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A new pandemic – new questions: postnatal care of infants born to mothers with suspected or confirmed COVID-19

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ABSTRACT

COVID-19 infection is primarily a community-acquired airborne respiratory infection, making pediatric and neonatal populations extremely vulnerable to the disease. Since the beginning of the coronavirus pandemic, many questions regarding mother and infant health have arisen, one of the most discussed issues being the management of infants born to mothers with suspected or confirmed COVID-19. Is it advisable to separate the child from the positive mother immediately after birth? What are the recommendations for breastfeeding? Are there any short and long-term follow-up indications or are there any possible long-term complications that we should take into account in those children? And not lastly, what are the most respectful and ethical measures both for mother and infant? We aim to analyze and compare the existing guidelines regarding the management of infants born to mothers with suspected or confirmed COVID-19 and to discuss the similarities and discrepancies between the available protocols.

Keywords: COVID-19, newborn, guideline, neonatal care

BACKGROUND

A global pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in December 2019 spreading from Wuhan, China throughout the whole world [1]. SARS-CoV-2 is a highly contagious positive-sense single-strand RNA virus that spreads in three main ways: aerosol transmission, through close contact, or via respiratory droplets [2]. There is limited evidence to confirm the occurrence of vertical transmission of SARS-CoV-2 (mother to child, either in utero or peripartum) [3–5]. However, some studies reported a low risk of vertical transmission in the third trimester, similar to those pathogens that cause congenital infection [6–10]. Shah et al. proposed a list of criteria for diagnosing congenital SARS-CoV-2 infection: mother with a positive polymerase chain reaction (PCR) test for SARS-CoV-2 either prenatally or within 2–3 weeks of birth, associated with a positive PCR test within 12 h of birth in child [4]. In symptomatic cases, the evidence of SARS-CoV-2 infection (by PCR test) in one umbilical cord blood or amniotic fluid prior to the rupture of membranes is enough for diagnosis.

Although initially scientific reports described a lower susceptibility to the virus among pediatric population, Cardenas et al. showed that the transmission rate is the same in children as it is in adult

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subjects [11]. As regarding clinical manifestations of pediatric COVID-19 infections, those vary and differ from the ones seen in adult patients [12]. Nonetheless, not only symptomatic forms or severe diseasses that common in pediatric patients but also death rates are low [13]. Moreover, the prevalence of SARS-CoV-2 infection in this population might be underestimated as a result of the high number of asymptomatic individuals, which means there is less testing done in these subjects, leading to fewer confirmed cases [13]. Pediatric patients with COVID-19 tend to develop mild upper respiratory tract infections associated with symptoms as rhinorrhoea, nasal congestion, sore throat, and fever [14]. Anedda et al, reported that while children are less affected by SARS-CoV-2 infection compared to the adult population, there are some high-risk groups, such as infants (0-1-year-old) or children dealing with pre-existing comorbidities (bilateral hydronephrosis, congenital heart disease, obesity, diabetes, asthma or chronic lung disease, sickle cell disease, or immunosuppression) [13].

Regarding the neonates, being difficult to distinguish the potential symptoms of COVID-19 in the newborn from the common symptoms of mild respiratory distress syndrome, transient newborn tachypnea, and neonatal sepsis, Chinese experts have proposed a proactive testing protocol [12]. In addition, official bodies of the Chinese state, such as the National Health Commission of China, have recently proposed screening and tracking infants born to COVID-19-positive women [15].

METHODS

We conducted literature research for guidelines and consensuses regarding clinical practice for infants born to mothers with suspected or confirmed COVID-19. We performed a systematic search on PubMed and EMBASE databases using keywords: ”COVID-19” OR ”SARS-CoV-2” AND “newborn” OR ”infant” OR ”neonate“ AND ”guideline” OR ”consensus” OR “protocol” from the time of their inception to May 2021 (Figure 1). National or international clinical practice guidelines and guidance documents with recommendations for the management of infants born to mothers with suspected or confirmed COVID-19 were eligible for inclusion. Websites of national pediatric associations and bibliographies of all included guidelines were examined to identify further relevant resources.

RESULTS

Clinical practice guidelines from the following countries were included in this review: Australia, Brazil, Canada, China, India, Ireland, Italy, Spain, and Turkey, as well as the recommendations provided by the World Health Organization (WHO), Centers for Disease Control and Prevention (CDC) and American Academy of Pediatrics (AAP). We focused on: rooming-in, breastfeeding, testing, and follow-up recommendations (Table 1).

