Research Letter

Association of the Delta (B.1.617.2) Variant of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) With Pregnancy Outcomes

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INTRODUCTION

Cases of coronavirus disease 2019 (COVID-19) due to the Delta (B.1.617.2) variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) were initially documented in India in late 2020.[1] The Delta variant has since become much more widespread, having been identified in more than 140 countries as of August 2021.[2] Data suggest that the Delta variant may be associated with more severe disease in the general population, with an increase in transmissibility and vaccine-breakthrough infections.[3–5]

Universal screening for SARS-CoV-2 has been used in labor and delivery at our institution since early in the pandemic to identify both symptomatic and asymptomatic infections. With the summer 2021 surge in COVID-19 cases (fourth wave), more than 95% of infections detected in our hospital have been identified as the Delta variant.

The objective of this analysis was to evaluate disease severity and maternal and neonatal outcomes during the fourth wave, largely representing the Delta variant. We also compared this cohort with a 2020 cohort of patients with COVID-19.

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

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METHODS

We conducted a retrospective cohort study at a single academic center. The study was approved by University of Texas Medical Branch at Galveston Institutional Review Board. All pregnant individuals presenting to our obstetric triage and labor and delivery unit undergo nasopharyngeal swab to detect SARS-CoV-2 infection, with either the Abbot ID NOW COVID 19 or Xpert Express SARS-CoV-2 polymerase chain reaction test, per manufacturer protocols. To minimize selection bias, we excluded patients with positive test results who were transferred to our unit from outside referring hospitals. Test results are positive, negative, or invalid. Invalid results are generally followed by repeat testing. For this analysis, individuals testing positive were categorized as asymptomatic, symptomatic not requiring oxygen support, or symptomatic requiring oxygen.

The present cohort was comprised of pregnant individuals testing positive for SARS-CoV-2 infection between July and August 2021, during which more than 95% of SARS-CoV-2 cases at our institution were attributed to the Delta variant of the virus. Relevant patient characteristics and maternal and neonatal outcomes were collected. Maternal and perinatal outcomes were then compared with those of a historic cohort before the dissemination of the Delta variant, from March to July 2020. The same criteria were used in both periods to classify the asymptomatic, symptomatic, and symptomatic requiring oxygen support groups. Initiation of oxygen support in both cohorts was followed by using the published protocol.[6] Perinatal outcome was a composite of neonatal intensive care unit admission, hypoxic ischemic encephalopathy, sepsis, respiratory support, seizures, birth trauma, meconium aspiration syndrome, hypotension requiring pressors, subgaleal

Table 1. Characteristics of Patients Who Tested Positive for the 2021 Delta Variant of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), Stratified by Severity

