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*COVID-19, pregnancy, and breastfeeding*: What is the current medical consensus on how COVID-19 may affect pregnant individuals who contract the virus? Likewise, what is the current medical consensus on COVID-19 and breastfeeding?

## 1. Background

Coronavirus disease 2019 (COVID-19) is a respiratory viral illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which has rapidly spread throughout the world. COVID-19 is thought to have originated in Wuhan, China with the first case reported in December 2019 (1). As of July 1st<sup>th</sup>, 2020, cases in the U.S. have totaled to 2,624,873and deaths have totaled to 127,299 (2). Although transmission and spread are still under current research, COVID-19 is thought to spread primarily through respiratory droplet with a higher rate of transmission compared to seasonal influenza and measles, with each case estimated to infect 2-3 people (1). Clinical severity varies from self-limiting, mild cold-like symptoms to more critical cases with multi-organ failure necessitating intensive care unit admissions. However, based on data from previous similar coronavirus outbreaks such as MERS and SARS, pregnant women are thought to be at a higher risk for more complicated clinical course. Given normal changes during pregnancy to the immune system, patients with COVID-19 are considered to be high risk and extensive precautions have been recommended to ensure proper hygiene and social

distancing with potential exposures (3). With a constant stream of new information, medical bodies such as Center for Disease Control (CDC), American College of Obstetricians and Gynecologists (ACOG), Royal College of Obstetricians and Gynecologists (RCOG), and American Academy of Pediatrics (AAP), continue to update their recommendations regarding pregnancy and breastfeeding in the COVID-19 era.

## 2. COVID-19 and Pregnancy

#### a. Disease course and severity

According to data early in the pandemic, compared to previous coronavirus outbreaks (MERS and SARS), COVID-19 appeared to be more mild in terms of complications during pregnancy. Furthermore, these early studies suggested that pregnancy does not seem to alter the disease course of COVID-19. A study which followed 43 COVID-19 positive pregnant patients in New York City described both asymptomatic and symptomatic presentations. Of the 43 patients, 37 (86%) showed mild disease, 4 (9.3%) showed moderate disease, and 2 (4.7%) showed severe disease (4). These figures are consistent with disease severity in non-pregnant COVID-19 positive patients. A systemic review of 295 pregnant patients demonstrated a rate of ICU admission of 4.7%, is also consistent with the non-pregnant population (5). A study involving 427 pregnant women infected by COVID-19 supported that pregnancy generally had good outcomes. However, this study also highlights the racial disparity among COVID-19 patients. 56% of the patients in this study were black/ethnic minority, and the study concluded black/ethnic minority is a significantly associated with admission due to COVID-19 (6). ACOG released a statement regarding the racial disparity and disproportionate rates in communities of color and maintain that the main factors contributing to these disparities are social determinants of health, access to healthcare and structural racism.

While data from earlier in the pandemic suggested that pregnant women are not at increased risk, a study released by the CDC in June 2020 highlighted data shows that pregnant women may be a particularly vulnerable population. Using data from National Notifiable Diseases Surveillance System a study by the CDC analyzed an estimated 8207 COVID-19 cases in pregnant women from January 22–June 17 (7). Data from this study showed increased hospitalization rates (31.5% vs 5.8%) and increased ICU admission rates (1.5% and 0.9%) in pregnant women vs non-pregnant women. After adjusting for confounding factors, the study concluded that pregnant women are 5.4 times more likely to be hospitalized and 1.5 times more likely to be admitted to the ICU. However, death rates between pregnant and non-pregnant women seems to be similar. Limitations to this study include unavailability of data distinguishing hospitalizations for COVID-19 from hospital admissions for pregnancy-related conditions, and missing key data such as demographics, underlying conditions, and symptoms. However, because of this study, CDC released a statement warning that pregnant people may be at an increased risk for severe illness from COVID-19. ACOG also released a statement in light of the new data brought forth by CDC and are currently considering modification to clinical guidelines (8). They also highlight the importance of including pregnant and lactating patients safely in clinical trials for vaccines. Overall, this new data suggests pregnant women with COVID-19 should be followed closely for worsening disease.

