Monoclonal antibody treatment of symptomatic COVID-19 in pregnancy: initial report

OBJECTIVE: Neutralizing monoclonal antibodies (mAbs) targeting the spike protein of SARS-CoV-2 have been shown to reduce disease progression and hospitalization in those at a high risk of disease progression.[1] The United States Food and Drug Administration (FDA) provided emergency use authorization (EUA) for neutralizing mAbs in November 2020, which included a warning for pregnant and lactating women. Mounting evidence showing that COVID-19 has a disproportionate effect on pregnant women with higher rates of viral infection and disease severity[2] prompted the inclusion of pregnancy as a criterion for mAb therapy in the United States earlier this year.[3] Although other monoclonal antibodies and their transplacental passage have been well-studied in pregnancy,[4] there are no data on the safety or efficacy of anti-spike protein neutralizing mAbs. To our knowledge, there is no previously published report of the treatment of COVID-19 with mAbs in pregnancy (PubMed, August 8, 2021; search terms: "Monoclonal antibody," "pregnancy," and "COVID-19").

STUDY DESIGN: These cases were collected as a part of a quality improvement project at a single academic medical center that was deemed exempt by the Human Research Protection Office. Pharmacy records were reviewed to identify patients who received the SARS-CoV-2 neutralizing antibodies between November 2020 and July 2021. The charts of these patients were reviewed in detail to extract COVID-19 and pregnancy-related data. The patients met strict FDA EUA criteria to be considered for mAb therapy.[5] Clinical disease severity was based on the National Institutes of Health (NIH) classifications.[6] The products used at our institution included bamlanivimab and casirivimab plus imdevimab, based on the availability at the time of treatment.

RESULTS: We reviewed data from 813 patients who received mAb therapy at our institution during the study period. Of note, 4 of these patients were pregnant at the time of infusion, and the maternal ages ranged from 26 to 34 years; their gestational ages ranged from 11 to 32 weeks. In addition, 2 of the 4 patients were overweight and the other 2 were obese. All had symptomatic COVID-19 at the time of diagnosis and were confirmed positive based on nasopharyngeal polymerase chain reaction testing. Furthermore, 2 of the 4 patients met the FDA EUA criteria for therapy based on immunosuppressive conditions—one based on diabetes mellitus and the other (the fourth patient) based on body mass index (BMI). Two patients had moderate disease at the time of treatment and the others were categorized as mild. All patients received casirivimab plus imdevimab and tolerated the infusion without immediate complication. One patient experienced disease progression after mAb therapy, developing shortness of breath and thus meeting the NIH criteria for moderate disease. None of the 4 pregnant women required additional outpatient visits or hospitalizations related to their COVID-19 diagnosis. No abnormalities in anatomy or growth were identified on ultrasound or at the time of delivery for any of the pregnancies. Two patients are still pregnant at this time and have no additional pregnancy complications. One pregnancy ended in term vaginal delivery of a healthy neonate in the setting of pregnancy-related hypertension and another pregnancy ended in preterm delivery after maternal trauma in an unrelated event (Table).

CONCLUSION: In this case series of maternal mAb therapy in pregnancy, we found no evidence of pregnancy complications or treatment failure. All 4 patients avoided progression to severe disease and none required additional COVID-19-related medical visits or hospitalizations. Anti-spike protein neutralizing antibodies are human immunoglobulin G1 kappa with unadulterated Fc receptors, which should allow for facilitated diffusion across the placenta,[4] raising the concern for transplacental passage. However, there were no fetal effects noted in our small cohort. Given the ongoing severity of the COVID-19 pandemic, especially during pregnancy, more information regarding the safety and efficacy of neutralizing mAbs in pregnancy is vital.

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The authors report no conflict of interest.

TABLE
Patient characteristics and outcomes

Patient	Age (y)	BMI (kg/m^2)	Existing pregnancy complications	Gestational age at treatment (wk + d)	COVID-19 severity at treatment	Symptom day at time of mAb infusion	Worst COVID-19 severity after treatment	Additional COVID-19 care required	Pregnancy outcomes
Patient A	25	32.7	Diabetes, hypertension	11+1	Mild	2	Mild	None	Currently 25 wk pregnant
Patient B	34	27.8	Postsplenectomy	32+0	Moderate	8	Moderate	None	36-wk delivery of normally grown fetus; maternal trauma
Patient C	29	37.0	Obesity	31+3	Mild	4	Moderate	None	37-wk delivery of normally grown fetus; diagnosis of gestational hypertension
Patient D	24	29.4	Shingles	32+0	Moderate	2	Moderate	None	Currently 38 wk pregnant

BMI, body mass index; *mAb*, monoclonal antibodies.

Hirshberg. Monoclonal antibody treatment of symptomatic COVID-19 in pregnancy. Am J Obstet Gynecol 2021.

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 https://doi.org/10.1016/j.ajog.2021.08.025

SARS-CoV-2 and the subsequent development of preeclampsia and preterm birth: evidence of a dose-response relationship supporting causality

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OBJECTIVE: Pregnant women affected with a severe SARS-CoV-2 infection have worse clinical outcomes than nonpregnant women with SARS-CoV-2, which can include the greater risks for admission to the intensive care unit, the use of invasive mechanical ventilation, the need for extracorporeal membrane oxygenation, and death. In addition, SARS-CoV-2 infection is a risk factor for fetal death and preterm birth. Early during the COVID-19 pandemic, a preeclampsia-like syndrome was reported in pregnant women with SARS-CoV-2.[1] This association has been confirmed by case series,[2] systematic reviews, and meta-analyses.[3] An important issue is whether COVID-19 causes preeclampsia. One of the Bradford Hill criteria to assess causality is the existence of a dose-response relationship between an exposure and the outcome of interest, which, in this case, is the severity of the SARS-CoV-2 infection and the likelihood of preeclampsia. This study was conducted to address this question.