

Coronavirus disease 2019 (COVID-19): Pregnancy issues

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INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the virus that causes coronavirus disease 2019 (COVID-19). Information about COVID-19 is evolving rapidly, and interim guidance by multiple organizations is constantly being updated and expanded. This topic will discuss issues related to COVID-19 during pregnancy and delivery.

VIROLOGY AND EPIDEMIOLOGY

General issues regarding the virology, geographic distribution, route of transmission, period of infectivity, and immunity of SARS-CoV-2 are reviewed separately.

PREVENTION

Pregnant women should follow the same recommendations as nonpregnant persons for avoiding exposure to the virus. Women with epidemiologic history of contact should be monitored.

Pregnant women with children should exercise caution. COVID-19 in children is usually mild and may be asymptomatic, although severe cases have been reported. Given the possibility of transmission of SARS-CoV-2 from asymptomatic individuals (or presymptomatic individuals within the incubation period), the Centers for Disease Control and Prevention recommend that children not have playdates with children from other households; that they remain ≥ 6 feet from people from other households when playing outside; and that they wear cloth face coverings in public settings where other social distancing measures are difficult to maintain.

Pregnant health care workers have additional concerns. Some human resources units suggest that pregnant health care workers in the third trimester, particularly ≥ 36 weeks, stop face-to-face contact with patients to help reduce their risk of acquiring infection and its consequences. More commonly, they give pregnant health care workers the option of reassignment or limiting their exposure to patients with confirmed or suspected COVID-19, especially during higher risk procedures (eg, aerosol-generating procedures).

CLINICAL MANIFESTATIONS

All pregnant women should be monitored for development of symptoms and signs of COVID-19, particularly if they have had close contact with a confirmed case or persons under investigation. Signs and symptoms of potential concern include fever or chills, new cough, and shortness of breath; other reported symptoms include sore throat, muscle aches, rhinorrhea/nasal congestion, diarrhea, anorexia, nausea/vomiting, headache, and possibly abnormalities in smell and/or taste. In a cohort of 118 pregnant women diagnosed with COVID-19 during the Wuhan epidemic, fever, cough, and shortness of breath occurred in 75, 73, and 7 percent of patients, respectively. Clinical manifestations (signs and symptoms, laboratory and imaging findings) are similar to those in nonpregnant individuals.

Complications of infection include acute respiratory distress syndrome, arrhythmias, acute cardiac injury, and shock.

Classification of disease severity

In the United States, the National Institutes of Health have categorized disease severity as:

- Asymptomatic or presymptomatic infection – Positive test for SARS-CoV-2 but no symptoms.
- Mild illness – Any signs and symptoms (eg, fever, cough, sore throat, malaise, headache, muscle pain) without shortness of breath, dyspnea, or abnormal chest imaging.
- Moderate illness – Evidence of lower respiratory disease by clinical assessment or imaging and a saturation of oxygen (SaO₂) >93 percent on room air at sea level.
- Severe illness – Respiratory frequency >30 breaths per minute, SaO₂ ≤93 percent on room air at sea level, ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO₂/FiO₂) <300, or lung infiltrates >50 percent.
- Critical illness – Respiratory failure, septic shock, and/or multiple organ dysfunction.

Disease severity has also been categorized as (Wu classification)]:

- Mild – No or mild symptoms (fever, fatigue, cough, and/or less common features of COVID-19).
- Severe – Tachypnea (respiratory rate >30 breaths per minute), hypoxia (oxygen saturation ≤93 percent on room air or PaO₂/FiO₂ <300 mmHg), or >50 percent lung involvement on imaging).
- Critical (eg, with respiratory failure, shock, or multiorgan dysfunction).

COURSE IN PREGNANCY

Limited available data suggest that pregnancy and childbirth do not increase the risk for acquiring SARS-CoV-2 infection, do not worsen the clinical course of COVID-19 compared with nonpregnant individuals of the same age, and most infected mothers recover without undergoing delivery. The patient group most commonly affected by severe disease includes older adults (>60 years), particularly with comorbidities, and most pregnant women are younger than middle age; however, they may have comorbid conditions that increase their risk (eg, hypertension, diabetes, severe obesity, severe asthma, cardiovascular disease). It is known that some patients with severe COVID-19

have laboratory evidence of an exuberant inflammatory response (similar to cytokine release syndrome), which has been associated with critical and fatal illnesses. Whether the normal immunosuppression of pregnancy affects the occurrence and course of this response is unknown.

In pregnant women who develop COVID-19 pneumonia, early data show approximately the same rate of intensive care unit (ICU) admissions as in the nonpregnant population but an increased risk of preterm and cesarean delivery. A preliminary report from the United States indicated 4 of 143 pregnant COVID-19 patients were admitted to an ICU, but these data were incomplete. In an initial United States experience from New York City including 43 pregnant patients with confirmed COVID-19, the disease course was mild in 37 (86 percent), severe in 4 (9.3 percent), and critical in 2 (4.7 percent). In a larger cohort of 147 pregnant patients in the WHO-China Joint Mission Report and a separate report of 118 pregnant patients in Wuhan, 8 percent were severely ill, and 1 percent were critically ill. These percentages are similar to those of nonpregnant, reproductive-age adults. Severe sequelae of maternal infection include prolonged ventilatory support and need for extracorporeal membrane oxygenation (ECMO).

A single maternal death has been reported in the medical literature, and several anecdotal reports exist.

It is important to note that in one report from New York City, 10 of 14 patients who were asymptomatic on admission for an obstetric indication and found to be SARS-CoV-2-positive on universal screening went on to develop symptoms during their delivery admission or postpartum. Of the 14 initially asymptomatic patients, 4 remained asymptomatic, 8 developed mild symptoms, and 2 developed severe/critical disease.

