Special Considerations in Pregnancy

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Summary Recommendations

There is current guidance from the Centers for Disease Control and Prevention, the American College of Obstetricians and Gynecologists, and the Society for Maternal-Fetal Medicine detailing the management of pregnant patients with COVID-19. This section of the COVID-19 Treatment Guidelines complements that guidance. The following are key considerations regarding the management of COVID-19 in pregnancy:

- Pregnant people should be counseled about the increased risk for severe disease from SARS-CoV-2 infection and receive recommendations on ways to protect themselves and their families from infection.
- If hospitalization for COVID-19 is indicated for a pregnant patient, care should be provided in a facility that can conduct maternal and fetal monitoring, when appropriate.
- General management of COVID-19 in pregnant patients should include:
  - Fetal and uterine contraction monitoring based on gestational age, when appropriate
  - Individualized delivery planning
  - A multispecialty, team-based approach that may include consultation with obstetric, maternal-fetal medicine, infectious disease, pulmonary-critical care, and pediatric specialists, as appropriate
- The COVID-19 Treatment Guidelines Panel (the Panel) recommends against withholding COVID-19 treatments or vaccination from pregnant or lactating individuals specifically because of pregnancy or lactation (AIII).
- In general, the therapeutic management of pregnant patients with COVID-19 should be the same as for nonpregnant patients, with a few exceptions (AII). Notable exceptions include:
  - The Panel recommends against the use of molnupiravir for the treatment of COVID-19 in pregnant patients unless there are no other options and therapy is clearly indicated (AIII).
  - There is insufficient evidence for the Panel to recommend either for or against the use of therapeutic anticoagulation in pregnant patients with COVID-19 who do not have evidence of venous thromboembolism. See Antithrombotic Therapy in Patients With COVID-19 for more information.
- For details regarding therapeutic recommendations and pregnancy considerations, see Therapeutic Management of Nonhospitalized Adults With COVID-19, Therapeutic Management of Hospitalized Adults With COVID-19, and the individual drug sections.
- There are limited data on the use of COVID-19 therapeutic agents in pregnant and lactating people. When making decisions about treatment, pregnant or lactating people and their clinical teams should use a shared decision-making process that takes several factors into consideration, including the severity of COVID-19, the risk of disease progression, and the safety of specific medications for the fetus, infant, or pregnant or lactating individual. For detailed guidance on using COVID-19 therapeutic agents during pregnancy, refer to the pregnancy considerations subsections in Antiviral Therapy and Immunomodulators.
- The decision to feed the infant breast milk while the lactating patient is receiving therapeutic agents for COVID-19 should be a collaborative effort between the patient and the clinical team, including infant care providers. The patient and the clinical team should discuss the potential benefits of the therapeutic agent and evaluate the potential risk of pausing lactation on the future of breast milk delivery to the infant.

Rating of Recommendations: A = Strong; B = Moderate; C = Weak
Rating of Evidence: I = One or more randomized trials without major limitations; Ila = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

Epidemiology of COVID-19 in Pregnancy

Although the overall risk of severe illness is low, pregnant people with COVID-19 are at a higher risk of severe disease than nonpregnant people. After adjustments have been made for age, race/ethnicity, and
underlying medical conditions, pregnant women have significantly higher rates of intensive care unit (ICU) admission (10.5 vs. 3.9 cases per 1,000 cases; adjusted risk ratio [aRR] 3.0; 95% CI, 2.6–3.4), mechanical ventilation (2.9 vs. 1.1 cases per 1,000 cases; aRR 2.9; 95% CI, 2.2–3.8), extracorporeal membrane oxygenation (0.7 vs. 0.3 cases per 1,000 cases; aRR 2.4; 95% CI, 1.5–4.0), and death (1.5 vs. 1.2 cases per 1,000 cases; aRR 1.7; 95% CI, 1.2–2.4). An ongoing systematic review and meta-analysis of 149 studies also described increased odds of ICU admission and mechanical ventilation among pregnant and recently pregnant patients with COVID-19 when compared with nonpregnant patients of reproductive age. Compared with pregnant women and recently pregnant women without COVID-19, pregnant women with COVID-19 were at a higher risk of preterm birth and stillbirth.

