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Pregnancy and infant outcomes following SARS-CoV-2 infection in pregnancy during delta variant predominance – Surveillance for Emerging Threats to Pregnant People and Infants

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Abstract

BACKGROUND: SARS-CoV-2 infection in pregnancy is associated with an increased risk of adverse birth outcomes such as preterm birth, stillbirth, and maternal and infant complications. Previous research suggests an increased risk of severe COVID-19 illness and stillbirth in pregnant people during delta variant predominance in 2021; however, those studies did not assess timing of infection during pregnancy, and few of them described COVID-19 vaccination status.

OBJECTIVE: Using a large population-based cohort, this study compared pregnancy and infant outcomes and described demographic and clinical characteristics of pregnant people with SARS-CoV-2 infection prior to and during the delta variant period.

STUDY DESIGN: This retrospective cohort analysis included persons with confirmed SARS-CoV-2 infection in pregnancy from 6 US jurisdictions reporting to the Surveillance for Emerging Threats to Pregnant People and Infants Network. Data were collected through case reports of polymerase chain reaction-positive pregnant persons and linkages to birth certificates, fetal death records, and immunization records. We described clinical characteristics and compared frequency of spontaneous abortion (<20 weeks of gestation), stillbirth (≥20 weeks), preterm birth (<37 weeks), small for gestational age, and term infant neonatal intensive care unit admission between the time periods of pre-delta and delta variant predominance. Study time periods were determined by when variants constituted more than 50% of sequences isolated according to regional SARS-CoV-2 genomic surveillance data, with time periods defined for pre-delta (March 3, 2020–June 25,

2021) and Delta (June 26, 2021–December 25, 2021). Adjusted prevalence ratios were estimated for each outcome measure using Poisson regression and were adjusted for continuous maternal age, race and ethnicity, and insurance status at delivery.

RESULTS: Among 57,563 pregnancy outcomes, 57,188 (99.3%) were liveborn infants, 65 (0.1%) were spontaneous abortions, and 310 (0.5%) were stillbirths. Most pregnant persons were unvaccinated at the time of SARS-CoV-2 infection, with a higher proportion in pre-delta (99.4%) than in the delta period (78.4%). Of those with infections during delta and who were previously vaccinated, the timing from last vaccination to infection was a median of 183 days. Compared to pre-delta, infections during delta were associated with a higher frequency of stillbirths (0.7% vs 0.4%; adjusted prevalence ratio, 1.55; 95% confidence interval, 1.14–2.09) and preterm births (12.8% vs 11.9%; adjusted prevalence ratio, 1.14; 95% confidence interval, 1.07–1.20). The delta period was associated with a lower frequency of neonatal intensive care unit admission (adjusted prevalence ratio, 0.74; 95% confidence interval, 0.67–0.82) than in the pre-delta period. During the delta period, infection during the third trimester was associated with a higher frequency of preterm birth (adjusted prevalence ratio, 1.41; 95% confidence interval, 1.28–1.56) and neonatal intensive care unit admission (adjusted prevalence ratio, 1.21; 95% confidence interval, 1.01–1.45) compared to the first and second trimester combined.

CONCLUSION: In this US-based cohort of persons with SARS-CoV-2 infection in pregnancy, the majority were unvaccinated, and frequencies of stillbirth and preterm birth were higher during the delta variant predominance period than in the pre-delta period. During the delta period, frequency of preterm birth and neonatal intensive care unit admission was higher among infections occurring in the third trimester vs those earlier in pregnancy. These findings demonstrate population-level increases of adverse fetal and infant outcomes, specifically in the presence of a COVID-19 variant with more severe presentation.

Keywords

adverse perinatal outcomes; COVID-19; delta variant; fetal death; pregnancy; preterm birth; SARS-CoV-2; stillbirth

Introduction

SARS-CoV-2 infection in pregnancy is associated with an increased risk of adverse birth outcomes such as preterm birth, stillbirth, and maternal and infant complications.[1] Previous research using administrative datasets or national surveillance data suggest an increased risk of severe COVID-19 illness in pregnant people.[2,3] The delta variant (B.1.617.2) represented the majority of US cases during July to December 2021 and was characterized by higher rates of hospitalization, intensive care unit admission, and death among the unvaccinated, likely due to a higher propensity for infection and greater replication in the lower respiratory tract.[4,5] Reports of pregnant people with COVID-19 during delta showed higher frequency of maternal morbidity and mortality and stillbirth.[6,7] A previous study conducted on SARS-CoV-2 infections before the emergence of the delta variant found differential risks of adverse pregnancy outcomes, with a higher proportion of preterm births when infection occurred in the third trimester than in the first and second trimesters.[8] However, studies of adverse

perinatal outcomes associated with the delta variant did not report on timing of infection during pregnancy, and a few studies report on COVID-19 vaccination status.

