Society for Maternal-Fetal Medicine
High-risk pregnancy experts

COVID-19 and Pregnancy: What Maternal-Fetal Medicine Subspecialists Need to Know

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The Society for Maternal-Fetal Medicine (SMFM) COVID Task Force

On March 11, 2020, the World Health Organization declared the COVID-19 outbreak [caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)] a pandemic. In light of this declaration, communication to obstetric care providers about this disease and how best to advise pregnant patients is imperative. This document complements the American College of Obstetricians and Gynecologists (ACOG) Practice Advisory and rapidly evolving guidance from the Centers for Disease Control and Prevention (CDC), with a specific focus on maternal, fetal, and neonatal implications.

What is known about COVID-19 disease severity in pregnancy?

Available data indicate that pregnant patients with COVID-19 are at an increased risk for severe illness compared with nonpregnant patients. Therefore, the CDC included pregnancy as an "increased risk" category for severe COVID-19. Specifically, pregnant patients are at a 3-fold increased risk for both ICU admission (adjusted risk ratio [aRR] 3.0, 95% CI 2.6–3.4) and invasive ventilation (aRR 2.9, 95% CI 2.2-3.8) compared with nonpregnant patients. Additionally, pregnant individuals are at a 2.4-fold increased risk for needing extracorporeal membrane oxygenation (ECMO) (aRR 2.4, 95% CI 1.4-4.0) and 70% increased risk of death from COVID-19 (aRR 1.7, 95% CI 1.2-2.4). Women with comorbidities and women aged 35 years or older appeared to have a particularly elevated risk of adverse maternal outcomes. Latina and Black women are also disproportionately affected by severe maternal morbidity and mortality. Although non-Hispanic Black and Black patients made up 14.1% of the total sample, they represent 36.6% of deaths overall, including 26.5% of deaths among pregnant patients. The Delta variant has been linked to increased risk of severe-critical disease, ICU admission, need for ventilation, and death in pregnant patients.

Severe-critical COVID-19 infection in pregnant patients, compared with asymptomatic pregnant patients or those without COVID, has been associated with adverse perinatal

outcomes, such as an increased risk of hypertensive disorders and preterm delivery at less than 37 weeks of gestation (16.4%).

What are the considerations for vaccination?

Vaccination is the best method to reduce maternal and fetal complications of SARS-CoV-2 infection The increased risk for pregnant people to experience a progression to severe-critical illness and the increased pregnancy risks that occur for those with severe-critical illness highlights the clinical importance of vaccination for pregnant individuals and family members. SMFM, the CDC, and other organizations representing maternal and public health professionals recommend that pregnant, postpartum, and lactating people and those considering pregnancy receive the COVID-19 vaccination. SMFM and ACOG recommend that pregnant people receive a COVID-19 booster shot at least 5 months after their primary series for mRNA-based vaccines (ie, Pfizer or Moderna) and at least 2 months after their primary vaccination for the Janssen vaccination. As with the primary series, the booster dose can be given at any stage during pregnancy and postpartum. There are no trimester-specific data to guide the timing of vaccination, and given the risk COVID-19 poses to maternal health and pregnancy, we recommend vaccination at any point during pregnancy. For further information, see **SMFM: Provider Considerations for Engaging in COVID-19 Vaccine Counseling With Pregnant and Lactating Patients**.

Who should be tested for SARS-CoV-2?

CDC guidance recommends that pregnant patients admitted with suspected COVID-19 or who develop symptoms concerning for COVID-19 during admission be prioritized for testing. Clinicians are also encouraged to test these patients or other causes of respiratory illness, such as influenza, when appropriate.

What outpatient treatments are available in pregnancy for mild to moderate COVID-19?

SMFM supports the NIH COVID-19 treatment guidelines and suggests that shared decision-making and acknowledgment of the limitations of the existing data should occur when considering treatment for pregnant patients. However, therapies that would otherwise be given should not be withheld specifically due to pregnancy or lactation. Therapies including monoclonal antibodies and antiviral medications can and should be provided to pregnant patients with COVID-19 who meet clinical qualifications. Other therapies may become available as well.

The following pertains to outpatient treatment for pregnant patients:

- Paxlovid (nirmatrelvir [PF-07321332] tablets and ritonavir tablets) is an antiviral medication. There are no human pregnancy data available on nirmetrelvir, but

ritonavir is used extensively in pregnancy with documented safety. Practitioners should consider drug-drug interactions.
- Sotrovimab is a monoclonal antibody. It is available as a single infusion and is effective against the Omicron variant. There has been limited supply and may only be available to patients at the highest risk of progression to severe disease.
- Remdesivir (3-day outpatient regimen) is an antiviral medication. There has been documented use of remdesivir throughout the pandemic. This regimen requires multiple IV infusions, which can be logistically difficult.

