



Expert consensus for managing pregnant women and neonates born to mothers with suspected or confirmed novel coronavirus (COVID-19) infection

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ABSTRACT

Objective: To provide clinical management guidelines for novel coronavirus (COVID-19) in pregnancy.

Methods: On February 5, 2020, a multidisciplinary teleconference comprising Chinese physicians and researchers was held and medical management strategies of COVID-19 infection in pregnancy were discussed.

Results: Ten key recommendations were provided for the management of COVID-19 infections in pregnancy.

Conclusion: Currently, there is no clear evidence regarding optimal delivery timing, the safety of vaginal delivery, or whether cesarean delivery prevents vertical transmission at the time of delivery; therefore, route of delivery and delivery timing should be individualized based on obstetrical indications and maternal–fetal status.

Keywords

COVID-19; Expert consensus; Management guidelines; Neonates; Pregnant women

Synopsis

Currently, there is no clear evidence regarding optimal delivery timing or route of delivery for pregnant women with COVID-19 infection; these should be individualized based on obstetrical indications and maternal–fetal status.

1 INTRODUCTION

In late December 2019, multiple unexplained pneumonia cases appeared in Wuhan City, Hubei Province, China. On January 12, 2020, WHO officially named this virus “2019 New Coronavirus (2019-nCoV)” [1], now named COVID-19. As of 10:00AM CET on February 24, 2020, WHO recorded a total of 79 331 confirmed cases globally: China had 77 262 confirmed cases and outside of China had 2069 cases (www.who.int). Confirmed cases of COVID-19 infection were also found in Southeast Asia, Europe, North America, and elsewhere, attracting worldwide attention. Other coronaviruses, such as severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) have caused more than 10 000 infected patients worldwide. The mortality rate of MERS-CoV infection approaches 37% [2–5]. The mortality rate of SARS-CoV infection is 10% in the general population and as high as 25% in pregnant women [6]. China has adopted infection control measures to isolate exposed people and suspected cases in accordance with international standards.

Chinese health officials continue to regularly update diagnosis and treatment protocols and educate and update the public and front-line healthcare providers [7]. China developed the 5th edition of the National Health and Medical Commission Diagnostic Standard with suspected or probable COVID-19 infection in response to this recent epidemic [8]. On February 5, 2020, a multidisciplinary teleconference comprising maternal–fetal medicine and other experts in or from China and the USA was held to discuss recommendations specific to the management of pregnant patients. From this meeting come the recommendations discussed below (Fig. 1). These recommendations are likely to evolve as the course of this novel disease unfolds.

Isolation and screening

Women with symptoms suggestive of COVID-19 should be immediately isolated in a single room for screening, and movement of the patient throughout the facility should be limited. Confirmed cases should be treated in a negative pressure room or isolation ward. Women with signs of critical illness should be immediately transferred to an intensive or critical care unit with negative pressure or equivalent [8]. Hospitals should establish a dedicated negative pressure operating room for pregnant women who must deliver with confirmed COVID-19 infection, and a dedicated neonatal negative pressure isolation room for newborns should be established. Ideally, these rooms will be close to one another, to limit traffic and movement of persons under investigation (PUI) or women and infants with known infection. Visitation may also

need to be limited, as close familial contacts may still be within the window in which they are infectious but asymptomatic.

Initial treatment and diagnostic confirmation

It is critical to distinguish COVID-19 from the following infectious and non-infectious diseases, and to continue to pay close attention and appropriately treat patients with other infections (Table 1). There is currently no clear evidence of definitive treatment for COVID-19, and the mainstay of treatment is supportive care.

1. Even while screening, provide supportive care: ensure adequate rest and sleep; ensure enough caloric intake; provide supplemental oxygen or respiratory support as needed; and maintain fluid and electrolyte balance.
2. Initiate broad-spectrum antimicrobial therapy to cover community-acquired pneumonia while initiating the diagnostic work-up.
3. In an effort to reduce a rising number of deaths due to severe COVID-19 disease, Chinese health officials have begun to recommend starting antiretroviral agents even though there is little empiric data supporting their efficacy. These may include:
 - (a) Alpha-interferon inhalation (5 million U each time for adults, add 2 mL of sterile water for injection, twice per day). The use of this drug in early pregnancy has the risk of hindering fetal growth and development and fully informed consent should be obtained [9].