While the course of the infection in pregnant persons is similar to that in nonpregnant persons, there are added issues during pregnancy, such as timing of prenatal care visits and screening tests in uninfected women and, in infected women, potential pregnancy complications, timing and management of labor and delivery, and postpartum care (mother-newborn separation, breastfeeding, infant care, postpartum depression risk). These issues are reviewed below.

Pregnancy complications — Hyperthermia, which is common in COVID-19, is a theoretical concern as elevation of maternal core temperature from a febrile illness during organogenesis in the first trimester may be associated with an increased risk of congenital anomalies, especially neural tube defects, or miscarriage. Use of acetaminophen in pregnancy, including in the first trimester, has been shown overall to be safe and may attenuate the pregnancy risks associated with fever exposure.

Infected women, especially those who develop pneumonia, appear to have an increased frequency of preterm birth. In a systematic review including 51 pregnant patients with well-documented COVID-19, 39 percent delivered before 37 weeks of gestation, 26 percent (9/34) had prelabor rupture of membranes, and 12.5 percent (6/48) had preterm labor. Almost all of the patients (96 percent [46/48]) were delivered by cesarean, and many of these cases appeared to be elective based on the potential consequences of the infection. There was one case each of preeclampsia and gestational hypertension. The only fetal death occurred in a critically ill woman with multiorgan failure on ECMO. The other 48 neonates were in good condition at birth. It is important to emphasize that available data are generally of low quality, reflecting small numbers of cases and a disproportionate number of patients intubated with COVID-19 pneumonia. In women with severe COVID-19 in the third trimester, there appears to be a bias to intervene catalyzed by the belief that management of the mother's respiratory disease will be improved by delivery; however, this hypothesis is unproven.

Vertical transmission

The criteria that should be used for definitive diagnosis of vertical transmission of SARS-CoV-2 are unclear. One suggestion is a neonatal nasopharyngeal swab positive for virus within one to two hours of birth and before contact with an infected individual, and an elevated immunoglobulin M (IgM) level for the virus in cord blood.

To date, SARS-CoV-2 has not been detected in cord blood, amniotic fluid, or placenta. Maternal viremia rates appear to be low (1 percent in one study), suggesting placental seeding and vertical transmission are unlikely. In reviews including up to 51 pregnant women with COVID-19, no cases of intrauterine transmission have been documented. Subsequently, several possible cases based on newborn laboratory and/or clinical findings have been reported, but SARS-CoV-2 testing on fetal blood, amniotic fluid, and placenta was either negative or not performed. Many of these infants were delivered by cesarean and had positive nasopharyngeal cultures for SARS-CoV-2 on days 1 or 2 of life, an elevated IgM level, and/or pneumonia. Positive IgM results are not definitive evidence of in utero infection, and, in many of these cases, early infant infection may have been due to postnatal contact with infected parents or caregivers.

APPROACH TO DIAGNOSIS

The possibility of COVID-19 should be considered in patients with new-onset fever/chills and/or respiratory tract symptoms (eg, cough, dyspnea). It should also be considered in patients with severe lower respiratory tract illness without any clear cause. Residing in or travel to a location where there is community transmission of SARS-CoV-2 or close contact with a confirmed or suspected case of COVID-19 in the past 14 days should heighten suspicion.

Patients who meet the testing criteria should undergo testing for SARS-CoV-2 RNA by reverse-transcription polymerase chain reaction (RT-PCR) on a nasopharyngeal swab specimen, ideally in addition to testing for other respiratory pathogens (eg, influenza, respiratory syncytial virus). Criteria for testing and diagnostic issues are discussed in detail separately. This testing should occur in a location designed to reduce the risk of passing the infection to uninfected persons, such as at dedicated "walk-in" or "drive-in" testing locations from which results can be made readily available to the obstetric providers.

A positive RT-PCR generally confirms the diagnosis of COVID-19, although false-positive tests are possible. False-negative tests on initial testing appear to be common. Sensitivity depends on the precise RT-PCR assay, the type of specimen obtained (nasopharyngeal specimens have higher sensitivity than oropharyngeal or nasal specimens), the quality of the specimen, and duration of illness at the time of testing. If the initial nasopharyngeal test is negative but the suspicion for COVID-19 remains and determining the presence of infection is important for management or infection control, the test should be repeated. In such cases, the World Health Organization also recommends testing lower respiratory tract specimens (eg, sputum, bronchoalveolar lavage), if possible. Infection control precautions for COVID-19 should continue while repeat evaluation is being performed.

A chest radiograph is sufficient for initial evaluation of pulmonary complications in most hospitalized patients with COVID-19. A single chest radiograph carries a very low fetal radiation dose of 0.0005 to 0.01 mGy. Computed tomography (CT) should be performed, if indicated, as the fetal radiation dose for a routine chest CT is also low and not associated with an increased risk of fetal anomalies or pregnancy loss. Some authorities have advocated pulmonary ultrasound for quick diagnosis of

pneumonia in pregnant women, which in certain locations would be the quickest way to ascertain high suspicion of maternal COVID-19 infection.

PRENATAL CARE

Preventing exposure in the community

Social distancing and hygienic measures are reviewed separately.

Patients with potential exposure

Pregnant patients with an epidemiologic history of contact with a person with confirmed, probable, or suspected COVID-19 should self-isolate and be monitored for symptoms. The incubation period is up to 14 days. Diagnostic testing for SARS-CoV-2 infection depends on test availability.

If testing is performed, those who test positive for SARS-CoV-2 and remain asymptomatic can discontinue isolation seven days after the date of their first positive SARS-CoV-2 test.

Further evaluation and management of patients who become symptomatic depend on illness severity, underlying comorbidities, and clinical status. Those with at least moderate illness are typically hospitalized.

