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Outcomes of pregnant patients treated with REGEN-COV during the COVID-19 pandemic

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BACKGROUND: Pregnant patients with SARS-CoV-2 infection are at increased risk for severe disease including hospitalization, intensive care admission, ventilatory support, and death. Although pregnant patients were excluded from investigational trials for pharmacologic treatments for COVID-19 illness, the National Institutes of Health treatment guidelines state that efficacious treatments should not be withheld from pregnant patients. An infusion of casirivimab and imdevimab (REGEN-COV), a monoclonal antibody therapy, was shown to reduce the risk of COVID-19–related hospitalization or death from any cause and resolved symptoms and reduced SARS-CoV-2 viral load more rapidly than placebo. In July of 2021, the Food and Drug Administration released an Emergency Use Authorization for REGEN-COV. Although pregnant persons were not included in the original trials, given the higher risk of morbidity and mortality in the pregnant population, our institution offered REGEN-COV to our pregnant patients beginning in August of 2021. Side effects after REGEN-COV administration are rare and thought to be secondary to COVID-19 rather than REGEN-COV.

OBJECTIVE: This study aimed to track safety and clinical outcomes in unvaccinated pregnant patients who received REGEN-COV and to compare these outcomes with those of a contemporary cohort of patients who tested positive for SARS-CoV-2 and were eligible but did not receive REGEN-COV. Our hypothesis was that REGEN-COV administration during pregnancy is safe, and that pregnant persons who received REGEN-COV would experience less severe COVID-19 respiratory illness, with decreased length of hospital stay, rates of intensive care unit admission, and need for oxygen and other COVID-19 therapeutics.

STUDY DESIGN: This is a retrospective cohort study of pregnant patients who either tested positive for SARS-CoV-2 or had a known exposure to a COVID-19–positive person, and were therefore eligible for REGEN-COV at our institution. Within this cohort, we compared those who received REGEN-COV with those who did not between March and October of 2021 at Grady Memorial Hospital in Atlanta, Georgia. The main outcomes studied were perinatal outcomes, safety data, and the clinical course of SARS-CoV-2 infection.

RESULTS: From March to October of 2021, 86 pregnant people tested positive for SARS-CoV-2 via real-time polymerase chain reaction or had a confirmed exposure. In this group, 36 received REGEN-COV and 50 did not. There were no instances of infusion rate adjustment or discontinuation, anaphylaxis, or death among individuals who received REGEN-COV. One individual experienced worsening shortness of breath >24 hours after administration, which was classified as an infusion-related reaction. There were no significant differences in perinatal outcomes, length of hospitalization, rates of intensive care unit admission, additional pharmacologic treatment for COVID-19, or oxygen requirement between the 2 groups.

CONCLUSION: Administration of REGEN-COV is safe in pregnancy and did not increase adverse maternal, neonatal, or obstetrical outcomes. There was not a statistically significant difference in COVID-19–related outcomes in our high-risk population. Given the likely safety of this drug in pregnancy and its known benefits in the nonpregnant population, we advocate for the continued use of this therapy and encourage the development of future studies to enroll a larger and more diverse cohort to explore its efficacy further.

Keywords: adverse events, casirivimab and imdevimab, COVID-19, maternal morbidity, monoclonal antibodies, neonatal morbidity, novel therapies, pregnancy, REGEN-COV, SARS-CoV-2

Introduction

The global COVID-19 pandemic has been a devastating public health crisis resulting in over 5.7 million deaths.[1–4] Pregnant patients are at increased risk for severe disease, including hospitalization, intensive care admission, ventilatory support, and death from COVID-19.[5–7] The recent B.1.617.2 Delta variant, which peaked in the Southeastern United States during the late summer of 2021, led to adverse perinatal outcomes including stillbirth, preterm birth, and poor neonatal outcomes.[8,9]