COVID-19 TESTING

All the selected guidelines include specific recommendations regarding COVID-19 assessment. Most of the papers (9/12) underline the importance of general testing for all infants born to mothers with COVID-19. AAP takes into account the financial impact allowing centers with limited testing resources to make testing decisions on a case-by-case basis [18]. Also, testing should be prioritized for neo-

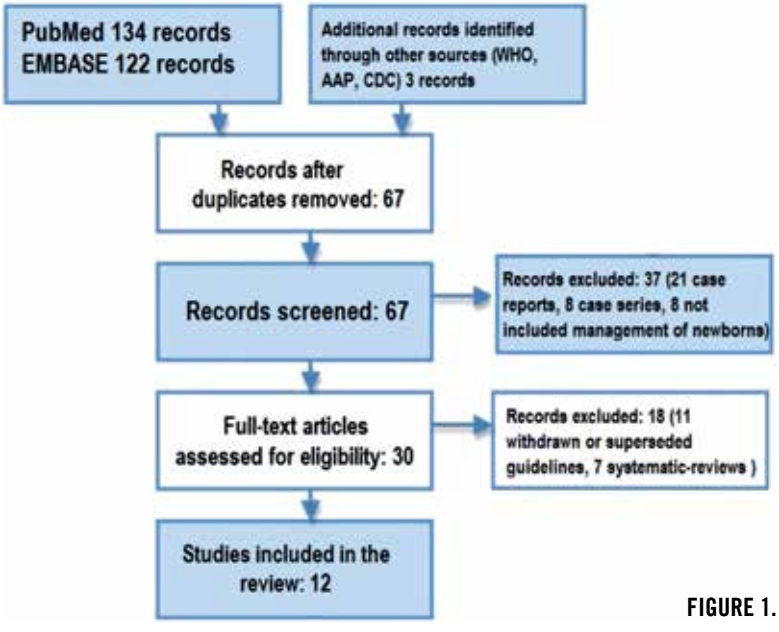

FIGURE 1. Literature search PRISMA diagram flow

TABLE 1. Recommendations for infants born to mothers with suspected or confirmed COVID-19

Guideline	Rooming-in	Breastfeeding	Testing	Follow-up
WHO [16]	Stay with mother	Allowed (hygiene precautions)	All infants	Not specified
CDC [17]				Close outpatient follow-up after discharge in suspected or confirmed COVID-19
AAP [18]	Temporary separation (become less infectious) or allowed to stay with mother her with distancing (at least 6 feet)		All infants* Centers with limited testing resources - testing decisions on a case-by-case basis.	Frequent outpatient follow-up (via phone, telemedicine, or office visit) through 14 days after birth for positive newborns
Australia [19]	Stay with mother		All infants	Not specified
Brazil [20]	Stay with mother; keep distance (2 m)		Only symptomatic infants	
Canada [21]	Stay with mother		All infants	Reevaluation after 48–72 h by a pediatrician
China [22]	Isolation room	Milk formula, breastfeeding discouraged		Reevaluation after 2–3 weeks
India [23]	Allowed to stay with mother	Allowed with hygiene precautions	If the mother had COVID-19 infection within 14 days before birth or contact in postnatal period	Telephone follow-up or home visit by a healthcare worker
Ireland [24]			Only symptomatic infants	Provide post-discharge advice about indications for readmission and the possible course of the disease
Italy [25]			All infants	At 14 and 28 days (testing only for research protocols)
Spain [26]				Follow-up criteria to be defined
Turkey [27]	Allowed to stay with mother if both positive and well. If negative to positive mother - separation or rooming-in according to mother's request			Not specified

nates with signs suggestive of COVID-19 as well as neonates with SARS-CoV-2 exposure requiring higher levels of care or who are expected to have prolonged hospitalizations (>48-72 hours depending on delivery mode). For neonates with manifestations suggestive of COVID-19, alternative diagnoses should be taken into consideration. The diagnosis is based on a positive SARS-CoV-2 RNA test by reverse transcription polymerase chain reaction (RT-PCR) using nasopharynx, oropharynx, or nasal swab samples. Serologic investigations are not recommended for neonatal diagnosis. Interestingly, contamination of umbilical cord blood may occur due to cross-contamination with maternal blood during sample collection. A fetal/neonatal peripheral blood sample or testing of another sterile or non-sterile sample is needed to confirm the diagnosis [28].

The recommendations of the guidelines from Brazil and India are to test only symptomatic infants and to use a case-by-case analysis to decide whether to test or not an asymptomatic infant born to a positive mother.