(b) Lopinavir/ritonavir (200 mg/50 mg, per capsule) two capsules, twice per day.

Lopinavir/ritonavir has been used in the treatment of pregnancy with HIV and the data show no significant teratogenicity [10]; the concentration in breast milk is very low, and no lopinavir/ritonavir is detected in breastfed infants [11–14].

The use of antiretroviral medications has not been recommended worldwide, and providers should consider the most up-to-date recommendations for the use of specific agents in accordance with international and local guidelines.

4. Monitor clinically: closely monitor vital signs and oxygen saturation; perform arterial blood gas analysis and review chest imaging as needed; monitor complete blood count, comprehensive metabolic panel, C-reactive protein, and other biochemical indicators of end-organ function and coagulation status.

5. Identify the pathogen: ensure adequate supplies and measures are in place to collect all necessary samples for pathogen testing.

Diagnostic imaging

Chest imaging is critical for the complete evaluation of COVID-19 infection and should not be withheld in pregnant women. Both X-ray and computed tomography (CT) use radiation. Impact on the fetus is related to the gestational age at the time of the examination and the dose of radiation exposure [8]. Routine diagnostic imaging doses are much lower than 1 Gy, the threshold for early embryonic injury [15, 16].

There have been no reports of fetal malformations, restricted growth, or miscarriage

at exposures below 50 mGy [17]. The minimum radiation dose associated with developmental delay is above 610 mGy [18–21].

According to data cited in clinical guidelines from the American College of Radiology [22] and the American College of Obstetrics and Gynecology [23], when pregnant women undergo a single chest X-ray examination, the fetus will receive a radiation dose of 0.0005–0.01 mGy. CT is associated with a fetal radiation dose of 0.01–0.66 mGy [16]. During the CT examination, intravenous iodine contrast agent can enter the fetal circulation and amniotic fluid through the placenta, but animal studies have shown that it has no teratogenic or mutagenic effects [24–26].

Due to a favorable risk– benefit ratio, X-ray, and CT should be used for pregnant women as clinically necessary, with informed consent. Abdominal shielding and limiting exposure times to the minimum necessary may reduce the total fetal radiation dose.

Management of confirmed cases

While the actual clinical course in pregnancy with COVID-19 is still being elucidated, it is recommended that symptomatic pregnant women be admitted and isolated in an intensive care or critical care unit with negative pressure rooms. Pregnant women may have better uteroplacental oxygenation while lying in a lateral-decubitus position, regardless of the mother's respiratory status.

1. Antimicrobial coverage: for pregnant women with suspected or confirmed secondary bacterial infections, antibacterial treatment should be initiated to ensure broad-spectrum coverage. Antibiotics should be tailored to drug sensitivity results [27]. In patients with localized abscess, adequate drainage is required at the same time to ensure healing [28].
2. Fluid management: critically ill patients without shock should be treated with conservative fluid management measures [29]; when septic shock occurs, volume resuscitation and norepinephrine are used to maintain mean arterial blood pressure (MAP) at 60 mm Hg or above [28].
3. Oxygenation: most pregnant women require an SpO₂ of 95% and above to maintain adequate fetal oxygenation [30, 31]. Oxygen should be given immediately to prevent hypoxemia and reduce the work of breathing and respiratory failure or arrest. Oxygen may be given via high-flow or non-rebreather mask, according to the patient's clinical condition. Humidification therapy devices, non-invasive ventilation (NIV), or endotracheal intubation may be necessary [33–36]. In recent years, clinically, the use of extracorporeal membrane lung oxygenation technology (ECMO) has been indicated to reduce the death of patients with pulmonary infection [37–40], but its use during pregnancy should be limited and less invasive therapy initiated early, with the aim of preventing and treating severe respiratory complications [36].
4. Severe acute renal failure due to sepsis: hemodialysis may be required should severe sepsis lead to renal failure, and should electrolyte imbalances be so impaired that they are life-threatening and unresponsive to conservative management.