#### b. Complications during pregnancy and risk to neonate

In a review article of 162 pregnant women with COVID-19, the most common symptom is fever (50%) followed by cough (34%) and dyspnea (16%) (9). Most common maternal complication is pneumonia (85%). Serious complications such mortality is reported at 2% and mechanical ventilation is required in 4% of patients in this study. This is in contrast with other coronavirus outbreaks such as SARS and MERS which showed a mortality of 18% and 25%, respectively and mechanical ventilation in 35% and 41% of patients, respectively. The most common complications during pregnancy are preterm birth (38%) and cesarean section (85%). Further increases in preterm birth and cesarean sections are seen in women who develop pneumonia. Although cases of mortality have been reported, they have often been limited to cases secondary to severe disease with both maternal and fetal mortality. Overall, there appears to be no indication that COVID-19 infection in the mother leads to increased risk of neonatal morbidity or mortality. CDC and ACOG both acknowledge the increased frequency of preterm birth, but have maintained that it is unclear if COVID-19 is the cause of this observation (7,8).

A major point of concern is the risk of viral transmission to the neonate. A Paris case study recently demonstrated transplacental transmission of COVID-19 in a neonate born to a mother in mother infected in her last trimester of pregnancy. (22) In a case series in which 9 women underwent cesarean delivery after diagnosis of COVID-19, testing amniotic fluid, cord blood and breastmilk were negative for viral load, suggesting no vertical transmission (12). There are however, cases of possible intrauterine transmission. Reports of IgM antibodies in neonatal serum at birth suggest possible intrauterine infection (13,14). The limited data is inconclusive evidence for vertical transmission in all cases, and as a result vaginal deliveries are not contraindicated at this time. Despite this, a large majority of patients have electively decided to undergo cesarean section (13). Additionally, increased rates of cesarean sections have been largely preformed electively due to belief that prompt delivery would improve respiratory disease. While CDC and ACOG state that intrauterine transmission is uncommon, both indicate the need for more data (9, 10). With emerging evidence of possible vertical transmission, RCOG states that vertical transmission is possible (15).

While COVID-19 is not an indication to alter route of delivery, a study in Spain which compared vaginal delivery and cesarean section in COVID-19 patients, higher rates of clinical

deterioration were seen in pregnant women delivering via cesarean section (Adjusted OR, 13.4; 95% CI, 1.5-121.9; P = .02) (16). In this study clinical deterioration was defined as the need for oxygen supplementation after delivery. These results have not altered clinical guidelines in regards to route of delivery, but they certainly raise concerns of potential adverse outcomes in COVID-19 mothers who undergo cesarean section.

Although vertical transmission in utero does not seem to pose a significant risk to the fetus, a potential risk early in pregnancy is hyperthermia associated with COVID-19. Studies have shown that fever during the first trimester is associated with increased rates of congenital anomalies, neural tube defects, and miscarriage (17). Unfortunately, limited data currently exists on the effects of COVID-19 infection and early pregnancy.

#### c. Hypercoagulability

Recent studies have shown increased risk of hypercoagulability and subsequent thromboembolic events in COVID-19 patients (19). Lab testing on these patients suggest that they may benefit from prophylactic anticoagulation therapy. This issue particularly effects pregnant women as normal physiologic changes during pregnancy affect coagulation, thus compounding the effects of COVID-19. As a result, the RCOG recommends low molecular weight heparin to all pregnant women with confirmed or suspected COVID-19 (13). ACOG recently updated their recommendation regarding anticoagulation in pregnant patients, stating it is reasonable to consider anticoagulation therapy given increased risk in pregnant patients, however no specific treatment is recommended (9).

### d. Steroid use

Use of steroids have been a point of concern in regards to management of pregnant women with COVID-19. The World Health Organization (WHO) recommends the avoidance of steroid use due to the evidence from previous coronavirus outbreaks that there is delayed viral clearance (20). Additionally, use of steroids has shown an increase in mortality in patients with influenza. However, in situations of preterm labor, corticosteroid use is vital to inducing fetal lung maturity. Additionally, the dosage of steroids given for prematurity are not likely to cause harm in the context of COVID-19. ACOG has recommended that while decisions may certainly be individualized, the clear benefits of betamethasone in pregnancies between 24 weeks and 34 weeks of gestation at a high risk for preterm birth outweigh the risks. However, in pregnant women with confirmed or suspected COVID-19, administration of betamethasone between 34-37 weeks may not be beneficial and thus ACOG recommends against the use of steroids during this period (8). The CDC has yet to comment on the use of corticosteroids in pregnancy.

