

Caring for Pregnant Patients with Asthma during the COVID-19 Pandemic

There is increasing information about COVID-19 and pregnancy. We hope the following information will be useful to practicing allergists and their patients.

Does pregnancy increase the need for critical care in the setting of COVID-19 infection?

Historically, pregnant individuals have been thought to be at increased risk of severe morbidity and mortality from specific respiratory infections, such as flu and SARS. As of October 13, 2020, a total of 26,364 cases of COVID-19 in pregnant women were reported to the Centers for Disease Control and Prevention (CDC) with a total of 45 deaths. In an analysis of approximately 400,000 women aged 15 to 44 years with symptomatic COVID-19, intensive care unit (ICU) admission, invasive ventilation, extracorporeal membrane oxygenation, and death were more likely in pregnant women than in nonpregnant women.

Risk of receiving invasive ventilation in pregnant women aged 35 to 44 was 3.6 times that of non-pregnant women (1). However, the data did not distinguish hospitalizations for COVID-19 from hospital admissions for pregnancy-related conditions or for delivery. A recent meta-analysis of 77 studies from China, Europe and the United States reported that high body mass index, chronic hypertension, and pre-existing diabetes were associated with severe COVID-19 in pregnancy. Pre-existing comorbidity was a risk factor for admission to the ICU (odds ratio (OR) 4.21, 95% confidence interval (CI) 1.06-16.72) and invasive ventilation (OR 4.48, 95% CI 1.40-14.37) (2). Pregnant women should be counseled about the potential risk for severe illness from COVID-19 and conscientiously take the same precautions as the general public to prevent infection, particularly if they have comorbid conditions mentioned above. If they do become sick, prompt management of symptoms is important.

Is timing of delivery affected by COVID-19?

Having severe symptoms or complications from any illness might affect timing of delivery. Reports of women hospitalized with symptoms of COVID-19 during the second and third trimesters of pregnancy have included preterm deliveries, but it is not clear if these were due to the mother's infection or other reasons (3). For women with suspected or confirmed COVID-19 in the third trimester who recover, it is reasonable to attempt to postpone elective delivery until a negative test result is obtained in an attempt to avoid transmission to the neonate.

Does COVID-19 present an increased risk of adverse perinatal and fetal outcomes?

Maternal SARS-CoV-2 infection may lead to perinatal complications directly or indirectly through placental dysfunction. Placental abnormalities such as malperfusion and functional impairment have been reported in pregnant women with COVID-19, potentially leading to outcomes such as preterm birth, intrauterine growth restriction, low birth weight and possibly early pregnancy loss (4). As noted above, some pregnant women with COVID-19 have had preterm births, and early reports showed a higher rate of delivery by caesarean sections.

A UK study compared rates of stillbirth and preterm delivery in pre-pandemic and pandemic cohorts. The incidence of stillbirth was significantly higher during the pandemic period (9.31 per

1,000 births) versus the pre-pandemic period (2.38 per 1,000 births). There was no increase in the incidence of preterm births. Interestingly, none of the women who experienced stillbirths had symptoms suggestive of SARS-CoV-2 infection, so the reasons for this increase remain unclear (5). A recent meta-analysis reported that pregnant women with COVID-19 are at increased risk of delivering a preterm birth (OR 3.01, 95% CI 1.16-7.85). However, this is based on a small number of studies with significant heterogeneity (2).

A recent multinational cohort study from 73 centers in 22 different countries found that earlier gestational age at infection (first trimester), maternal ventilator support and low birth weight are risk factors associated with adverse perinatal outcomes (6). A U.S. matched case control study of 61 cases of pregnant women with COVID-19 infection found that odds of adverse outcomes such as preeclampsia, venous thromboembolism, maternal ICU admission, and maternal death, were 3.4 times more likely in the case group compared to uninfected matched comparison pregnancies. In addition, neonatal outcomes such as respiratory distress syndrome, intraventricular hemorrhage, and neonatal death, were 1.7 times more likely in the case group. This was largely driven by those patients with severe disease. In fact, those patients with mild COVID-19 had outcomes similar to matched controls (7).

PRIORITY, a prospective U.S. cohort study, recently reported early findings in 263 infants born to mothers with confirmed SARS-CoV-2 during pregnancy. NICU admission, preterm birth and pneumonia or respiratory tract infection through 6 to 8 weeks of age did not differ between those born to mothers testing positive to SARS-CoV-2 and those born to mothers testing negative. However, infants born to mothers who first tested positive 0 to 14 days prior to delivery were also born earlier.

Among 3,912 infants with known gestational age born to women with SARS-CoV-2 infection in another study, 12.9% were preterm (<37 weeks), which was higher than a national estimate of 10.2% (8).

In a recent study where all women presenting in labor underwent COVID-19 testing, 65% of women with positive tests were asymptomatic, and those who tested positive were more likely to have preeclampsia (7.7% versus 4.3%; prevalence ratio, 1.84; 95% CI, 1.004-3.36). COVID-19 illness severity may also affect pregnancy outcome (9). In a cohort study of 252 SARS-Co-V-2 positive pregnant women, severe or critical illness prior to 37 weeks gestation was associated with pregnancy loss and preterm birth (10).

Can maternal SARS-CoV-2 infection be transmitted to the fetus?