Vaccination during pregnancy is highly effective in reducing severe disease, provides protection to the infant, and therefore is recommended for pregnant people.[9–11] The Centers for Disease Control and Prevention (CDC) strengthened communications recommending vaccines to pregnant persons in August, 2021 in response to the growing body of evidence associating COVID-19 with adverse outcomes and with indication of increased deaths and stillbirths among pregnant people with COVID-19 during the delta variant period.[12] Although vaccine uptake among pregnant persons increased in late 2021, vaccine hesitancy persisted, and only approximately 31% of pregnant people were considered fully vaccinated (ie, received 2 mRNA doses or 1 Janssen dose) by September 2021.[13,14]

Few studies have reported on birth outcomes, timing of infection, and vaccination status during the delta variant predominance period in the United States. This study aimed to describe characteristics of pregnant people with SARS-CoV-2 infection, including vaccination status at the time of infection, and frequency of adverse birth and infant outcomes prior to and during the delta predominance period. We also explored the associations, by trimester, of infection during the delta period, because previous studies using this cohort reported differences in frequency of adverse outcomes by trimester.[8]

Materials and Methods

This analysis utilized data from the following 6 US jurisdictional health departments reporting to the Surveillance for Emerging Threats to Pregnant People and Infants Network by September 15, 2023: Massachusetts, Missouri, New Jersey, Pennsylvania (excluding Philadelphia), City of Philadelphia, and Tennessee. The jurisdictions were included based on reported cases during the delta period and ability to link data to birth certificates, fetal death records, and immunization registries to obtain outcomes and COVID-19 vaccination status. We included pregnant people with known birth outcomes and SARS-CoV-2 infection during pregnancy between March 3, 2020 and December 25, 2021. Infection was confirmed using the first SARS-CoV-2-positive polymerase chain reaction (PCR) result during pregnancy, and gestational age was calculated based on estimated date of delivery. For this analysis, we restricted to only the first infection during a pregnancy. Reinfections, defined as a positive PCR result >90 days from the first positive, accounted for 3.1% of the population, and did not impact the main findings when they were excluded.

Because sequencing of every infection is impossible, we utilized a methodology that used time periods as a proxy for variant predominance.[15,16] The delta predominance period was defined as the time when the delta variant accounted for 50% or more of sequenced isolates in each US Department of Health and Human Services region. The pre-delta (March 3, 2020–June 26, 2021) and delta (June 27, 2021–December 25, 2021) time periods approximately correspond to variant predominance in the United States and differed by 1 to 3 weeks by region.[17]

Pregnancy outcomes included live births, spontaneous abortion (<20 weeks of gestation) and stillbirth (≥20 weeks of gestation). Preterm birth (<37 weeks of gestation) was analyzed among live births with infection at <37 weeks to capture the population at risk. Small for gestational age was calculated among all infants based on INTERGROWTH-21st standards,[18] and neonatal intensive care unit (NICU) admission was reported among term, liveborn infants. Associations between trimester of infection and pregnancy outcomes were also assessed among infections occurring during the delta period.

Unadjusted and adjusted prevalence ratios (PRs and aPRs) of outcome measures were estimated using Poisson regression. Estimates were adjusted for continuous maternal age, race and ethnicity, and insurance status at delivery. Analyses were performed using R version 4.2.2 (R Foundation), and statistical significance was defined as a *P* value of <.05. This activity was reviewed by the CDC and was conducted consistent with applicable federal law and policy.[19]

Results

A total of 56,856 pregnant persons infected with SARS-CoV-2 were included, with 38,828 (68.3%) infected during the pre-delta period and 18,028 (31.7%) during the delta period (Table 1). The median maternal age was 29.5 years with 59.5% aged 25 to 34 years, which did not differ by time period. In the pre-delta period, 51.2% were White non-Hispanic and 23.7% were Hispanic/Latino compared to 64.4% White non-Hispanic and 12.7% Hispanic/Latino in the delta period. Medicaid was the most common insurance at delivery among pregnant people with infection during the pre-delta period (47.3%), whereas private insurance was most common during delta (43.1%). The trimester of infection was similar across variant periods with the third trimester being most frequent (40.4%), followed by second trimester (33.8%), then first trimester (25.9%). Underlying health conditions were similar across variant periods with 36.6% having at least 1 condition and 28.5% with pre-pregnancy obesity. Gestational diabetes and pregnancy-induced hypertension were reported among 9.3% and 9.1% of pregnant persons and were similar across variant periods. In the pre-delta period, 99.4% of pregnant persons infected with SARS-CoV-2 were unvaccinated compared to 78.4% in the delta period. Of those vaccinated, median time since last vaccination dose to infection during pregnancy was 32 days in pre-delta compared to 183 days in the delta period. There were 29 maternal deaths reported overall with 16 during the pre-delta period (0.41/1000 pregnant persons) and 13 during the delta period (0.72/1000 pregnant persons).