Routine prenatal care in asymptomatic women

The American College of Obstetricians and Gynecologists (ACOG) and the Society for Maternal-Fetal Medicine have issued guidance regarding prenatal care during the COVID-19 pandemic (available at acog.org and SMFM.org). It includes general guidance for testing and preventing spread of COVID-19, algorithms, and suggestions for modifying traditional protocols for prenatal visits. These modifications, which should be tailored for low- versus high-risk patients (eg, multiple gestation, hypertension, diabetes), include telehealth, reducing the number of in-person visits, timing of visits, grouping tests (eg, aneuploidy, diabetes, infection screening) to minimize maternal contact with others, restricting visitors during visits and tests, timing of indicated obstetric ultrasound examinations (eg, gestational age, fetal anomaly, fetal growth, placental attachment), and timing and frequency of use of nonstress tests and biophysical profiles.

There are many ways to reduce the time patients, including patients with high-risk pregnancies, are in the office. For example, the clinician can order a 75 gram two-hour oral glucose tolerance test (GTT) instead of a glucose challenge test and 100 gram three-hour GTT (in women with positive results); cell-free DNA screening can be used (at >10 weeks) for Down syndrome screening rather than the combined test (ie, nuchal translucency on ultrasound and serum analytes). Ideally, every woman should have telehealth capabilities and a means for measuring blood pressure at home.

In the author's practice, during the pandemic, most low-risk pregnant women come to the office only for in-person prenatal visits at 12, 20, 28, and 36 weeks of gestation (ie, at gestational ages when ultrasound and/or laboratory tests can be also performed) to minimize person-to-person contacts. Some practices are encouraging that even these visits occur by telehealth. When an outpatient office visit occurs, all patients and health care workers wear at least a surgical mask; no partner is allowed, but video communication is encouraged.

The psychological impact of COVID-19 should also be recognized and support offered. In one study, approximately one-third of respondents reported moderate to severe anxiety.

Medical management of pregnant women with COVID-19

Home care

Most pregnant patients with known or suspected COVID-19 have mild disease that does not warrant hospital-level care in the absence of obstetric problems (eg, preterm labor). Patient instructions and other aspects of home care are similar to that in nonpregnant persons.

The US Food and Drug Administration has expanded its approval for use of noninvasive fetal and maternal monitoring devices in the home in patients who require fetal and/or maternal monitoring for conditions unrelated to COVID-19. This can help reduce patient and health care provider contact and potential exposure to COVID-19 during the pandemic.

Hospitalized patients

Pregnant hospitalized patients should be cared for by a multispecialty team. Guidelines for management of hospitalized patients with COVID-19, including evaluation and care of critically ill patients, are reviewed elsewhere.

Additional issues in pregnant women include:

- **Fetal monitoring** – A specific management issue in pregnant patients is fetal monitoring in those who are at a viable gestational age. The need for and frequency of fetal testing depend upon gestational age, stability of maternal vital signs, other maternal comorbidities, and discussions with the patient and her family that consider the possibly increased risks of stillbirth and perinatal morbidities in the absence of testing as well as the possible risks from increased contact with health care personnel performing this testing. For hospitalized patients, a Bluetooth-enabled external fetal monitor can transmit the fetal heart rate tracing to the obstetric provider. The monitor can be used continuously in unstable hospitalized patients in whom cesarean delivery would be performed for a persistent nonreassuring fetal heart rate pattern. An abnormal tracing might also help guide maternal oxygen therapy. In patients with stable oxygen saturation (SaO₂), a nonstress test can be performed twice daily, as one option.
- **Monitoring for preterm labor** – Monitoring pregnant patients for signs and symptoms of preterm labor is a routine component of obstetric care and should be a component of maternal monitoring of pregnant patients hospitalized in nonobstetric settings.
- **Maternal oxygenation level** – Among critically ill COVID-19 patients, profound acute hypoxemic respiratory failure from acute respiratory distress syndrome (ARDS) is the dominant finding. General supportive care of the critically ill patient with COVID-19 pneumonia is similar to that in patients with ARDS due to other causes. Common complications of COVID-19-related ARDS include acute kidney injury, elevated liver enzymes, and cardiac injury (eg, cardiomyopathy, pericarditis, pericardial effusion, arrhythmia, sudden cardiac death). During pregnancy, maternal peripheral oxygen saturation (SpO₂) should be maintained at ≥95 percent, which is in excess of the oxygen delivery needs of the mother. If SpO₂ falls below 95 percent, an arterial blood gas is obtained to measure the partial pressure of oxygen (PaO₂): Maternal PaO₂ greater than 70 mmHg is desirable to maintain a favorable oxygen diffusion gradient from the maternal to the fetal side of the placenta.

In the intensive care unit (ICU), severely ill patients with COVID-19 are often managed in the prone position. Some ICUs have extended this approach to pregnant women, although even a semi-prone position can be a difficult position in which to place a pregnant woman in the last half of pregnancy.

- Use and type of venous thromboembolism (VTE) prophylaxis – Direct data on thromboembolic risk with COVID-19 are limited but suggest an increased risk. The American Society of Hematology, the Society of Critical Care Medicine, and the International Society of Thrombosis and Haemostasis recommend routine pharmacologic VTE prophylaxis in patients hospitalized with COVID-19 unless there is a contraindication (eg, bleeding, severe thrombocytopenia). We initiate prophylaxis in all pregnant women with COVID-19 admitted to the hospital for management of an antepartum obstetric or medical disorder and all postpartum women with the infection.

Unfractionated heparin is generally preferred in pregnant women who might be proximate to delivery because it is more readily reversed than low molecular weight heparin. Low molecular weight heparin is reasonable in women unlikely to be delivered within several days and those who are postpartum.

- Safety of antiviral drug therapy – Several agents are being evaluated for treatment of COVID-19. Although some of these agents are clinically available for other indications (eg, hydroxychloroquine or chloroquine), their use for COVID-19 remains investigational. At some hospitals, pregnant women with severe COVID-19 are being offered remdesivir in a compassionate-use protocol.

