

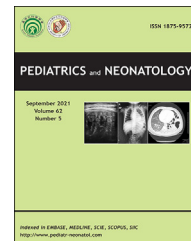


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Review Article

Delivery management of suspected or confirmed COVID-19 positive mothers

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The Coronavirus Disease-2019 (COVID-19) pandemic has brought catastrophic impact on the world since the beginning of December 2019. Extra precautionary measures against COVID-19 during and after delivery are pivotal to ensure the safety of the baby and health care workers. Based on current literature, it is recommended that delivery decisions be discussed between obstetricians and neonatologists prior to delivery, and designated negative pressure delivery rooms should be arranged for COVID person under investigation (PUI). During delivery, a minimal number of experienced staff attending delivery should don personal protective equipment (PPE) and follow the neonatal resuscitation program (NRP). Positive pressure ventilation is best used in a negative pressure room if available. At-risk babies should be transported in an isolette, and tested for COVID-19 in a negative pressure room soon after bathing. Skin-to-skin contact and breast milk feed should continue under certain circumstances. Although newborns with COVID-19 infections often present with symptoms that mimic sepsis and one third of affected patients may demand some form of respiratory support, short-term prognoses are favorable and most recover within two weeks of symptoms onset. In this article, we will further elaborate on topics covering timing and mode of delivery, antenatal steroid, vertical transmission, delivery room management, airway management, transport, testing and isolation after birth, skin-to-skin contact, breast milk feeding, clinical features, outcomes, and

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discharge plans. In addition, we also share our experiences of encountering neonates born of suspected COVID-19 positive mothers.

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1. Introduction

Coronavirus Disease-2019 (COVID-19), a newly-identified coronavirus, appeared in Wuhan, China at the beginning of December 2019, and spread rapidly worldwide. Taiwan, has reported 1048 confirmed and 10 mortality cases with no confirmed newborn cases as of April 5th, 2021. Although COVID-19 cases are rare in infants and neonates with the majority either with mild or no symptoms,¹ severe illness requiring invasive ventilation has been reported.² Chang Gung Memorial Hospital, Linkou Branch (Linkou CGMH), the nearest tertiary referral center to the Taiwan Taoyuan International Airport,³ serves northern Taiwan with over 350 deliveries per month. Since the beginning of January 2020, the neonatology department has promptly developed a delivery room management protocol for pregnant women who were considered as patient under investigation (PUI) or confirmed cases of COVID-19. All precautionary measures were made based on literature review and discussed among experts in the fields of neonatology, pediatric infection, and obstetrics. In this article, we will discuss and address critical issues of delivery management of suspected COVID-19 positive mothers and share our experiences in managing babies born to suspected COVID-19 positive mothers. Most importantly, Taiwan's government has implemented strict regulations in order to achieve low rates of infection in the country; therefore, our policy ensures a stringent strategy in accordance with the Taiwan CDC's guidance and recommendations.

2. Important issues regarding suspected or confirmed COVID-19 positive mothers

2.1. Timing and mode of delivery

According to the American College of Obstetricians and Gynecologists (ACOG)'s recommendations, COVID-19 alone is not an indication for pregnancy termination or delivery, and to this date there is no definite evidence for the optimal timing of delivery; however, early delivery may be warranted if the pregnant woman is critically ill.^{4,5} In addition, the mode of delivery should be based on the progression of labor and by obstetric decisions⁶ since there is no beneficiary evidence of delivery via cesarean section.^{4,5,7–9} Furthermore, owing to the risk of possible perinatal adverse events such as preterm birth, fetal distress, miscarriage and intrauterine growth restriction seen in pregnant women with COVID-19 infection,¹⁰ it is crucial for neonatologists to don full personal protective equipment (PPE) when attending deliveries for high-risk neonates. To avoid possible spread of the disease, it is

recommended that a designated isolated area and delivery room be arranged for COVID-19 PUI and test-confirmed mothers.