Obstetric and Perinatal Outcomes in Patients With COVID-19

An observational cohort study of all pregnant patients at 33 U.S. hospitals with a singleton gestation and a positive result on a SARS-CoV-2 virologic test evaluated maternal characteristics and outcomes across disease severity. The data suggested that adverse perinatal outcomes were more common in patients with severe or critical disease than in asymptomatic patients with SARS-CoV-2 infection, including an increased incidence of cesarean delivery (59.6% vs. 34.0% of patients; aRR 1.57; 95% CI, 1.30–1.90), hypertensive disorders of pregnancy (40.4% vs. 18.8%; aRR 1.61; 95% CI, 1.18–2.20), and preterm birth (41.8% vs. 11.9%; aRR 3.53; 95% CI, 2.42–5.14). The perinatal outcomes for those with mild to moderate illness were similar to those observed among asymptomatic patients with SARS-CoV-2 infection.

Among 1,249,634 delivery hospitalizations in the United States from March 2020 through September 2021, women with COVID-19 had an increased risk of stillbirth, which was defined as fetal death at >20 weeks’ gestation (aRR 1.90; 95% CI, 1.69–2.15). The risk of stillbirth was higher during the time period that the Delta variant was the dominant variant in the United States (aRR 4.04; 95% CI, 3.28–4.97) than during the pre-Delta period (aRR 1.47; 95% CI, 1.27–1.71).

A retrospective cohort analysis collected data from 14,104 pregnant or recently postpartum individuals who delivered at U.S. hospitals that participated in the Gestational Research Assessments for COVID-19 (GRAVID) study. Compared with pregnant individuals who did not have SARS-CoV-2 infection, patients with COVID-19 during pregnancy had an increased risk of meeting the composite endpoint of maternal death or severe morbidity related to hypertensive disorders of pregnancy, postpartum hemorrhage, or infection. Eighty percent of the patients in this cohort tested positive for SARS-CoV-2 infection during the third trimester. The primary composite endpoint occurred in 13.4% of patients with COVID-19 during pregnancy or within 6 weeks postpartum and in 9.4% of those without COVID-19 (aRR 1.41; 95% CI, 1.23–1.61). When compared with those who did not have a positive SARS-CoV-2 test result, pregnant patients who had SARS-CoV-2 infection prior to 28 weeks’ gestation had a subsequent increased risk of fetal/neonatal death (aRR 1.97; 95% CI, 1.01–3.85), preterm birth at <37 weeks (aRR 1.29; 95% CI, 1.02–1.63), and hypertensive disorders of pregnancy with delivery at <37 weeks’ gestation (aRR 1.74; 95% CI, 1.19–2.55). There were no significant differences between these groups of patients in the risk of preterm birth at <34 weeks, any major congenital abnormalities, or a size for gestational age of less than the fifth or tenth percentiles. There were also no significant differences between these groups in the rates of gestational hypertension overall or preeclampsia with severe features. These data suggest that those with SARS-CoV-2 infection early in gestation may also have an increased risk of subsequent adverse pregnancy outcomes.

Vertical Transmission of COVID-19

Although vertical transmission of SARS-CoV-2 is possible, current data suggest that it is rare. A review of 101 infants born to 100 women with SARS-CoV-2 infection at a single U.S. academic medical center
found that 2 infants (2%) had indeterminate SARS-CoV-2 polymerase chain reaction (PCR) results, which were presumed to be positive; however, the infants exhibited no evidence of clinical disease. It is reassuring that the majority of the infants received negative PCR results after rooming with their mothers and breastfeeding directly (the mothers in this study practiced appropriate hand and breast hygiene).

Data collected by the Centers for Disease Control and Prevention (CDC) as part of the Surveillance for Emerging Threats to Mothers and Babies Network showed that among 4,038 infants born to people with COVID-19, for whom laboratory testing information was available and who were tested during the delivery hospitalization, 227 infants (5.6%) had positive PCR results for SARS-CoV-2.9

The published data to date were largely collected prior to the emergence of the Omicron variants. The risk of vertical transmission may vary based on viral dynamics and the transmissibility of the circulating variants in a community; however, the variant-specific factors that are associated with vertical transmission have not been determined. For additional information on vertical transmission and infants born to people with SARS-CoV-2 infection, see Special Considerations in Children.

