



Novel Corona Virus Pandemic and Neonatal Care: It's Too Early to Speculate on Impact!

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Abstract

The entire world is reeling under the effects of the novel corona virus pandemic. As it is a new infection, our knowledge is evolving constantly. There is limited information about impact of corona virus on neonatal care in relation to newborns with confirmed or suspected COVID-19. In this article, we summarize the current approach to this infection in relation to newborn babies. We discuss the basic aspects of the infection, the approach of care to novel corona virus disease 2019 (COVID-19) in positive pregnant women, the likely presentation in newborns (as per current knowledge), and the approach to the management of neonates with infection or at risk of the infection. Children are less susceptible to COVID-19 infection and generally have a mild course. There is a lower risk of severe disease among pregnant women and neonates. It was recommended to follow the current protocols for management of symptomatic newborn with isolation precautions, antibiotics, and respiratory support.

Keywords Neonatal · COVID-19 · Novel corona virus · Pregnancy · Personal protective equipment · PCR

Abbreviations

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| CSD | Cesarean section deliveries |
| CPAP | Continuous positive airway pressure |
| EBM | Expressed breast milk |
| NICU | Neonatal intensive care unit |
| COVID-19 | Novel corona virus disease 2019 |
| PPE | Personal protective equipment |
| RT-PCR | Reverse transcriptase-polymerase chain reaction |

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| SARS-CoV-2 | Severe acute respiratory syndrome coronavirus 2 |
| WHO | World Health Organization |

Introduction

Since December 2019, when the novel corona virus-related infections were reported in the Wuhan province in China, the world has witnessed a situation never seen before. The virus

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has now been reported in most countries around the world and since March 11, 2020, has been declared a pandemic by the World Health Organization (WHO) [1]. There has been a high case fatality rate, and as of now (mid-June 2020), close to 8 million cases and nearly 440,000 deaths have been reported [2]. As it is a new infection and disease characteristics are still being elucidated in many settings, the exact protocols that we follow in different age groups will need regular updates.

The knowledge on COVID-19 in neonates is only based on a recent experience over the past 6 months or so. Children are less susceptible to COVID-19 infection and generally have a mild course in newborns, and children experience with significantly lower death rates [3, 4]. Moreover, there is limited information about the impact of corona virus on neonatal care in relation to newborns with confirmed or suspected COVID-19 [5, 6]. In this article, we discuss the basic aspects of the infection, the approach of care to novel corona virus disease 2019 (COVID-19) in positive pregnant women, the likely presentation in newborns (as per current knowledge), and the approach to the management of neonates with infection or at risk of the infection.

Novel Coronavirus Infection—Brief Outline

The novel coronavirus, named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), belongs to the family of viruses called Beta coronavirus, similar to the one causing SARS-1 outbreak in 2002–2003 [7]. It is a single-stranded RNA virus with a helical capsid with radiating spikes (hence the name corona), and the disease is referred to as coronavirus disease 2019 (COVID-19). Later on, on February 2020, the Coronavirus Study Group of the International Committee on Taxonomy of Viruses issued a statement announcing an official designation for the novel virus: severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [8]. The virus spreads by airborne (aerosol and droplet generation by atomization while coughing, sneezing, or even talking) and droplet contact spread and has a high attack rate [2, 9]. Although the elderly people with co-morbidities are at high risk, so far, newborns and children are relatively spared from serious complications [10]. Symptoms of COVID-19 appear to be less severe in infants and children in comparison than that of adult patients [1, 11–13]. The diagnosis is made by positive reverse transcriptase-polymerase chain reaction (RT-PCR) test result for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) usually on swabs taken from deep intranasal and oropharyngeal swabs [2, 9]. The antibody testing and other tests to assess immune status are not fully developed yet.

