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Original Research

Neutralizing Monoclonal Antibodies for Coronavirus Disease 2019 (COVID-19) in Pregnancy

A Case Series

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OBJECTIVE: To describe outcomes associated with monoclonal antibody use in pregnant persons with mild-to-moderate coronavirus disease 2019 (COVID-19).

METHODS: We present a retrospective case series of pregnant patients who received anti–severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) monoclonal antibody infusions at a single center from April 1, 2021, through October 16, 2021. Pregnant patients who had a positive SARS-CoV-2 polymerase chain reaction (PCR) test result and mild-to-moderate COVID-19 symptoms were eligible for monoclonal antibody infusion. Exclusion criteria for administration included need for supplemental oxygen, hospitalization due to COVID-19, and positive SARS-CoV-2 PCR test result more than 7 days before screening. All patients received either bamlanivimab plus etesevimab or casirivimab plus imdevimab based on availability and dosing instructions of the product and emerging resistance patterns in the community.

RESULTS: During the study period, monoclonal antibody infusions were administered to 450 individuals at our institution, of whom 15 were pregnant. Of the 15 pregnant persons receiving monoclonal antibody, six (40%) had full-vaccination status at the time of infusion. Two individuals (13%, CI 0–31%) experienced systemic reactions during the infusion, both resulting in temporary changes in the fetal heart rate tracing that recovered with maternal and intrauterine resuscitative efforts. One patient delivered after infusion for worsening maternal and fetal status; the remainder of the patients did not require admission for COVID-19.

CONCLUSION: In this case series, pregnant persons who received anti–SARS-CoV-2 monoclonal antibody infusions had generally favorable outcomes.

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Each author has confirmed compliance with the journal's requirements for authorship.

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Financial Disclosure

Christina Han disclosed receiving funding from Roche Sequencing. Yalda Afshar and Christina U. Pham disclosed that the U.S. Food and Drug Administration granted emergency use authorization for the use of monoclonal antibody infusions in SARS-CoV-2–infected individuals with mild-to-moderate symptoms with risk factors for disease progression. Although pregnant people were not included in the original EUA, it is now well-established that pregnant individuals are at higher risk of severe morbidity and mortality from COVID-19. Guidelines from the Society for Maternal-Fetal Medicine, therefore, noted that all therapies that are recommended for nonpregnant individuals should also be made available to the obstetric population. Christina U. Pham also disclosed receiving funding from Gilead. The other authors did not report any potential conflicts of interest.

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Anti–severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) monoclonal antibodies have been used to reduce morbidity and risk for hospitalization in patients at increased risk for progression to severe coronavirus disease (COVID-19).[1,2] These antibodies are directed against the receptor-binding domain of the spike protein of SARS-CoV-2, thereby preventing binding of the spike protein to its receptor on target host cells

and facilitating antibody-dependent phagocytosis by macrophages.[1,2] This, in turn, can reduce the viral load by up to 70% according to Weinreigh et al.[2]

Currently available formulations of SARS-CoV-2 monoclonal antibodies include bamlanivimab plus etesevimab[3] and casirivimab plus imdevimab.[4] The U.S. Food and Drug Administration (FDA) granted emergency use authorization for these preparations in individuals with SARS-CoV-2 infection with mild-to-moderate COVID-19 symptoms with risk factors for disease progression. Although pregnant people were not included in the original emergency use authorization,[3,4] it is now well established that pregnant individuals are at higher risk for severe morbidity and mortality from COVID-19.[5,6] Guidelines from the Society for Maternal-Fetal Medicine, therefore, note that all therapies that are recommended for nonpregnant individuals should also be made available to the obstetric population.[7] Given the lack of data on use of anti–SARS-CoV-2 monoclonal antibodies, we aim to describe the outcomes of monoclonal antibody use in pregnancy.

METHODS

We present a retrospective case series of pregnant patients who received anti–SARS-CoV-2 monoclonal antibody infusions at a single quaternary care center from April 1, 2021, through October 16, 2021. This study was approved by the institutional review board at the University of California, Los Angeles (IRB #21-001607), and informed consent was obtained from the patients discussed in detail.

Pregnant patients who had a positive SARS-CoV-2 polymerase chain reaction (PCR) test result were identified. Symptomatic patients were evaluated and triaged by maternal–fetal medicine subspecialists and confirmed to have met criteria for monoclonal antibody administration. Pregnancy was considered an independent risk factor for progression of COVID-19; no additional risk factors were necessary for entry into treatment. Exclusion criteria for administration included need for supplemental oxygen, hospitalization due to COVID-19, and positive SARS-CoV-2 PCR test result more than 7 days before screening. In our center, pregnancy was considered to be an independent risk factor for disease progression after June 8, 2021, when the FDA updated the emergency use authorizations to include pregnant people. Appendix 1, available online at http://links.lww.com/AOG/C585, contains the institutional protocols in force during the study period.