Maternal Characteristic	Asymptomatic (n=23)	Symptomatic Not Requiring Oxygen Support (n=30)	Symptomatic Requiring Oxygen Support (n=8)	P[a]
Age (y)	27 (16–43)	26 (15–38)	35 (29–37)	.41
Gestational age at symptom onset or diagnosis (wk)	37 (17–40)	33 (14–40)	36 (27–38)	.01
Gestational age at delivery (wk)[b]	39 (27–40)	39 (30–40)	37 (36–38)	.16
Gravidity	3 (1–11)	3 (1–7)	3 (2–5)	.64
Parity	2 (0–6)	1 (0–4)	1 (0–3)	.40
Time from symptom onset to clinical evaluation (d)	NA	2 (0–14)	2 (0–3)	.53
BMI (kg/m^2)	32 (20–61)	31 (19–47)	33 (31–75)	.59
Health care workers	1 (4)	1 (3)	0 (0)	1
Medical comorbidities				.15
None	16 (70)	17 (57)	3 (38)	
Asthma	2 (9)	1 (3)	1 (12)	
Preeclampsia	2 (9)	1 (3)	0 (0)	
Chronic hypertension	0 (0)	0 (0)	0 (0)	
Gestational diabetes	0 (0)	3 (10)	1(12)	
Pregestational diabetes	1 (4)	2 (7)	0 (0)	
1 or more	0 (0)	5 (17)	1 (12)	
Other	2 (9)	1 (3.3)	2 (25)	
COVID-19 vaccine	2 (9)	2 (7)	0 (0)	1
Prior positive SARS-CoV-2 test result	4 (17)	5 (17)	4 (50)	.13
Fever	NA	14 (47)	3(38)	<.001
Myalgia	NA	11 (37)	4 (50)	.002
Malaise	NA	10 (33)	4 (50)	.001
Chills or rigor	NA	8 (27)	0 (0)	.007
Cough	NA	20 (67)	7(88)	<.001
Headache	NA	15 (50)	1 (12)	<.001
Shortness of breath	NA	8 (27)	8 (100)	<.001
Runny nose	NA	5 (17)	1 (12)	.1
Sore throat	NA	5 (17)	0 (0)	.08
Diarrhea	NA	3 (10)	1 (12)	.2
Chest pain	NA	0 (0)	0 (0)	N/A
Anemia[c]	8 (35)	6 (20)	3 (38)	1
Leukocytosis[d]	2 (9)	0 (0)	1 (13)	.41
Lymphopenia[e]	4 (17)	6 (20)	7 (88)	.001
Thrombocytopenia[f]	3 (13)	2 (7)	2 (25)	.75
Elevated BUN[g]	0 (0)	0 (0)	0 (0)	NA
Elevated creatinine[h]	0 (0)	0 (0)	0 (0)	NA
Acute kidney injury	0 (0)	0 (0)	0 (0)	NA
Elevated AST[i]	0 (0)	3 (10)	4 (50)	.1
Elevated ALT[i]	0 (0)	2 (7)	4 (50)	.27
Abnormal chest X-ray or CT	0 (0)	0 (0)	7 (88)	NA
ICU admission	0 (0)	0 (0)	3 (38)	.002
Invasive mechanical ventilation	0 (0)	0 (0)	1 (12)	.1
Nasal cannula	0 (0)	0 (0)	8 (100)	<.001
Face mask	0 (0)	0 (0)	2 (25)	.01
High-flow nasal cannula	0 (0)	0 (0)	5 (62)	<.001
Delivery at less than 37 wk[k]	4/18 (22)	4/12 (33)	1/3 (33)	.56
Stillbirth[k]	0 (0)	1/12 (8)	0 (0)	.4
Vaginal delivery[k]	10/18 (55)	7/12 (58)	1/3 (33)	.77
Indication for cesarean[l]				.345
Obstetric	8/8 (100)	4/4 (100)	2/2 (100)	1
COVID-19	0 (0)	0 (0)	0 (0)	

(*continued*)

Table 1. Characteristics of Patients Who Tested Positive for the 2021 Delta Variant of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), Stratified by Severity (*continued*)

Maternal Characteristic	Asymptomatic (n=23)	Symptomatic Not Requiring Oxygen Support (n=30)	Symptomatic Requiring Oxygen Support (n=8)	P[a]
Postpartum hemorrhage	0 (0)	0 (0)	1/3 (33.33)	.1
Hospital duration (d)	1 (0–7)	1 (0–12)	7 (6–12)	.1
Neonatal composite[k,m]	9/18 (50)	3/11 (33)	1/3 (33)	.89

NA, not applicable; BMI, body mass index; COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; BUN, blood urea nitrogen; AST, aspartate aminotransferase; ALT, alanine aminotransferase; CT, computed tomography; ICU, intensive care unit.
Data are median (range), n (%), or n/N (%) unless otherwise specified.
[a] Kruskal Wallis test, Pearson χ^2 test, or Fisher exact test.
[b] Eighteen asymptomatic patients, 12 patients in the symptomatic not requiring oxygen support group, and three patients in the symptomatic requiring oxygen support group had delivered by the time this article was written. The rest of the pregnancies in our cohort are ongoing.
[c] Defined as less than 11 g/dL in the first and third trimesters and less than 10.5 g/dL in the second trimester.
[d] Defined as white blood count greater than 11.1 10*3/uL.
[e] Defined as lymphocyte count less than 1.32 10*3/uL.
[f] Defined as platelet count less than 150 10*3/uL.
[g] Defined as BUN greater than 23 mg/dL.
[h] Defined as creatinine greater than 1.04 mg/dL.
[i] Defined as AST greater than 40 units/L.
[j] defined as ALT greater than 35 units/L.
[k] Denominator reflects total deliveries in each group.
[l] Denominator reflects total cesarean deliveries in each group.
[m] Defined as occurrence of any of the following: perinatal death, respiratory support, hypoxic ischemic encephalopathy, seizure, meconium aspiration syndrome, birth trauma, neonatal intensive care unit admission, intracranial or subgaleal hemorrhage, or hypotension requiring pressors.

or intracranial hemorrhage, and perinatal death. Data were analyzed using STATA 16. Shapiro-Wilk test was used for normality, χ^2 or Fisher exact for categorical variables, and Mann–Whitney–Wilcoxon or Kruskal Wallis test for continuous data, as appropriate. Statistical significance was determined by $P<.05$.

