

Coronavirus Disease 2019 (COVID-19) and Pregnancy

Responding to a Rapidly Evolving Situation

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As the world confronts coronavirus disease 2019 (COVID-19), an illness caused by yet another emerging pathogen (severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]), obstetric care providers are asking what this means for pregnant women. The global spread has been swift, and many key questions remain. The case-fatality rate for persons cared for in the United States and whether asymptomatic persons transmit the virus are examples of questions that need to be answered to inform public health control measures. There are also unanswered questions specific to pregnant women, such as whether pregnant women are more severely affected and whether intrauterine transmission occurs. Although guidelines for pregnant women from the American College of Obstetricians and Gynecologists and the Centers for Disease Control and Prevention have been rapidly developed based on the best available evidence, additional information is critically needed to inform key decisions, such as whether pregnant health care workers should receive special consideration, whether to temporarily separate infected mothers and

their newborns, and whether it is safe for infected women to breastfeed. Some current recommendations are well supported, based largely on what we know from seasonal influenza: patients should avoid contact with ill persons, avoid touching their face, cover coughs and sneezes, wash hands frequently, disinfect contaminated surfaces, and stay home when sick. Prenatal clinics should ensure all pregnant women and their visitors are screened for fever and respiratory symptoms, and symptomatic women should be isolated from well women and required to wear a mask. As the situation with COVID-19 rapidly unfolds, it is critical that obstetricians keep up to date.

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In December 2019, a cluster of cases of pneumonia of unknown cause began to emerge in Wuhan, China. On December 31, 2019, China notified the World Health Organization (WHO) of the outbreak, and shortly thereafter, on January 7, 2020, a novel coronavirus was identified as the causative pathogen. Just 2 days later, Chinese investigators shared the genetic sequence of the virus, later named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) because of its sequence similarity to the virus that caused a worldwide outbreak of severe acute respiratory syndrome (SARS) in 2002–2003. On January 30, 2020, the WHO declared the outbreak of illness with this novel coronavirus (now known as *coronavirus disease 2019* or *COVID-19*) a Public Health Emergency of International Concern.¹ On March 11, the WHO declared a pandemic, indicating global spread of this novel coronavirus.

This situation is rapidly evolving. As of March 17, 2020, more than 189,000 persons have been diagnosed with COVID-19 globally, with more than 7,500 deaths and spread to more than 150 countries and regions, including more than 5,000 cases identified in



the United States.² Community transmission (cases without connection to travel) is now well documented in the United States. However, these cases likely represent the tip of the iceberg given the limitations on testing in the United States thus far. More than 700 publications have appeared in the medical literature and document the most common symptoms of fever, fatigue, and dry cough. Laboratory findings include lymphopenia, prolonged prothrombin time, and elevated lactate dehydrogenase; radiography findings include bilateral patchy shadows or ground glass opacity of the lungs on chest computed tomography scan.³ Diagnostic testing using real-time reverse transcription-polymerase chain reaction has moved from the Centers for Disease Control and Prevention (CDC) to include state public health laboratories and, most recently, commercial laboratory options,⁴ and work to develop a serology test for COVID-19 has begun.⁵ Fortunately, pregnant women have not been forgotten. Three case series, for a total of 31 pregnancies affected by COVID-19, have been published,^{6–8} and a WHO report from China provides limited information on 147 pregnancies.⁹ Reviews examining features during pregnancy of diseases caused by other coronaviruses (eg, SARS and Middle East respiratory syndrome [MERS]), in the context of limited information on COVID-19 during pregnancy, have been published.^{1,10} Guidelines for pregnant women have quickly been made available through the American College of Obstetricians and Gynecologists (ACOG),¹¹ and responses to frequently asked questions about COVID-19 and pregnancy have been posted by the CDC.¹²

However, many key questions remain about COVID-19 in general and specific to pregnant women. One critical question about COVID-19 relates to the case-fatality rate of the disease. Early data from Wuhan, China, suggested that 4.3% of 138 hospitalized patients with COVID-19 died³; however, it was recognized that early estimates can overestimate the case-fatality rate because mild or asymptomatic cases are often missed early in an outbreak. Later data from the Chinese Center for Disease Control and Prevention based on more than 70,000 cases suggested a lower case-fatality rate of 2.3%¹³; recent data reported in the media from Iran have suggested a higher case-fatality rate of just less than 9%.¹⁴ South Korea has reported 75 deaths among 8,236 confirmed cases for a lower case-fatality rate of 0.9%.¹⁵ The case-fatality rate depends not only on the disease and complete ascertainment of cases, but on the health care provided to affected patients and the age and health of the population studied. Given the small number of cases in the United States and the limited testing per-

formed thus far, the case-fatality rate for persons cared for in the United States is unknown.

Important questions regarding transmission of SARS-CoV-2 also remain. One vital question is whether persons who are asymptomatic can transmit the virus; case reports have suggested asymptomatic transmission is possible, but how often this occurs is unknown.^{16,17} Because of the possibility of SARS-CoV-2 transmission when a person touches a contaminated surface, another critical issue is how long the virus can survive on surfaces. A recent review article suggests that coronaviruses could survive as long as 9 days depending on the surface and the type of coronavirus.¹⁸ Answers to these questions are essential to guidance on infection control and disinfection and other public health control measures and will require careful study, including examination of seroprevalence among patients who never show symptoms and additional studies of virus persistence and inactivation.