2.2. Antenatal steroid

A recent systemic review indicated that in the COVID-19 pandemic era the most common adverse pregnancy outcome was preterm birth; additionally, according to the American CDC's Morbidity and Mortality Weekly Report (MMWR), studies showed an increase in preterm births among the general U.S. population as compared to 2019.^{11,12} Currently, antenatal steroid prior to delivery is still recommended for all preterm deliveries between 24 + 0 and 33 + 6 weeks of gestation.^{4,8} Some studies show a favorable combined maternal and infant outcome, while others recommended antenatal steroid below 32 weeks of gestation for hospitalized PUI women and below 30 weeks of gestation for those admitted to the intensive care unit (ICU).¹³ However, the decisions are best reached by multidisciplinary team decision-making.¹⁴

2.3. Vertical transmission

The question of whether Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) can infect the neonate via vertical transmission has been an issue of debate since the beginning of the COVID-19 pandemic. Although many researchers have proposed intrauterine infection of SARS-CoV-2 is expected to be low based on experience that respiratory viruses seldom contribute to vertical transmission to fetuses, it is still necessary to identify possible spread of the virus through the placenta, amniotic fluids, umbilical cord blood and maternal blood exposure. The SARS-CoV-2 genome has been found in umbilical cord blood in addition to vaginal mucosa and placenta of pregnant women,¹⁵ and evidence of vertical transmission has grown recently with one of the first reports published in February 2020 by Wang et al.¹⁶ However, solidifying evidence of vertical transmission has yet been established,^{10,17–19} and whether vertical transmission exists regarding SARS-CoV-2 still warrants further investigation.

2.4. Delivery room management

According to the World Health Organization (WHO), COVID-19 is transmitted via droplet, and personnel exposed to an infected person within 1 m without proper protective equipment are at exceptionally high risk for contracting the disease.²⁰ Due to the possible airborne characteristic of the SARS-CoV-2, the neonatal intensive care units (NICU) should

assemble comprehensive management protocols for babies delivered by PUI or confirmed mothers prior to delivery, not only to prevent neonates from contracting the virus but also to protect health care personnel during delivery and management. We also believe it is imperative that delivery decisions must be made together between neonatologists and obstetricians. All deliveries should proceed in an isolated negative pressure room with the minimum number of staff,²¹ and all personnel must be dressed in PPE, including gown, N95 respiratory masks, or air-purifying respirator, goggles, and gloves during delivery, standby and transport of the newborn.^{7,9,22} In situations where insufficient negative pressure rooms are available during an outbreak or in limited resource areas, at least a designated delivery room should be accessible, equipped with an infant warmer situated more than 2 m from the mother.²³ Furthermore, until further evidence emerges, most current guidelines propose the continuation of delayed cord clamping based on a lack of evidence of vertical transmission.⁹

Additionally, the resuscitation of the newborn at least 2 m away from the delivery table or provision of a curtain separating these areas is recommended.^{22,24} Resuscitation following standard neonatal resuscitation program (NRP) guidelines were carried out by most facilities.^{7,22,25} In order to achieve minimal contact time of exposure both during delivery attendance and subsequent necessary procedures, we recommend that prior simulation training programs must be established and rehearsed preceding delivery.²⁶

2.5. Management of the airway

Natural infection of SARS-COV-2 is known to occur via respiratory route, and infection can be transmitted quickly by respiratory droplets containing the virus¹; therefore, types of ventilatory support during delivery and the postnatal period are important. In the midst of the pandemic, shortages of negative pressure rooms are common; however, it is highly recommended that all patients requiring continuous positive airway pressure (CPAP) or any form of ventilation be placed in a negative pressure room.²⁷ Noninvasive ventilatory support such as nasal intermittent positive pressure ventilation, nasal CPAP and nasal cannula are open system devices that may generate a high potential risk for droplet and airborne transmission; therefore, the use of high-efficiency particulate air (HEPA) filter is recommended to minimize the risk of aerosolization.⁹ If the PUI is a preterm or high-risk newborn requiring bag-mask ventilation, a HEPA filter should be placed between the mask and the T-piece resuscitator with the filter replaced every 8–12 h.²⁸ Furthermore, all personnel performing resuscitation or intubation must don full PPE. Furthermore, reduction in frequency of pulmonary hygiene is proposed in addition to the use of in-line suctioning catheter when available.²⁷

