

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

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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 recent <u>American College of Obstetricians and Gynecologists (ACOG) Practice Advisory</u> and rapidly evolving guidance from the Centers for Disease Control and Prevention (CDC), with a specific focus on maternal, fetal, and neonatal implications.¹

How is COVID-19 spread?

SARS-COV-2 is primarily spread through person-to-person contact via respiratory droplets, which are relatively heavy, fall from the air before evaporating, and are unlikely to spread more than 6 feet.² Transmission may also occur via aerosolized droplets that remain suspended in air, through contact with contaminated surfaces, and via a fecal-oral route, although further data outside of laboratory settings are needed to establish efficiency and clinical significance. It is currently unknown if the virus can be spread through semen or vaginal secretions. Asymptomatic, presymptomatic, and symptomatic people have all been shown to spread the virus.

Infection prevention measures are of critical importance for preventing the spread of infection. The CDC recommends that all individuals take measures to prevent the spread of COVID-19 by practicing frequent hand washing, social distancing, and wearing a mask or face covering when around others. Face masks and cloth face coverings are critical tools in the fight against the spread of COVID-19. There is increasing evidence that cloth face coverings and face masks help prevent individuals with COVID-19 from spreading the virus.³⁻⁵ In addition, masking can help decrease the chance that an individual will contract the virus.⁶ The CDC provides general recommendations for infection prevention in the management of COVID-19⁷ (https://www.cdc.gov/coronavirus/2019-ncov/infection-control/control-recommendations.html).

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

There are not enough data to determine with certainty whether pregnant women are more susceptible to acquiring the SAR-CoV-2 virus. However, recent reports from the CDC and elsewhere suggest that pregnancy is an independent risk factor for COVID-19 disease severity.

Initial reports from the CDC comparing hospitalized pregnant persons to nonpregnant persons of reproductive age with SARS-CoV-2 infection (Morbidity and Mortality Weekly Review [MMWR], June 25, 2020) indicated that pregnant persons were more likely to have severe disease.⁸ After adjusting for age, presence of underlying medical conditions, and race/ethnicity, pregnant women were 1.5 times more likely to be admitted to the intensive care unit (ICU) (1.5% vs 0.9%; 95% CI, 1.2–1.8) and 1.7 times more likely to receive mechanical ventilation (0.5% vs 0.3%; 95% CI, 1.2–2.4) than those who were not pregnant. These initial data did not show an increased risk of death in pregnant versus nonpregnant patients. However, data were not available to distinguish hospitalization for COVID-19–related reasons from hospital admission for pregnancy-related reasons. Furthermore, the authors could not determine whether escalations in care were due to worsening COVID-19– related clinical morbidity or to either obstetric morbidity (eg, postpartum hemorrhage) or obstetric-related concerns (eg, lowered threshold for escalation of care given potential airway concerns in the context of pregnancy).

An updated MMWR was published on November 6, 2020.⁹ Using the National Notifiable Disease Surveillance System, the authors identified women of reproductive age (15-44 vears) who were hospitalized with laboratory-confirmed symptomatic SARS-CoV-2 infection. Pregnancy status was available for 409,462 women (35.5%); the 5.7% of women (n=23,434) who were pregnant were compared with nonpregnant women (n=386,028). As with the prior MMWR, their findings again demonstrated that pregnant women with COVID-19 are at an increased risk for severe disease, specifically 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 women had 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 older women appeared to have a particularly elevated risk of adverse maternal outcomes. Women of color, specifically Latina or Black women, also continued to be disproportionately affected by severe maternal morbidity and mortality. Specifically, while non-Hispanic Black and Black patients made up 14.1% of the total sample, they represented 36.6% of deaths overall, including 26.5% of deaths among pregnant women. These findings have been replicated in other CDC reports.^{10, 11}

Although the data continue to have limitations, including missing data (64%), reporting bias, and limited detail regarding obstetric vs disease-related indications for hospitalization, they consistently demonstrate that pregnancy is an independent risk for severe disease. The CDC has now added pregnancy to its list of high-risk categories.

Based on these data, the CDC now recommends that pregnant women be counseled about the potential risk for severe illness from COVID-19, and measures to prevent infection with SARS-CoV-2 should be emphasized for pregnant women and their families, specifically masking, social distancing, and handwashing. Although relative risks are increased, this information should be provided in the context of overall low absolute risks for invasive ventilation (2.9 per 1,000), ECMO (0.7 per 1,000), and death (1.5 per 1,000).

Who should be tested for SARS-CoV2?