Likewise, several questions remain about pregnant women and their newborns. Preliminary information suggests that pregnant women are not more severely affected than the general population¹; however, the numbers of pregnant women reported have been small, and comparison is needed with nonpregnant women of similar age rather than with all persons with COVID-19, a population that is older (median age is approximately 50 years) and has underlying conditions. A small study that compared pregnant women with a matched control group of nonpregnant women of similar age suggests that pregnant women with SARS may have an increased risk of severe disease and death.¹⁹ Whether intrauterine or perinatal transmission occurs is also unknown. Among the small number of pregnancies reported thus far, no evidence of transmission to the neonate has been observed; however, these women were nearly all infected in the third trimester and most underwent cesarean delivery.^{6–8} The effects of the virus earlier in pregnancy are completely unknown; no neonates have been delivered to women infected in the first and second trimesters of pregnancy.

The paucity of evidence challenges some of the key decisions that need to be addressed. For example, one question that has arisen is whether pregnant health care workers should receive special consideration. During the 2009 H1N1 influenza pandemic, in which pregnant women were more likely to develop complications than nonpregnant women,^{20,21} the CDC recommended that pregnant women should strictly adhere to the same measures that were recommended for all health care personnel, although certain work accommodations, such as avoidance of aerosol-generating procedures on infected patients, could be offered as an option.²² In contrast, the CDC



recommended that pregnant health care workers not care for patients with Ebola virus disease, given the severity of illness in mothers and their neonates, the high risk of transmission, and the challenges related to the required personal protective equipment for Ebola care.²³ Whether special accommodations should be made for COVID-19 require better data on the severity of COVID-19 in pregnant women.

Other areas of controversy relate to temporary separation of infected mothers and their newborns. Preliminary data suggest that children are mildly affected with COVID-19,²⁴ but the level of risk to a newborn is largely unknown.

Another question is related to breastfeeding. Limited data have suggested that SARS-CoV-2 is not transmitted through breast milk,⁶ but numbers on which to determine evidence-based recommendations are too small.

So where does this leave obstetricians and their pregnant patients? As with previous emerging pathogens, we need to base recommendations on the best information available now, recognizing that data are limited and recommendations will likely change in the future. Certain recommendations are well supported. The best way to prevent the spread of COVID-19 is to implement measures that we use every year to limit the spread of seasonal influenza. Patients should be instructed to avoid contact with ill persons, avoid touching their face, cover coughs and sneezes, wash hands frequently, disinfect contaminated surfaces, and stay home when sick. Prenatal clinics should ensure all pregnant women and their visitors are screened for fever and respiratory symptoms, and symptomatic women should be isolated from well women and required to wear a mask.

Additional measures, such as limiting visitors in labor and delivery units and postpartum wards, might be appropriate depending on levels of community transmission.¹ In areas of widespread transmission, community mitigation strategies such as cancellation of mass gatherings, school closures, and promotion of teleworking have been implemented,²⁵ and ensuring that pregnant women and their families have preparedness plans that address how their families respond to these measures is appropriate.²⁶ Given that pregnant women are relatively unique in that prenatal care requires frequent, routine health care visits, which might place them at greater risk of having contact with ill persons, adjustments to the health care system might also be necessary. During the SARS epidemic in 2002–2003, some health care systems in Canada had well pregnant women use separate facilities for labor and delivery.²⁷ Finally, owing to possible disruptions to health care delivery, pregnant

women might benefit from having copies of their health care records.²⁶

As the situation with COVID-19 rapidly unfolds, it is critical that obstetricians keep up to date on transmission in their area and on national guidance. Obstetricians should know who to contact at their hospital as well as their local or state health department if questions about testing or management arise. Obstetricians should regularly check the CDC website (www.cdc.gov) for clinical updates and sign up to receive Health Alert Network messages (<https://emergency.cdc.gov/han/updates.asp>), the CDC's primary method for sharing urgent public health information by email. The CDC website has a wide range of information for health professionals on a number of topics, including clinical care (eg, availability of investigational therapeutics such as remdesivir), infection control, guidance for evaluating persons suspected of having COVID-19, and inpatient obstetric health care guidance, among others. This information is regularly updated as new information becomes available. Staying up to date on local disease activity by following state or local health department websites is also necessary. Obstetricians should also regularly check updated information on ACOG's website (www.acog.org), including Practice Advisories, which are brief, focused statements that are rapidly issued in response to urgent clinical issues. The websites for both ACOG and *Obstetrics & Gynecology* (greenjournal.org) provide direct links to the CDC for easy access to these critical resources.

COVID-19 is the latest in a series of diseases caused by emerging pathogens in the past two decades, from SARS to 2009 H1N1 influenza to Ebola and Zika virus disease. As with those previous outbreaks, we must work to stay up to date with the latest data and recommendations, share what we know and do not know with our patients, and continue to be strong advocates for our patients, ensuring that their needs are addressed. Our patients deserve nothing less.

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