Pregnant Women with COVID-19: Impact on Maternal/Neonatal Health

Currently, there is no evidence of higher risk of severe disease and complications among pregnant women with COVID-19 compared with healthy non-pregnant adults [14–18]. There is only limited data on the impact of the current COVID-19 outbreak on women affected during pregnancy and newborns. Currently, no data was suggesting an increased risk of miscarriage in pregnant women with COVID-19 infection. In women with symptomatic COVID-19, there may be an increased risk of fetal compromise in active labor [19]. Women have been advised to avoid water births to prevent the risk of disease transmission through feces. Data from China found severe complications in 8% of pregnant women with COVID-19 [14]. However, the high rate of cesarean section deliveries (CSD) in Chinese reports is concerning, and subsequent reports from different countries have not confirmed any need to consider CSD apart from the obstetric and maternal condition-based decisions. Martinez et al. [15] reported delivery details of 72 COVID-19 positive mothers in Spain, and the CSD decision was based on obstetric decision (just over 40% CSD rate). The study could not demonstrate the presence of coronavirus in placenta, amniotic fluid, or cord blood in the cases [16]. The maternal outcome was slightly worse (in terms of needing respiratory support) for mothers undergoing CSD, and the newborn outcome was not different. Only 3 of the 72 newborns were positive on the initial test, and all of these were negative on the repeat test at 48 h. Two of the babies developed infection after 2 days, likely acquired from the mother, but all babies were well and asymptomatic [15]. Besides, initial reports on the COVID-19 infected pregnant women in Wuhan indicated that most of them were in their third trimester, few on second trimester, and none identified at first trimester [20]. However, the study showed that the fetus of the SARS-CoV infected mother in the first trimester of pregnancy would develop intrauterine growth restriction (IUGR); therefore, more attention should be paid on the prevention of COVID-19 in the first trimester of pregnancy [21].

There is no evidence that COVID-19 has an effect on fetal development [22]; however, increased potential risk of preterm delivery has been emphasized [23]. An analysis of 23 studies involving pregnant mothers with COVID-19 demonstrated a preterm delivery rate of 47% [24]. One of the major complications of preterm deliveries, necrotizing enterocolitis, may overburden the obstetrics and neonatal services [23].

How Do Neonates Get Infected?

Recent studies from the UK and other countries confirmed that vertical transmission due to COVID-19 can occur, although the rate is low [14–18]. It is encouraging that horizontally infected

neonates had shown a mild clinical profile with good outcomes [10, 25]. Early Chinese reports suggested that vertical transmission of SARS-CoV-2 does not occur, as amniotic fluid, vaginal mucus, placenta, umbilical cord, cord blood, and neonatal stool specimens tested negative for the virus [19, 26]. Congenital SARS-CoV-2 infection, with virus present in a neonate's nasopharynx at the time of birth, may occur, with a frequency not yet defined. There are reports of perinatal spread especially where the mother is symptomatic just prior to delivery; this could be explained by the relatively high viral load in symptomatic mothers [15, 19, 27].

PCR is a highly sensitive test, and even vaginal secretions in the baby's nose can cause positivity. Results from cord sample and liquor samples are not clear-cut. In another series of 7 neonates born by CSD in Zhongnan Hospital of Wuhan University, 3 newborns showed high IgM levels to COVID-19, suggesting antenatal infection (as IgM does not cross placenta); however, false positive tests cannot be ruled out [28]. Recent UKOSS (UK) study confirmed that vertical transmission due to COVID-19 can occur; however, the rate is low [29]. The study followed up 427 pregnant women admitted to the hospital with confirmed COVID-19 infection, and 243 women had given birth. Among the infants delivered, 5% ($n = 12$) tested positive, and six infants tested positive within the first 12 h of birth. IgM antibodies were detected (cord blood serum) in 3 infants who were tested negative and were all asymptomatic.

Postnatal transmission from parents or carers who have the infection (or are asymptomatic carriers) is the commonest reason a baby may get infected. The role of breast milk in spreading is also being debated, as there have been reports of breast milk being positive for the virus where the mother was symptomatic around delivery [30]. However, the World Health Organization (WHO) as well as other bodies like the Canadian Pediatric Society encourage breast feeding either directly or as expressed milk after parents have been explained the risk and benefits [31, 32]. A recent study has reported that Neonatal COVID-19 infection is uncommon, uncommonly symptomatic, and the rate of infection is no greater when the baby is born vaginally, breastfed, or allowed contact with the mother [33]. Another recent case study published in *Nature Communication* reported transplacental transmission of COVID-19 from a positive pregnant mother during the last trimester to her offspring which occurred due to maternal viremia, placental infection, and neonatal viremia following placental infection [34].

Obstetric and Neonatal Team Members: Infection Control and Prevention

During this crisis, obstetrics and neonatal departments in most hospitals need to plan major changes in their daily health

professional team as there may be shortages of staff due to the infection or replacement in other positions [18]. Further, stress for being infected and possibly infecting families, overwork with long shifts, isolation, restrictions on socialization, and death of relatives or colleagues may decrease their performance [18, 35].