- Remdesivir is a novel nucleotide analogue that has activity against SARS-CoV-2 in vitro and related coronaviruses (including severe acute respiratory syndrome [SARS] and Middle East respiratory syndrome-related coronavirus [MERS-CoV]) both in vitro and in animal studies. It has been used without reported fetal toxicity in some pregnant women with Ebola and Marburg virus disease and is being used to treat, on a compassionate-use basis, pregnant patients with severe COVID-19. Randomized trials of the drug during the COVID-19 pandemic have excluded pregnant and breastfeeding women.

- Both hydroxychloroquine and chloroquine have been reported to inhibit SARS-CoV-2 in vitro, but data from early randomized trials generally do not suggest a benefit. Hydroxychloroquine crosses the placenta. Accumulation in fetal ocular tissues has been observed in animal studies, but fetal ocular toxicity has not been observed in humans, which is reassuring given that the drug has been widely used by pregnant women for treatment of systemic lupus erythematosus or for prevention of malaria. Adverse maternal effects include abnormal heart rhythms (QT interval prolongation and ventricular tachycardia).

Several other drugs are being used in research studies. One such drug is lopinavir-ritonavir, which is primarily used for treatment of HIV infection, including during pregnancy. It crosses the placenta and may increase the risk for preterm delivery, but an increased risk of teratogenic effects has not been observed in humans. Investigational drugs for COVID-19 that are known to be teratogenic include ribavirin and baricitinib.

Use of standard medications for managing pregnancy complications

- Antenatal betamethasone – For the general population, the Centers for Disease Control and Prevention (CDC) recommend avoiding glucocorticoids in COVID-19-positive persons because they have been associated with an increased risk for mortality in patients with influenza and delayed viral clearance in patients with MERS-CoV infection. However, the CDC have not addressed use of antenatal glucocorticoids to reduce neonatal morbidity and mortality from preterm birth in pregnant COVID-19-positive patients.

Because of the clear benefits of antenatal betamethasone administration between 24+0 and 33+6 weeks of gestation in patients at high risk of preterm birth within seven days, ACOG continues to recommend its use for standard indications to pregnant patients with suspected or confirmed COVID-19. However, for pregnant patients with suspected or confirmed COVID-19 at 34+0 to 36+6 weeks of gestation and at risk of preterm birth within seven days, the benefits to the neonate are less clear, and ACOG has advised not administering a course of betamethasone to such patients. However, these decisions may need to be individualized, weighing the neonatal benefits with the risks of potential harm to the pregnant patient.

- Low-dose aspirin – For pregnant women without COVID-19, ACOG has stated that low-dose aspirin should continue to be offered as medically indicated (eg, prevention of preeclampsia). For those with suspected or confirmed COVID-19 for whom low-dose aspirin would be indicated, the decision to continue the drug should be individualized. For example, continuing preeclampsia prophylaxis is likely not worthwhile in severely or critically ill patients or near term. A panel from the National Institutes of Health has stated that persons with COVID-19 who are taking nonsteroidal anti-inflammatory drugs (NSAIDs) for a comorbid condition should continue therapy as previously directed by their health care provider.

Concern about possible negative effects of NSAIDs was raised by anecdotal reports of a few young, nonpregnant patients who received NSAIDs (ibuprofen) early in the course of infection and experienced severe disease. However, there have been no clinical or population-based data that directly address the risk of NSAIDs. Given the absence of data, the European Medicines Agency and the World Health Organization do not recommend avoiding NSAIDs in COVID-19 patients when clinically indicated.

- Tocolysis – In women with known or suspected COVID-19, our preferred tocolytic is nifedipine. It is a suitable alternative to indomethacin, which is subject to the concerns discussed above, and to beta sympathomimetics, which can further increase the maternal heart rate.

Follow-up of women who recover from COVID-19

An ultrasound to assess fetal growth is reasonable a few weeks following maternal recovery, especially in patients who had severe illness. Very limited COVID-19-specific data on fetal growth are available. Fetal growth restriction was reported in two of three pregnancies complicated by SARS and delivered five and seven weeks after onset of illness. The placentas showed areas of fetal thrombotic vasculopathy, which may have been caused by SARS-related coagulopathy or placental hypoxia during the acute maternal illness.

Timing delivery in infected women

For most women with preterm COVID-19 and nonsevere illness who have no medical/obstetric indications for prompt delivery, delivery is not indicated and ideally will occur sometime after a negative testing result is obtained or isolation status is lifted, thereby minimizing the risk of postnatal transmission to the neonate.

In women with severe illness, there are multiple issues to consider, and timing of delivery needs to be individualized. Whether the mother's respiratory disease will be improved by delivery and the risk of postnatal transmission in the delivery room when maternal symptoms are acute are both unclear. It should also be noted that maternal antibody production and, in turn, passive newborn immunity may not have had time to develop.

For the hospitalized patient with COVID-19 with pneumonia but not intubated, some authorities have advocated consideration of delivery in pregnancies >32 to 34 weeks. The rationale is that delivery is performed before the pulmonary situation worsens and ongoing maternal hypoxemia places the fetus at risk of compromise. Most authorities do not advocate delivery prior to 32 weeks, even though the maternal situation may worsen in the second week, given the known morbidity and mortality of very preterm infants.

Timing of delivery of the hospitalized pregnant woman intubated and critically ill with COVID-19 is challenging. After 32 to 34 weeks, some have advocated delivery if the patient is stable, but this could exacerbate the maternal condition. Between viability and <32 weeks, continuing maternal support with fetal monitoring is usually suggested for perinatal benefit as long as the maternal situation remains stable or improving. In some situations, maternal extracorporeal membrane oxygenation may be necessary.

MANAGEMENT OF LABOR AND DELIVERY

Although many asymptomatic patients are concerned about leaving their home because of the COVID-19 pandemic, the American College of Obstetricians and Gynecologists (ACOG) continues to recommend following existing evidence-based guidance regarding home birth.

