Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Increasing oxygen requirements and disease severity in pregnant individuals with the SARS-CoV-2 Delta variant

OBJECTIVE: According to the Centers for Disease Control and Prevention (CDC), the Delta (B.1.617.2) variant of SARS-CoV-2 became the most common variant in certain regions of the United States in July 2021. More than 80% of cases detected in Ohio starting the first week of July, were attributed to the Delta variant.[1]

Although the Delta variant was found to be associated with an increase in disease severity and oxygen requirement in the nonpregnant population,[2] there are limited data on its impact on pregnant individuals.[3,4] This study aimed to determine whether the Delta variant was associated with increased oxygen requirement and disease severity in the pregnant population.

STUDY DESIGN: This was a single academic center retrospective cohort study conducted at The Ohio State University Wexner Medical Center. All pregnant individuals who had a positive molecular test for COVID-19 by reverse transcription polymerase chain reaction (RT-PCR) from March 2020 through October 2021 were included. The cohort was divided into 2 groups on the basis of the Delta variant becoming the dominant variant in Ohio starting July 2021. The Delta variant group included positive patients from July 2021 to October 2021, and the pre-Delta (including B.1.1.7, B.1.351, P.1) variants group included positive patients from March 2020 to June 2021. Individuals were not routinely sequenced for the different variants at our institution.

TABLE 1
Maternal characteristics and pregnancy outcomes

Maternal characteristics (n)	Delta variant group (n=99)	Pre-Delta variant group (n=325)	*P* value
GA at diagnosis[a] (wk+d)	29+3 (23+3 to 35+6)	31+5 (17+6 to 37+3)	.64
Nulliparity[b]	25 (25.3)	75 (23.1)	.69
Age[c] (y)	29.0 (5.5)	29.5 (5.4)	.48
Medical history[b]			
Respiratory disease[d]	7 (7.1)	37 (11.4)	.22
Chronic hypertension	14 (14.1)	33 (10.2)	.27
Pregestational diabetes	5 (5.05)	23 (7.1)	.64
BMI at COVID-19 diagnosis[a] (kg/m^2)	33.0 (26–39)	31.0 (26–37)	.11
Partial COVID-19 vaccine series[b]	21 (21.1)	27 (8.3)	<.01[e]
Completed COVID-19 vaccine series[b]	17 (17.2)	21 (6.5)	<.01[e]
Pregnancy outcomes (n)	Delta variant group (n=97)[f]	Pre-Delta variant group (n=325)	*P* value
Gestational diabetes[b]	2 (2.1)	30 (9.2)	.02[e]
Hypertensive diseases of pregnancy[b,g]	11 (11.3)	41 (12.6)	.74
Cesarean delivery[b]	6 (6.2)	111 (34.2)	<.01[e]
Postpartum hemorrhage[b]	2 (2.1)	16 (4.9)	.39
Preterm delivery <37 wk[b]	21 (21.7)	59 (18.2)	.44
Intrauterine fetal demise[b]	1 (1.0)	6 (1.9)	.99

BMI, body mass index; *GA*, gestational age.

[a] Data are presented as median (interquartile range); [b] Data are presented as n (%); [c] Data presented as mean (±standard deviation); [d] Respiratory diseases include asthma, chronic obstructive pulmonary disease, or any other known underlying respiratory condition; [e] Significant at $P<.05$; [f] Two with data missing as still pregnant; [g] Hypertensive diseases of pregnancy include gestational hypertension; preeclampsia; hemolysis, elevated liver enzymes, and low platelet count syndrome; or eclampsia.

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TABLE 2
COVID-19 characteristics, severity, treatments, and outcomes

COVID-19 characteristics and treatments	Delta variant group (n=99)	Pre-Delta variant group (n=325)	aOR (95% CI)
Primary outcome[a]	18 (18.2)	22 (6.8)	2.76 (1.38–5.50)[b]
Highest level of oxygen supplementation required	6 (6.1)	15 (4.6)	1.19 (0.41–3.04)
Nasal cannula	7 (7.1)	1 (0.3)	22.18 (3.84–418.9)[b]
HFNC	5 (5.1)	6 (1.9)	2.56 (0.71–8.87)
Mechanical ventilation/ECMO			
Moderate/severe/critical disease severity[c]	23 (23.2)	34 (10.5)	2.30 (1.24–4.21)[b]
Admission to hospital for COVID-19	18 (18.2)	51 (15.7)	1.27 (0.61–2.03)
Admission to ICU for COVID-19	9 (9.1)	7 (approximately 2.2)	4.25 (1.51–12.39)[b]
Symptomatic	80 (80.8)	195 (60.0)	2.84 (1.66–5.02)[b]
Laboratory abnormalities[d]	26 (26.3)	41 (12.6)	2.31 (1.24–4.25)[b]
Abnormal findings on chest imaging	23 (23.2)	28 (8.62)	2.93 (2.56–5.40)[b]
Receipt of corticosteroids	18 (18.2)	20 (6.2)	3.05 (1.50–6.05)[b]
Receipt of remdesivir	20 (20.2)	21 (6.5)	3.29(1.67–6.47)[b]
Maternal death from COVID-19	2 (2.0)	0 (0)	—
Subgroup analysis of maternal oxygen supplementation and disease severity with Delta variant for vaccinated vs unvaccinated			
Variable (n)	Vaccinated (n=17)	Unvaccinated (n=82)	*P* value
Primary outcome[a]	0 (0)	18 (22.0)	.04[b]
Moderate/severe/critical disease severity[c]	0 (0)	22 (26.8)	.01[b]
Symptomatic	15 (88.2)	65 (79.3)	.51
Laboratory/chest imaging abnormalities[d]	1 (5.9)	25 (30.5)	.04[b]
Admission to hospital for COVID-19	0 (0)	18 (22.0)	.04[b]
Admission to ICU for COVID-19	0 (0)	9 (11.0)	.35
Maternal death from COVID-19	0 (0)	2 (2.0)	.99

Data are presented as number (percentage). aOR presented for obesity (body mass index>30 kg/m^2) and co-occurring medical conditions (respiratory disease, chronic hypertension, and pregestational diabetes).

aOR, adjusted odds ratio; *CI*, confidence interval; *ECMO*, extracorporeal membrane oxygenation; *HFNC*, high-flow nasal cannula; *ICU*, intensive care unit.