Because of the increased risk of severe COVID-19 illness in the pregnant population, the National Institutes of Health (NIH), the American College of Obstetricians and Gynecologists (ACOG), and the Society for Maternal-Fetal Medicine (SMFM) have all issued statements indicating that therapies that would otherwise be given should not be withheld specifically because of pregnancy or lactation status.[1,10,11] Monoclonal antibody treatment has previously been shown to be an effective treatment against other viruses such as Ebola and influenza viruses. Consequently, there was a push to study the role of monoclonal antibodies and their use for protection against COVID-19 illness. Monoclonal antibodies showed promising results in early efficacy trials and are thought to help rapidly decrease the high viral loads found in patients with hypoxemia, thereby preventing the progression to severe disease.[12–14] In the summer of 2021, a combination of the monoclonal antibodies casirivimab and imdevimab (REGEN-COV, Regeneron Pharmaceuticals, Tarrytown, NY) was shown to reduce the risk of COVID-19–related hospitalization or death from any cause and resolved symptoms more rapidly than placebo in a nonpregnant population.[15,16] In July 2021, the United States Food and Drug Administration

Cite this article as: Levey NH, Forrest AD, Spielman DW, et al. Outcomes of pregnant patients treated with REGEN-COV during the COVID-19 pandemic. Am J Obstet Gynecol MFM 2022;4:100673.

2589-9333/$36.00
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http://dx.doi.org/10.1016/j.ajogmf.2022.100673

AJOG MFM at a Glance

Why was this study conducted?

It has been well-established that REGEN-COV is a safe and effective therapy for treatment of nonpregnant people with SARS-CoV-2 infection; however, little is known about this therapy in the pregnant population.

Key findings

We described a retrospective cohort study of 86 pregnant people at our institution who tested positive for or had a known exposure to the SARS-CoV-2 virus, 36 of whom received REGEN-COV. There were no significant adverse safety events among those who received monoclonal antibodies. REGEN-COV, however, was not associated with decreased length of hospitalization or intensive care unit admission in our cohort.

What does this add to what is known?

This is a large study investigating the administration of REGEN-COV to pregnant people.

(FDA) released an Emergency Use Authorization for the use of REGEN-COV to prevent progression to severe disease for patients with mild to moderate COVID-19 illness or for postexposure prophylaxis.[17,18]

As with many previous treatments for COVID-19, pregnant patients were excluded in the efficacy and safety trials.[1] Given the higher risk of morbidity and mortality in the pregnant population, however, our institution began offering REGEN-COV to pregnant patients who either tested positive for SARS-CoV-2 or had a close contact who tested positive for SARS-CoV-2 in August 2021. Few studies have investigated the use of this novel monoclonal antibody combination in the pregnant population; the existing literature is limited to 3 small case series.[7,19,20]

The objective of this study was to examine outcomes in pregnant patients who received REGEN-COV and compare these outcomes with those of a similar cohort of patients who tested positive for SARS-CoV-2 but did not receive REGEN-COV. This study aimed to provide information on the safety and clinical outcomes of the use of REGEN-COV in the pregnant population. Our primary hypothesis was that REGEN-COV administration during pregnancy is safe, and that the pregnant persons who received REGEN-COV would experience less severe COVID-19 respiratory illness, with decreased length of hospital stay, rates of intensive care unit (ICU) admission, and need for oxygen and other COVID-19 therapeutics.

Materials and Methods

This was a retrospective cohort study comparing 2 groups of pregnant persons: those who tested positive for or had a close contact with someone who tested positive for SARS-CoV-2 who received REGEN-COV therapy, and those who tested positive for SARS-CoV-2 but did not receive REGEN-COV therapy. Our cohort included all pregnant patients who tested positive for SARS-CoV-2 between March 2021 and October 2021, and pregnant persons who received REGEN-COV because they were considered a close contact to someone who tested positive. Patients were excluded if they did not meet criteria for REGEN-COV at our institution, which included patients who required oxygen or other therapeutics such as remdesivir or dexamethasone at time of diagnosis, or who had received the COVID-19 vaccination series. The patients from the REGEN-COV group presented between August and October of 2021, at which time there was widespread access to the monoclonal antibodies at our institution, whereas the time period of the control group was from March to October of 2021.

Study group demographics and health information such as maternal age, race or ethnicity, and medical comorbidities were abstracted by the study authors from the electronic medical record or through the Grady Obstetric and Gynecological Outcomes database. Relevant maternal and birth outcomes were also collected. Descriptive statistics were performed to evaluate the maternal demographic and clinical characteristics of patients who were diagnosed with SARS-CoV-2 infection during the study period. Planning data were not available to address sample size and power considerations for this small retrospective study. A 2-sample *t*-test for continuous variables was used to compare demographic and clinical characteristics, perinatal outcomes, and clinical course of SARS-CoV-2 infection between the REGEN-COV and the control group. Proportions were compared by study group using the chi-square test for categorical variables, except in cases where expected cell counts were <5, for which an exact chi-square test was used. A 2-sided P value of <.05 indicated statistical significance.

