Safety of breast/chest-feeding by those infected by SARS-CoV-2

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Purpose of review
One important question from the outset of the pandemic has been whether a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-infected person's milk might be a vehicle for SARS-CoV-2 transmission. This review summarizes the most recent data on this topic.

Recent findings
A SARS-CoV-2 sIgA response in milk after infection is very common. To date, there has been no evidence that SARS-CoV-2 transmits via human milk. Though viral RNA has been identified in a minority of milk samples studied, infectious virus particles have not.

Summary
The highly dominant transmission route for SARS-CoV-2 is via inhalation of respiratory droplets containing virus particles. Other routes of transmission are possible, including fecal–oral, trans-placental, and to a much lesser extent, via a contaminated surface. SARS-CoV-2 cannot transmit via human milk. There is no evidence that infants should be separated from SARS-CoV-2-infected mothers who are well enough to establish or continue breastfeeding.

Keywords
coronavirus disease 2019, human milk, lactation, severe acute respiratory syndrome coronavirus 2, secretory IgA

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative virus of the COVID-19 pandemic, has infected more than 235 million people worldwide, causing more than 4.8 million deaths. The highly dominant transmission route for SARS-CoV-2 is via inhalation of respiratory droplets containing virus particles, some of which may be extremely small, forming what are considered airborne particles forming an aerosol [1]. These droplets are formed from exhalation of any kind by an infected person, including breathing, talking, or even more so, from sneezing, coughing, or singing. Though risk of contact with these aerosols are considerably higher when a social distance is not maintained, it has been demonstrated that transmission can occur over long distances indoors [1]. Notably, infectious virus has been measured in the air for as long as 3 h after particles were dispersed [2]. It is now well documented that an infected person can transmit to another in as few as 3 days and infected people are typically the most likely to transmit (i.e. transmitting the highest viral loads) very early in this transmission window, often before symptoms are certain are most infectious just prior to and during the onset of symptoms. It fact, asymptomatic and/or presymptomatic transmission of SARS-CoV-2 is believed to account for nearly 60% of global transmission [3]. Though surface transmission is possible, and initially of notable concern at the outset of the pandemic, substantial evidence to date indicates that this mode of transmission is of virtually no consequence [4]. Significant levels of viable SARS-CoV-2 is found in an infected person's saliva; however, there is little evidence that oral transmission is a major route of infection, as the acidic stomach environment likely destroys the virus [5]. SARS-CoV-2 can replicate well in gut tissue and virus has been cultured from feces [6,7]. As such, there is

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KEY POINTS

- To date there is ample evidence indicating that SARS-CoV-2 does not transmit via human milk.
- Infected mothers do transmit antibodies in their milk that may protect their infants against SARS-CoV-2 infection.
- With proper hand hygiene and masking efforts, all evidence indicates that the risk to neonates from their infected mothers is virtually nil.
- Infants should not be separated from SARS-CoV-2-infected mothers who are well enough to establish or continue breast/chest-feeding.

evidence that a minority of cases globally may be because of fecal–oral transmission, particularly among children and/or where access to hygienic toileting is not available [6,7]. Viable virus has been detected in urine in certain cases, though this is not believed to be a source of significant global spread [7]. Determining the true risk of vertical transmission of SARS-CoV-2 from mother to infant *in utero* or during delivery via vaginal secretions is highly convoluted by respiratory exposure at birth, though placental infection has been documented using immunostaining of tissue [8].

HUMAN MILK: A KEY IMMUNOLOGICAL COMPARTMENT

Human milk is widely considered a critical contributor to infant health, and has been shown to be protective against diarrheal diseases, otitis media, asthma, allergy, obesity, diabetes, and certain cancers [9,10]. In low-income settings, human milk-feeding significantly reduces child mortality rates up to age 2 [11]. Although the true function and purpose of many of milk's components are still poorly understood, it is a highly complex biological fluid that not only consists of key nutritional elements for normal infant development and growth but also is a notable immunological compartment. The mucosa and its secretions of the oral, nasal and gastrointestinal tract form the first critical line of defense against a large number of infectious pathogens in our environment. The mucosal immune system is an essential barrier, and if this barrier is absent or damaged in some way, we are highly vulnerable to a myriad of infections [12]. Mature human milk contains ~0.6 mg/ml total immunoglobulin (Ig), though there is great variation among women sampled [13]. Milk IgG originates predominantly from serum with some local production in specific cases, though IgG constitutes only ~2% of total milk antibody (Ab) [14]. Approximately 90% of total milk Ab is IgA and ~8% IgM, nearly all in secretory (s) form [sIgA/sIgM; polymeric Abs complexed to j-chain and secretory component proteins] [12,14,15]. Nearly all sIgA/sIgM derives from the gut-associated lymphoid tissue (GALT), via the entero-mammary link, via vascular homing of antibody-secreting B cells from the gut to the mammary gland. Various animal studies have demonstrated this migration and homing during late pregnancy and lactation. Homing appears to be controlled hormonally, as well as by various adhesion factors on the B cells and the maternal vasculature including MadCAM-1, integrin $\alpha 4\beta 7$, CCL28, and CCR10 [16]. This link is an evolutionarily critical mechanism facilitating specific protection to a vulnerable infant against the pathogens in the maternal/infant environment sampled by the maternal GALT, and provides key immunological training for the infant [16]. The secretory component protein is a cleaved segment of the polymeric immunoglobulin receptor (pIgR), which transports this GALT/MALT-derived Abs into the milk. Infants benefit greatly from the sIgA provided in human milk, as the neonate mucosal immune system is relatively deficient in sIgA production as well as other key immune factors. Even past the neonatal period, these Abs can supplement the infant's own immunity to provide protection against pathogens against which the infant does not yet have immunological protection.