[a] Primary outcome=composite of any form of supplemental oxygen used; [b] Significant at $P<.05$; [c] Defined using the National Institutes of Health criteria: asymptomatic, no symptoms consistent with COVID-19; Mild illness, symptomatic without shortness of breath/dyspnea/abnormal chest imaging; moderate illness, evidence of lower respiratory disease during clinical assessment or imaging and those who have an oxygen saturation (SpO_2) ≥94%; severe illness, SpO2 <94% on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO_2/FiO_2) <300 mm Hg, a respiratory rate >30 breaths/min, or lung infiltrates >50%; critical illness, respiratory failure, septic shock, and/or multiple organ dysfunction; [d] Laboratory abnormalities: defined as platelet count <150 × 10^3 per uL, or prothrombin time >14 seconds, or partial prothrombin time >35 seconds, or creatinine >1 mg/dL, or aspartate aminotransferase greater than 40 units/L or alanine aminotransferase >35 units/L. Chest imaging abnormalities defined by changes consistent with COVID-19 on chest X-ray or computed tomography.

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Our primary outcome was need for oxygen supplementation, defined as any oxygen supplementation using a nasal cannula, a high-flow nasal cannula, mechanical ventilation, or extracorporeal membrane oxygenation (ECMO). Patients with oxygen saturation ≤94% on room air or those with severe or critical disease were started on oxygen supplementation (criteria applied across all time points during study period). The secondary outcomes included disease severity on the basis of the National Institutes of Health criteria (assigned at time of diagnosis or hospital admission),[5] hospitalization for COVID-19, COVID-19 symptoms, laboratory and imaging abnormalities, intensive care unit (ICU) admission, inpatient therapeutics use including remdesivir and corticosteroids, and maternal death. A subgroup analysis, comparing the outcomes for vaccinated and unvaccinated individuals, was performed in the Delta variant cohort. The clinical care of patients was similar regardless of their vaccination status.

The summary statistics were calculated for the baseline variables. Bivariate analyses were performed as appropriate. The association between infection with the Delta variant and the primary and secondary outcomes was determined using multivariable analysis, correcting for the clinically relevant

covariates such as body mass index (BMI) and major medical comorbidity (respiratory disease, hypertension, and pregestational diabetes). It was then expressed as adjusted odds ratio (aOR) with 95% confidence interval (CI). All the statistical analyses were performed using Stata version 15 (StataCorp, College Station, TX). A *P* value less than.05 was used for statistical significance. Because this was an exploratory study with convenience sampling, no power calculations or correction for multiple comparisons were performed. This study was approved by the University's institutional review board.

RESULTS: A total of 424 pregnant individuals tested positive for SARS-CoV-2 infection during the study period and were included. Maternal characteristics including age, BMI, gestational age at COVID-19 diagnosis, and medical comorbidities were comparable between the pre-Delta and the Delta groups (Table 1). Patients in the pre-Delta group had higher rates of gestational diabetes and were more likely to be delivered by cesarean delivery; no difference was noted in the rates of hypertensive diseases of pregnancy or preterm delivery between the 2 groups (Table 1).

Patients in the Delta variant group were more likely to require any form of oxygen supplementation (18.2% vs 6.8%; aOR, 2.76; 95% CI, 1.38−5.50) and have more severe disease (moderate, severe, or critical; 23.2% vs 10.5%; aOR, 2.30; 95% CI, 1.24−4.21) than those in the pre-Delta variant group (Table 2). In addition, they were more likely to have laboratory or imaging abnormalities and require admission to the ICU (Table 2). There were 2 maternal deaths in the Delta variant group compared with none in the pre-Delta variant group. Both the patients were unvaccinated.

The rate of COVID-19 vaccination was higher in the Delta variant group, with 17.2% of patients having completed the vaccination series compared with 6.2% in the pre-Delta variant group (Table 1). A subgroup analysis among COVID-19 patients in the Delta variant cohort showed that none of the vaccinated patients required oxygen supplementation, compared with 22% (*P*=.04) of the unvaccinated patients who also showed more severe forms of the disease (moderate, severe, or critical; 26% vs 0%; *P*=.01). In addition, the rates of laboratory or imaging abnormalities (30.5% vs 5.9%; *P*=.04) and admission to the hospital (22% vs 0%; *P*=.04) were all significantly higher in unvaccinated pregnant individuals with the Delta variant than in those who were unvaccinated (Table 2).

CONCLUSION: A significant increase in oxygen requirement and disease severity was seen in pregnant individuals affected by the SARS-CoV-2 Delta (B.1.617.2) variant. Vaccinated patients were less likely to develop severe disease or require oxygen supplementation with the Delta variant than the nonvaccinated population. The difference in the vaccination rate between the 2 groups may be explained by the increased availability and uptake of the vaccine during the Delta predominance. The results of our study support the importance of COVID-19 vaccination in the pregnant population, as it appears to be protective against severe forms of the disease. ■

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