Research Letter

Early Administration of Remdesivir and Intensive Care Unit Admission in Hospitalized Pregnant Individuals With Coronavirus Disease 2019 (COVID-19)

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Remdesivir has been shown to shorten the time to recovery in hospitalized patients with coronavirus disease 2019 (COVID-19). Data on its use in pregnancy are limited. In this single-center retrospective cohort study, our objective was to determine whether early remdesivir use in pregnant individuals is associated with decreased risk of admission to the intensive care unit (ICU). Forty-one pregnant patients were included in this study, and outcomes were compared between those who received remdesivir less than 7 days (early group) and 7 or more days (late group) from onset of patient-reported symptoms. Early remdesivir administration was associated with improved clinical outcomes, including lower rates of ICU admission, decreased length of hospitalization, and decreased progression to critical disease in pregnant individuals hospitalized with COVID-19.

(Obstet Gynecol 2022;00:1–3)
DOI: 10.1097/AOG.0000000000004734

INTRODUCTION

Remdesivir inhibits severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) replication. Data from clinical trials have demonstrated that remdesivir shortens the time to recovery in hospitalized adults with COVID-19.[1–3] Furthermore, earlier treatment initiation (less than 7 days from symptom onset) in high-risk individuals reduces the risk of hospitalization or death.[4] The U.S. Food and Drug Administration approved, under an emergency use authorization, the use of remdesivir for patients hospitalized with COVID-19.[5] Although data on use of remdesivir among pregnant individuals hospitalized with COVID-19 are limited, its use in pregnant patients has become standard at many hospitals.[6] The objective of our study was to investigate whether early administration of remdesivir in pregnant patients hospitalized with COVID-19 was associated with a decrease in intensive care unit (ICU) admission and disease severity.

METHODS

We performed a retrospective cohort study to examine outcomes for pregnant individuals hospitalized with COVID-19 who received remdesivir from April 2020 through October 2021. Infection with SARS-CoV-2 was confirmed by nucleic acid amplification tests. Patients qualified for remdesivir if they were admitted to the hospital with COVID-19, because pregnancy is considered a risk factor for progression to severe or critical disease based on the National Institutes of Health treatment guidelines.[7]

We compared outcomes of patients who received remdesivir less than 7 days (early group) or 7 or more days (late group) from onset of patient-reported symptoms. The primary outcome was ICU admission. Criteria for ICU admission included hypoxemic respiratory failure, septic shock, multiple organ dysfunction, and hemodynamic instability. Secondary outcomes included need for mechanical ventilation or extracorporeal membrane oxygenation, progression to critical disease, and

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Financial Disclosure
Nora Colburn reports receiving funding from Personal Health Insights. The other authors did not report any potential conflicts of interest.

ISSN: 0029-7844/22

length of hospital stay. Summary statistics were calculated for baseline variables, and bivariate analyses were performed as appropriate. All statistical analyses were performed using Stata 15. $P<.05$ was used for statistical significance. The study was approved by The Ohio State University's Institutional Review Board.

RESULTS

A total of 41 hospitalized pregnant individuals received remdesivir, 24 (58.5%) in the early group and 17 (41.5%) in the late group. None of the patients had received any dose of COVID-19 vaccination. Maternal characteristics including age, body mass index (BMI, calculated as weight in kilograms divided by height in meters squared), history of preterm birth, and medical comorbidities (including pregestational diabetes, pulmonary disease, and hypertension) were similar between the two groups (Table 1). Gestational age at diagnosis for the early group was higher than that for the late group (34 weeks [interquartile range 29–36] vs 28 weeks [interquartile range 22–32], $P=.02$).

The early group received remdesivir at a mean of 3 days from onset of symptoms (range 1–6 days), compared with a mean of 9 days (range 7–14 days) in the late group. The majority of patients in our cohort (n=34, 82%) received a 5-day course of remdesivir (range 3–10 days), with no difference in the mean number of doses between the two groups. Using National Institutes of Health criteria, disease severity at the time of first remdesivir dose was similar between the two groups. Patients in the early group were less likely to be admitted to the ICU (21% vs 59%, odds ratio 0.18, 95% CI 0.04–0.72) or to progress to critical disease (12% vs 41%, odds ratio 0.20, 95% CI 0.51–0.87) (Table 2). Additionally, those in the early group had shorter hospital stays (5 days [interquartile range 4–5.75] vs 11 days [interquartile range 4.5–15.5], $P<.01$). There were two maternal deaths in the late group, compared with none in the early group. Pregnancy outcomes were comparable between the two groups (Table 2).