This research was approved by the institutional review boards of the Emory University School of Medicine and Grady Memorial Hospital (Study ID 00003470).

Results

From March to October 2021, 86 pregnant people tested positive for SARS-CoV-2 via real-time polymerase chain reaction (PCR) or had a confirmed exposure and met inclusion criteria. In this group, 36 patients received REGEN-COV and 50 did not (Table 1). Most patients underwent testing for SARS-CoV-2 when they presented with symptoms (81% in the REGEN-COV group and 60% in the control group), although a small percentage tested positive after asymptomatic screening on labor and delivery (19% in the REGEN-COV group and 36% in the control group), and 2 individuals in the control group were tested because of a known exposure. Among the 36 individuals who received REGEN-COV in our

TABLE 1
Maternal demographic and clinical characteristics

Variables	REGEN-COV n=36	Control n=50	*P* value[a]
Maternal age at eligibility, mean (y), SD	29.2 (8.2)	27.2 (5.7)	.19
Race/ethnicity			.89
Non-Hispanic Black	30 (86)	40 (80)	
Non-Hispanic White	1 (3)	2 (4)	
Hispanic	4 (11)	8 (16)	
Other/missing	1 (3)	0	
Insurance			.31
Medicaid	32 (89)	45 (90)	
Commercial	3 (8)	1 (2)	
Self-pay	1 (3)	4 (8)	
Primary language			.12
English	30 (83)	45 (90)	
Spanish	3 (8)	5 (10)	
Other	3 (8)	0	
Parity			.77
Nulliparous	7 (19)	8 (22)	
Multiparous	29 (81)	28 (78)	
Medical comorbidities			
Obesity (BMI >30)	12 (33)	15 (30)	.74
Asthma	7 (19)	9 (18)	.87
Anemia	2 (6)	4 (8)	.70
Chronic hypertension	8 (22)	6 (12)	.21
Pregestational diabetes mellitus	2 (6)	2 (4)	1.00
Mental health	4 (11)	4 (8)	.72
Gestational age at REGEN-COV eligibility			.002
<14 wk	10 (28)	1 (2)	
14–28 wk	11 (31)	18 (36)	
>28 wk	15 (42)	31 (62)	
Indication for SARS-CoV-2 testing			.09
Asymptomatic testing	7 (19)	18 (36)	
Person under investigation	29 (81)	30 (60)	
COVID-19 exposure	0	2 (4)	

Data are number (percentage), unless otherwise specified.

BMI, body mass index; *SD*, standard deviation.

[a] Two-sample *t*-test, chi-square, or exact chi-square tests were used, as appropriate.

Levey. Outcomes of pregnant patients treated with REGEN-COV. Am J Obstet Gynecol MFM 2022.

cohort, most (94%) had positive SARS-CoV-2 PCR result, although 2 individuals (6%) received REGEN-COV as post-exposure prophylaxis without a positive test result (Table 2). All controls had a positive SARS-CoV-2 PCR result. Of the 50 participants who did not receive REGEN-COV, 8 (16%) were offered but declined and 35 (70%) were not offered. Of the 35 who were not offered, 17 (49%) tested positive before the widespread use of REGEN-COV at our institution. Of the patients who were offered, 5 patients initially accepted administration of REGEN-COV, then subsequently either did not show for their scheduled administration or were unable to be reached for mobile administration. Both the REGEN-COV and control cohorts consisted of patients who were majority non-Hispanic Black (86% and 80%, respectively; *P*=.89), had Medicaid insurance coverage (89% and 88%; *P*=.33), and were English-speaking (83% and 90%; *P*=.12). Both groups were more likely to be multiparous (81% and 78%; *P*=.77) (Table 1). Among all patients, the most common medical comorbidity was obesity, defined as body mass index >30 (33% and 30%; *P*=.74), and the second most common was chronic hypertension (22% and 12%; *P*=.21). In both groups, the most common gestational age at time of REGEN-COV eligibility was the third trimester (42% and 62%). Notably, 10 women were eligible and received REGEN-COV in the first trimester, whereas only 1 patient was eligible in the first trimester in the control group.