Clinical judgment, test availability, community spread, and other local policies should be used to decide which patients are tested for SARS-CoV2.¹² Signs and symptoms of COVID-19 range from mild to severe and include fever, myalgias, cough, and difficulty breathing as well as gastrointestinal symptoms and anosmia in some patients. According to the CDC, epidemiologic factors, such as the prevalence of SARS-CoV2 in the local community, may also be used to guide testing.

CDC guidance recommends that pregnant women admitted with suspected COVID-19 or who develop symptoms concerning for COVID-19 during admission should be prioritized for testing. Clinicians are also encouraged to test these women for other causes of respiratory illness, such as influenza. COVID-19 testing recommendations are likely to change frequently, and maternal-fetal medicine (MFM) subspecialists are encouraged to check the CDC website for evolving guidance.¹² For more information, please refer to the CDC guidance <u>Evaluating and Testing Persons for Coronavirus</u> <u>Disease 2019 (COVID-19)</u>.

Current testing for acute SARS-CoV2 is by viral detection [either polymerase chain reaction (PCR) or antigen], and availability varies by location. The FDA and CDC do not endorse the use of antibody testing to diagnose acute SARS-CoV2 infection.

Is there evidence of in-utero transmission of COVID-19?

Data suggest that receptors established for SARS-CoV-2 cell entry are only minimally expressed within the human placenta, indicating that SARS-CoV-2 is unlikely to infect the placenta through these established mechanisms and that in-utero transmission may be less likely.¹³ SARS-CoV-2 testing by PCR of samples of placenta, amniotic fluid, and cord blood from case series have rarely been positive, and positive cases are often due to contamination.^{14, 15} Several reports describe a few neonates with SARS-CoV-2 IgM detectable in cord blood. However, given the imperfect specificity of IgM and lack of clinical evidence of disease in the neonates, it is not clear that these cases actually represent in-utero transmission.^{16, 17} To date, only one published clinical case has demonstrated clear evidence of in-utero infection with clinical sequelae in the infant.¹⁴ In this case, maternal SARS-CoV-2 infection was diagnosed at 35 and 2/7 weeks of gestation in the context of clinical symptoms of COVID-19. The fetal heart rate tracing was nonreassuring, and a cesarean delivery was performed. The placenta, amniotic fluid, and neonatal blood, rectal, and nasopharyngeal samples tested positive for SARS-CoV-2 by PCR, and the neonate exhibited transient neurological compromise. Collectively, these data suggest that in-utero transmission of SARS-CoV-2 is rare but possible. It is important to emphasize the limitations of the data available, the novel nature of this virus, and that robust data from women who became infected with SARS-CoV-2 in the first or early second trimester of pregnancy are not yet available.

Whether infection earlier in pregnancy can lead to in-utero transmission has yet to be determined.

Does COVID-19 cause miscarriage or congenital anomalies?

The risk of miscarriage has been detailed in case reports and a case-controlled study comparing incident SARS-CoV-2 infection in first trimester miscarriages (n=100) to ongoing pregnancies (n=125); these have not shown any difference in incident infection.¹⁸

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 fetal loss or congenital anomalies associated with SARS-CoV-2 infection early in pregnancy.^{19, 20}

<u>Are women infected with COVID-19 at increased risk for preterm birth and stillbirth?</u> Preterm delivery has been reported among women positive for COVID-19 during pregnancy. However, it appears that some of these cases may be iatrogenic and not due to spontaneous preterm labor.^{21, 22,15}

Given the limited data available regarding COVID-19 during pregnancy, adverse obstetrical and perinatal outcomes reported with other respiratory viral infections have been extrapolated to COVID-19. Other respiratory viral infections during pregnancy, such as influenza, have been associated with adverse neonatal outcomes, including low birth weight and preterm birth, generally thought to be due to severe maternal illness. Infants have been born preterm, small for gestational age, or both to women with other coronavirus infections, including SARS-CoV and MERS-CoV, during pregnancy.^{23, 24} However, it is not clear that the implications and outcomes associated with COVID-19 are the same as with these other infections. Further data are urgently needed.

A study from the United Kingdom indicated a significantly higher incidence of stillbirth during the pandemic period (9.31 per 1000 births) as compared to during the prepandemic period (2.38 per 1000 births).²⁵ Although none of the stillbirths during the pandemic period were in patients with known COVID-19 infection, these findings pose questions regarding the impact of the pandemic and changes in the provision of routine obstetric care. The authors noted a decrease in hypertension during the pandemic period, which could represent underdiagnosis due to changes in care and monitoring. The study also showed that there were no significant changes in births at less than 37 weeks of gestation during the pandemic period (7.6 per 1000 births) versus before the pandemic (6.8 per 1000 births) and at less than 34 weeks of gestation during the pandemic period (3.7 per 1000 births) versus before the pandemic (2.5 per 1000 births). Importantly, lack of information on the causes of stillbirth and the rates of asymptomatic infection in the study population are limitations of these data.

