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To cite this article: Shirin Shahbazi Sighaldeh & Mohammad Ebrahimi Kalan (2020): Care of newborns born to mothers with COVID-19 infection; a review of existing evidence, The Journal of Maternal-Fetal & Neonatal Medicine, DOI: 10.1080/14767058.2020.1777969

To link to this article: https://doi.org/10.1080/14767058.2020.1777969

Published online: 23 Jun 2020.
Care of newborns born to mothers with COVID-19 infection; a review of existing evidence

Shirin Shahbazi Sighaldeha and Mohammad Ebrahimi Kalanb

aReproductive Health Department, Nursing and Midwifery School, Tehran University of Medical Sciences, Tehran, Iran; bDepartment of Epidemiology, Robert Stempel College of Public Health, Florida International University, Miami, FL, USA

ABSTRACT

Background: The novel Coronavirus disease 2019 (COVID-19) pandemic is already wreaking havoc on families and communities’ welfare. It is critical to discuss newborn care of infected mothers with COVID-19 based on the latest international guidelines and national guidelines of countries with the highest incidence of COVID-19 cases.

Objective: We discuss how to care for a newborn of a suspected or infected mother with COVID-19 using existing evidence.

Method: As of 16 April 2020, we reviewed articles and guidelines related to COVID-19 in the reproductive health field, mother, and newborn health. Our review yielded in 10 categories (i) the risk of diagnostic procedures in suspected mothers on fetus/infant health, (ii) the risk of intrauterine or postpartum transmission to the fetus/infant, (iii) appropriate method and delivery time in women with confirmed COVID-19, (iv) umbilical cord clamping and skin to skin contact, (v) clinical manifestations of infected infants, (vi) confirmation of infection in a suspected neonate/infant, (vii) instructions for infant’s care and how to feed her/him, (viii) bathing the baby, (ix) the criteria of discharging baby from the hospital, (x) the impact of isolation on the maternal mental health.

Results: Our findings showed that the possibility of intrauterine or perinatal transmission of COVID-19 is still questionable and ambiguous. However, what has been agreed upon in the existing texts and guidelines is that the close contact of mother and infant after birth can transmit the virus to the baby through droplets or micro-droplets.

Conclusions: Based on our findings, it is recommended to separate the baby from the mother with confirmed (or suspected) COVID-19 infection for at least 2 weeks. Since the motivation and stable situation of mothers allow breastfeeding during the isolation, infected mothers should be taught about breast expression skills, common breast problems, the symptoms of their baby’s infection, and the principles of personal hygiene to protect the infant against COVID-19 infection.

Introduction

The novel Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) has spread exponentially across the globe [1]. COVID-19 pandemic has posed critical challenges for public health, research, and medical communities worldwide. The SARS-CoV-2 spreads through saliva droplets or nasal secretions when an infected person coughs or sneezes [1], with existing evidence suggesting that the potential route of spreading through microdroplets released when talking [2]. These microdroplets can remain 20 min or more in stagnant air, thus maintaining social distance, wearing appropriate masks and air circulation may help mitigate the infection risk [2]. The vast majority of patients have mild or moderate symptoms and recover without the need for special treatment, but people with underlying conditions such as diabetes, chronic obstructive pulmonary disease (COPD), or cancer are more likely to develop a serious illness [1].

According to the World Health Organization (WHO), as of 27 May 2020, more than 5 million confirmed cases were reported globally with >340,000 deaths, mostly from the United States of America (USA) [1]. In the Eastern Mediterranean Region, Iran is considered as an epicenter of COVID-19 with the incidence of
140,000 confirmed cases with a death toll of 7508 as of 27 May 2020 [3].

According to a systematic review, COVID-19 may affect 1% to 5% of children [4] with more likely to present a mild or asymptomatic condition than adults [5–7]. Evidence shows that COVID-19 occurs in children with rapid recovery much shorter incubation period [8], and better disease prognosis compared to adults [9]. Children can be potential and silent carriers of the virus persistently because they can pass it through the stool even two weeks after improving respiratory symptoms [6]. That’s why Xing et al. warned about the spreading of the infection among children after reopening of kindergartens and schools [6].

During the COVID-19 pandemic, pregnant women and newborns represent a vulnerable population [10]. To date, although there is no strong evidence-based information showing if pregnant women have a greater chance of getting sick from COVID-19 than the general public [8,11–13], it is well established that pregnant women are at greater risk for severe illness with viruses from the same family as COVID-19 and other viral respiratory infections, such as influenza [14]. Additionally, some experts believe that the reported cases thus far are too limited to be convincing about virulence of COVID-19 infection among this population [15]. For example, in a study of 31 pregnant women, Yin et al. found that pregnant women were more likely to have severe and critical forms of COVID-19 [16]. Other studies, on the other hand, have reported the similar severity of the disease in pregnant and non-pregnant women [8,11–13].