The mean number of days from positive test to REGEN-COV administration was 3 (Table 2). Individuals received REGEN-COV either in the hospital setting (75%), where it was typically administered intravenously, or in 1 of our mobile community units (25%), where it was administered subcutaneously. There were no instances of infusion rate adjustment or discontinuation, anaphylaxis, or death in our cohort. One patient experienced worsening shortness of breath and new oxygen requirement >24 hours after administration. This patient went on to require dexamethasone and ICU admission. This may be considered an infusion-related reaction per the FDA, but also may have represented progression of disease.[18] There were no other symptoms of an infusion-related reaction in our cohort.

Among individuals who delivered (n=71), the mean gestational age at delivery was 37 weeks (*P*=.46) (Table 3). There was not a statistically significant

TABLE 2
Safety profile and adverse events in the cohort of patients who received REGEN-COV during pregnancy

Variables	REGEN-COV, n=36
Indication for REGEN-COV	
PCR-positive	34 (94)
Postexposure prophylaxis	2 (6)
Days from positive COVID-19 test to REGEN-COV administration, mean (SD)	3 (3)
Route of administration	
Intravenous (hospital)	27 (75)
Subcutaneous (community)	9 (25)
Adverse event	
Hypersensitivity reaction	0
Infusion-related reaction[a]	1 (3)
Anaphylaxis	0
Death	0
Infusion rate adjustment or discontinuation	0
Timing of event after administration	
<24 h	0
>24 h	1 (3)
Required hospital admission for COVID-19	9 (25)
Admission <24 h after REGEN-COV administration	8 (89)
Admission >24 h after REGEN-COV administration	1 (11)

Data are number (percentage), unless otherwise specified.

PCR, polymerase chain reaction; *SD*, standard deviation.

[a] Defined as fever, difficulty breathing, reduced oxygen saturation, chills, nausea, arrhythmia, chest pain or discomfort, weakness, altered mental status, headache, bronchospasms, hypotension, hypertension, angioedema, throat irritation, rash including urticaria, pruritis, myalgia, or vasovagal reaction.

Levey. Outcomes of pregnant patients treated with REGEN-COV. Am J Obstet Gynecol MFM 2022.

difference in rates of preterm delivery, with 29% in the REGEN-COV group delivering before 37 weeks vs 30% in the control group (*P*=.96). There was a statistically significant difference in mode of delivery between the 2 groups (*P*=.01), which seems to have been driven by the rate of cesarean delivery, which was 25% among those who received REGEN-COV and 40% among controls. There was no statistically significant difference when the indication for cesarean delivery was explored (*P*=.70) (Table 3). In both groups, the most common indication was nonreassuring fetal status (50% and 43%). There were no statistically significant differences in markers of neonatal morbidity between the 2 groups, including 5-minute Apgar <7 (0% and 9%; *P*=.29), need for resuscitation at delivery (46% and 34%; *P*=.33), neonatal ICU (NICU) admission (39% and 19%; *P*=.09), and neonatal demise (4% and 4%; *P*=1.0).

When patients who received REGEN-COV were compared with those who did not, the prevalence of symptoms at time of diagnosis was largely the same, including subjective fever, shortness of breath, and myalgias (Table 4). A statistically significant difference between the 2 groups was present only for cough, with 56% of patients who received REGEN-COV describing cough as a symptom vs only 26% of controls (*P*=.005). Similarly, the clinical findings were comparable between the 2 groups aside from documented fever >100.4°F, which was more common in the REGEN-COV cohort (19% and 4%; *P*=.03) (Table 4). Although there was not a statistically significant difference in length of hospitalization between the 2 groups (*P*=.51), >50% of controls remained inpatient for ≥2 days, whereas >50% of REGEN-COV patients were discharged after <2 days (Table 4). Of the 9 patients in the REGEN-COV group who were admitted to the hospital for COVID-19–related symptoms, 89% were admitted within 24 hours of REGEN-COV administration, and it is uncertain if hospitalization would have occurred regardless of the monoclonal antibody administration. There were no statistically significant differences between the REGEN-COV and control group in ICU admission (11% and 33%; *P*=.53), additional pharmacologic treatment for COVID-19 (6% and 8%; *P*=.70), or oxygen support (6% and 6%; *P*=1.0).