Strict precautions should be maintained by using personal protective equipments (PPE) with social distancing measures in the obstetric and neonatal wards to minimize staff exposure [18, 36]. Breaks should be spread out so colleagues do not eat or drink with each other without mask. If any team member has symptoms or has an infected family member, he/she should be self-isolated and tested. Asymptomatic contacts of this team member should be tested as well, and self-isolation in these cases depends on exposure risk and unit policy [35]. The PPE shortages are reported worldwide, and this should be considered in decision-making. Some hospitals have devised their own policies to reuse N95 or equivalent masks on a rotational basis.

Approach to Care: Mother Is COVID-19 Positive or Symptomatic with Suspected Infection

This is an increasingly common scenario as the virus spreads in the local community and the pregnant women are likely to get infected. Thankfully, thus far the disease has not been reported to be any more severe in pregnant women compared with other healthy adults, though mothers with co-morbidities will still be at high risk. Routine separation of the mother and baby is not promoted, and guidance on individualized care is recommended in pregnancy and delivery [12]. This has been well discussed in a recent article published by Chandrasekharan et al. [32]. From the obstetric and neonatal team's point of view, a clear plan has to be put in place preferably including the parents in the discussion—the following should be discussed [18, 32, 35, 37]:

1. Full PPE as per guidelines for all healthcare personnel involved in delivery process and attending the delivery (resuscitation of newborn). Be careful when baby needs suction, intubation, or mask ventilation as these are aerosol generating procedures. It is recommended to move babies between areas in an incubator as far as feasible.
2. Avoid close contact with the mother soon after birth (skin to skin care not given); delayed cord clamping should be done as per protocol.
3. If the mother is not symptomatic, the baby can be roomed in with the mother with a safe distance of 6 ft (2 m) between her bed and the crib. Except while feeding and during cares, the baby should be in the crib.

4. The mother should wear gloves while handling the baby (preferably) and should wear a mask while approaching or holding the baby or during feeding.
5. Breast feeding options should be discussed. If the mother is symptomatic, we could consider giving a formula and expressing and discarding the milk during the symptomatic phase (when the likelihood of viral shedding in milk is more, and also since the mother may be on antiviral treatment some of which may be relative contraindications during breast feeding). If mother is asymptomatic, she could either breast feed directly wearing a mask or express breast milk wearing a mask and an unaffected relative/carer could feed the baby.
6. Where the mother is symptomatic, especially if she is unwell to look after the baby, it is better to consider separation until the mother is asymptomatic. The baby can then be transferred to her and would use the approach to feeding as above. Due consideration should be given for formula feeds if expressed milk is not adequate or the mother is unable to express due to her condition. Depending on family circumstances and resource availability, the baby can be kept away from the mother either in a nursery setting or in a separate room and looked after by an unaffected family member, with plan to discharge home with them once stable. This option is not preferred if mother is symptomatic but can be offered in an asymptomatic mother if family prefers this option and resources permit the same. The parents should be involved in this decision, and they should be aware that despite these precautions, there is a small risk of the baby getting the infection, and this discussion should be documented.
7. The current recommendation is for the baby to get the test on day 1 (preferably before any direct contact with mother), and if positive, the test could be repeated on days 3–5 and further repeat if still positive. If initial test is negative, we could consider testing again after 48 h in case of a false negative first test. If the baby and mother are well, and the baby is negative, the baby could be discharged home. If the baby is positive for COVID-19, because of the unpredictable course, we could consider monitoring in the hospital until negative result is documented. As the condition evolves and we see more cases, testing to confirm in asymptomatic babies may not be needed—it should be feasible to manage asymptomatic COVID-19 positive babies at home as well after a period of initial stability, and routine repeat tests may not be needed as long as they are isolated and monitored adequately.