Table 2. Comparison of the 2020 and 2021 Coronavirus Disease 2019 (COVID-19) Cohorts

	COVID-19 Case Cohort		
	2020 (n=91) (5 mo)	2021 (n=61) (1.5 mo)	P*
Gestational age at time of diagnosis or symptom onset (wk)	36 (14–40)	33 (3–40)	.018
BMI 35 kg/m^2 or higher	32 (35)	25 (43)	.3
Medical comorbidities			.3
None	58 (63)	36 (59)	
Asthma	2 (2)	4 (6)	
Preeclampsia	9 (10)	3 (5)	
Chronic hypertension	4 (4)	0 (0)	
Gestational diabetes	2 (2)	4 (6)	
Pregestational diabetes	3 (3)	3 (5)	
1 or more	6 (7)	6 (10)	
Other	7 (8)	5 (8)	
Symptomatic	35 (38)	38(62)	.004
Oxygen requirement	4 (4)	8 (13)	.07
Invasive mechanical ventilation	0 (0)	1 (2)	.4
ECMO	0 (0)	1 (2)	.4
ICU admission	0 (0)	1 (2)	.4
COVID-19 vaccine	0 (0)	4 (6)	.4
Delivery at less than 37 wk	9/60 (15)	9/33 (27)	.1
Birth weight (g)	3,185 (570–4,410)	3,035 (2,010–4,080)	.2
Composite neonatal outcome	29/60 (48)	13/30 (43)	.6

COVID-19, coronavirus disease 2019; BMI, body mass index; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit.
Data are median (range), n (%), or n/N (%) unless otherwise specified.
* Mann–Whitney–Wilcoxon test, Pearson χ^2 test, or Fisher exact test.

RESULTS

A total of 61 of 1,737 pregnant individuals tested positive for SARS-CoV-2 infection from July to August 2021 (Table 1). Overall, 21% had a prior positive SARS-CoV-2 (polymerase chain reaction or antibody) test result before presentation to labor and delivery, and only four (6%) were vaccinated (Table 1).

The gestational age at time of diagnosis was significantly lower in symptomatic patients (Table 1). The most common laboratory abnormality was lymphopenia, with lower values in those requiring oxygen support. Patients requiring oxygen support were more likely to receive antibiotics, antiretrovirals, and corticosteroids.

Thirty-three patients had delivered by the time this article was written. In asymptomatic and symptomatic patients not requiring oxygen, all deliveries occurred for obstetric reasons; one of three deliveries in symptomatic patients requiring oxygen support was for worsening maternal COVID-19. Rates of preterm deliveries and composite neonatal outcomes did not differ among the groups (Table 1). One stillbirth occurred in a symptomatic patient not requiring oxygen support, and one case of postpartum hemorrhage and sepsis occurred in a patient requiring oxygen support. No neonates tested positive for SARS-CoV-2 infection during their delivery admissions.

DISCUSSION

The Delta variant was first identified in March 2021 in the United States[6] and has now become the main variant responsible for new infections in the Southeastern states with low vaccination rates. Compared with the Alpha variant of SARS-CoV-2, the Delta variant is 60% more transmissible and has resulted in substantially higher numbers of cases, hospitalizations, and deaths.[7]

Our group has previously reported our experience between March 2020 and July 2020, before the emergence of the Delta variant.[8] In comparison with the 2020 cohort, pregnant individuals who tested positive for SARS-CoV-2 infection in the fourth wave had a lower median gestational age at time of diagnosis or symptom onset and were more likely to be symptomatic (Table 2). In the latest wave, one patient required invasive mechanical ventilation, eight patients required oxygen support (13.1%), one patient was placed on extracorporeal membrane oxygenation, one patient had a term stillbirth, and three patients were admitted to the intensive care unit. In the pre-Delta cohort, 4.4% of patients required oxygen support and none of the other events were identified. In the current cohort, only 6% of patients were vaccinated and none of the patients requiring oxygen support were vaccinated. An important limitation of the current report is that, for many comparisons, we lacked adequate statistical power to discern meaningful differences among different risk factors or outcomes between the two study time periods.

Our study emphasizes the seriousness of the Delta variant in the obstetric population. U.S. Food and Drug Administration–approved COVID-19 vaccines have been shown to be highly effective against the Delta variant[5] and at preventing severe disease, hospitalizations, and death.[9] Hence, vaccination is the cornerstone for control of the pandemic. In the obstetric population, vaccination hesitancy is high. This Research Letter highlights the need to increase vaccination of pregnant and reproductive-aged individuals.

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