DISCUSSION

Because remdesivir inhibits SARS-CoV-2 viral replication,[8] it is plausible that its use in the early stages of the infection might lead to improved outcomes. In nonpregnant patients, early outpatient use of a 3-day remdesivir course was associated with decreased COVID-19–related hospitalization and death, with an acceptable safety profile.[4] Our study demonstrated that early administration of remdesivir was associated with improved clinical outcomes, including lower rates of ICU admission and decreased length of hospitalization

Table 1. Maternal and Coronavirus Disease 2019 (COVID-19) Characteristics*

Characteristic	Early Group (Less Than 7 d) (n=24)	Late Group (7 or More d) (n=17)	*P*
Gestational age at diagnosis (wk)	34 [29–36]	28 [22–32]	.02
Nulliparity	3 (13)	4 (24)	.42
Age (y)	29.4±4.7	32.1±5.4	.10
Medical comorbidities†	8 (33)	5 (29)	.99
BMI 30 or higher at COVID-19 diagnosis	20 (83)	12 (71)	.45
History of preterm birth (less than 37 wk)	5 (21)	2 (12)	.68
Disease severity at time of remdesivir receipt‡			
Mild or moderate	15 (62)	8 (47)	.36
Severe	9 (38)	9 (53)	
Laboratory abnormalities§	14 (58)	14 (82)	.17
Abnormal chest imaging‖	23 (96)	15 (88)	.56
Corticosteroid course for COVID-19	18 (75)	15 (88)	.43
Receipt of monoclonal antibodies before hospital admission	2 (8)	1(6)	.99

BMI, body mass index; COVID-19, coronavirus disease 2019.
Data are median [interquartile range], n (%), or mean±SD unless otherwise specified.
* Data were analyzed using Mann Whitney U test, χ^2 test, Fisher exact test, or Student *t* test, as appropriate.
† Medical comorbidities include respiratory disease (asthma, chronic obstructive pulmonary disease, or any other known underlying respiratory condition), chronic hypertension, and pregestational diabetes.
‡ Defined using National Institutes of Health criteria—mild illness: symptomatic without shortness of breath, dyspnea, or abnormal chest imaging; moderate illness: evidence of lower respiratory disease during clinical assessment or imaging and SpO2 94% or higher; severe illness: SpO2 lower than 94% on room air at sea level, PaO2/FiO2 ratio less than 300 mm Hg, respiratory rate higher than 30 breaths per minute, or lung infiltrates greater than 50%.
§ Laboratory abnormalities defined as platelet count less than 150×10^3/microliter, prothrombin time greater than 14 seconds, partial prothrombin time greater than 35 seconds, creatinine level greater than 1 mg/dL, aspartate aminotransferase level greater than 40 units/L, or alanine aminotransferase level greater than 35 units/L.
‖ Chest imaging abnormalities defined by changes consistent with COVID-19 on chest X-ray or computed tomography.

Table 2. Coronavirus Disease 2019 (COVID-19) and Pregnancy Outcomes*

Outcome	Early Group (Less Than 7 d)	Late Group (7 or More d)	OR (95% CI)†	P
COVID-19 outcomes				
n	24	17		
ICU admission	5 (21)	10 (59)	0.18 (0.04–0.72)‡	
Progression to critical disease§	3 (12)	7 (41)	0.20 (0.51–0.87)‡	
Oxygen supplementation				
HFNC	3 (13)	4 (24)	0.46 (0.11–2.00)	
Mechanical ventilation or ECMO‖	3 (12)	7 (41)	0.20 (0.51–0.87)‡	
Pregnancy outcomes				
n	21¶	12#		
Gestational diabetes	3 (14)	0 (0)		.28
Hypertensive disorders of pregnancy**	6 (29)	0 (0)		.07
Cesarean delivery	11 (52)	5 (42)		.72
Postpartum hemorrhage	2 (9)	1 (10)		.99
Preterm delivery for obstetric indications††	8 (38)	3 (25)		.70
Preterm delivery for worsening COVID-19	1 (5)	4 (33)		.05
Maternal death from COVID-19	0 (0)	2 (12)		.19

OR, odds ratio; ICU, intensive care unit, HFNC, high-flow nasal cannula, ECMO, extracorporeal membrane oxygenation; COVID-19, coronavirus disease 2019.
Data are n (%) unless otherwise specified.
* Data were analyzed by χ^2 test or Fisher exact test as appropriate.
† The association between early receipt of remdesivir and study outcomes was expressed as odds ratio with 95% CI.
‡ Significant at $P<.05$.
§ Defined using National Institutes of Health criteria—critical illness: respiratory failure, septic shock, multiple organ dysfunction.
‖ None of these patients were mechanically ventilated or on ECMO before initiation of remdesivir.
¶ Three patients with data missing were still pregnant at the time of manuscript submission.
# Five patients with data missing were still pregnant at the time of manuscript submission.
** Hypertensive disorders of pregnancy include gestational hypertension; preeclampsia; hemolysis elevated liver enzymes, and low platelet count (HELLP) syndrome, and eclampsia.
†† Obstetric indications include spontaneous preterm labor, preterm prelabor rupture of membranes, and preeclampsia with severe features.

among pregnant individuals hospitalized with COVID-19. Limitations to our study include nonrandom treatment allocation, which could have led to unmeasured differences between the two groups that may have influenced outcomes. In particular, those in the late group may have had more severe disease, which could have biased our findings. Additionally, our small sample size limited the ability to draw conclusions about low-frequency outcomes. In conclusion, early administration of remdesivir should be considered in hospitalized pregnant individuals owing to risk of severe or critical disease progression.

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PEER REVIEW HISTORY

Received January 13, 2022. Received in revised form January 26, 2022. Accepted February 3, 2022. Peer reviews are available at http://links.lww.com/AOG/C605.