Management of Babies Who Are COVID-19 Positive

In some cases, the babies have presented with fever, loose stools, and respiratory distress, but majority is asymptomatic [25]. Since community spread is noted in most countries, any symptomatic baby presenting with fever, diarrhea, unexplained respiratory distress, and other manifestations should have a COVID-19 PCR test sent. Even if the baby's test is positive, management is according to current protocols for symptomatic newborn with isolation precautions, antibiotics and respiratory support as indicated. Such babies should be nursed in incubators. Though the clinical outcome has been good, the neonates with COVID-19 are more likely symptomatic than older children who get the infection. Babies who are asymptomatic could be managed with the parents (rooming in). Babies are unlikely to be infectious unless aerosol generating events like crying or sneezing, but healthcare workers should wear full PPE while handling them. Stool may be infective as well, and precautions are essential while handling stools. Antipyretics like paracetamol can be used as normally indicated. If the baby is unwell with respiratory distress, antibiotic cover as per unit policy would be indicated. In babies presenting with gastrointestinal concerns, a period on intravenous (IV) fluids may be needed, but most of these symptoms appear to resolve over 2–3 days. Some babies present like acute bronchiolitis and may need a period of respiratory support. As high flow nasal cannula therapy and nasal continuous positive airway pressure (CPAP) are aerosol generating procedures, such babies should be in incubators, with expiratory flow tubing preferably within the incubator. The severe disease in adults is a result of an uncontrollable host inflammatory response, a cytokine storm [38], and luckily, this is less pronounced in children as a group including neonates and that could be a factor behind the milder manifestations in this age group. The Kawasaki like inflammatory syndrome described in older children has not been noted in newborns, but we should be alerted to record and publish such presentations if we encounter them. There are no reports so far regarding experience with antivirals and use of immunomodulators like hydroxychloroquine in neonates so far. The recent recovery study [33] in a mainly adult population (unpublished as of now) has reported improvement in patients needing oxygen or ventilatory support with the use of steroids, and if a newborn is sick with COVID-19-related complications, this could be a factor to consider, though not evidence based yet.

NICU Policies

All suspected or confirmed COVID-19 neonates are required to be admitted to neonatal intensive care units (NICUs) [39, 40]. Since community transmission places any individual at

risk of being asymptomatic and carrying the virus, it is advisable to minimize visiting hours (and allow only parents to visit) [41]. Skin-to-skin care and direct breast feeding while in NICU may need to be minimized in open layout NICUs [33]. Unfortunately, one of the negative effects of this practice would be exposure to bottle feeding, as cup feeding or syringe feeding needs closer contact and possible aerosol exposure. It was suggested that COVID-19 negative results of respiratory specimens or anal swabs should be obtained at least 48 h before discharge [39].

Oral Care in Neonates in COVID-19 Pandemic

General oral care recommendations such as oral hygiene care by gentle wiping of oral cavity using sterile gauze dipped in drinking water should be followed. Colostrum can serve as a beneficial oral care in newborn especially for preterm infants. Dental procedures are usually indicated when neonates have the presence of natal or neonatal teeth. Dental extraction is indicated when natal or neonatal teeth are associated with the following conditions: (i) mobility, (ii) inconvenience during sucking/breast feeding, (iii) oral ulceration, and (iv) supernumerary teeth [33]. During COVID-19 pandemic, the dentist must clinically evaluate oral cavity and history associated with feeding discomfort. The dentist should prefer early appointment during the beginning of weekday. Early appointment will prevent the neonate to expose to the patient crowd in the dental office and preventing cross-infection. Telephone conversation and teledentistry should be preferred mode of communication with dentists. Dental practices are considered the focal points for cross-infection, and dental care professionals must take precautions to minimize the risk of infection by adopting national/international infection control and prevention guidelines [42].

Evidence-Based Research

Since this is a novel infection, an ongoing coordinated multinational data collection [43] is critical to improve our knowledge on various aspects of this disease. Ventures like the EPICENTRE (EsPnIc Covid pEdiatric NeonaTal Registry) which is mainly focused on Europe, Vermont Oxford Network (VON) and the American Academy of Pediatrics Section on Neonatal-Perinatal Medicine (SONPM) tool in the USA, and BAPM tool (the UK) are some examples of coordinated multinational projects. As clinicians, we need to be alert to new information emerging which will guide us in further management—there is a website with all recent resources related to perinatal COVID (<https://perinatalcovid19.org/>) [44] which we would encourage colleagues to regularly refer to.

Conclusion and Recommendations

The current crisis is a unique situation faced by the medical fraternity worldwide. It is very important to share clinical and research information and disseminate unique presentations, as well as contribute wholeheartedly to the data collected by registries as mentioned above. As more neonates are affected with acute disease, it is possible that we will see a broader spectrum of problems and we should be alert to new presentations. More challenges will be faced like payment systems and insurance-related issues restricting more frequent testing (when governments scale down testing), and local teams should work together to formulate guidelines suitable to their system, so they can overcome such challenges by working together in a team.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

Consent for Publication All authors reviewed and approved the final version and have agreed to be accountable for all aspects of the work including any issues related to accuracy or integrity.

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