Data were extracted from electronic medical records by one investigator (M.R.), including patient demographics, COVID-19 symptoms, laboratory data, pregnancy data, fetal heart tracing data, and pregnancy and neonatal outcomes (if available). Per institutional protocol, patients at less than 20 weeks of gestation received their infusions at an outpatient site (infusion center or home infusion). Patients who were at 20 weeks of gestation or more received their infusions as a same-day infusion in the labor and delivery unit and were observed for 1 hour after the infusion. Patients who were at or beyond 24 weeks of gestation had either fetal nonstress tests before and after their infusion or continuous fetal monitoring during the observation period, per physician preference. Descriptive statistics are reported.

RESULTS

From April 2021 through October 2021, monoclonal antibody infusions were administered to 450 individuals through our center, of whom 15 were pregnant. All patients received either bamlanivimab plus etesevimab or casirivimab plus imdevimab based on availability and dosing instructions of the product and emerging resistance patterns in the community.[8] Pregnant individuals who received monoclonal antibodies were heterogeneous in age, body mass index, gestational age, insurance type, and presenting symptoms (Table 1). Forty percent of the pregnant individuals in this series were fully vaccinated.

Two patients (13%, CI 0–31%) developed an adverse reaction while under observation for infusion of monoclonal antibodies. None of the other 13 patients experienced adverse reactions, progression to severe disease, or adverse pregnancy outcomes to date. No adverse reactions were reported in the 435 nonpregnant individuals who received monoclonal antibody treatment, although chart review of the nonpregnant group was not performed, but all adverse events from the monoclonal antibodies are kept for internal review. Of the patients who had monoclonal antibody infusions, eight (53%) have delivered: one after a reaction as reported below, two at term with fetal growth restriction, and five at term with no complications.

The first patient with a reaction (patient 8, Table 1) presented at 36 2/7 weeks of gestation with a history of positive SARS-CoV-2 PCR test result 7 days earlier and risk factors of asthma and obesity. Presenting symptoms were mild, with sore throat and malaise. White blood cell count was 6.8×10^3/microliter. During the infusion, the patient developed tachypnea, wheezing, and shaking, followed by oxygen desaturation to 90%, which improved with supplemental oxygen. Concomitant with the reaction, fetal bradycardia

Table 1. Patient Demographics, Characteristics, and Outcomes

Patient No.	Monoclonal Antibody Type*	Risk Factor(s)	GA (wk)	Cough	Chest Pain	Loss of Taste	Congestion
1	Bamlanivimab/etesevimab	BMI higher than 25	20 0/7	x	x	x	
2	Casirivimab/imdevimab	Hypertension	37 0/7				x
3	Casirivimab/imdevimab	BMI higher than 25, GDM	22 3/7	x			x
4	Casirivimab/imdevimab	BMI higher than 25	29 2/7	x			x
5	Casirivimab/imdevimab	BMI higher than 25	29 1/7	x			
6	Casirivimab/imdevimab		36 0/7				
7	Casirivimab/imdevimab	BMI higher than 25	35 6/7				
8	Casirivimab/imdevimab	BMI higher than 25, asthma	36 2/7				x
9	Casirivimab/imdevimab	BMI higher than 25, asthma	38 0/3				
10†	Casirivimab/imdevimab	GDM	35 5/7	x			x
11	Casirivimab/Imdevimab	BMI higher than 25	28 4/7	x		x	x
12	Casirivimab/imdevimab	BMI higher than 25	34 5/7	x		x	x
13	Casirivimab/imdevimab		25 5/7	x			
14	Casirivimab/imdevimab	Asthma	15 2/7	x			x
15	Casirivimab/imdevimab	BMI higher than 25, smoker	8 0/6				

GA, gestational age; ADR, adverse drug reaction; BMI, body mass index; FGR, fetal growth restriction; GDM, gestational diabetes mellitus.
* Dosages of monoclonal antibodies were: 1) bamlanivimab 700 mg and etesevimab 1,400 mg, and 2) casirivimab 600 mg and imdevimab 600 mg.
† Received second dose of vaccine but had not reached 2 weeks postvaccination (patient 10).

was noted for 11 minutes to a nadir of 90 beats per minute, followed by tachycardia to 210 beats per minute an hour later. No maternal fever was noted. Intravenous diphenhydramine and crystalloid was administered once the reaction was recognized. A chest X-ray performed after the reaction revealed multifocal peripheral consolidation suspicious for COVID-19 pneumonia. The patient was placed on remdesivir and dexamethasone and ultimately delivered 36 hours later, at 36 3/7 weeks of gestation, for worsening respiratory status and nonreassuring fetal heart tracing. An uncomplicated primary cesarean delivery was performed under spinal anesthesia; the neonate had Apgar scores of 8 at 1 minute and 9 at 5 minutes. By postoperative day 1, the patient's respiratory symptoms had resolved and the patient was oxygenating well on room air; thus, remdesivir and dexamethasone were stopped. Neonate and mother were both discharged home on postoperative day 3.