In reports of a limited number of infants born to women with COVID-19 illness around the time of delivery, most newborns have not had evidence of infection. However, a small number of newborns have tested positive for the virus soon after delivery. This suggests the possibility that the virus could pass from a mother to a baby during pregnancy. A recent study measured viral load in COVID-19 positive pregnant mothers and found that it was not associated with COVID-19 positivity in neonates (11). In fact, risk of transmission to neonate by rooming-in and breastfeeding was low. In a meta-analysis including 230 women with COVID-19 and 156 newborns, the vertical transmission rate calculated by SARS-Co-V-2 nucleic acid tests was 3.91% (12). In the PRIORITY study described above of 263 infants born to mothers with confirmed SARS-CoV-2 during pregnancy, the estimated incidence of a positive infant SARS- CoV-2 test was

low at 1.1 %. In another study, among 610 (21.3%) infants with testing results, 2.6% had positive SARS-CoV-2 results, primarily those born to women with infection at delivery (8).

Are there special considerations for pregnant women with asthma?

Few data exist to indicate that having asthma is associated with an increased risk of becoming infected with COVID-19 or a more severe course in the non-pregnant infected patient. Recent reassuring data show that having asthma was not associated with an increased risk of hospitalization or even mortality in COVID-19 hospitalized patients. There are even fewer data for pregnant asthmatic women with COVID-19. However, the Centers for Disease Control and Prevention (CDC) does indicate that those with moderate to severe asthma might be at a higher risk for severe illness from COVID-19. In one study of 46 pregnant women with COVID-19 infection, four had asthma. Of the six women with severe disease in that study, two had asthma, but one was overweight and the other was obese with hypertension (13). Current recommendations emphasize the need to maintain asthma control during pregnancy. Reducing controller therapy could put pregnant women with asthma at increased risk of an asthma exacerbation necessitating medical care, which could then put them at an increased risk of being exposed to COVID-19.

Is breastfeeding safe during COVID-19 infection?

Breast milk provides protection against serious childhood infections. Women are often encouraged to continue breastfeeding or provide breast milk even when they are sick with a virus, such as the flu. Information about COVID-19 in breastfeeding women is limited at this time. Most case reports have not detected virus in the breastmilk of infected mothers. In a study of 18 women with confirmed SARS-CoV-2 infection, one breast milk sample had detectable SARS-CoV-2 RNA, but the viral culture for that sample was negative (14). No other breast milk samples from the 18 women had an evidence of infectious virus. In another study that included 24 mothers confirmed with COVID-19 and 19 with suspected infection, no breast milk samples tested positive for the SARS-Co-V-2 nucleic acid (15). This suggests that breast milk may not be a potential source of infection for the infant.

Are there any data on the safety of remdesivir in the management of critically ill pregnant COVID-19 patients?

Remdesivir was recently given Emergency Use Authorization (EUA) by the Food and Drug Administration (FDA). Data on the use in pregnancy is limited. Manufacturer safety data indicate no reproductive developmental toxicity in animals at clinically relevant doses. Embryonic toxicity was only noted when systemically toxic doses were administered to female animals before conception. A recent case report describes one pregnant patient who received compassionate use of remdesivir and developed transaminitis, which is a noted side effect of remdesivir (16).

Should pregnant and lactating women receive the COVID-19 vaccine?

On December 11, 2020, the FDA issued the first EUA for a vaccine for the prevention of COVID-19 in individuals 16 years of age and older. The EUA allows the Pfizer-BioNTech COVID-19 vaccine to be distributed in the United States. However, the vaccine was not specifically tested in pregnant women or in those who were breastfeeding. Developmental and reproductive

studies in animals to assess the potential effects on the fetus are underway. However, the FDA encourages vaccine companies to collect long-term data on how the vaccine performs in pregnant and lactating women. Without data, having a shared decision making dialogue with the pregnant patient regarding receiving the vaccine that considers exposure risk and underlying conditions will be essential. This is supported by the American College of Obstetricians and Gynecologists (ACOG) who recommends that COVID-19 vaccines should not be withheld from pregnant individuals who meet criteria for vaccination based on Advisory Committee on Immunization Practices (ACIP)-recommended priority groups and that pregnant individuals should be free to make their own decision in conjunction with their clinical care team (17).

Are there ongoing studies to which pregnant women could be referred?

Researchers are still learning how COVID-19 affects pregnant women. As part of their pregnancy studies, the organization MotherToBaby is interested in examining the short and long-term effects of COVID-19 in pregnancy and breastfeeding, as well as COVID-19 vaccination in pregnancy or during breastfeeding. This study will consist of phone calls over the course of the pregnancy and post-delivery or while breastfeeding, release of medical records related to the pregnancy and infant's development, and collection of breastmilk samples. If you have a pregnant or breastfeeding patient with COVID-19, or who has been vaccinated please consider enrolling them at mothertobaby.org or by calling (877) 311-8972.

Women diagnosed with COVID-19 from all countries may enroll in the International Registry of Coronavirus Exposure in Pregnancy (IRCEP). Women can enroll and provide information to the IRCEP via website and mobile app. The study will collect data on reproductive history, COVID-19 infection test, and symptoms. Women will complete monthly modules until post-partum, and medical records from the mother and neonate will be requested. If you have a pregnant patient with COVID-19, consider enrolling them at ircep.preregistry.com.

The Vaccines and Medications in Pregnancy Surveillance System (VAMPSS) also is continuing to study asthma medications during pregnancy. VAMPSS is a nationwide post-marketing surveillance system established to comprehensively monitor the use and safety of vaccines and medications during pregnancy, coordinated by the AAAAI. You can learn more about VAMPSS at the [AAAI website](#). If you have a pregnant patient with asthma, please consider enrolling them in the VAMPSS studies at mothertobaby.org or by calling (877) 311-8972.

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