During the pre-delta period, 99.4% of birth outcomes resulted in live births, 0.4% stillbirths, and 0.1% spontaneous abortions compared to 99.1% live births, 0.7% stillbirths, and 0.1% spontaneous abortions in the delta period (Table 2). The delta period was associated with a higher frequency of stillbirths than pre-delta (aPR, 1.55; 95% confidence interval [CI], 1.14–2.09). When restricting to infections at <37 weeks of gestation, 11.9% of births in pre-delta were preterm compared to 12.8% in delta (aPR, 1.14; 95% CI, 1.07–1.20). The proportion of indicated preterm births were similar across time periods, although there were substantial proportions with unknown indication (>50%). NICU admission among term, liveborn infants was 5.1% in the pre-delta period compared to 4.2% in delta period (aPR,

0.74; 95% CI, 0.67–0.82), with a greater proportion of missing for pre-delta than delta (8.1%, 2.2%). Small for gestational age was similar across pre-delta (5.4%) and delta (5.7%) periods (aPR, 1.07; 95% CI, 0.98–1.16).

Among pregnant people who experienced a stillbirth, median time from infection to stillbirth outcome in the pre-delta period was 29 days compared to 13 days in delta, with shorter days from infection to delivery among those with later trimester infection (Table 3). Across variant periods, most pregnant people who experienced a stillbirth were infected in the second trimester (43.9%), followed by third trimester (31.3%), then first trimester (24.8%).

During the delta period, infection during the third trimester was associated with a higher frequency of preterm birth than infection during the first and second trimesters combined (aPR, 1.41; 95% CI, 1.28–1.56) (Table 4). There was also a higher frequency of NICU admission (aPR, 1.21; 95% CI, 1.01–1.45) among term infants infected during the third trimester. Frequency of stillbirth and small for gestational age during the delta period was not statistically different by trimester of infection.

Discussion

Principal findings

SARS-CoV-2 infections during the delta variant period were associated with a higher frequency of stillbirth and preterm birth than during the pre-delta. During the delta period, third trimester infections were associated with increased frequency of preterm birth and NICU admission.

Results

Our study confirmed previous findings of increased frequency of preterm birth and stillbirth during the delta variant predominance period compared to pre-delta period, even after adjusting for age, race and ethnicity, and health insurance. The delta variant has been shown to have more propensity for infection and higher viral loads,[21] which may lead to more severe maternal illness and death and inducing abnormalities in the placenta leading to adverse fetal and/or infant outcomes.[22,23] During the delta variant period, third trimester infection was associated with an increase in preterm birth and NICU admission compared to first or second trimester infection; however, we did not find an association between timing of infection and stillbirth, although the frequency of stillbirth was higher during the delta period overall.

We found a lower frequency of NICU admission among term infants in the delta period although previous studies have reported either higher risk or no difference between the pre-delta and delta predominance periods.[24,25] This may be due to differential missingness in the pre-delta period compared to the delta predominance period. Future analyses can assess the impacts of disease severity and whether vaccination status modifies the association.

Clinical implications

This analysis included infections beginning in March, 2020, before the Emergency Use Authorization (EUA) by the US Food and Drug Administration of the Pfizer-BioNTech COVID-19 vaccine in December 2020. We described timing from last vaccination to infection in each variant period, which aligned with the timing of COVID-19 vaccination distribution in the US. Out of 38,828 pregnant persons infected in the pre-delta period, 38,589 (99.4%) were unvaccinated. Although pregnant people were eligible to receive vaccination immediately after the EUA, the CDC strengthened communications recommending vaccines to pregnant persons in August, 2021 after indication of increased deaths and stillbirths among pregnant people with COVID-19.[12] The delta period, spanning from June to December of 2021, included a larger proportion of pregnant persons with infection who received 1 dose (n=788, 4.4%) and 2 or more doses (n=3062, 17.0%). However, the majority of this cohort with PCR-confirmed infections was unvaccinated at the time of infection. Among those who were previously vaccinated, the median timing of last vaccination to infection was 183 days during delta, which corresponds to protection in the first few months after vaccination and waning immunity after 150 days.[26] This finding provides additional support for the importance of COVID-19 vaccination during pregnancy and staying up to date with vaccinations to prevent adverse maternal, fetal, and infant outcomes.