Comment

Principal findings

In this cohort study of pregnant patients who were SARS-CoV-2–positive or exposed to SARS-CoV-2, there were no serious adverse events, instances of anaphylaxis, need for cessation of infusion, or deaths among those who received REGEN-COV. When compared with a similar cohort of SARS-CoV-2–positive patients who did not receive REGEN-COV, there were no significant differences between the 2 groups in the number of severe maternal morbidity (SMM) events, need for oxygen support, ICU admission, or length of hospital stay. There were also no statistically significant differences in obstetrical outcomes between the 2 groups aside from mode of delivery, with cesarean delivery being more common among controls. These findings indicate that REGEN-COV is a safe therapy for COVID-19 infection during all trimesters of pregnancy and support the recommendations from the NIH, ACOG, and SMFM.

Results in the context of what is known

REGEN-COV administration has shown promising results in early efficacy trials in the nonpregnant population.[12,21]

TABLE 3
Obstetrical outcomes

Variables	REGEN-COV n=24, 12 undelivered	Control n=47, 3 undelivered	*P* value[a]
Gestational age at delivery, mean (SD)	36.8 (4.3)	37.4 (2.8)	.46
Mode of delivery			.01
Vaginal	14 (58)	28 (60)	
Operative (vacuum or forceps)	4 (17)	0	
Cesarean delivery	6 (25)	19 (40)	
Indication for cesarean delivery	n=6	n=19	.70
Planned cesarean delivery	2 (33)	3 (21)	
Arrest of labor	1 (17)	5 (36)	
Nonreassuring fetal status	3 (50)	6 (43)	
Missing	1 (17)	5 (36)	
Infants born before 37 wk	7 (29)	14 (30)	.96
Indication for delivery before 37 wk	n=7	n=14	
Hypertensive disorder	2 (29)	2 (14)	
Fetal growth restriction	1 (14)	2 (14)	
Premature rupture of membranes	0	6 (43)	
Placental disorder	0	3 (21)	
Spontaneous	3 (43)	3 (21)	
SARS-CoV-2 infection	1 (14)	0	
Nonreassuring fetal status	0	4 (29)	
Infant birthweight, mean (SD), g	2691 g (844)	2845 g (714)	.42
Neonatal morbidity			
5-min Apgar <7	0	4 (9)	.29
Neonatal resuscitation	11 (46)	16 (34)	.33
Median length of NICU stay, d (range)	18 (2–40)[b]	22 (0–86)[c]	
Admitted to NICU	9 (38)	9 (19)	.09
Neonatal demise	1 (4)[d]	2 (4)[e]	1.00

Data are number (percentage), unless otherwise specified.

NICU, neonatal intensive care unit; *SD*, standard deviation.

[a] Two-sample *t*-test, chi-square, or exact chi-square tests were used, as appropriate; [b] Two were still admitted and were not included in the calculation; [c] One was transferred to another hospital on day of life 0 and not included in the calculation; [d] Neonatal demise at day of life 34 owing to suspected sepsis; [e] One neonatal demise on day of life 1 owing to pulmonary hyperplasia secondary to oligohydramnios after preterm premature rupture of membranes; 1 neonatal demise on day of life 1 owing to pulmonary hyperplasia secondary to congenital diaphragmatic hernia.

Levey. Outcomes of pregnant patients treated with REGEN-COV. Am J Obstet Gynecol MFM 2022.

Studies in the pregnant population have been limited to small case series,[7,19,20] and all 3 only report that REGEN-COV was not associated with any adverse events. Further, side effects after REGEN-COV administration are rare and thought to be secondary to COVID-19 rather than REGEN-COV.[22] Our results support these findings because we found no significant adverse events in patients after administration of REGEN-COV. One possible isolated infusion-related reaction was documented after a patient was found to have a new oxygen requirement and onset of shortness of breath 24 hours after REGEN-COV administration, although it is difficult to elucidate whether this was a true infusion-related reaction or represented a progression of COVID-19 illness that was independent of monoclonal antibody administration. Given that this symptom occurred >24 hours after REGEN-COV exposure and that shortness of breath is a hallmark of COVID-19, we suspect that this more likely represents progression of disease. A similar safety profile with a paucity of adverse outcomes was found in the existing literature on REGEN-COV in the nonpregnant population.[7,19,20]

Two of the case series on monoclonal antibody administration in pregnancy reported on disease severity, and stated that patients who received monoclonal antibodies did not experience disease progression, but this was not compared with a similar cohort that did not receive REGEN-COV.[20] Our study did include a comparison group, and we found that patients who received REGEN-COV did not seem to have different disease progression or a change in clinical course when compared with a roughly equivalent group of patients who did not receive REGEN-COV. However, our small cohort study was not powered to assess this clinical comparison. Nevertheless, our study compared perinatal outcomes between similar groups of patients, and found almost no difference, except in the rate of cesarean delivery.