ROOMING-IN

Rooming-in is an evidence-based practice that promotes keeping healthy newborn babies and their mothers together in post-labor recovery rooms. Separating a mother from a child has both ethical and emotional implications. According to WHO, skin-to-skin contact and practicing rooming-in throughout the day and night are encouraged, whether the mothers or the newborns have suspected, probable, or confirmed COVID-19 [16]. However, infection prevention measures (i.e., wearing a mask, and practicing hand hygiene) should be taken as there is a potential risk of transmission [17]. In those cases with suspected or confirmed infection in mothers, CDC considers that there is no potential risk of virus transmission if the following three criteria are simultaneously met: at least 10 days have passed since their symptoms first appeared, at least 24 hours have passed since their last fever without the use of antipyretics, and their other symptoms have improved. If these criteria are not met, the

mother may temporarily separate from the newborn. Also, if the mother is too ill to take care of the newborn, or the newborn is at risk of developing severe illness (prematurity, underlying medical conditions), the healthcare providers should take into consideration the temporary separation [28].

The first guideline released by AAP at the beginning of the COVID-19 pandemic recommended that the mother should be separated from her child to minimize the risk of neonatal SARS-CoV-2 infection [18]. The early approach to mother-infant separation was based on limited knowledge regarding the prenatal and postnatal transmission of the virus. This recommendation has been changed as a result of the studies which showed that the risk of contracting the virus is the same even if the mothers are separated from their newborns or not [29]. Although the most recent recommendations of the AAP support the rooming-in system, it is highly indicated that the mother should keep a safe distance of at least 6 feet from her child whenever possible.

The AAFP (American Academy of Family Physicians) also encourages parent-infant bonding and advises against the separation of the mother from her newborn if circumstances allow. For the protection of the child, some key steps need to be followed: wearing a mask and a gown, practicing rigorous hand hygiene, and limiting contact with the newborn when not breastfeeding [30].

Many countries and governments (The Government of Western Australia, the Canadian Paediatric Society, the National Neonatology Forum of India and the Indian Academy of Pediatrics, the Ministry of Health of Brazil, the Institute of Obstetricians and Gynaecologists of the Royal College of Physicians of Ireland, the Italian Society on Neonatology (SIN) and the Turkish Neonatal Society) have aligned to the WHO recommendations, suggesting that full-term newborns who are not requiring NICU admission should be roomed-in with their mother whenever possible, following the hygiene precautions. Separating mothers with SARS-CoV-2 infection from their children may delay bonding and skin-to-skin contact which is highly needed immediately after birth [24].

On the opposite, the guideline from China recommends immediate separation of the newborn from the positive mother using an isolation room towards reducing the risk of spreading the virus. Patients with COVID-19 were treated in special tertiary-level hospitals, in isolated buildings, reserved for hospitalizations of severe infectious diseases. Even infected or suspected newborns were hospitalized in these wards, NICU teams being assigned to take care of them. Infected newborns were placed in incubators in order to reduce the potential for airborne transmission between patients and medical staff [15].

There are two situations where separation could be accepted: mothers who are too ill to care for their infants or who need higher levels of care, and neonates at higher risk for severe illness (preterm infants, infants with underlying medical conditions, infants needing higher levels of care).

BREASTFEEDING

It is a well-known fact that breastfeeding brings many benefits to the neonate, as well as to the mother. Breast milk is an important source of nutrients for the newborn, it provides immunity to protect the newborn against infections and it decreases the infant's mortality rate.

All the included papers, except for the Chinese guideline, encourage breastfeeding [22]. In China, parental visitation, including the breastfeeding ones, were suspended during the hospitalization of the newborn [15].

Moreover, WHO underlines the idea that infants born to mothers with suspected, probable, or confirmed COVID-19 should be fed according to standard infant feeding guidelines, with special precautions when necessary [31]. The recommendation is that breastfeeding should be initiated within the first hour after birth or as soon as the mother can breastfeed. Although WHO supports breastfeeding, a list of precautions should be taken into account: using a mask that covers both mouth and nose, hands washing for a minimum of 20 seconds before and after touching the infant, and cleaning and disinfecting surfaces.

Based on available evidence regarding COVID-19 infection in neonates, the risk of disease is low; the infection is frequently asymptomatic, while the consequences of not breastfeeding and separation between mother and child can be significant.

FOLLOW-UP RECOMMENDATIONS

The impact of COVID-19 maternal infection on children's development is not established. Although seven of the included guidelines provide recommendations for follow-up after discharge, there are not yet any clear criteria for the frequency and the eligible infants for specific follow-up strategies. According to AAP, neonates with suspected or confirmed COVID-19, or ongoing exposure, require close outpatient follow-up after discharge, with frequent outpatient follow-up (via phone, telemedicine, or office visit) through 14 days after birth for positive newborns, but there are no available protocols to decide the frequency and the indications for retesting in these categories [18].