**Racial and Ethnic Disparities Among Pregnant People With COVID-19**

Between January 22 and June 7, 2020, 8,207 pregnant women with COVID-19 were reported to CDC. Among these women, 46% were reported to be Hispanic and 22% were reported to be Black. Those proportions were higher than the proportions of Hispanic and Black women who gave birth in 2019 (24% and 15%, respectively), suggesting that pregnant people who are Hispanic or Black may be disproportionately affected by SARS-CoV-2 infection.10 These disparities have been reported in the nonpregnant population as well.11 It is important to note that these disparities are related to social determinants of health, current and historic inequities in access to health care and other resources, and structural racism. The American College of Obstetricians and Gynecologists (ACOG) has published guidance on addressing health equity during the COVID-19 pandemic.

**Prevention of COVID-19 in Pregnancy**

Pregnant people should be counseled about the increased risk for severe disease from SARS-CoV-2 and the measures they can take to protect themselves and their families from infection. Non-pharmacologic measures include practicing physical distancing, washing hands regularly, and wearing a face covering as per guidance from the CDC.

**COVID-19 Vaccines**

Pregnant people should be counseled about the benefits of COVID-19 vaccination, which include a decreased risk of severe disease and hospitalization for the pregnant person and a decreased risk of hospitalization for the infant in the first 6 months of life.12 The Society for Maternal-Fetal Medicine (SMFM), the ACOG, and the CDC recommend that all eligible persons, including pregnant and lactating individuals and those who are planning to become pregnant, receive a COVID-19 vaccine or vaccine series. This includes booster doses, if the person is eligible. The CDC has published up-to-date guidance regarding COVID-19 vaccination, including guidance for administering vaccines to pregnant and lactating individuals. COVID-19 vaccines can be administered regardless of trimester and in concert with other vaccines that are recommended during pregnancy.13

Pregnant people were not included in the initial COVID-19 vaccine studies. However, there is a growing body of observational data that supports the efficacy and safety of administering COVID-19 vaccines to this population. At this time, the mRNA COVID-19 vaccines and the recently authorized Novavax vaccine are preferred over the Johnson & Johnson/Janssen vaccine for all eligible individuals, including pregnant and lactating people.13,14 For the most up-to-date clinical recommendations, see the CDC.
guidelines on using COVID-19 vaccines. The ACOG and SMFM provide guidance for counseling pregnant and lactating patients about COVID-19 vaccination.\textsuperscript{13,15}

Efficacy

A prospective cohort study of 131 subjects at 2 academic medical centers compared the immunogenicity and reactogenicity of the mRNA COVID-19 vaccines in pregnant and lactating women and nonpregnant controls. The study also compared vaccine-generated immunity to the immune response to natural SARS-CoV-2 infection among pregnant participants.\textsuperscript{16} Maternal immunoglobulin (Ig) G antibody levels were similar after vaccination in pregnant and lactating women and in nonpregnant controls, and the antibody response did not differ by trimester of vaccination. There were significantly higher levels of antibodies in vaccinated pregnant women compared with pregnant women who had had natural SARS-CoV-2 infection during the previous 4 to 12 weeks. In addition, maternal receipt of a COVID-19 vaccine series was protective against infant hospitalization with COVID-19 in the first 6 months of life.\textsuperscript{12}