Infection control precautions

- Prehospital notification of possible infection – The Centers for Disease Control and Prevention (CDC) recommend that pregnant patients who have confirmed or suspected COVID-19 notify the obstetric unit before arrival so that the facility can make appropriate infection control preparations. The obstetric unit should ensure that their infection control practices for these patients are consistent with CDC guidelines.
- Evaluation of all patients presenting to the hospital – All patients should be screened for signs and symptoms of COVID-19, as well as whether they have had close contact with a confirmed case or persons under investigation, before entering the hospital for admission to the labor and delivery unit]. Screening can include checking temperature and asking about fever and/or new cough, shortness of breath, sore throat, muscle aches, rhinorrhea/nasal congestion, and smell and taste abnormalities. The CDC advise prioritizing the testing of pregnant women with suspected COVID-19 at admission or who develop symptoms of COVID-19 during admission.

Asymptomatic patients and presymptomatic patients may present to the labor and delivery unit, which has implications for the health care staff and management of the newborn. For this reason, testing all patients upon presentation may be appropriate. The author's hospital and others in areas with a high rate of infection have begun using a rapid SARS-CoV-2 test on all patients admitted to the labor and delivery unit. We believe this information is useful to inform infection control precautions both intrapartum and postpartum, including newborn care. During the New York City pandemic, 215 pregnant women admitted to two New York City hospitals for delivery were screened for COVID-19, and 33 (15 percent) were SARS-CoV-2-positive. Of the 33 women, 4 (12 percent) were symptomatic and 29 (88 percent) were asymptomatic on admission. Among the 29 asymptomatic women who tested positive, 3 developed a postpartum fever, and at least 1 of these patients was presumed to have COVID-19. One additional patient who tested negative on admission became symptomatic postpartum, and repeat SARS-CoV-2 testing was positive.

The evaluation and diagnosis of women admitted to labor and delivery with suspected COVID-19 are similar to that of other patients admitted to the hospital with suspected disease. The CDC advise prioritizing the testing of pregnant women with suspected COVID-19 at admission or who develop symptoms of COVID-19 during admission.

- Use of personal protective equipment on labor and delivery – The author and others recommend that all clinicians with person-to-person contact wear a surgical mask in the health care setting, under the assumption that every patient and health care colleague might be infected with COVID-19. During active labor in particular, there are concerns of viral dissemination when the patient is forcefully exhaling.

To address asymptomatic and presymptomatic transmission, we also suggest that all asymptomatic patients wear a cloth face covering, at a minimum, consistent with CDC guidance. If a patient arrives to the health care facility without a cloth face covering, a face mask should be used if supplies are available.

- Care of COVID-19-positive inpatients – Ideally, pregnant COVID-19 inpatients should be cared for in specially equipped (eg, negative-pressure) rooms in antepartum, intrapartum, and postpartum COVID-19-only units, similar to other adult COVID-19 inpatients who are usually placed in dedicated COVID-19-only units, halls, or hospitals. Patients with suspected or confirmed COVID-19 are normally instructed to wear a face mask, including during labor and delivery, which may be difficult during active pushing.

Infection control precautions regarding pregnant patients with confirmed or suspected infection are similar to those for other hospitalized patients and are reviewed separately.

- Support persons on labor and delivery – Perhaps the most controversial issue regarding infection control for women in labor and delivery units is whether to allow a support person. Most facilities recognize that a support person is important to many laboring women and permit one support person who must remain with the laboring woman (may not leave her room and then return).

The support person should be screened for fever and other symptoms before entering the building and in accordance with hospital policies. Those with any symptoms consistent with COVID-19, exposure to a confirmed case within 14 days, or a positive test for COVID-19 within 14 days should not be allowed to attend the labor and birth. If screening is negative, we require that the support person wear a cloth face covering, at a minimum, consistent with CDC guidance. If the support person arrives at the health care facility without a cloth face covering, a face mask should be issued if supplies are available.

A support person who screens positive should not be permitted in the hospital. In such cases and when additional support persons are desired, they can be a part of the patient's labor and delivery via video.

Route of delivery

COVID-19 is not an indication to alter the route of delivery. Cesarean delivery is performed for standard obstetric indications.

Even if vertical transmission is confirmed as additional data are reported, this would not be an indication for cesarean delivery since it would increase maternal risk and would be unlikely to improve newborn outcome. Reports of COVID-19 infection in the neonate have generally described mild disease.

Screening patients scheduled for induction or cesarean delivery

Patients should be screened for COVID-19 and can undergo pre-induction/pre-cesarean laboratory testing the day before a planned induction or cesarean delivery. We evaluate symptomatic patients to determine whether it is feasible to reschedule until results of COVID-19 testing are available. This requires balancing the risks of continuing the pregnancy in the setting of a positive or negative test result. In particular, if the result is positive, the patient may become more severely ill over time since symptoms are often more severe in the second week of the illness.

In asymptomatic women, inductions of labor and cesarean deliveries with appropriate medical indications should not be postponed or rescheduled; this includes 39-week inductions or cesarean deliveries after patient counseling.

Analgesia and anesthesia — In patients with known or suspected COVID-19, neuraxial anesthetic is not contraindicated and has several advantages in laboring patients: it provides good analgesia and thus reduces cardiopulmonary stress from pain and anxiety and, in turn, the chance of viral dissemination, and it is available in case an emergency cesarean is required, thus obviating the need for general anesthesia. The Society of Obstetric Anesthesia and Perinatology suggests considering suspending use of nitrous oxide for labor analgesia in these patients because of insufficient data about cleaning, filtering, and potential aerosolization of nitrous oxide systems. They also urge consideration of limiting use of intravenous, patient-controlled analgesia because of the risk of respiratory depression.