Among this population, cardiopulmonary adaptive alters present during pregnancy (e.g. elevated heart rate and stroke volume, and reduced pulmonary residual capacity) which may increase the risk of hypoxemia and contribute to the increased severity [14]. Thus, health care providers should consider pregnant women and their infants as a high-risk population in control and prevention strategies during pulmonary-associated pandemics like COVID-19 [11,17–20]. One of the main concerns associated with COVID-19 is the potential impact on the newborn and its detrimental consequences [17]. Concerns about how to care for a baby after birth, such as breastfeeding, vaccination, or neonatal screening, are among the major concerns of mothers during COVID-19 pandemic [21].

Maternal-neonatal transmission of respiratory viruses occurs mainly through close contact, transmission through droplets (caregivers, family members, and family visitors), hospital-acquired infections, and exposure to sources of infection from public places [22]. Currently, it is unclear if COVID-19 can cross through the placental route to the fetus. In limited case series reported to date, no evidence of virus has been found in the breast milk of women infected with COVID-19 that can be transmitted through breast milk (i.e. presence of SARS-CoV-2 in the breast milk) [23]. Similar to their mothers, newborns appear to be a high-risk population against COVID-19 infection due to weakened immune systems [24]. Additionally, potential transmission of SARS-CoV-2 infectious between infected newborns raises another concern during this pandemic [8].

The National Health Commission of China (2020) also recommended postponing the routine follow-up visits of infants during strict quarantine in early February. They installed an app on parents’ smartphones and asked them to monitor their baby’s skin bilirubin [25].

In Iran, pediatricians from Research Institute for Children’s Health have developed an algorithm based on diagnostic and therapeutic standards to treat children who are suspected of having COVID-19 infection (children who have a dry cough, fever, with or without fever [26]. There are no accurate statistics on the number of infants infected with the COVID-19 infection in Iran and beyond, but given that COVID-19 is more contagious than Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) [18], infants are not immune to the infection and they are at greater risk of being infected by their parents or caregivers. It seems that designing such an algorithm and strategies for newborns can be very useful. Herein, we discuss how to care for a newborn of a suspected or infected mother with COVID-19 using existing evidence.

**Search method**

A systematic search of the literature that was published from 1 January 2020, up through to 30 March 2020, was carried out using two electronic databases including PubMed and Google Scholar. Additionally, we searched for statements or guidelines from the US Center for Disease Control and Prevention (CDC) and WHO. The search was updated on April 14, 2020. The search was based on keywords taken from the Mesh system, including COVID-19 and pregnancy; SARS-CoV-2 and pregnancy; Coronavirus and pregnancy; 2019-nCoV and pregnancy; and then COVID-19 all and its equivalents with breastfeeding, neonatal care and newborn such as COVID-19 and breastfeeding; SARS-
CoV-2 and neonatal care; Figure 1 and newborn.
COVID-19 and neonatal care and so on.

As shown in flowchart 1, during this period, of the 1,461 articles related to COVID-19 extracted from our search databases and gray literature, 57 articles were eligible since they were about COVID-19 and reproductive health. One article was deleted due to the French language [27]. We reviewed only the abstract section of papers because their full text was in the Chinese language [28–30]. One paper was deleted in this level because it was written entirely in the Chinese language [31]. We also reviewed gray papers by searching medRxiv and letters to editors.

Results

The risk of diagnostic procedures in suspected mothers on fetus/infant health

The computed tomography (CT) images have shown higher sensitivity in detecting the possibility of viral pneumonia caused by SARS-CoV-2. This diagnostic procedure has been used in pregnant women who are suspected of COVID-19 infection [12]. Hence, among afflicted mothers, anxiety about the effect of COVID-19 on their child begins from the fetal period of their children because mothers worried about the detrimental effects of radiation on their fetus’s health. According to data from the American College of Radiology and the American College of Obstetricians and Gynecologists [17], when a single chest CT scan is performed for suspected mothers, the radiation dose to the fetus is only between 0.01 and 0.66 mGy which is negligible, while harmful effects of radiation such as microcephaly, fetal growth restriction and cognitive impairment on the fetus/infant were observed with doses higher than 610 mGy. Therefore, pregnant women should be reassured that diagnostic procedures will not harm their fetus/infant.

Risk of intrauterine or postpartum transmission to the fetus/infant

Regarding the effect of maternal infection on fetal health, Chen et al. studied 9 pregnant women with pneumonia caused by COVID-19 and they did not find any fetal death, neonatal death, or birth asphyxia. The neonatal Apgar score was normal. Amniotic fluid, umbilical cord blood, throat swab, and breast milk were examined in six of these nine cases, which were reported negative for the SARS-CoV-2 [12].