Antibody Transfer to the Neonate

The available data indicate that vaccine-derived antibodies are passively transferred to the neonate during pregnancy and lactation.\textsuperscript{17} A case control study that was conducted at 20 pediatric hospitals in 17 states in the United States from July 1, 2021, to January 17, 2022, assessed the relationship between maternal vaccination with a 2-dose mRNA COVID-19 vaccine during pregnancy and pediatric hospitalization for COVID-19.\textsuperscript{12} In this study, 379 infants aged <6 months were hospitalized. One hundred seventy-six of these infants had COVID-19 and were considered case infants; the remaining 203 infants did not have COVID-19 and were considered control infants. Sixteen percent of the mothers of the case infants had received 2 COVID-19 vaccine doses during pregnancy compared with 32\% of the mothers of control infants. Maternal completion of a 2-dose primary mRNA COVID-19 vaccination series during pregnancy led to a decrease in the number of infant hospitalizations for COVID-19 during the first 6 months of life (61\% decrease; 95\% CI, 31\% to 78\%). There were no statistically significant differences between the case infants and control infants in the presence of underlying medical conditions or the occurrence of premature birth. Of the 43 case infants who were admitted to the ICU, 88\% had mothers who were unvaccinated. These data further support the CDC’s recommendation for COVID-19 vaccination in people who are pregnant, breastfeeding, or trying to become pregnant or who might become pregnant in the future.\textsuperscript{18}

Safety

A study that used data from 3 vaccine safety reporting systems in the United States reported that the frequency of adverse events among 35,691 vaccine recipients who identified as pregnant was similar to the frequency observed among nonpregnant patients. Local injection site pain, nausea, and vomiting were reported slightly more frequently in pregnant people than in nonpregnant people. Other systemic reactions were reported more frequently among nonpregnant vaccine recipients, but the overall reactogenicity profile was similar for pregnant and nonpregnant patients.

The CDC is enrolling pregnant patients in the v-safe COVID-19 Vaccine Pregnancy Registry to collect and analyze data related to COVID-19 vaccination in pregnant people and their infants. As of May 2, 2022, 23,779 pregnant people in the United States have been enrolled. Surveillance data from 3,958 pregnant patients who were enrolled in the registry showed that, among 827 people who completed their pregnancies, there were no safety signals among obstetric or neonatal outcomes when rates of pregnancy loss (spontaneous abortion or stillbirth), preterm birth, congenital anomalies, infants who were small for gestational age, and neonatal death were compared to historic incidences in the peer-reviewed literature.\textsuperscript{19}

Pre-Exposure Prophylaxis With Anti-SARS-CoV-2 Monoclonal Antibodies

Pregnancy does not preclude the use of anti-SARS-CoV-2 monoclonal antibodies (mAbs) as pre-exposure prophylaxis (PrEP). Similar to nonpregnant patients, pregnant patients qualify for PrEP with
anti-SARS-CoV-2 mAbs if they are unable to mount an adequate immune response to vaccination or they cannot receive a COVID-19 vaccine due to the potential for a severe reaction to the vaccine or its components. As IgG mAbs, the authorized anti-SARS-CoV-2 mAbs would be expected to cross the placenta. There are no data on the use of these mAbs in pregnant patients; however, other IgG products have been safely used in pregnant people when their use is indicated. Therefore, authorized anti-SARS-CoV-2 mAbs should not be withheld during pregnancy.

Managing COVID-19 in Pregnancy

As in nonpregnant patients, SARS-CoV-2 infection can present in pregnant patients as asymptomatic/presymptomatic disease or with a wide range of clinical manifestations, from mild symptoms that can be managed with supportive care at home to severe disease and respiratory failure that requires ICU admission. The illness severity, underlying comorbidities, and clinical status of pregnant patients with symptoms that are compatible with COVID-19 should be assessed to determine whether in-person evaluation for potential hospitalization is needed.

If hospitalization is indicated, care should be provided in a facility that can conduct maternal and fetal monitoring, when appropriate. The management of COVID-19 in the pregnant patient may include:

- Fetal and uterine contraction monitoring based on gestational age, when appropriate
- Individualized delivery planning
- A multispecialty, team-based approach that may include consultation with obstetric, maternal-fetal medicine, infectious disease, pulmonary-critical care, and pediatric specialists, as appropriate

In general, the recommendations for managing COVID-19 in nonpregnant patients also apply to pregnant patients.