Clinical implications

Although there was no observed difference in clinical outcomes or COVID-19 progression between the control and study group, clinically relevant information regarding obstetrical outcomes, tolerability, and general safety can be gleaned from this population. There was no significant difference in need for oxygen support, ICU admission, or length of hospital stay between the control group and the group receiving REGEN-COV, although our study may have been underpowered for these outcomes. In addition, our cohort was a high-risk population, as indicated by the comparatively high rates of SMM in both groups (6% and 2%, *P*=.3), and therefore differences in outcomes between the 2 groups may have been

TABLE 4
Clinical course of SARS-CoV-2 infection

Variables	REGEN-COV n=36	Control n=50	*P* value[a]
Symptoms present at diagnosis			
Subjective fever	4 (11)	4 (8)	.72
Cough	20 (56)	13 (26)	.005
Shortness of breath	8 (22)	8 (16)	.47
Myalgias	8 (22)	7 (14)	.32
Sore throat	4 (11)	3 (6)	.45
Congestion	5 (14)	6 (12)	1.00
Loss of taste or smell	1 (3)	6 (12)	.23
Nausea or vomiting	3 (8)	2 (4)	.65
Headache	3 (8)	1 (2)	.30
Chest pain	6 (17)	2 (4)	.06
Clinical findings present	11 (31)	8 (16)	.11
Temperature >100.4°F	7 (19)	2 (4)	.03
HR >110 BPM	7 (19)	6 (12)	.34
Hypotension <100/60 mm Hg	0	0	
Hypoxia O_2 <95%	6 (17)	6 (12)	.54
Leukocytosis or leukopenia	1 (3)	2 (4)	1.00
Fetal distress	1 (3)	0	.42
Abnormal chest imaging	7 (58.3)	6 (67)	1.00
Viral pneumonia	3 (25)	6 (67)	.09
Length of hospital admission for treatment of COVID-19 infection, n (%)	n=9	n=6	.51
<2 d	5 (56)	1 (17)	
2–4 d	3 (33)	3 (50)	
>4 d	1 (11)	2 (33)	
Required ICU admission	1 (11)	2 (33)	.53
Required pharmacologic treatment for SARS-CoV-2	2 (6)	4 (8)	.70
Remdesivir or other antiviral	2 (6)	3 (6)	—
Tocilizumab	0	1 (2)	—
Other	0	1 (2)	—
Required oxygen support			1.00
Nasal cannula or high-flow	2 (6)	3 (6)	—
BiPAP	0	0	—
Mechanical ventilation	0	0	—
Required delivery for COVID-19	1 (3)	0	.42
Severe maternal morbidity event	3 (6)[b]	1 (2)[c]	.30

Data are number (percentage), unless otherwise specified.

BiPAP, bilevel positive airway pressure; *BPM*, beats per minute; *HR*, heart rate; *ICU*, intensive care unit.

[a] Two-sample *t*-test, chi-square, or exact chi-square tests were used, as appropriate. This *P* value reflects all clinical findings; [b] The first patient was admitted to the ICU for shock secondary to postpartum hemorrhage, the second for urosepsis, and the third (who also received intubation) for cardiac arrest of unknown etiology; [c] One patient was admitted to the ICU for COVID-19 pneumonia.