Fan et al. [32], examined the placenta, umbilical cord blood, amniotic fluid, and breast milk of two physicians with COVID-19. They did not detect SARS-CoV-2 in these products. One infant developed mild fever and lymphopenia, three days after birth. On day four, diffuse haziness was seen in both lungs of the baby, but no patchy consolidation was observed on CT images. The baby responded to antibiotic treatment and was discharged from the hospital on day 8.

In the second baby, only mild pneumonia and lymphopenia were seen, which responded to antibiotics in two days. In successive follow-ups no traces of SARS-CoV-2 were found in breast milk. The researchers concluded that both cases showed a low risk of intrauterine and vertical transmissions, but every baby may be at high risk of transmitting the virus from mother to child after birth [32]. Wang et al. also did not find any evidence of COVID-19 virus in pregnancy products and infants of infected mothers [33]. Schwartz and Graham believe that in some cases, a viral infection can be transmitted to the baby through the birth canal or during lactation, but these mechanisms are very unusual in the case of viral infections [34]. Cao et al. conclude that there is no information about the mother-to-fetus/infant transmission of the virus during the perinatal period and vaginal delivery, and also no evidence of intrauterine transmission has been reported so far [8]. Additionally, other investigators have not confirmed vertical transmission of the virus from an infected mother to the newborns [19,35–37].

Zhang et al. using data of 81,026 confirmed COVID-19 cases in China, identified 4 nucleic acid-confirmed neonatal infections. At the time of disease onset, two newborns were at isolation and the other two were not isolated. The authors’ findings support intrauterine transmission potential [30].

In a study done by Zhu et al. they found that nine babies born to infected mothers with COVID-19 had negative pharyngeal swabs tested by real-time reverse-transcription polymerase chain reaction (rRT-PCR), which supports the notion that the SARS-CoV-2 Coronavirus cannot be transmitted vertically from mother to baby. Nevertheless, they recommended that due to the limited sample size of their study, further studies are warranted to achieve a strong conclusion about vertical transmission of SARS-CoV-2. In this study, there was fetal distress in 6 infants. For this reason, the researchers assumed that this event may be related to COVID-19. So, before the childbearing of an infected mother, gynecologists should ask a neonatal specialist who is an expert in resuscitation, be ready in the delivery room. They reported one neonatal death in their analysis but the baby’s throat swab obtained nine days after delivery, was negative for COVID-19.
The youngest baby has been infected with COVID-19 thirty hours after birth. The baby was born on 2 February 2020 at a hospital in Wuhan, China, from a mother who was ill, and on February 5th, it was reported that the baby had confirmed COVID-19 infection. The baby’s vital signs were stable, without fever or cough, but he had shortness of breath, abnormal liver tests, and abnormal radiography [34].

In nine women at Zhongnan Hospital in China, samples of whole blood, serum, oral swabs, urine, and feces were tested. Additionally, milk of all 9 mothers was tested for associated RNA of SARS-CoV-2. All aforementioned tests were reported negative. Similarly, at Tongji Hospital, samples of two newborns and the breast milk of their infected mothers were tested and reported to be negative for RNA of SARS-CoV-2 [34].

In a retrospective study, Zhang et al. compared the neonatal outcomes of two groups of mothers, including 16 mothers with confirmed COVID-19 infection and 45 healthy mothers. All of whom gave birth at 36 weeks by cesarean section. None of the babies were infected after birth and there was no significant difference between newborns in terms of neonatal distress, meconium in amniotic fluid, and neonatal asphyxia [30]. In another study, Yin et al. could not detect the presence of SARS-CoV-2 in amniotic fluid, placenta, neonatal throat, and anal swab and breast milk samples of 31 infected mothers [16].

Chen et al. in a study of swabs from the throats of three infants whose mothers infected with COVID-19 at the end of pregnancy, found that all samples were negative for the nucleic acid of COVID-19. No pathological findings were found in the placenta of these infants and they were negative for the nucleic acid of SARS-CoV-2 [11]. In a recent report from outcomes of 13 newborns born to infected mothers, 1 of 9 samples of stool and 1 from 3 samples of breast milk was positive for Coronavirus nucleic acid [38].

In Iran, there is a case report of a 15-day-old infant infected with COVID-19. The baby had a fever, sweating, respiratory problems, and motility, but no cough or runny nose and gastrointestinal symptoms were detected. The baby was under care in the newborn intensive care unit (NICU). Her parents had recently cough, fever, and sweating. The infant was tested positive for COVID-19. The baby was discharged 6 days after hospitalization, with good condition. The researchers suggested that because of various clinical and laboratory symptoms that infants may have, it is logical that we do rt-PCR for infants with symptoms of COVID-19 infection [39].