We found a higher frequency of preterm birth in the delta period (12.8%) than in the pre-delta period (11.9%). This could be due to increased disease severity during the delta period and/or changes in obstetric management of SARS-CoV-2-positive pregnant persons throughout the course of the pandemic. Although this analysis did not observe differences in indication of preterm birth, previous studies have established a higher percentage of preterm births among pregnant persons with COVID-19 and have noted that increased disease severity is a contributing factor to both spontaneous and indicated preterm births.[27,28]

Research implications

Previous research reported that the risk of stillbirth among pregnant persons with SARS-CoV-2 infection was higher than in those without infection.[7] DeSisto et al also found a higher risk of stillbirth among pregnant persons in the delta period (2.7%) than in the pre-delta period (1.0%). Although statistically significant, the magnitude of association was lower in this analysis (0.7% vs 0.4%), which may reflect differences in inclusion because our study included all persons with laboratory confirmation of SAR-CoV-2, including asymptomatic and mild illness. The elevated risk in the delta period may be attributed to disease severity. There is limited evidence to suggest that the more severe delta variant results in a greater prevalence of placental abnormalities,[22] although these abnormalities may be a result of more severe disease and not necessarily attributed specifically to the delta variant. Additional research is needed to address disease severity and COVID-19, and compare placental changes of those with infection with comparators without infection.

Strengths and limitations

This analysis was subject to at least 4 limitations. First, due to a reliance on data from fetal death records for ≥20 weeks of gestation and birth certificates, and a potential lack

of medical encounters, spontaneous abortions were under-ascertained in our study and should be interpreted with caution. Second, the jurisdictions were dependent on obtaining COVID-19 vaccination based on linkages to immunization registries. Cases that were not linked may represent those unvaccinated or vaccinated; however, those records were not included in the state registries. Thus, our findings may misclassify vaccination coverage or time of infection since last vaccination. Third, due to the reliance on linked data, we were unable to ascertain preterm birth indication or COVID-19 disease severity for the majority of cases. However, there is evidence of increased disease severity during the delta predominance and the impact on birth and fetal outcomes.[3,6] Fourth, we defined the pre-delta and delta periods based on >50% cases by the end of the surveillance week in each US region. Although these percentages were based on regionally representative data, misclassification is possible but likely nondifferential.

This analysis had several strengths including a large population-based cohort of persons with SARS-CoV-2 infection during pregnancy, data on timing between infection and outcome, and vaccination status at the time of infection.

Conclusion

Frequency of stillbirth and preterm birth following SARS-CoV-2 infection in pregnancy were higher during the delta variant predominance period than during the pre-delta period. These findings highlight the impact of COVID-19 in pregnancy on adverse fetal and infant outcomes, specifically in the presence of a variant with more severe presentation, and support recommendations for pregnant people and those who may become pregnant to stay up to date with COVID-19 vaccines.

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AJOG MFM at a Glance

Why was this study conducted?

The increased severity of the SARS-CoV-2 delta variant resulted in an increase in adverse perinatal outcomes. This population-based study aimed to investigate outcomes, timing of infection, and describe vaccination status among pregnant people with SARS-CoV-2 infection during the delta variant predominance period.

Key findings

SARS-CoV-2 infection during the delta variant predominance period was associated with a higher frequency of stillbirth and preterm birth than the pre-delta period. Most pregnant persons with SARS-CoV-2 infection were unvaccinated, and third trimester infection during delta predominance was associated with a higher frequency of preterm birth and neonatal intensive care unit admission than infection in earlier trimesters.

What does this add to what is known?

These findings demonstrate population-level increases of adverse fetal and infant outcomes, specifically in the presence of a COVID-19 variant with more severe presentation.

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TABLE 1

Demographics of pregnant people with SARS-CoV-2 infection by variant predominance period