Levey. Outcomes of pregnant patients treated with REGEN-COV. Am J Obstet Gynecol MFM 2022.

less obvious because of the high risk of morbidity at baseline. The threshold for hospital admission and ICU transfer may be lower in pregnant patients than in nonpregnant patients, and thus these markers may not have been as indicative of disease severity in this population. Furthermore, there was no routine protocol for ICU transfer at our institution, thus it varied between providers. Another factor that could have played a role was that all members of the REGEN-COV study group tested positive for SARS-CoV-2 during the peak of the Delta variant wave, whereas many patients (26%) from the control group tested positive before June 2021, before the peak of the Delta wave in the Southeast United States. Given that the Delta variant was associated with more severe disease, if we had been able to recruit a completely chronologically comparable cohort, we may have observed some significant differences in markers of disease progression.[23] Although this represents the largest cohort to be published to date, it is still small, and thus was not powered to reflect clinically significant differences in outcomes. For example, although administration of REGEN-COV did not seem to significantly alter the clinical course in our cohort, a statistically nonsignificant difference was found in the length of hospital stay and ICU admission. Among the small number of individuals who were admitted to the hospital for COVID-19 illness, most of the REGEN-COV patients were admitted for <2 days, whereas most of the controls were admitted for >2 days, which is a finding that may be amplified by a larger study cohort. Of the patients who received REGEN-COV and required hospital admission, 89% were admitted within 24 hours of receiving REGEN-COV. This highlights the fact that the overwhelming majority of patients in the REGEN-COV group who required hospitalization were hospitalized at the time of REGEN-COV administration, instead of presenting later for worsening disease. This may suggest that REGEN-COV had an influence on prevention of progression to severe disease.

Finally, we observed no statistically significant differences in obstetrical outcomes between the control group and the study group aside from mode of delivery, with cesarean delivery having been more common among controls. The reason for this is unclear, especially because there was no significant difference in the indication for cesarean delivery between the control and the study group. COVID-19 infection has been associated with an increase in cesarean delivery, but the retrospective nature of this study does not allow us to state the role that COVID-19 disease may have played in the higher rate of cesarean delivery in our control group.[24] Notably, there was a trend toward more frequent NICU admission of neonates born to mothers who received REGEN-COV. However, at our institution, the threshold for NICU admission is relatively low because there is not a special care nursery to serve as a step-down unit. Median length of NICU stay, therefore, was a much more accurate indicator of neonatal morbidity, and a difference was not observed between the 2 groups when this statistic was examined (18 and 22 days, respectively).

Research implications

This study adds to the growing body of evidence suggesting that the use of monoclonal antibodies is safe in the pregnant population and does not seem to be associated with adverse events. However, further research is needed to determine whether monoclonal antibodies add any additional clinical benefit in pregnant persons, and whether they are the best therapeutic option for persons presenting with mild to moderate disease. In addition, given that different variants of SARS-CoV-2 seem to affect pregnant persons differently, more research needs to be done at different time points to gauge overall efficacy.

Strengths and limitations

This was a large cohort study evaluating the safety and clinical outcomes of pregnant patients receiving REGEN-COV and included a patient population at high risk of progression to severe disease. Although our control group was not entirely contemporary to our study group, our study nevertheless provided important preliminary insight on the efficacy of REGEN-COV in this population. Despite this being a large study on the use of REGEN-COV in pregnancy to date, the sample size was underpowered to detect small but clinically important outcome differences, and the retrospective nature of our study precluded us from being able to always accurately determine whether a reaction was secondary to the drug or because of the progression of COVID-19 illness. Finally, as previously mentioned, the control group included patients predating the predominance of the SARS-CoV-2 Delta variant, and thus we may have compared outcomes of different strains of the virus. However, given that the Delta variant was associated with more severe disease, the lack of significant differences between the 2 groups may indicate REGEN-COV's efficacy against the more pathogenic variants, although research in a larger, prospective cohort will be needed to answer these questions.

Conclusions

Our findings indicate that REGEN-COV is a safe therapy for SARS-CoV-2 infection in pregnancy and support the recommendations from NIH, ACOG, and SMFM. Although our study did not document a clinical benefit from REGEN-COV use, it did not establish a negative impact of REGEN-COV on outcomes, which also lends some credence to its safety in pregnancy. In addition, although this was not its focus, our study included a diverse and historically medically underserved population, indicating that REGEN-COV is an acceptable therapeutic to many within this group. We therefore advocate for continued use of monoclonal antibody therapy for all pregnant persons. ■

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Received Mar. 30, 2022; revised May 13, 2022; accepted June 1, 2022.

The authors report no conflict of interest.

This research was funded by the Emory Medical Care Foundation and the Emory Woodruff Health Sciences Synergy Award.

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