According to a case report published in the Journal of American Medical Association (JAMA) [40] a baby was born on 22 February 2020, to a mother with a cesarean section at a hospital in Wuhan, China. Maternal vaginal discharge was negative for Coronavirus. The baby had no abnormal symptoms and his lung CT images and rt-PCR tests of pharyngeal swabs were negative, but the baby had a high level of Immunoglobulin G (IgG) and Immunoglobulin G (IgM) between 2 h and 16 days after birth. The baby was isolated in a negative pressure room and was discharged from hospital on March 18. The authors concluded that elevated levels of IgG in the baby may be a sign of maternal or neonatal infection, and high levels of IgM and laboratory evidence of inflammation and abnormal liver tests may indicate that the baby was infected with COVID-19 in the mother’s womb. The limitations of this study are that only one case was examined and the placenta and amniotic fluid were not examined [40]. Lackey et al. emphasized that IgM antibodies present in the serum of SARS-CoV-2 negative infants cannot cross the placental barrier. Thus, these findings indicate that the baby had an infection (and the production of these antibodies) in the uterus [41].

Appropriate method and time of delivery in women with COVID-19

Mode of childbearing is determined by routine midwifery indications and there is no benefit in performing cesarean section for all [10,32,42]. However, most studies have reported that cesarean section is performed for infected pregnant women with COVID-19 [11,12,22,30,32,43,44]. Wu et al. in their case series of 13 Chinese pregnant women with COVID-19 concluded that a vaginal delivery may be a safe delivery option because in all women vaginal secretion specimens were negative for the novel Coronavirus [38].

Regarding the time of delivery for women with COVID-19, it is stated that the virus is not an indication for childbirth, but in the case of severe maternal symptoms, termination of pregnancy is recommended [19,42]. If the mother’s symptoms are severe and the gestational age is less than 23 to 24 weeks–when the fetus is not yet viable–termination of pregnancy is recommended [19,42]. If the fetal age is between 26 and 34 weeks, the time of delivery will be determined by the condition of the mother and fetus. If the fetus is 34 weeks or older, due to a high chance of survival, late preterm delivery is possible [42]. Thus, it is logical for women who are pregnant in the third trimester, to
delay childbirth [32]. If the mother’s symptoms are mild, the pregnancy could be closely monitored and continued until the term [42].

**Umbilical cord clamping and skin to skin contact**

The International Society of Ultrasound in Obstetrics & Gynecology (ISUOG) and existing evidence recommend that the umbilical cord should be clamped quickly to reduce the risk of vertical transmission [17,29] and the infant should be sent to a resuscitation facility for evaluation by a pediatrician [17]. Nevertheless, the Royal College of Obstetricians and Gynecologists (RCOG) recommend that umbilical cord clamping may be done routinely because during vaginal delivery it is unlikely that the risk of vertical transmission change with one more minute of perfusion through the placenta. Most likely, COVID-19 transmission occurs in the postpartum period and through normal routes [45]. Additionally, studies from the USA maintained that delayed umbilical cord clamping (DCC) does not increase the risk of vertical transmission, and therefore, it should be performed for at least 60 s if the baby is vigorous. However, in some centers, immediate cord clamping is preferred for example when the mother is symptomatic (fever, cough, and other respiratory symptoms), to minimize exposure in the delivery room [10].

Concerning the skin-to-skin contact, WHO recommends that mothers or infants with suspected, probable, or confirmed COVID-19 can remain together with skin-to-skin contact, especially immediately after birth during the initiation of breastfeeding [10,46]. Nevertheless, some experts do not recommend skin-to-skin contact between mothers and newborns at the time of COVID-19 infection [47] since they believe that the transmission of SARS-CoV-2 through the skin-to-skin contact cannot be ruled out. Taken together, it seems that shared decision-making with the parents before delivery regarding the potential risks and benefits of skin-to-skin contact is the best option [10].

**Clinical manifestations of infected infants**

Newborns might catch SARS-CoV-2 through close contact with infected patients or asymptomatic virus carriers. The disease might have an insidious onset and be nonspecific [33]. For example, in preterm infants’ symptoms may be nonspecific and include instability of body temperature, gastrointestinal symptoms, and respiratory problems including fever, cough, runny nose, nausea and vomiting, diarrhea, and abdominal pain. A number of infants may also develop acute respiratory distress syndrome [4,8]. Other symptoms are lethargy and feeding intolerance [10].

In infected newborns, the initial symptoms may be fever, cough, or diarrhea. Although vertical transmission of COVID-19 has not confirmed yet, the perinatal infection may cause premature labor, respiratory distress, thrombocytopenia accompanied by abnormal liver function, and even death [22]. For instance, the late-onset respiratory distress has been described in several infants 1–3 weeks after birth and/or discharge from the hospital [10].