Perinatal care considerations

Fetal monitoring

Electronic fetal heart rate monitoring and/or ultrasound should be used to evaluate the fetal status dependent upon the gestational age. Doppler assessment for the presence of fetal heart tones suffice in the previable period. More advanced monitoring is recommended once the fetus reaches viability. Routine diagnostic procedures such as amniocentesis are not recommended in mothers with active infection. Should amniocentesis be considered as part of a diagnostic work-up (such as evaluation for intra-amniotic inflammation and infection), the risks and benefits of such procedures should be discussed with the patient and appropriate informed consent obtained.

Delivery timing

COVID-19 infection alone is not an indication for pregnancy termination, and decisions regarding delivery timing must be individualized. In most cases, the improvement of the mother's condition will improve the fetal status. Ideally, if women can be successfully treated, pregnancies should be allowed to continue to term. Conversely, if a pregnant woman is critically ill, her clinical deterioration may lead to intrauterine fetal demise or loss of both mother and infant. In such circumstances, early delivery may be warranted. The indications for early delivery depend upon: the mother's clinical status; gestational age; and fetal well-being. Pregnant women who

are critically ill due to COVID-19 infection in the previable period (which varies regionally, generally <26 weeks in China, <23–24 weeks in the USA) may require early delivery as a life-saving measure, despite a high risk of neonatal death. In women with severe COVID-19 infection at 26–33⁺⁶ weeks of gestation, the safety of the mother and fetus should be taken into account. At a gestational age of 34 weeks or above, the fetus likely has a high intact survival rate and late preterm delivery may be considered. Before any preterm delivery, antenatal corticosteroids and magnesium sulfate for neuroprotection should be given to any mother with a potentially viable fetus. The risk of vertical transmission during peak infection and while symptoms are very acute is unknown, and maternal antibody production and passive immunity may not yet have had time to develop. Therefore, early delivery should be recommended only as the risk–benefit ratio to the individual mother and fetus demands intervention.

Mode of delivery

Delivery should be performed in a negative pressure isolation ward whenever possible. Movement between the patient’s antepartum treatment room and dedicated operating room should be limited, and the patient should wear a surgical mask outside isolation rooms. The mode of delivery should be based on the usual obstetric indications, as there is no clear benefit of delivery via cesarean in women with COVID-19 infection. Regional epidural anesthesia or general anesthesia can be used for delivery in pregnant women with COVID-19 pneumonia, and the decision

about mode of analgesia should be discussed with the anesthesiology team. If intubation is required due to poor maternal status, general endotracheal anesthesia should be used for cesarean delivery [36].

Placental disposal

The placenta of pregnant women with COVID-19 infection should be treated as biohazardous waste; when the placental tissue sample needs to be tested, it should be disposed of according to local and national regulations.

Neonatal care

Delayed cord-clamping for neonates from pregnant women infected with COVID-19 is not recommended and the neonate should be cleaned and dried immediately.

Previous, limited data on pregnant women with SARS-CoV infection have shown a low probability of vertical transmission from mother to fetus [41, 42]. A single case of COVID-19 has been reported in a neonate at 30 hours of life. Therefore, newborns of mothers with suspected or diagnosed COVID-19 infection should be isolated for 14 days after birth and closely monitored for clinical manifestations of infection. The mother and newborn may need to be isolated separately until both are cleared, pending further clinical outcome data. Strict hand hygiene should be maintained, and the breasts should be cleaned before pumping. At present, it is uncertain whether the COVID-19 virus exists in breast milk and breastfeeding is not recommended. Once cleared to breastfeed, there should be no adjustment of medications. Women should

pump regularly to ensure lactation, and supportive psychological care should be provided as needed.

Personal protection and prevention strategies

Pregnant women are uniquely susceptible to severe disease in the setting of viral infections. At present, there are no effective drugs or preventive vaccines available targeting COVID-19. Personal protection and patient isolation are key to controlling further infection and viral spread [43, 44]. We recommend the following advice to all patients who live in endemic areas:

1. Always maintain good personal hygiene habits. Wash hands with soap and water; all medical staff should wear masks. Avoid close contact with others; reduce participation in large-scale public events, dinners, and other places with large crowds.
2. Be proactive: stay abreast of the latest recommendations regarding COVID-19 infection.
3. Those with suspected symptoms should seek medical treatment and follow all recommendations regarding treatment and contact isolation in accordance with their doctor's advice.