General anesthesia (intubation and extubation) is considered an aerosolizing procedure, so special personal protective equipment (ie, N-95 masks, etc) should be worn by all involved health care providers during such a cesarean delivery.

Magnesium sulfate

In women with respiratory compromise, the use of magnesium sulfate for maternal seizure prophylaxis and/or neonatal neuroprotection should be decided on a case-by-case basis since the drug may further depress respirations. Consultation with maternal-fetal medicine and pulmonary/critical care specialists is advised.

Labor management

Generally, management of labor is not altered in women giving birth during the COVID-19 pandemic or in women with confirmed or suspected COVID-19. Person-to-person contact and time in the labor unit and hospital should be limited, as safely feasible. For patients who require cervical ripening, outpatient mechanical ripening with a balloon catheter is an option. For inpatient cervical ripening, using two methods (eg, mechanical and misoprostol or mechanical and oxytocin) decreases the time from induction to delivery, compared with using one agent only.

SARS-CoV-2 has not been detected in vaginal secretions or amniotic fluid, so rupture of fetal membranes and internal fetal heart rate monitoring may be performed for usual indications, but data are limited. It should be noted that labor, and particularly pushing, often causes loss of feces, which can contain the virus and spread the infection.

We believe that use of interventions that can increase risk of infection and have not been proven beneficial, as for example the use of the birth ball or peanut ball, should be limited. As intrapartum oxygen has no proven fetal benefit, the practice of oxygen therapy for fetal resuscitation should be abandoned; the nasal cannula and face mask used are in contact with the maternal respiratory tract

and secretions, so handling of such equipment increases contamination/exposure between patient and provider. Lastly, we advocate not delaying pushing in the second stage.

Delivery procedures

For women with known or suspected infection, ACOG has stated that delayed umbilical cord clamping is highly unlikely to increase the risk of transmitting pathogens from an infected mother to the fetus; however, many institutions have chosen to prohibit this practice in term infants, in whom the benefits are modest, to minimize newborn exposure to any virus in the immediate environment and reduce the chances that the newborn will require phototherapy for jaundice. Many institutions also prohibit skin-to-skin contact in these cases, although the World Health Organization has not advised against this. One expert group suggested leaving the vernix caseosa in place for 24 hours after birth since it contains antimicrobial peptides. However, the American Academy of Pediatrics advises bathing newborns as soon as reasonably possible after birth to remove virus potentially present on skin surfaces.

Umbilical cord blood banking can be performed if planned; the risk of COVID-19 transmission by blood products has not been documented and is unclear at present.

Intrapartum and postpartum fever

COVID-19 infection should be part of the differential diagnosis of intrapartum and postpartum fever, particularly when accompanied by respiratory symptoms and reduced oxygenation. Such patients should be tested for the virus, along with evaluation for common causes of intrapartum and postpartum infection (eg, chorioamnionitis, endometritis).

POSTPARTUM CARE

Maternal monitoring

- For patients with known or suspected COVID-19 who are asymptomatic, postpartum maternal monitoring is routine.
- For patients with mild illness, we check vital signs and monitor intake and output every 4 hours for 24 hours after vaginal delivery and 48 hours after cesarean delivery.
- For patients with moderate illness, we perform continuous pulse oximetry monitoring for the first 24 hours or until improvement in signs and symptoms, whichever takes longer. The type and frequency of follow-up laboratory studies and chest imaging (initial or repeat) are guided by the patient's course. Several institutional protocols are available.
- For patients with severe or critical illness, very close maternal monitoring and care on the labor and delivery unit or intensive care unit are indicated.

Infant evaluation

The infants of mothers with COVID-19 are considered COVID-19 suspects, and they should be tested, isolated from other healthy infants, and cared for according to infection control precautions for patients with confirmed or suspected COVID-19. Where testing capacity is available, neonates should be tested for SARS-CoV-2 infection as soon as possible and within the first 24 hours of age using available molecular assays. Repeat testing should be performed at approximately 48 hours of age if the infant is still at the birth facility. Both the throat and nasopharynx should be sampled, but one

swab may be used to conserve swabs and polymerase chain reaction testing reagents. A separate rectal swab can be obtained if such testing is available at their center.

Mother-baby contact

Temporary separation of mothers with known or suspected COVID-19 from their newborns has been proposed to reduce the risk of mother-baby transmission, but may also have adverse consequences. For example, not rooming-in and avoiding skin-to-skin contact can be stressful for mothers; disrupt breastfeeding; and have negative effects on newborn stress, feeding, and bonding.

The World Health Organization (WHO) has opined that mothers who have suspected, probable, or confirmed COVID-19 virus infection should be enabled to remain together and practice skin-to-skin contact. The Centers for Disease Control and Prevention (CDC) advise determining whether to separate a mother with known or suspected COVID-19 and her infant on a case-by-case basis, using shared decision making between the mother and the clinical team. Factors to consider include:

- The mother's and infant's clinical conditions.
- Whether the mother's infection is suspected (no SARS-CoV-2 test result) or confirmed, and the infant's SARS-CoV-2 testing result (separation is not necessary if the infant has a positive test).
- The mother's desire to breastfeed.
- The facility's ability to accommodate mother-baby separation or colocation.
- The mother's ability to maintain separation when she goes home, if she has not met criteria to discontinue temporary separation.
- Other risks and benefits of temporary separation of a mother with known or suspected COVID-19 and her infant.

If mother-baby separation is implemented, the following should be considered:

- Infant COVID-19 suspects should be isolated from other healthy infants and cared for according to the Interim Infection Prevention and Control Recommendations for Patients with Suspected or Confirmed Coronavirus Disease 2019 (COVID-19) in Healthcare Settings.
- If another healthy family member is providing infant care (eg, diapering, bathing, feeding), they should use appropriate personal protective equipment (healthy family members should wear a gown, gloves, face mask, and eye protection).