Therapeutic Management of COVID-19 in the Setting of Pregnancy

To date, most SARS-CoV-2-related clinical trials have excluded individuals who are pregnant and lactating. In cases where lactating and pregnant individuals have been included in studies, only a small number have been enrolled. This makes it difficult to provide evidence-based recommendations on the use of anti-SARS-CoV-2 therapies in these vulnerable patients and potentially limits their treatment options. When possible, pregnant and lactating individuals should not be excluded from clinical trials of COVID-19 therapeutic agents or vaccines.

The COVID-19 Treatment Guidelines Panel (the Panel) **recommends against** withholding COVID-19 treatments from pregnant or lactating individuals specifically because of pregnancy or lactation (AIII). For details regarding therapeutic recommendations and pregnancy considerations, see [General Management of Nonhospitalized Adults With Acute COVID-19](https://www.covid19treatmentguidelines.nih.gov/) and the individual drug sections.

Utilizing a shared decision-making process and acknowledging the limitations of available data in pregnancy, the pregnant patient and the clinical team should consider the safety of the medication for the pregnant or lactating individual and the fetus, as well as the severity of maternal disease. For detailed guidance on the use of COVID-19 therapeutic agents during pregnancy, refer to the pregnancy considerations subsections in [Antiviral Therapy](https://www.covid19treatmentguidelines.nih.gov/) and [Immunomodulators](https://www.covid19treatmentguidelines.nih.gov/).

In general, the therapeutic management of pregnant patients with COVID-19 should be the same as for nonpregnant patients, with a few exceptions (AIII). Notable exceptions include:

- The Panel **recommends against** the use of molnupiravir for the treatment of COVID-19 in pregnant patients unless there are no other options and therapy is clearly indicated (AIII). Fetal
toxicity has been reported in animal studies of molnupiravir. However, when other therapies are not available, pregnant people with COVID-19 who are at high risk of progressing to severe disease may reasonably choose molnupiravir therapy after being fully informed of the risks, particularly if they are beyond the time of embryogenesis (i.e., >10 weeks’ gestation). There is currently a lack of data on the use of molnupiravir in lactating people, and molnupiravir may cause adverse effects in infants who are exposed to the drug through breastfeeding. Because of this, the Food and Drug Administration Emergency Use Authorization for molnupiravir states that lactating people should not breastfeed their infants during treatment with molnupiravir and for 4 days after the final dose. Pumping and discarding breast milk to maintain supply during this time is recommended.

- Pregnant patients were not included in most of the clinical trials that evaluated therapeutic anticoagulation in the setting of COVID-19, and there is a potential for increased maternal risks if bleeding occurs during pregnancy. Therefore, there is insufficient evidence for the Panel to recommend either for or against the use of therapeutic anticoagulation in pregnant patients with COVID-19 who do not have evidence of venous thromboembolism.

Timing of Delivery
The ACOG provides detailed guidance on the timing of delivery and the risk of vertical transmission of SARS-CoV-2.

In most cases, the timing of delivery should be dictated by obstetric indications rather than maternal diagnosis of COVID-19. For people who had suspected or confirmed COVID-19 early in pregnancy and who recovered, no alteration to the usual timing of delivery is indicated.

Post-Delivery
Therapeutic management in postpartum patients should follow guidelines for nonpregnant patients. However, the use of anticoagulation therapy in the immediate postpartum period should be individualized, as there may be an increased risk of bleeding, especially after an operative delivery.

The majority of studies have not demonstrated the presence of SARS-CoV-2 in breast milk; therefore, breastfeeding is not contraindicated for people with laboratory-confirmed or suspected SARS-CoV-2 infection. Precautions should be taken to avoid transmission to the infant, including practicing good hand hygiene, wearing face coverings, and performing proper pump cleaning before and after breast milk expression.

The decision to feed the infant breast milk while the patient is receiving therapeutic agents for COVID-19 should be a joint effort between the patient and the clinical team, including infant care providers. The patient and the clinical team should discuss the potential benefits of the therapeutic agent and evaluate the potential risk of pausing lactation on the future of breast milk delivery to the infant.

Specific guidance on the post-delivery management of infants born to individuals with known or suspected SARS-CoV-2 infection, including breastfeeding recommendations, is provided by the CDC and the American Academy of Pediatrics and in Special Considerations in Children.

References