**Confirmation of infection in a suspected newborn/infant**

In infected mothers, the infant should be tested at or beyond 24 h after birth [10]. Separate swabs of the nasopharynx, oropharynx, and rectum are recommended. A second test 24 h later may be valuable for confirmation [10].

Infants who infected with COVID-19 tend to have mild clinical symptoms and their CT imaging findings are not as typical as adults’, therefore, diagnosis of COVID-19 should be made based on three major findings including CT imaging, epidemiological history, and nucleic acid detection [48].

According to Shah et al. classification system and case definition for SARS-CoV-2 infection, congenital infection in alive born newborn will be confirmed in the following conditions: (i) when there is detection of the virus by PCR in umbilical cord blood or neonatal blood collected within first 12 h of birth or amniotic fluid collected prior to rupture of membrane; (ii) Neonatal infection acquired intrapartum can be confirmed when there is detection of the virus by rt-PCR in nasopharyngeal swab at birth and 24–48 h of age; (iii) neonatal infection acquired postpartum can be confirmed when there is detection of the virus by rt-PCR in nasopharyngeal/rectal swab at ≥48 h of birth in a newborn whose respiratory sample tested negative by rt-PCR at birth [49].

**Instructions for infant’s care and how to feed her/him**

The American College of Obstetricians and Gynecologists (ACOG) and the US CDC recommend the separation of mother and baby in separate rooms if the mother is infected or suspected to have infection [23,50]. CDC temporary guidelines for breastfeeding in infected or suspected mothers also state that if
the mother wants to breastfeed the baby, she should be milked by hand or pump [51]. The WHO recommends that women with COVID-19 can feed their baby directly by her breast or she could feed her baby by expressed milk or using donor milk [52].

The Chinese Expert Consensus believes that all suspected or infected infants (including babies who are born to infected/suspected pregnant women) should be admitted to the NICU [29]. In general, all infants before admission to the NICU should be screened for COVID-19 by collecting clinical and non-clinical history from their parents. The high-risk infants should be isolated at least 14 days in a separate room. Infants are more vulnerable to infection due to their still-developing immune system, so standard precautions should be taken in the care of infants until their status is determined [29]. National Health Commission of the People's Republic of China [53] recommends that babies born to infected or suspected mothers with COVID-19 should be kept isolated in a unit designed to care for them up to ~14 days. They also emphasized that mothers must not feed their babies by breast milk until their recovery [53].

According to the instructions of the Ministry of Health and Medical Education of Iran, the COVID-19 suspicious mother is not prohibited from breastfeeding, if the mother’s diagnosis is conclusive the baby should be quarantined for 2 weeks and the mother could feed the baby by her breast milk or formula or donor milk, depending on mother’s condition [54]. According to temporary instructions from the International Society of Ultrasound in Obstetrics & Gynecology (ISUOG), if the mother is very ill, separation of mother and baby is the best option, and milk expression should be done to maintain milk production. If the mother is asymptomatic and has a mild illness, breastfeeding, and rooming-in can be done with the help of the mother and health care provider [17]. RCOG has a less strict guideline and recommends that infected or suspected mothers do not need to be separated from their baby and they can be kept together during the postpartum time. The mother can express her milk and then feed the infant through a caregiver [45]. The USA experts classify the relationship between mother and baby and infant nutrition, based on parental preference, the number of hospitalized patients, and the economic status of the community [10]. In general, they have introduced three options to parents and health care providers. These options range from formula feeding and expressed breast milk to direct breastfeeding [10]. According to Italian Society of Neonatology (SIN) and Union of European Neonatal & Perinatal Societies (UENPS), if an infected or suspected mother is asymptomatic at delivery, rooming-in is feasible and direct breastfeeding is allowed but if the mother is too sick to care for the newborn, the newborn has to be managed separately and fed fresh expressed breast milk [55]. More details on these guidelines are given in Table 1.

### Bathing the baby

An early bath to minimize exposure can be considered in stable term newborn infants born to a mother with suspected or confirmed COVID-19 infection [10].

### Baby discharge criteria from hospital

If the infant is positive but asymptomatic, he/she can be discharged but may need to be quarantined at home. If the infant is negative and asymptomatic, he/she can be discharged to be cared for by a non-infected, asymptomatic caregiver [56]. If the infant is positive and symptomatic, the temperature should be normal for more than three days; respiratory symptoms and radiographic findings should be shown significant improvement; and nasal, pharyngeal, and sputum swabs, should be negative for COVID-19 for two consecutive days (i.e. 24 h apart) [57].

### The impact of isolation on the maternal mental well-being

Because the separation of the infected mother from the baby and the lack of breastfeeding can lead to the deprivation of the mother and baby from “bonding,” resulting in more maternal stress during the postpartum time, it is recommended that the health providers, in addition to helping the mothers’ physical health, also consider the mothers’ mental health and facilitate mental supports during this health crisis [17].