Not only handling but also disposal of dirty diapers has become an extremely important measure,

Chinese specialists paying special attention in this regard, due to reporting prolonged excretion of fecal virus for several weeks after clinical recovery. Therefore, the correct handling of diapers or materials contaminated with other secretions (especially respiratory) is a significant measure in China in order to reduce the possibility of the disease spreading both inside tertiary units and after discharge [15].

Aiming to avoid frequent outpatient visits and to reduce unnecessary hospitalizations during the COVID-19 epidemic, China has launched a new online program to monitor indirect hyperbilirubinemia in newborns, using a smartphone app called Biliscan, available in Asia, Europe and Africa, through which parents can monitor transcutaneous bilirubin (TCB) levels. Thus, before discharging the newborn, parents download and install the application on their smartphone and practice using the software under the guidance of medical staff, receiving a color calibration card for home use. The doctor then offers advice to the parents and schedules the next online consultation, based on the answers obtained to the questionnaire and the TCB level. If the TCB level is above the 95th percentile in the first week after birth, exceeds 15 mg/dL after the age of 7 days, or there is an increase in bilirubin levels above 5 mg/dL in the last 24 hours, the baby will be scheduled for outpatient clinical evaluation. Newborns with significant hyperbilirubinemia will be hospitalized, avoiding outpatient day phototherapy, as the outpatient setting increases the risk of transmitting SARS-CoV-2 infection [15]. This neona-tal hyperbilirubinemia follow-up program has been used in tertiary hospitals in China and has proven to be a feasible and effective solution for newborns with ABO hemolysis after discharge.

DISCUSSIONS

The American Academy of Pediatrics (AAP) and Society of Obstetricians and Gynecologists (SOGC) recommend that newborns of a COVID positive mother to be considered suspected for COVID-19 [18,32]. According to AAP, all these infants should be tested by reverse transcription polymerase chain reaction (RT-PCR) at approximately 24 hours after birth and, if negative, retested at approximately another 24 hours after [18]. In case of early discharge of the asymptomatic newborns, prior to 48 hours of age, a single test at 24 to 48 hours of age is enough. However, it is advisable to establish the diagnosis by two positive tests, because one single positive RT-PCR test may also be explained by active viral replication or by viral fragments acquired during vaginal delivery [33].

One of the most efficient measures to prevent the spreading of the SARS-CoV-2 infection is vaccination. Randomized controlled trials have been run in order to evaluate the efficacy of these vaccines and their side effects, but pregnant and breastfeeding women were not included in these trials. Based on the available information about the technologies used in the vaccine development, CDC states that the authorized vaccines are not a risk for lactating women and babies fed with breastmilk, therefore breastfeeding mothers can receive the COVID-19 vaccine. Vaccine-induced antibodies have been identified in umbilical cord blood and breast milk samples, meaning that vaccination of the mother can lead to possible fetal and neonatal immunization [34].

According to French National Authority for Health (Haute Autorité de Santé; HAS), it is recommended that the first consultation for the neonates born to mothers with COVID-19 should be within the first 24 h of arrival at home with the midwife, then a consultation between the 6th and 10th day postpartum, preferably at the pediatrician's or general practitioner's practice, in accordance with the safety protocol in place [35]. However, the impact of early maternal infection during pregnancy on child development is not yet known, requiring close monitoring of the child at each visit.

Besides the healthcare aspects, this pandemic raised some ethical issues regarding the separation of the newborn from the mother and the initial disapproval of breastfeeding. There is no evidence suggesting that COVID-19 in mothers who are otherwise healthy leads to serious illness in newborns. However, the healthcare professionals faced many difficulties regarding the best practice to choose while working with limited evidence.

Globally, multiple efforts are made to understand the consequences of Sars-CoV-2 infection on pregnant women and infants.

In conclusion, the impact of maternal COVID-19 and its risk on newborn future development are still not well known. All the guidelines and the consensus papers regarding infants born to mothers with suspected or confirmed Sars-CoV-2 infection seek to provide safety for newborns without compromising the benefits of early contact. Most of the guidelines underline the benefits of rooming in breastfeeding. However, some situations require special neonatal care (preterm newborns, NICU admission) and in these scenarios, the decisions are frequently made on a case-by-case basis. A questionnaire could be used as a practical tool for the physicians, the results aiming to help direct public health decisions and clinical guidance for the most suitable care in case of affected pregnant women and infants.

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