An MMWR released on September 16, 2020, reported a preterm delivery rate of 8.9% among 43,571 births and a stillbirth rate of 3.2% among pregnant women with SARS-CoV-2 infection, both symptomatic and asymptomatic.^{10, 11} The study was unable to assess

whether these outcomes were predominantly among those with more severe disease.

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

Should obstetric care appointments be altered?

Alternate prenatal care schedules have been proposed as a strategy to control the spread of COVID-19. Community mitigation efforts are important, although the implementation of 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 be provided necessary prenatal care and antenatal surveillance when indicated.

Do women with COVID-19 need additional antenatal surveillance?

During acute illness, fetal management should be similar to that provided to any similarly ill pregnant woman. 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.

Very little is known about the natural history of pregnancy after a patient recovers from COVID-19. 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. Given how little is known about this infection, a detailed mid-trimester anatomy ultrasound examination may be considered following periconception or first-trimester maternal infection. Interval growth assessments could be considered depending on the timing and severity of infection, with the timing and frequency informed by other maternal risk factors. Antenatal testing is reserved for routine obstetrical indications. Please see <u>The Society for Maternal-Fetal Medicine COVID-19</u> <u>Ultrasound Practice Suggestions</u> for further information. Signs and symptoms of preterm labor should also be reviewed.

Are there delivery considerations?

In general, maternal COVID-19 infection itself is not an indication for delivery.²¹ Timing of delivery, in most cases, should not be dictated by maternal COVID-19 infection. For women infected early in pregnancy who recover, no alteration to the usual timing of delivery is necessary. For women 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 (e.g., 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 women who are critically ill, preterm delivery may be considered if it is thought that it could potentially improve maternal status. Athough intrauterine transmission rarely occurs, data do not support that mode of delivery impacts this risk.

Therefore, cesarean delivery is not recommended to reduce the risk of viral infection.

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

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 just before the individual develops symptoms when viral replication may be high. At this time, the CDC recommends that infants born to mothers with known SARS-CoV2 at the time of delivery should be considered to have suspected infection and should be tested and isolated from other healthy infants. The determination of whether to keep a mother with known or suspected COVID-19 and her 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 team²⁶ (https://www.cdc.gov/coronavirus/2019-ncov/hcp/inpatient-obstetric-healthcare-guidance.html). Rooming-in with precautions has been endorsed by the American Academy of Pediatrics.²⁷ Providers are encouraged to check the <u>CDC site</u> frequently regarding this topic, as new guidance is added often.

How can a postpartum visit be altered?

In areas where there are ongoing high rates of community transmission of SARS-CoV-2, it is reasonable to modify postpartum care to include telehealth. ACOG's <u>Managing Patients</u> <u>Remotely: Billing for Digital and Telehealth Services</u> 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 LARC utilization if desired.

What is the guidance for pregnant health care workers?

Evidence shows that the risks to health care workers (HCWs) can be mitigated with the appropriate use of personal protective equipment (PPE). Approximately 330,000 HCWs are expected to be pregnant or recently postpartum during the pandemic. No available data on pregnant HCWs that stratifies risk by exposure, gestation, underlying comorbidities, or sociodemographic risks exist. Pregnant HCWs should follow the CDC risk assessment and infection control guidelines for HCWs with potential exposure to patients with suspected or confirmed COVID-19. While pregnant HCWs may continue to work, facilities may consider limiting their exposure to patients with confirmed or suspected COVID-19, especially during higher-risk procedures (eg, aerosol-generating procedures). However, in settings with a higher burden of disease or limited staffing, this may not be feasible. The above recommendations should also be applied to other HCWs considered to be at higher risk for severe complications of infection, such as older

adults; people with chronic medical conditions (heart disease, diabetes, and lung disease); or those who are immunocompromised.

<u>Summary</u>

It is important for MFM subspecialists to learn about COVID-19 to optimize patient care and to protect themselves. This is a rapidly changing landscape, and new information will continue to be updated frequently. As data on pregnancy accumulate, SMFM will continue to provide guidance to our members.

For questions related to labor and delivery considerations and ultrasound practice suggestions during the COVID-19 pandemic, 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

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