### Discussion and conclusion

The possibility of mother-to-fetus transmission of SARS-CoV-2 is currently a highly debated concept in perinatal medicine community [26,49]. Concerns about the effect of COVID-19 on the fetus and the infant are important issues in the field of reproductive health and fetal-maternal medicine. According to the literature, the first and safe option to diagnose COVID-19 is a chest CT scan because so far the dose of radiation emitted to the fetus from CT is very low and has no
There is insufficient evidence on the safety of breastfeeding (ie, recommending breastfeeding) and, on the one hand, the need for separation mother and baby:

i. If the mother is very ill, separation of mother and baby is the best option, and milk expression should be done to maintain milk production

ii. If the mother is asymptomatic and has a mild illness, breastfeeding and rooming-in can be done with the help of the mother and health care provider.
harmful effects. The neonatal consequences of mothers with COVID-19 infection have been reported to be the same as those of non-infected mothers. For this reason, researchers believe that compared to acute respiratory syndrome Coronavirus (SARS-CoV) and Middle East respiratory syndrome Coronavirus (MERS-CoV), which were associated with serious maternal and neonatal consequences, SARS-CoV-2 is not considered a high-risk virus for mother and baby [58] and the majority of newborns born to mothers with SARS-CoV-2 infection either do not become infected or exhibit mild-to-moderate symptoms at birth [49]. As of this writing, in COVID-19 related studies, there have been no reports of infant and fetal deaths. Additionally, amniotic fluid, whole blood, umbilical cord, placenta, oral swabs, serum, urine, and infant stools are reported negative for the Coronavirus.

In discussed studies, the Apgar score of infants of infected mothers was reported to be normal after birth. However, there are a few reports of respiratory distress and acute respiratory distress syndrome (ARDS) in infants of infected mothers. Therefore, performing this quick assessment on a baby at 1 and 5 min after birth can help to identify the typical and potential symptoms of COVID-19.

Although some experts have ruled out the risk of intrauterine transmission, others have been cautious about this risk [41]. They argue that although negative samples of pregnancy products and newborns make the possibility of intrauterine transmission small, the report of viral antibodies in an infant’s blood whose rt-PCR test was negative and some cases of fetal distress in some infants of infected mothers, make it hard draw a definite conclusion in this regard.

Although the possibility of prenatal transmission for COVID-19 has been ruled out previously [8,34], a study done by Nie and colleagues among 26 newborns, reported perinatal transmission in one newborn. They emphasized that this case could not be a case of vertical transmission because the cord blood and placental samples were both negative for SARS-CoV-2 [58]. Therefore, both intrauterine transmission and perinatal transmission of the virus both are still challenging and ambiguous, and more studies are needed to draw definitive conclusions about them. Simultaneously, what researchers have more clearly understood is the significant risk of mother-to-baby virus transmission after birth. It means babies who are born to mothers with confirmed COVID-19 can acquire the infection post-delivery [59]. For this reason, breastfeeding has been banned despite the lack of Coronavirus in the milk of infected mothers. In addition to the prohibition of breastfeeding, it is recommended that the baby be