THE HUMAN MILK IMMUNE RESPONSE TO SARS-CoV-2 INFECTION

A SARS-CoV-2 sIgA response in milk after infection is very common. We and others have reported SARS-CoV-2-specific Abs in milk obtained from donors with previously confirmed or suspected infection [17–20]. Our work has so far determined that SARS-CoV-2 infection elicits a robust specific milk IgA response in at least 90% of cases, which is very strongly correlated with a robust specific secretory Ab response. This is relevant for the effective protection of a human milk-fed infant, given the high durability of secretory Abs in the relatively harsh mucosal environments of the infant mouth and gut [14,15]. Notably, our studies have demonstrated that this sIgA response is neutralizing, and that even after 7–10 months, only 36% of samples exhibited more than 10% decrease in specific IgA endpoint titers, whereas 57% of samples actually exhibited an increase in specific IgA titer. These highly durable or even increased titers may be reflective of long-lived plasma cells in the GALT and/or mammary gland, as well as continued antigen stimulation in these compartments, possibly by other human coronaviruses, or repeated exposures to SARS-CoV-2.

HUMAN MILK IS NOT A VEHICLE FOR SARS-CoV-2 TRANSMISSION

Undoubtedly, milk from a COVID-19-recovered person is highly likely to contain a high amount of specific sIgA that may have a protective effect on the human milk-fed infant. One major, important question from the outset of the pandemic has been whether a SARS-CoV-2-infected person's milk might be a vehicle for SARS-CoV-2 transmission. This question stirred considerable panic, and caused mothers and babies to be separated, particularly at birth, often with adverse consequences to establishment of the breast/chest-feeding relationship, in some cases, irrevocably [21]. Now, more than 18 months into the pandemic, this question has been explored by several groups. To date, there has been no evidence that SARS-CoV-2 transmits via human milk. Numerous studies of colostrum and mature milk from women with acute SARS-CoV-2 infection have failed to find any viral RNA in milk samples. This includes several early studies conducted in Wuhan, China that examined milk from infected mothers of newborns by RT-PCR ([22–30]; reviewed in [31,32▪,33▪]). One early study from Italy and several of the Chinese reports documented both symptomatic and asymptomatic SARS-CoV-2-infected infants with probable mother-to-infant transmission (likely via respiratory droplets) or unknown transmission routes, still with no evidence of viral RNA in the mothers' milk samples [29,30,34]. Notably, as cases of infected mothers continued to be analyzed, viral RNA was ultimately identified in a small minority of milk samples studied [35–37]. In a single case, SARS-CoV-2 RNA was detected in milk at days 4, 5, and 7 after symptom onset, with subsequent samples found to be negative [35]. In another study that included 18 women providing 64 milk samples, 1 milk sample had detectable SARS-CoV-2 RNA, on the day of symptom onset [36]. Subsequent samples were negative for viral RNA. Notably, collection methods in these reports do not always include masking, cleaning of the chest, or even handwashing to avoid contamination of viral RNA from the donor's respiratory droplets. Indeed, viral RNA in such studies has been found on the chest skin [18]. It is also critical to note that even where viral RNA was detected in milk, infectious SARS-CoV-2 particles were not. Several meta-analyses to date have failed to find evidence of worsened health outcomes for infants of any age breast/chest-fed by infected mothers, or increased rates of infection for these infants compared with those who are formula-fed [38,39]. In one prospective study of 19 women in New York City testing positive for SARS-CoV-2 infection at delivery, RT-PCR of colostrum samples found all but one to be negative for viral RNA, with no evidence of infection in the baby of the mother with the positive milk sample, nor in any other baby in the study [40]. A larger NYC-based study of mothers with confirmed or suspected SARS-CoV-2 infection at delivery included 101 newborns monitored and tested whereas the mothers were still in hospital, with 55 followed for 10–25 days after birth [41▪▪]. This study found only two infants to be SARS-CoV-2-positive (very low viral load) just after birth, with none of the infants in the study exhibiting any COVID-19 disease, despite most newborns feeding directly from the mother (with appropriate mask and hand hygiene encouraged) and rooming-in [41▪▪].

CONCLUSION

Given the clear safety profile of milk from SARS-CoV-2-infected mothers, the significant amount of immunological data demonstrating a robust and rapid specific Ab response, and the general immense benefits of human milk-feeding, particularly in low-income countries, the WHO, CDC, and all major relevant associations recommend that infants not be separated from SARS-CoV-2-infected mothers and that breast/chest-feeding should be established and not disrupted (depending on the mothers' desire to do so), in combination with masking and other hygiene measures [42,43].

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Conflicts of interest

There are no conflicts of interest.

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