities of spike-reactive T cells. As milk lymphocytes are capable of withstanding the gastric environment, infiltrating the gut mucosa, entering blood circulation and being distributed into infant tissues, further studies are needed to investigate whether milk transferred spike-reactive T cells could mediate protection against viral infection in the infant upper respiratory tract and gut.

Other ingredients in breast milk that protect against COVID-19

Many bioactive molecules (such as LF, breast milk oligosaccharides, lactadherin, anti-protease and antioxidant factors, etc.) could provide passive protection to the baby. Among them, LF is widely distributed in milk, colostrum and most exocrine secretions that bathe mucosal surfaces. Recently, it has been considered to be one of the bioactive

inhibitors for SARS-CoV-2 (Mattar *et al.*, 2021) and causes extensive research. Naidu *et al.* (2020) suggested LF's charge neutralization ability may also act as blocking viral adhesion to the proteoglycan-rich host cell surface (Naidu *et al.*, 2020). Moreover, the interaction between the virus and the host can be interfered by it without internalization in the cell, which is especially effective in the throat, salivary glands, and upper respiratory tract in the early expansion phase of the virus. For example, heparan sulfate proteoglycans (HSPGs) have been proved to be a necessary co-factor for SARS-CoV-2 infection and promote specific attachment to ACE2 receptors and the internalization of the virion (Hu *et al.*, 2021). LF can bind to them on the cell surface and prevent infection by blocking the interaction between SARS-CoV-2 and HSPGs. Besides, LF could also selectively inhibit cathepsin L, a lysosomal peptidase critical for endocytosis and a cell entry pathway used by SARS-CoV-2.

In addition to the interaction with host cells, LF can also modulate the immune response. On one hand, oral administration can improve the generation of CD+3, CD+4, and CD+8 lymphocytes population, and enhance T cell cytotoxic activities, natural killer cell cytotoxicity, and serum cytokine levels (Kawakami *et al.*, 2015). On the other hand, excessive inflammation could be suppressed by LF. As well known, the virus could cause the propagation of the pro-inflammatory state, and LF in breast milk not only to promote the differentiation of CD4+ T cells into Th1 cells to block many inflammatory cytokines such as IL-1β, IL-6 and TNF-α, but also to stimulate pro-inflammatory macrophages to shift toward anti-inflammatory macrophages.

From the above results, these intrinsic functional properties make maternal-LF a potent innate defense factor to prevent the spread of COVID-19 from mother to newborn, and may also explain why infants have low COVID-19 morbidity and mortality. In addition, given its wide availability, limited cost, and lack of adverse effects, LF could be suggested as both a non-toxic health eement to prevent infection and an adjunct therapy for those who have developed COVID-19. However, more research to verify the dosage and efficacy is still needed.

Limitations

There are limitations to this review. Firstly, we excluded non-English language studies. Secondly, our review only included data from mRNA vaccines. Several other COVID-19 vaccines remain under investigation.

Conclusion

Although SARS-CoV-2 RNA has been detected in breast milk, the rate is extremely low and the samples are almost impossible to contain viable viral particles. This seems to invalidate the hypothesis that the virus could be transmitted via maternal milk. Moreover, vaccine mRNA is not present in milk samples, or is only detected in very low levels in some cases. Similarly, the PEG was not found at significant levels in milk after vaccination. These results, consistent with no significant side effects noted in breastfeeding infants, support the safety of vaccination during lactation.

Breast milk of lactating women after infection or mRNA COVID-19 vaccination contains various bioactive molecules like Abs and LF. They can prevent infants' airways and gastrointestinal tract from infections. Interestingly, breast milk after vaccination contains a majority of IgG, whereas an IgA-dominated response was observed in the breast milk of infected women. This difference may be ascribed to the various exposure routes of lactating women to viral antigens. In addition, LF could help infants modulate the overactive inflammatory response of the gastrointestinal caused by SARS-CoV-2 and counteract the activation of the cytokine-storm. Therefore, provided that precautions (wearing masks during breastfeeding, sterilizing breast pumps and washing hands frequently with soap and water, etc.) are taken to avoid spreading the virus to the infants, infected and vaccinated lactating women should continue to breastfeed their infants uninterruptedly to enhance infants' immunity and prevent severe adverse symptoms of SARS-CoV-2 infection.

Authors' Contribution: The authors confirm contribution to the paper as follows: Fei Chen designed the original idea and wrote the original draft; Chun Luan, Zichun Wei, Dechen Cai, Zhiwen Cui and Yuyang Li contributed to the bibliographic search and in the original draft writing. Hao Wu, Xiaoxia Zhang and Xiaoli Wu edited and reviewed the final version of the manuscript. All authors have approved the final version of the manuscript.

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