Conclusion

Recommendations for managing pregnant women and neonates born to mothers with suspected or confirmed COVID-19 infection are summarized in Table 2.

Author contributions

DC and HY initiated the study; DC wrote the draft abased on expert advice for all authors in this manuscript; KF and MB made essential revisions for this manuscript.

Conflicts of interest

The authors have no conflicts of interest.

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FIGURE LEGENDS

Figure 1. Flowchart of consultation process for pregnant women with suspected COVID-19 infection.

Table 1. Differential diagnosis of acute severe respiratory distress.

Category	Examples
Viral pneumonia	Influenza, parainfluenza, adenovirus, respiratory syncytial virus, SARS, MERS
Bacterial pneumonia	<i>Mycobacterium pneumococcus</i> , <i>Streptococcus pneumoniae</i> , aspiration pneumonia
Non-infectious lung disease	Vasculitis, dermatomyositis, cardiogenetic pulmonary edema, cardiac disease

Abbreviations: MERS, Middle East respiratory syndrome; SARS, severe acute respiratory syndrome.

Table 2. Summary of management recommendations

No.	Recommendations	Quality	Importance
1	Medical centers should standardize screening, admission, and management of all pregnant women infected with COVID-19. Management should be coordinated in accordance with local, federal, and international guidelines; the public should be informed about the risks of adverse pregnancy outcomes.	Moderate	Critical
2	All pregnant women should be asked whether they have a history of travel to endemic areas or contact with others confirmed to have COVID-19 and should be screened for clinical manifestations of COVID-19 pneumonia.	High	Critical
3	Pregnant women with suspected COVID-19 infection should undergo lung imaging examinations (CXR, CT) and diagnostic testing for COVID-19 as soon as possible.	High	Critical
4	Pregnant women who have a suspected or confirmed COVID-19 infection should be encouraged to report symptoms immediately. They should be screened promptly by qualified medical personnel and directed to present to the appropriate hospital if clinically required. Hospitals with isolation rooms or negative pressure wards should preferentially admit these patients into those units rather than have the patient triaged and transferred between multiple clinics and facilities.	High	Critical
5	For pregnant women with confirmed COVID-19 infection, routine antenatal examination delivery should be carried out in a negative pressure isolation ward whenever possible, and the medical staff who take care of these women should wear protective clothing, N95 masks, goggles, and gloves before contact with the patients.	Low	Critical
6	The timing of childbirth should be individualized. Timing should be based on maternal and fetal well-being, gestational age, and other concomitant conditions, not solely because the pregnant patient is	Low	Important

	infected. The mode of delivery should be based on routine obstetrical indications, allowing vaginal delivery when possible and reserving cesarean delivery for when obstetrically necessary.		
7	In pregnant women with COVID-19 infection who need a cesarean delivery, it is reasonable to consider regional analgesia. If the maternal respiratory condition appears to be rapidly deteriorating, general endotracheal anesthesia may be safer; multidisciplinary planning with the anesthesiology team is recommended.	Very low	Important
8	It is currently uncertain whether there is vertical transmission from mother to fetus, but limited cases have shown no evidence of vertical transmission in patients with COVID-19 infection in late-trimester pregnancy. Neonates should be isolated for at least 14 days. During this period, direct breastfeeding is not recommended. It is recommended that mothers pump milk regularly to ensure lactation. Breastfeeding may not be safe until COVID-19 is ruled out or until both mother and neonate clear the virus. Multidisciplinary team management with neonatologists is recommended for newborns of mothers with COVID-19 pneumonia.	Low	Important
9	It is recommended that obstetricians, neonatologists, anesthesiologists, critical care medical specialists, and other medical professionals jointly manage pregnant women with COVID-19 pneumonia and strictly prevent cross-infection. Medical staff caring for these patients must monitor themselves daily for clinical manifestations such as fever and cough. If COVID-19 infection pneumonia occurs, medical staff should also be treated in isolation wards.	Low	Important
10	All staff engaged in obstetrics should receive training for COVID-19 infection control.	High	Critical

Note: The quality and importance of evidence reported in this paper has been adapted from the quality and importance of evidence criteria described in the Canadian Task Force on Preventive Health Care

(https://canadiantaskforce.ca/wp-content/uploads/2016/12/procedural-manual-en_2014_Archived.pdf).