If separation is indicated (mother is on transmission-based precautions) but not implemented, other measures may be utilized to reduce potential mother-to-infant transmission and include:

- Physical barriers (eg, a curtain between the mother and newborn) can be constructed, and the newborn can be kept ≥ 6 feet away from the mother.
- The mother can wear a face mask and practice hand hygiene when in close contact with her infant, particularly when feeding.
- If another healthy adult is in the room, they can care for the newborn.

After hospital discharge — After hospital discharge, the American Academy of Pediatrics advises:

- A mother with COVID-19 infection should maintain a distance of at least six feet from the newborn and use a face mask and hand hygiene for newborn care until (1) she is afebrile for 72 hours without

use of antipyretics, and (2) at least seven days have passed since symptoms first appeared. For discontinuation of home isolation in nonpregnant persons, the CDC also suggest improvement in respiratory symptoms (eg, cough, shortness of breath).

- A mother with COVID-19 infection whose newborn requires ongoing hospital care should maintain separation until (1) she is afebrile for 72 hours without use of antipyretics, and (2) her respiratory symptoms are improved, and (3) at least two consecutive SARS-CoV-2 nasopharyngeal swab tests collected ≥ 24 hours apart are negative.

For mothers with laboratory-confirmed COVID-19 who have never been symptomatic, the CDC suggest discontinuing isolation when at least seven days have passed since the date of their first positive COVID-19 diagnostic test. For three days following discontinuation of isolation, they should continue to stay ≥ 6 feet away from others and wear a mask over their nose and mouth whenever they are in settings where other persons are present.

Breastfeeding and formula feeding — It is unknown whether the virus can be transmitted through breast milk. The only report of testing found no virus in the maternal milk of six patients. However, droplet transmission could occur through close contact during breastfeeding.

Breastfeeding should be encouraged. In addition to its many other benefits, breast milk is a passive source of antibodies and other anti-infective factors and, thus, may provide passive antibody protection for the infant.

If mother and baby separation has been implemented, ideally, the infant is fed expressed breast milk by another healthy caregiver until the mother has recovered or has been proven uninfected, provided that the other caregiver is healthy and follows hygiene precautions. Expressing breast milk is important to support establishment of the maternal milk supply.

Before pumping, ideally with a dedicated breast pump, the mother should wear a mask and thoroughly clean her hands and breasts with soap and water and clean pump parts, bottles, and artificial nipples. The CDC have issued guidance about cleaning breast pumps. If possible, the pumping equipment should be thoroughly cleaned by a healthy person.

If feeding by a healthy caregiver is not possible, mothers with confirmed COVID-19 or symptomatic mothers with suspected COVID-19 should take precautions to prevent transmission to the infant during breastfeeding (wear a mask, hand and breast hygiene, disinfect shared surfaces that the symptomatic mother has contacted).

Ideally, women who choose to formula feed should have another healthy caregiver feed the infant. If this is not possible or desired, such women must also take appropriate infection control precautions, as described above, to prevent transmission through close contact when feeding.

Analgesia

Nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly used for treatment of postpartum pain. As discussed above, concern about possible negative effects of NSAIDs in patients with COVID-19 was raised by anecdotal reports of a few young, nonpregnant patients who received NSAIDs (ibuprofen) early in the course of infection and experienced severe disease. However, there have been no clinical or population-based data that directly address the risk of NSAIDs. Given the absence of data, the European Medicines Agency and WHO do not recommend avoiding NSAIDs when clinically indicated. Given the uncertainty, we suggest using acetaminophen as the preferred analgesic agent, if possible, and if NSAIDs are needed, the lowest effective dose should be used.

Permanent and reversible contraception

Permanent contraception (tubal sterilization) does not add significant additional time or risk when performed at an uncomplicated cesarean birth and thus should be performed if planned. Permanent contraception after a vaginal birth is more of an elective procedure, so such decisions should be made on a local level, based upon available resources.

If not performed or if a reversible contraceptive method is desired, an alternative form of contraception should be provided (eg, immediate postpartum long-acting reversible contraception or depot medroxyprogesterone acetate) as long as the patient desires one of these methods. This avoids additional outpatient postpartum visits.

Discharge from hospital

We suggest early discharge postpartum, such as one day after vaginal delivery and a maximum of two days after cesarean delivery, to limit the patient's personal risk in the hospital environment.

Candidates for mother-infant separation after discharge and criteria for discontinuation of separation are discussed above.

Postpartum office visit

Modifying or reducing postpartum outpatient care is appropriate to reduce the risk of inadvertent exposure. For example, it may be possible to perform early postpartum assessments, including wound and blood pressure checks, with telehealth. A comprehensive postpartum visit may still be important by 12 weeks, especially in patients with comorbidities and in patients who lose insurance coverage at that time.

All postpartum patients should still be screened for postpartum depression four to eight weeks after delivery. The most widely used instrument is the self-report, 10-item Edinburgh Postnatal Depression Scale, which can be completed in less than five minutes, but alternatives are available. As discussed above, the psychological impact of COVID-19, which may include moderate to severe anxiety, should also be recognized and support offered.

PREGNANCY REGISTRIES

Registries are being developed to collect data of how COVID-19 affects pregnancy and newborns. For example:

- Pregnancy CoRonavirus Outcomes RegIsTrY (PRIORITY) is the official United States registry led by the University of California, San Francisco.
- International Registry of Coronavirus Exposure in Pregnancy (IRCEP) is another registry led by an international group of investigators.

SELECTED RESOURCES

In the United States, the American College of Obstetricians and Gynecologists, the Society for Maternal-Fetal Medicine, and the Centers for Disease Control and Prevention have issued guidance regarding prenatal, intrapartum, and postpartum care during the COVID-19 pandemic. This includes

general guidance for testing and preventing spread of COVID-19 and suggestions for modifying traditional protocols for prenatal visits, obstetric ultrasound examinations, use of nonstress tests and biophysical profiles, planned induction or cesarean delivery, and contact with the infant.