The second patient who developed a reaction (patient 13, Table 1) presented at 25 5/7 weeks of gestation, 2 days after a positive SARS-CoV-2 PCR test result, with mild symptoms of myalgia and fatigue. She had no additional risk factors. Approximately 12 minutes after the completion of the infusion, she reported difficulty breathing but did not have tachypnea or low oxygen saturation. Mild hypertension was noted, with systolic blood pressure of 142 mm Hg. Two consecutive fetal decelerations were noted for 7 minutes and 5 minutes each, during which oxygen supplementation, oral acetaminophen, and intravenous diphenhydramine, methylprednisolone, and crystalloid were administered. On recovery from the decelerations, the fetal heart tracing remained reassuring over an hour of monitoring and the patient was discharged home with no further sequelae. The rest of the patient's pregnancy was uncomplicated. The patient underwent an induction of labor at 39 weeks of gestation and had an uncomplicated vaginal delivery.

DISCUSSION

To date, there is limited information on the use of anti–SARS-CoV-2 monoclonal antibodies in pregnancy.[9,10] Our report describes outcomes of fetal heart monitoring for all patients who received their infusion after 24 weeks of gestation. In the original trials in nonpregnant populations, reactions were

Patient No.	Myalgias	Shortness of Breath	Headache	Fatigue	Days of Symptoms	Fully Vaccinated	ADR	Delivered
1					7	No	No	Yes
2					2	No	No	Yes (FGR)
3					3	No	No	Yes
4		x			4	Yes	No	Yes
5	x				1	No	No	Yes
6	x		x	x	3	No	No	Yes
7				x	2	Yes	No	Yes
8					7	No	Yes	Yes
9	x		x		2	No	No	Yes
10†					2	No†	No	Yes
11	x			x	5	Yes	No	Yes
12					6	No	No	Yes (FGR)
13	x			x	2	Yes	Yes	Yes
14					4	Yes	No	Yes
15	x				5	Yes	No	Yes

noted in 0.2–2.3% of the infused individuals, compared with 1.4% of placebo-infused individuals.[11] Most of these events, described as pruritus, flushing, rash, and facial swelling, occurred during the infusion and were reported as mild in severity. These reported reactions in nonpregnant individuals differed slightly from the respiratory symptoms noted by the two pregnant patients in this report.

Our internally developed institutional protocol includes the screening and counseling of all candidates by maternal–fetal medicine specialists, specifically regarding the risks of COVID-19 in pregnancy and the lack of available evidence on the risks and utility of monoclonal antibody infusion in pregnancy. The two cases with prolonged fetal heart tracing decelerations could not be causatively attributed to the infusions and, particularly in patient 8, could have been a result of worsening underlying COVID-19; however, the temporal association of the fetal heart tracing aberrations to the monoclonal antibody infusion is important to note. These cases have been reported to MedWatch, the FDA Safety Information and Adverse Event Reporting system.

In this case series, pregnant persons who received anti–SARS-CoV-2 monoclonal antibody infusions had generally favorable outcomes. Two patients who experienced reactions during the monoclonal antibody infusions also concomitantly exhibited temporary fetal heart tracing abnormalities, which recovered in the short term with maternal and intrauterine resuscitative efforts. Given the risks of severe disease progression that SARS-CoV-2 infection poses to pregnant individuals, we believe that anti–SARS-CoV-2 monoclonal antibodies should continue to be offered to pregnant individuals, with shared decision making regarding fetal heart tracing monitoring when appropriate and availability of supportive medications to treat infusion reaction and provide intrauterine resuscitation. Furthermore, the original trials demonstrated increased efficacy of anti–SARS-CoV-2 monoclonal antibodies in individuals who are seronegative for SARS-CoV-2.[2] As such, institutions may consider triaging patients based on comorbidities or seronegative status, when serologic testing is available. Raising the threshold of entry into treatment with anti–SARS-CoV-2 monoclonal antibody infusion may allow for better selection of pregnant candidates who may benefit from infusions.

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