2.6. Transport of patients

Following initial management of the newborn, the baby should be transferred from the radial warmer into an isolette inside the negative pressure delivery room, while placing the isolette as far away from the delivery table as

possible to minimize contact with contaminated areas. The patient should then be transferred to an isolated room via the isolette,^{7,25} during which time, all personnel responsible for standby, transfer and care for the newborn don full aerosol precaution PPE.^{7,25,29,30}

2.7. Testing and isolation after birth

The American Centers of Disease Control and Prevention (CDC) and the American Academy of Pediatrics (AAP) suggest using reverse transcription polymerase chain reaction (RT-PCR) for SARS-CoV-2 RNA as the gold standard test for acute infection, but the optimal timing and frequency of testing has yet to be established. It is suggested that the specimen be obtained via nasopharyngeal, oropharyngeal, or nasal swab.^{25,31} Subsequent tests are arranged in response to different scenarios: those who test negative and positive initially. According to the AAP's recommendation, facilities may convert to the use of universal precautions if two tests disclose negative results at least 24 h apart for newborns who need continual hospital care. On the other hand, for those who test positive for their initial result, a follow up test should be done repetitively 48–72 h apart until two consecutive negative results are obtained.³²

The AAP also recommends that bathing newborns at the earliest possible time after birth is optimal to facilitate the removal of potential virus residues on the skin.³² Some researchers suggest that the newborn stay with the mother under appropriate precautions in a designated isolation room if clinically stable; others, however, suggest mother and child be isolated separately,⁴ in which case, video visits may be considered to help alleviate parental distress.²⁶ It is also advised that physicians inform the parents regarding separation from their baby prenatally to reduce stress and prevent conflict. The AAP and the WHO declare room-in may be practicable for low-risk mothers with only mild symptoms,^{20,27} provided that the newborn be separated 2 m from the mother or there is a physical shield such as a curtain in between to ensure most extensive protection.³³ However, vast differences in each country's epidemic status should be taken into consideration, and management should comply with the CDC's policy and regulations.

2.8. Skin-to-skin contact and breast milk feeding

Skin-to-skin contact has been shown to have multiple beneficiary effects on newborns,³⁴ so most guidelines reach a consensus that skin-to-skin contact should continue disregarding maternal COVID-19 infection if appropriate PPE³⁵ (surgical mask) is worn along with appropriate hand hygiene. Moreover, AAP also advocate skin-to-skin care per usual center practice.

Breast milk is well known for its benefits of carrying numerous defensive factors against infectious diseases and advantages on the development of immune system.³⁶ Although documentations of virus in breast milk have been reported,³⁷ detection of viral RNA by RT-PCR does not correspond with infectivity. The WHO and the AAP recommend breast milk feeds following appropriate breast and hand hygiene, and that breast milk may be fed to the infant by designated caregivers.³⁸ All breast milk pumping

equipment must be cleaned in between pumping periods according to standard hospital policies, which stipulate disinfecting the pump with cleanser and washing all pump attachments with hot soapy water.

2.9. Clinical features, outcomes and discharge plans

Although children seem to be less severely influenced by COVID-19 infection than adults, in some populations, neonates exhibit more severe disease than older children.³⁹ Symptoms often mimic sepsis, which includes temperature instability (mostly hyperthermia), respiratory distress, hypoxia, gastrointestinal intolerance and lethargy.^{39–41} Gale et al. noted that 42% of neonatal cases suffered severe disease, and that 33% of babies required respiratory support.³⁹ Although the long-term consequences of neonatal infection are as yet unknown, studies show favorable prognoses in neonates as most symptomatic newborns recover within one to two weeks of symptom onset.^{39,41,42}

The discharge timing is solely based upon the baby's clinical condition; some experts recommend two consecutive negative tests prior to discharge and that neonates be taken care of by an asymptomatic and uninfected caretaker. If the baby tests positive and is ready for discharge, Francis et al. suggest quarantine at home.^{32,38} However, currently in Taiwan, all COVID-19 patients must be hospitalized in isolation per Taiwan CDC guidelines and may only be

discharged after achieving the discharge criteria for confirmed COVID-19 cases.⁴³