All of the above have similar efficacy at preventing hospitalization and death; however, no trials have specifically evaluated efficacy in a pregnant population.

- Molnupiravir is an antiviral medication with a reported 30% efficacy. Although the EUA recommends against its use in pregnancy due to mutagenicity concerns, this drug may be reasonably considered for use in pregnancy if there are no other therapies available and with documented counseling that the patient understands the risks and benefits.

The NIH guidelines also recommend that monoclonal antibody therapy can be offered as a treatment for infected individuals and that postexposure prophylaxis should be considered for inadequately vaccinated individuals exposed to SARS-CoV-2 depending on the sensitivity of circulating variants; this should also include pregnant individuals.

The CDC also recommends that COVID-19 vaccination does not need to be delayed following receipt of monoclonal antibody therapy or convalescent plasma therapy.

What is the evidence for perinatal infection among neonates born to pregnant people with SARS-CoV-2 infection?

Using data from the Surveillance for Emerging Threats to Mothers and Babies Network (SET-NET), the CDC reported that among >25,000 liveborn infants with available PCR test results, 4% tested positive on SARS-CoV-2 PCR, with a higher positivity rate among preterm infants and mothers with infection <14 days from delivery. These and other data suggest that perinatal infection does occur with an estimated frequency of 1% to 4%. However, further research is needed on transmission dynamics, specifically regarding in utero, intrapartum, and early neonatal risk of infection

Does COVID-19 cause miscarriage or congenital anomalies?

The risk of miscarriage has been detailed in case reports and a case-control study comparing incident SARS-CoV-2 infection in first trimester miscarriages (n=100) with ongoing pregnancies (n=125); these studies have not demonstrated that COVID-19 infection is associated with a greater chance of miscarriage.

At this time, no data describing the risk of structural anomalies associated with infection in the first and second trimesters exist. There are mixed data regarding the risk of congenital malformations in the setting of maternal fever in general. Overall, at this time, data are insufficient to suggest an increased risk of congenital anomalies associated with

SARS-CoV-2 infection early in pregnancy.

Does SARS-CoV-2 infection during pregnancy increase the risk of preterm birth or stillbirth?

An MMWR released on September 16, 2020, reported a stillbirth rate of 3.2% among pregnant patients with symptomatic and asymptomatic SARS-CoV-2 infection. An MMWR released on November 19, 2021, found that the adjusted risk of stillbirth in patients with a COVID-19 diagnosis documented at delivery hospitalization was 4 times higher than the risk in patients without COVID-19 infection who delivered during the period of Delta variant predominance. A higher severity of maternal illness was associated with the risk of stillbirth. In addition, case series of patients with COVID-19 who experienced stillbirth had evidence of fibrin deposition and trophoblast necrosis on placental pathology. These studies have critical gaps (eg, missing data on the gestational age at the time of SARS-CoV-2 infection and the timing of stillbirth in relation to the infection). This potential increase in the risk of stillbirth supports the strong recommendation for COVID-19 vaccination during pregnancy.

An observational cohort study showed that pregnant patients with severe-critical COVID-19 illness were at increased risk of perinatal complications compared with those with mild-moderate or asymptomatic illness. Severe-critical COVID-19 also is associated with an increased risk of cesarean delivery, hypertensive disorders of pregnancy, and preterm birth.

Should obstetric care appointments be altered?

SMFM continues to encourage patients with high-risk conditions to receive necessary prenatal care and antenatal surveillance when indicated during this pandemic.

Alternate prenatal care schedules have been proposed as a strategy to control the spread of COVID-19. Community mitigation efforts are important, although implementing such strategies depends on local practice and population factors and resources. Where available, telehealth (including telephonic and other remote services) can be used to allow access to care for these patients while implementing community mitigation efforts. Obstetrician-gynecologists and other prenatal care practitioners should ensure that patients with high-risk conditions continue to receive necessary prenatal care and antenatal surveillance when indicated.

Do pregnant people with COVID-19 need additional antenatal surveillance?

During acute illness, fetal management should be similar to that provided to any similarly ill pregnant patients. Continuous fetal monitoring in the setting of severe illness should be considered only after fetal viability, when delivery would not compromise maternal health, or as another noninvasive measure of maternal status.