- American College of Obstetricians and Gynecologists COVID-19 information
- Society for Maternal-Fetal Medicine
- World Health Organization
- Centers for Disease Control and Prevention:
 - Pregnancy and Breastfeeding
 - Interim Considerations for Infection Prevention and Control of Coronavirus Disease 2019 (COVID-19) in Inpatient Obstetric Healthcare Settings
- A dedicated website (www.pregnancy covid19.com) with several helpful pregnancy-specific links and information, including information for patients.

PREGNANCY REGISTRY PRIORITY

(Pregnancy CoRoNaVirus Outcomes RegIsTrY) is a nationwide United States study of pregnant or recently pregnant women who are either under investigation or who have been confirmed to have COVID-19 infection. Providers and patients can send information via priority.ucsf.edu.

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately.

INFORMATION FOR PATIENT

SUPToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients.

SUMMARY AND RECOMMENDATIONS

- Pregnant women should follow the same recommendations as nonpregnant persons for avoiding exposure to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (COVID-19). We suggest that pregnant health workers in the third trimester, particularly those ≥ 36 weeks, stop face-to-face contact with patients.
- Clinical manifestations of COVID-19 in pregnant women are similar to those in nonpregnant individuals. A positive test for SARS-CoV-2 generally confirms the diagnosis of COVID-19, although false-positive and false-negative tests are possible.

- Pregnancy does not appear to increase susceptibility to infection or worsen the clinical course, and most infected mothers recover without undergoing delivery. However, severe disease necessitating maternal intensive care unit admission and need for extracorporeal membrane oxygenation can occur.
- Infected women, especially those who develop pneumonia, appear to have an increased frequency of preterm birth and cesarean delivery. These complications are likely related to severe maternal illness as intrauterine infection does not appear to occur, but this is still under investigation.
- The American College of Obstetricians and Gynecologists (ACOG) and the Society for Maternal-Fetal Medicine (SMFM) have issued guidance regarding prenatal care during the COVID-19 pandemic (available at acog.org and SMFM.org), including general guidance for testing and preventing spread of COVID-19, suggestions for modifying traditional protocols for prenatal and postnatal visits and hospital discharge, and algorithms for assessment and management. These modifications are tailored for low- versus high-risk pregnancies
- For the general population, the Centers for Disease Control and Prevention recommend avoiding glucocorticoids in COVID-19-positive persons because of the potential for adverse effects on the course of the disease. Because of the clear benefits of antenatal betamethasone administration between 24+0 and 33+6 weeks of gestation in patients at risk of preterm birth within seven days, ACOG continues to recommend its use for standard indications to pregnant patients with suspected or confirmed COVID-19.
- For most women with preterm COVID-19 and nonsevere illness who have no medical/obstetric indications for prompt delivery, delivery is not indicated and ideally will occur sometime after a negative testing result is obtained or isolation status is lifted, thereby minimizing the risk of postnatal transmission to the neonate. Severely ill patients at least 32 to 34 weeks of gestation with COVID-19 pneumonia may benefit from early delivery.
- Generally, management of labor is not altered in women giving birth during the COVID-19 pandemic or in women with confirmed or suspected COVID-19. SARS-CoV-2 has not been detected in vaginal secretions or amniotic fluid, so rupture of fetal membranes and internal fetal heart rate monitoring may be performed for usual indications, but data are limited. COVID-19 is not an indication to alter the route of delivery. The partner/support person should be screened in accordance with hospital policies and those with any symptoms consistent with COVID-19, exposure to a confirmed case within 14 days, or a positive test for COVID-19 within 14 days should not be allowed to attend the labor and birth.
- In patients with known or suspected COVID-19, neuraxial anesthetic is not contraindicated and has several advantages in laboring patients. The Society of Obstetric Anesthesia and Perinatology suggests suspending use of nitrous oxide for labor analgesia in these patients because of insufficient data about potential aerosolization of nitrous oxide systems.
- At delivery of patients with known or suspected COVID-19, some institutions have chosen to prohibit delayed cord clamping in term infants, in whom the benefits are modest, to minimize newborn exposure to any virus in the immediate environment and reduce the chances that the newborn will require phototherapy for jaundice.
- Nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly used for treatment of postpartum pain; however, there are anecdotal reports of possible negative effects of NSAIDs in patients with

COVID-19. Given the uncertainty, we use acetaminophen as the preferred analgesic agent, if possible, and if NSAIDs are needed, the lowest effective dose should be used.

- Infants born to mothers with known COVID-19 are COVID-19 suspects and should be tested, isolated from other healthy infants, and cared for according to infection control precautions for patients with confirmed or suspected COVID-19.
- Whether to separate a mother with known or suspected COVID-19 and her infant is determined on a case-by-case basis. If the infant tests positive, separation is unnecessary. If separation is indicated (mother is on transmission-based precautions) but not implemented, other measures may be utilized to reduce potential mother-to-infant transmission, including physical barriers and ≥ 6 feet separation, personal protective equipment and hand hygiene, and utilization of other healthy adults for infant care (feeding, diapering, bathing).
- The virus has not been found in breast milk, but data are limited. Droplet transmission to the newborn could occur through close contact during feeding. In mothers with confirmed COVID-19 or symptomatic mothers with suspected COVID-19, to minimize direct contact, ideally, the infant is fed expressed breast milk by another caregiver until the mother has recovered or been proven uninfected, provided that the other caregiver is healthy and follows hygiene precautions. In such cases, the mother should wear a mask and thoroughly clean her hands and breasts before pumping; the pump parts, bottles, and artificial nipples should be cleaned as well. If she breastfeeds the infant directly, similar personal hygienic precautions should be taken.
- Several agents are being evaluated for treatment of COVID-19. Remdesivir is the most promising and has been used without reported fetal toxicity in some severely ill pregnant women.

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