3. Our experience with suspected COVID-19 positive mothers

The first case was referred to our institution on March 1, 2020, a 32-year-old woman (gravida 1, para 0) without remarkable systemic disease due to suspected preterm premature rupture of membrane at 31 + 4 weeks of gestation. She developed a low-grade fever with progressive exertional dyspnea and throat irritation. The dyspnea worsened on March 5, and an oxygen mask of 5L/min was needed to maintain an oxygen saturation of 90–95%. The obtained chest radiograph revealed bilateral lower lobes pneumonia. During the time that COVID-19 infection could not be ruled out, she was immediately transferred to a negative pressure room for preparation of cesarean section due to maternal respiratory compromise. The second case, a 31-year-old (gravida 1, para 0) HBV carrier, was pregnant at 38 + 5 weeks of gestation who developed sudden onset dyspnea with desaturation. The chest radiograph disclosed left lower lobe pneumonia. She was moved to a negative pressure room for intubation and emergency C/S due to impending respiratory failure. The attendance of pediatricians during delivery followed a protocol developed at the beginning of January (Fig. 1).

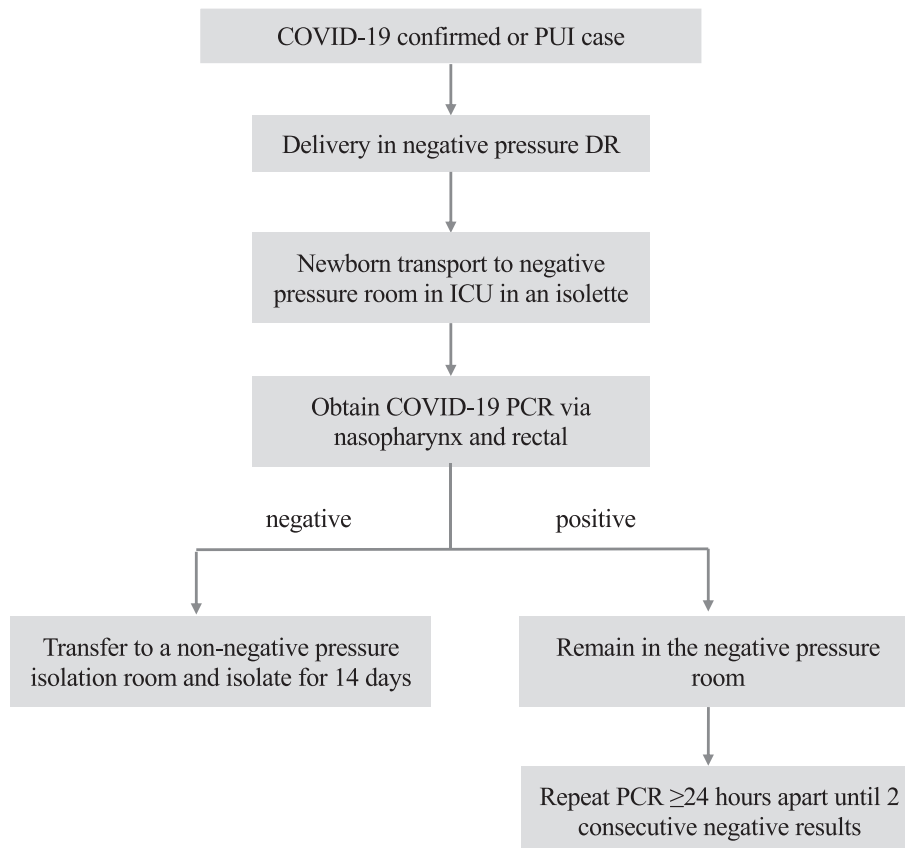


Figure 1 Flowchart of management of COVID-19 confirmed or PUI mothers and neonates.

A designated COVID-19 bag equipped with all the necessities for delivery attendance was prepared prior to delivery as listed in [Table 1](#). This bag remains with the patient until the newborn tests negative for COVID-19. Once the decision for delivery is made, a radial warmer is transported to the negative pressure delivery room, and the entire delivery process is attended by an experienced pediatrician and nurse equipped with PPE.