In the setting of a mild infection, management similar to that for a patient recovering from influenza is reasonable. It should be emphasized that patients can decompensate after several days of apparently mild illness, and pregnant individuals should be instructed to call or be seen for care if symptoms worsen, particularly if shortness of breath develops.

Very little is known about the natural history of pregnancy after a patient recovers from COVID-19. An international multicenter retrospective cohort study found that infection in the second trimester was associated with an increased risk of composite adverse obstetric outcomes while adverse neonatal outcomes were associated with third-trimester infection. Given how relatively little is known about COVID infection, a detailed midtrimester anatomy ultrasound examination may be considered following periconception or first-trimester maternal infection. Interval growth assessments also may be considered depending on the timing and severity of infection, with the timing and frequency informed by other maternal risk factors. Although epidemiologic data suggest an increased risk for stillbirth, the data are inconclusive to inform recommendations for fetal surveillance, and antenatal testing should be reserved for routine obstetric indications. Please see **The Society for Maternal-Fetal Medicine COVID-19 Ultrasound Practice Suggestions** for further information.

Are there delivery considerations?

In general, maternal COVID-19 infection itself is not an indication for delivery. Timing of delivery, in most cases, should not be dictated by maternal COVID-19 infection. For individuals infected early in pregnancy who recover, no alteration to the usual delivery timing is necessary. For indivudals infected at or near term, the timing of delivery should be individualized. Specifically, this decision must balance the possibility of clinical deterioration with expectant management, the health services and support implications of immediate delivery (eg, the presence of a support person in labor), and the increased risks of exposure to healthcare workers when delivery occurs in a time of high viremia. For critically ill patients, the timing of delivery should be individualized with shared decision-making with the patient or healthcare proxy, and preterm delivery may be considered if it is thought to potentially improve maternal status. Data do not support that mode of delivery impacts the risk for perinatal infection. Therefore, cesarean delivery is not recommended to reduce the risk of viral infection.

For additional intrapartum recommendations, please refer to **Society for Maternal-Fetal Medicine and Society for Obstetric and Anesthesia and Perinatology Labor and Delivery COVID-19 Considerations.**

What protective measures can be taken for the neonate?

Current evidence suggests that the risk of a neonate acquiring SARS-CoV-2 from its mother is low. However, there is a potential risk of SARS-CoV-2 transmission to the neonate via contact with infectious respiratory secretions from the mother, caregiver,

or other persons with SARS-CoV-2 infection, including immediately before the individual develops symptoms when viral replication may be high. At this time, the CDC recommends that infants born to individuals with known SARS-CoV-2 at the time of delivery should be considered to have suspected infection and should be tested and isolated from other healthy infants. Determining whether to keep a mother with known or suspected COVID-19 and infant together or separated after birth should be made on a case-by-case basis, using shared decision-making between the mother and the clinical team (https://www.cdc.gov/coronavirus/2019-ncov/hcp/inpatient-obstetric-healthcare- guidance.html). Rooming-in with precautions and breastfeeding are endorsed by the American Academy of Pediatrics. Providers are encouraged to check the CDC site frequently regarding this topic, as new guidance is added often.

How can a postpartum visit be altered?

In areas with ongoing high rates of community transmission of SARS-CoV-2, it is reasonable to modify postpartum care to include telehealth. ACOG's **Managing Patients Remotely: Billing for Digital and Telehealth Services** provides resources on policies and coding for telehealth to support these services.

Contraception is a core component of the postpartum visit, and contraceptive choices may be limited by telehealth. Obstetric clinicians should discuss contraception options with patients during prenatal care and attempt to confirm a plan prior to delivery to facilitate immediate postplacental long-acting reversible contraception utilization if desired.

Summary

It is important for MFM subspecialists to learn about COVID-19 to optimize patient care and protect themselves. **This is a rapidly changing landscape, and new information will continue to be updated frequently.**

For questions related to labor and delivery considerations, ultrasound practice suggestions during the COVID-19 pandemic, and COVID-19 vaccination during pregnancy, please refer to SMFM's other resources:

Society for Maternal-Fetal Medicine and Society for Obstetric and Anesthesia and Perinatology Labor and Delivery COVID-19 Considerations

The Society for Maternal-Fetal Medicine COVID-19 Ultrasound Practice Suggestions

SMFM: Provider Considerations for Engaging in COVID-19 Vaccine Counseling With Pregnant and Lactating Patients

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