# 3. COVID-19 and Breastfeeding

In terms of breastfeeding, both ACOG and CDC have maintained that viral loads of COVID-19 in breastmilk are not detectable and breastfeeding is not contraindicated (9,10). AAP, supports and encourages breastfeeding in mothers with COVID-19 (18). Although there is lack of data that demonstrates viral transmission through breast milk, shared decision making is recommended as there is still a risk of transmission through respiratory droplet when feeding. As a result, CDC, ACOG, AAP recommend use of a facemask and proper hand hygiene while feeding. If the decision is to use a breast pump, the baby should ideally be fed by a healthy individual (9,10,19). If using a breast pump, proper cleaning of all parts of the pump is recommended after use. Overall, the benefit of breastfeeding includes decreased risk of infection, increased maternal well-being and sustainability given potential shortage of other feeding options; all of which outweigh the risks of potential airborne exposure from the mother.

Although limited data exists regarding the presence of COVID-19 antibodies in the breastmilk and potentially transferring immunity, assumptions can be made based on data regarding previous coronavirus antibodies in breastmilk. In these studies, the presence of antiviral antibodies depends on the timing of maternal infection. For example, median time of the presence of antibodies after infection for SARS-CoV was 17 days (21).

## 4. Conclusion

Overall, our understanding of COVID-19 and pregnancy is limited by the amount of data available in the medical literature. As a result, medical recommendations are rapidly evolving as new data is brought forth. The statements and recommendations by CDC, ACOG, RCOG, and AAP as it relates to the effects of COVID-19 and pregnancy are outlined in table 1. With recent data, the medical community, particularly CDC and ACOG, have released statements warning that pregnant women may represent a vulnerable population and may develop more severe disease compared to the general healthy counterparts. Clinical course in most cases manifests with cold-like symptoms, fevers and pneumonia. However long-term effects of COVID-19 on pregnancy have vet to be elucidated. Furthermore, most studies to date have described cases of pregnant women in the 3<sup>rd</sup> trimester or presenting in labor. Therefore, further studies would be needed to understand the effect of COVID-19 on pregnancy in the earlier stages of gestation. The most common fetal complications are mainly limited to preterm birth and cesarean sections and further studies will be needed to understand long term effects. CDC, ACOG, and AAP are all in consensus that there is inconclusive data to suggest viral transmission through either trans placental exchange or breastmilk. As a result, vaginal delivery unless contraindicated for other medical reasons and breastfeeding are both encouraged.

The consensus is that COVID-19 does not affect the general management of pregnancy/labor and proper precautions similar to the non-pregnant population should be maintained. The studies which societies and organizations have based their recommendations on have been on cases in the earlier stages of the pandemic and are largely limited to third-trimester presentations. Thus, a better understanding of the effects of COVID-19 on pregnancy, birth and post-partum care will require more data including a larger set of patients across the all stages of pregnancy. Further investigations should also be targeted at racial disparities and possible contributing socioeconomic factors in regards to COVID-19 and pregnancy.

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	Risk of Infection/Severity of disease	Risk to Baby	Anticoagulation	Breastfeeding
CDC(1)	Potentially at risk for more severe disease	Vertical transmission unlikely Increased risk of pre-term birth	May be increased risk for thrombosis – no specific recommendation regarding treatment	If breastfeeding- proper precautions are encouraged
ACOG(2)	No increased risk for severe infection or mortality	Cases of reported vertical transmission, but uncommon	May be increased risk for thrombosis – reasonable to consider anticoagulation	No concern for transmission through milk – still risk for respiratory droplet
RCOG(3)	Most cases are mild/moderate flu-like symptoms	Vertical transmission may be possible – further investigation is needed	All pregnant women with suspected or confirmed COVID- 19 should receive heparin treatment	No contraindication
AAP(4)	-	-	-	Support breastfeeding

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