### Table 1. Continued.

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<th>Source</th>
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<td>Royal College of Obstetricians and Gynaecologists (RCOG)</td>
<td>• Also, if it is not possible to separate the mother and baby due to lack of facilities, the mother and baby can be kept in the same room. Because the virus may be transmitted by airborne droplets more than breast milk, breastfeeding mothers should wash their hands thoroughly and use three-ply surgical masks before contact the baby. If the mother and baby are in the same room, the baby’s cut should be kept at least two meters away from the mother’s bed and a physical barrier such as a curtain should be used.9 • According to the RCOG: i. An infected or suspected mother does not need to be separated from the baby and they can be kept together during the postpartum time ii. The mother can express her milk and then feed the infant with the help of a caregiver. • Also, the neonatologist should discuss the benefits and disadvantages of rooming-in as well as breastfeeding with the infant family. • For infected mothers whose infants are still negative or pending a test for COVID-19, three options can be considered: i. The infant can receive formula or donor milk. The mother can pump her milk until she is asymptomatic with two negative tests for COVID-19 at least 24-hour apart ii. The mother has to wear a mask, wash her breast with soap, and then express breast milk. A healthy family member or a nurse can feed the expressed milk to the baby in a separate room. This approach continues until the mother meets the same criteria as in the First option. iii. The mother can wear a surgical mask, wash her hands and breasts with soap and water, and breastfeed the baby. These precautions continue until the fever of mother and other symptoms subside and has two negative tests for COVID-19 at least 24-hour apart. • The first option is suitable for resource-rich settings with low patient volume, the second is suitable when resources are starting to fall with modest patient volume, and the last option for the poor and underdeveloped settings with a large influx of patients. • If an infected or suspected mother is asymptomatic at delivery, rooming-in is feasible and direct breastfeeding is allowed, under strict measures of infection control. • When a mother is too sick to care for the newborn, the newborn has to be managed separately and fed freshly expressed breast milk. There is no need to pasteurize breast milk because human milk is not believed to be a vehicle of coronavirus.</td>
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<td>Italian Society of Neonatology (SIN) and Union of European Neonatal &amp; Perinatal Societies (UENPS)</td>
<td>• According to the RCOG: i. An infected or suspected mother does not need to be separated from the baby and they can be kept together during the postpartum time ii. The mother can express her milk and then feed the infant with the help of a caregiver. • Also, the neonatologist should discuss the benefits and disadvantages of rooming-in as well as breastfeeding with the infant family. • For infected mothers whose infants are still negative or pending a test for COVID-19, three options can be considered: i. The infant can receive formula or donor milk. The mother can pump her milk until she is asymptomatic with two negative tests for COVID-19 at least 24-hour apart ii. The mother has to wear a mask, wash her breast with soap, and then express breast milk. A healthy family member or a nurse can feed the expressed milk to the baby in a separate room. This approach continues until the mother meets the same criteria as in the First option. iii. The mother can wear a surgical mask, wash her hands and breasts with soap and water, and breastfeed the baby. These precautions continue until the fever of mother and other symptoms subside and has two negative tests for COVID-19 at least 24-hour apart. • The first option is suitable for resource-rich settings with low patient volume, the second is suitable when resources are starting to fall with modest patient volume, and the last option for the poor and underdeveloped settings with a large influx of patients. • If an infected or suspected mother is asymptomatic at delivery, rooming-in is feasible and direct breastfeeding is allowed, under strict measures of infection control. • When a mother is too sick to care for the newborn, the newborn has to be managed separately and fed freshly expressed breast milk. There is no need to pasteurize breast milk because human milk is not believed to be a vehicle of coronavirus.</td>
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9WHO [52]; 8WHO [3]; 2WHO [1]; 6Wang L et al. [29]; 7National Health Commission of the People’s Republic of China [53]; 5Iranian Scientific Breastfeeding Promotion Society [54]; 4Poon et al. [17]; 3RCOG [45]; 1Chandrasekharan et al. [10]; 6Davanzo et al. [63].
isolated and kept away from the mother after birth for about two weeks.

Since micro-droplets can transmit the virus to the newborn, advising mothers to be separate from their baby sounds perfectly reasonable. According to the scientific community (e.g. WHO, SIN, ISoug), after two weeks of isolation if the infected mother is not ill and tends to breastfeed, she can feed her baby directly by her breast milk. Hand washing before touching the baby and wearing a face mask during breastfeeding is the most effective preventive measures against COVID-19 [55]. Formula feeding can be applicable given that feeding babies with breast milk is almost impossible. Although scientists suggest that feeding the baby by mother’s breast milk could be an option if parents and providers accept the risk of transmission, they strongly emphasized that in resource-rich setting formula feeding is preferable [10].

Regardless of the setting in which the mother is hospitalized, the preference of formula feeding may be somewhat understandable. Because in mothers who are being treated with antiviral drugs the safety of breast milk remains unknown [10]. Since one of the three samples of breast milk tested in the study of Wu et al. was positive for Coronavirus nucleic acid, they recommended that breast milk safety be investigated in further studies [38]. On the other hand, it is believed that in Coronavirus pandemic breastfeeding should be promoted especially when there is a shortage of formula [59] and in order to prevent emotional trauma for the nursing baby and enhancing their immune responses by the specific secretory IgA antibodies producing in the milk of infected mothers [60].

According to WHO, if a woman wants to keep her milk supply, she should express at least every 3 h and
if it seems to be decreasing after a few weeks, she should express every 30–60 min and at least every 3 h during the night. Another important recommendation of WHO is that a woman should express her breast milk because the breast will be easily hurt if another person tries to express it [61]. This organization also has recommended that syringe pumps are more efficient than rubber bulb pumps, and it is easier to clean and to sterilize (Figure 2). The disadvantages of rubber bulb pumps are that they can easily carry infection, which is especially dangerous if more than one woman uses the same pump. For sanitizing cups or other appliances, in normal condition, WHO recommends pouring boiling water into them for a few minutes [61]. But during COVID-19 pandemic, Marinelli and Lawrence suggest the disinfecting of milk containers with viricidal agents made from sodium hypochlorite mainly for protecting from spreading the virus by the surfaces of these containers [62]. There is no need to pasteurize breast milk because human milk is considered safe, not a vehicle of Coronavirus [63].