Management of newborn is executed according to the initial steps of NRP; however, due to the possibility of aerosol spread, positive pressure ventilation (PPV) is avoided, and early intubation using endotracheal tubes with HEPA filter is performed when the patient is distressed and requires PPV. A pulse oximeter is connected for monitoring heart rate and saturation, and an end-tidal carbon dioxide (EtCO₂) monitor confirms endotracheal intubation. Endotracheal intubation is performed by the most experienced pediatrician on site, and the difficult airway response team is alerted.

After the patient stabilizes, the newborn is immediately transferred to a negative pressure room in the pediatric ICU and tested for COVID-19 using PCR analysis obtained from both oropharyngeal and rectal swabs. Once the test is negative, the patient is transferred to an isolation room apart from other unaffected infants for a total of 14 days. Protective gowns, gloves, standard procedural masks, and goggles are required when caring for these newborns. If the newborn tests positive, a repeated PCR is performed at least 24 h apart from the previous examination, and the patient will remain in the negative pressure room until two consecutive negative results, followed by transfer to a non-negative pressure isolation room for further isolation of 14 days. While in isolation, family visits are prohibited, and breast milk feeding is restricted until the mother is confirmed to be negative for COVID-19 infection.

Although our initial protocol may seem to contradict global recommendations for management in the delivery room, and prohibits family visits and breast milk feeding, the basis of our initial approach originates from our hospital's experience on the 2003 SARS outbreak in Taiwan and Taiwan CDC's Interim Guidelines for Clinical Management of SARS-CoV-2 Infection⁴³ prior to the emergence of global guidance.

4. Limitation

Our review has included comprehensive guidelines ranging from different global organizations; however, some limitations of this review exist including the lack of our own country's experience as there are no reported COVID-19

confirmed newborns in Taiwan and we are unable to provide the most updated recommendations as world-wide guidelines are updated rapidly in accordance to the emergence of new information regarding COVID-19. We recommend each facility should adhere to each country's policy and regulations when encountering COVID-19 cases.

5. Conclusion

Since the beginning of the COVID-19 pandemic, debate over whether COVID-19 can be transmitted via vertical transmission has yet to reach a definitive conclusion. The general principal of separating the PUI mother and the newborn by 2 m during and after delivery is proposed until the mother has proven negative for COVID-19 infection. Neonatologists should attend to deliveries of high-risk babies and don full PPE during the entire process, and a negative pressure room is required if CPAP or any form of mechanical ventilator is used. Some of the common symptoms are hyperthermia, respiratory distress and gastrointestinal intolerance, and most neonates achieve favorable prognoses. Breast milk can be pumped after appropriate hand and breast hygiene and the infant can be fed by a designated caretaker. Discharge is based on the baby's clinical condition but should adhere to each country or hospital's discharge criteria. Recommendations for delivery management of suspected or confirmed COVID-19 mothers are summarized in the [Supplementary Table](#).

At Linkou Chang Gung Memorial hospital, we recognized the importance of early preparation for managing newborns delivered by PUI or COVID-19 confirmed mothers, and the neonatologists coordinated with gynecologists and infectious disease specialists to develop a standardized protocol for the delivery of high-risk babies. While we anticipate that our policies and procedures may be beneficial to other institutions, though each center must establish and revise its guidelines to provide the most suitable care for patients.

Declaration of competing interest

All authors declare no conflicts of interest.

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Table 1 Check list for designated COVID-19 bag for delivery attendance.

<input type="checkbox"/>	Neopuff™ Infant Resuscitator
<input type="checkbox"/>	Disposable inflatable ambulatory bag
<input type="checkbox"/>	HEPA filter
<input type="checkbox"/>	Laryngeal mask airway (LMA)
<input type="checkbox"/>	Pulse oximeter with disposable cable
<input type="checkbox"/>	Umbilical vein (UV) catheter
<input type="checkbox"/>	Epinephrine

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.pedneo.2021.06.004>.