According to a Cochrane study initiation of milk expression sooner after birth when not feeding at the breast, relaxation, massage, warming the breasts, hand expression, and lower cost pumps may be as effective, or more effective, than large electric pumps [64]. These statements tell us that breastfeeding requires a lot of patience, skills, and motivation from mother. Thus, if the mother is not skilled enough or the mother’s general condition is not good enough to express her milk herself (according to WHO recommendation), another nutritional method, i.e. formula will be chosen. In this regard, Davanzo stated that the practice of routine separation of the newborn infant from her mother, can damage the mother–baby relationship and the re-beginning of breastfeeding will be difficult [55].

In addition to the mother’s inability to start or continue breast milk expression, she may also be concerned about the safety of her milk. Therefore, it is important to reassure the mother that her milk is safe. Interestingly, almost a decade ago, veterinary medicine investigators have reported the detection of some antibodies against some viruses such as Coronavirus in colostrum of non-immunized, naturally infected cows [65]. The authors claimed that these antibodies can develop passive immunity against Coronavirus in their suckling calves [65]. Also, Davanzo believes that in the light of limited scientific evidence breast milk cannot be considered a vehicle of Coronavirus infection, but it contains some specific antibodies that can help the baby become stronger against the virus [54]. During the SARS outbreak, at ~130 days after illness onset, antibodies of SARS-CoV were detected in the breast milk of a pregnant woman, with no evidence of virus [62,66]. This highlights the importance of further research on human breast milk antibodies that can have protective roles and lead to passive immunity in the infant of infected mothers. Another important point is the possibility of respiratory distress in preterm or term babies of pregnant women who have a serious or critical infection. Thus, all pregnant women with COVID-19 infection should be admitted to the hospitals that are equipped with NICU.

**Recommendation**

- Breastfeeding can be encouraged in infected or suspected mothers. This should be based on informed decision making and in full compliance with measures of infection control. If there are concerns about compliance with preventive measures, or the parents are worried about the safety of the milk, bottle-feeding will be a better option.
- Parents should be taught that if a baby is in close contact with a sick person, such as his mother, the risk of infection is very high, so both the infected mother and other suspected or infected people should be kept away. Also, no one should visit the baby except the healthy parent and caregiver with personal protective equipment (PPE).
- The mother should be trained on how to breastfeed (with all three methods of hand, syringe, or pump). In the first few times of breast expression, the trainer should observe mother to make sure that the milk is properly expressed.
- Mother and other family members should be advised to disinfect the pump or other milk containers with agents made from sodium hypochlorite.
- Before discharge, mothers should be taught about conditions that can help the breast milk to come out better during breast expression, including relaxation, massage, and warming the breasts.
- If parents decide to consume formula because of reasons such as fear of milk safety, teach them how to clean the bottle well.
- Because the baby does not breastfeed, milk stasis can lead to problems such as full breast, breast tenderness, and inflammation of the breast. The symptoms of these problems should be explained to the mother. Additionally, the suitable interval between breast expression and how to disinfect the equipment, such as a bottle or pump, after each feeding should be taught to the parents.
• The person who is going to take care of the baby during two weeks of isolation should be taught how to breastfeed the baby and the principles of personal hygiene should be emphasized, including regular hand washing and PPE.

• Because the symptoms of the onset of infection in the baby may be nonspecific or gastrointestinal disorders, the first symptoms may be, so these symptoms should be taught to caregivers and parents and they should be warned that when they see these symptoms, the baby should be taken immediately to an emergency room.

• Using appropriate masks by parents and the child’s caregiver, the type of gloves, and the correct way to wash the hands should be given high priority.

• Follow up on the detection of initial symptoms of infection after discharge by phone calls or virtual networks.

• Parents should be informed about national screening, vaccination, and routine visits programs during the COVID-19 pandemic.

• Researchers should introduce ways to help the mothers do breast expression more effectively and encourage them to continue to do so until the end of the baby’s isolation period.

• It is critical to update national/international guidelines to offer a practical guide to the health care providers, physicians, and parents.

• Finally, further studies are strongly recommended to assess the safety of breast milk.

Acknowledgments

Special thanks to the Education Department and Midwifery team of Kamali Hospital in Karaj, Iran, for sending us the Iran’s Ministry of Health guideline on Breastfeeding and Neonatal Care in COVID-19 pandemic.

Author contributions

SSS designed the work and collected the relevant articles. SSS, and MEK, contributed to the review of articles, to draw conclusion and to write recommendations.

Disclosure statement

No potential conflict of interest was reported by the author(s).

ORCID

Shirin Shahbazi Sighaldeh http://orcid.org/0000-0003-4043-923X
Mohammad Ebrahimii Kalan http://orcid.org/0000-0001-7709-5392

References