		Total N (%)	Pre-delta, n (%) (March 3, 2020 - June 26,2021)	Delta, n (%) (June 27-Dec. 25, 2021)
Total[a]		56,856 (100.0)	38,828 (68.3)	18,028 (31.7)
Age	(Median, IQR)	29.5 (25.3–33.4)	29.5 (25.3–33.3)	29.5 (25.1–33.4)
	<20 y	2760 (4.9)	1798 (4.6)	962 (5.3)
	20–24 y	10,720 (18.9)	7239 (18.6)	3481 (19.3)
	25–29 y	16,991 (29.9)	11,803 (30.4)	5188 (28.8)
	30–34 y	16,839 (29.6)	11,484 (29.6)	5355 (29.7)
	35–39 y	7912 (13.9)	5353 (13.8)	2559 (14.2)
	40+y	1615 (2.8)	1138 (2.9)	477 (2.6)
	Unknown	19 (0.0)	13 (0.0)	6 (0.0)
Race/ethnicity	American Indian or Alaska Native	323 (0.6)	207 (0.5)	116 (0.6)
	Asian non-Hispanic	1943 (3.4)	1510 (3.9)	433 (2.4)
	Black non-Hispanic	8524 (15.0)	5840 (15.0)	2684 (14.9)
	Hispanic/Latino	11,483 (20.2)	9195 (23.7)	2288 (12.7)
	Native Hawaiian or Other Pacific Islander	168 (0.3)	117 (0.3)	51 (0.3)
	Other race non-Hispanic	1057 (1.9)	706 (1.8)	351 (1.9)
	White non-Hispanic	31,477 (55.4)	19,864 (51.2)	11,613 (64.4)
	Unknown	1881 (3.3)	1389 (3.6)	492 (2.7)
Insurance status at delivery	Medicaid	25,237 (44.4)	18,384 (47.3)	6853 (38.0)
	Private	22,482 (39.5)	14,709 (37.9)	7773 (43.1)
	None/self-pay	712 (1.3)	469 (1.2)	243 (1.3)
	Other	674 (1.2)	474 (1.2)	200 (1.1)
	Missing/not reported	7751 (13.6)	4792 (12.3)	2959 (16.4)
Trimester of infection	First trimester	14,702 (25.9)	10,158 (26.2)	4544 (25.2)
	Second trimester	19,201 (33.8)	12,839 (33.1)	6362 (35.3)
	Third trimester	22,953 (40.4)	15,831 (40.8)	7122 (39.5)
Trimester of prenatal care initiation[b]	First trimester	42,624 (74.0)	29,326 (74.5)	13,298 (73.0)

		Total N (%)	Pre-delta, n (%) (March 3, 2020 - June 26,2021)	Delta, n (%) (June 27-Dec. 25, 2021)
	Second trimester	8404 (14.6)	5912 (15.0)	2492 (13.7)
	Third trimester	1550 (2.7)	1056 (2.7)	494 (2.7)
	Unknown trimester	3137 (5.4)	1820 (4.6)	1317 (7.2)
	No prenatal care	1034 (1.8)	630 (1.6)	404 (2.2)
	Unknown	814 (1.4)	597 (1.5)	217 (1.2)
Parity	Nulliparous	12,563 (22.1)	8564 (22.1)	3999 (22.2)
	Multiparous	32,679 (57.5)	21,597 (55.6)	11,082 (61.5)
	Unknown	11,614 (20.4)	8667 (22.3)	2947 (16.3)
Underlying health conditions	Any underlying condition	20,825 (36.6)	13,937 (35.9)	6888 (38.2)
	Pre-pregnancy obesity	16,214 (28.5)	10,546 (27.2)	5668 (31.4)
	Pre-pregnancy diabetes	898 (1.6)	634 (1.6)	264 (1.5)
	Chronic hypertension	2099 (3.7)	1407 (3.6)	692 (3.8)
	Chronic lung disease	1524 (2.7)	1171 (3.0)	353 (2.0)
	Cardiovascular disease	498 (0.9)	393 (1.0)	105 (0.6)
	Renal disease	95 (0.2)	72 (0.2)	23 (0.1)
	Liver disease	362 (0.6)	234 (0.6)	128 (0.7)
	Autoimmune condition	237 (0.4)	186 (0.5)	51 (0.3)
	Immunosuppressive condition	301 (0.5)	249 (0.6)	52 (0.3)
	Disability	62 (0.1)	49 (0.1)	13 (0.1)
Pregnancy complications	Gestational diabetes	5309 (9.3)	3798 (9.8)	1511 (8.4)
	Pregnancy-induced hypertension[c]	5151 (9.1)	3493 (9.0)	1658 (9.2)
Vaccination status at first infection in pregnancy	0 doses	52,727 (92.7)	38,589 (99.4)	14,138 (78.4)
	1 dose	895 (1.6)	107 (0.3)	788 (4.4)
	2 doses	3079 (5.4)	92 (0.2)	2987 (16.6)
	3 doses	72 (0.1)	2 (0.0)	70 (0.4)
	4 doses	5 (0.0)	0 (0.0)	5 (0.0)
	Unknown timing	78 (0.1)	38 (0.1)	40 (0.2)
Days since last vaccination[d]	(Median, IQR)	176 (100–229)	32 (22 –65)	183 (113–231)

		Total N (%)	Pre-delta, n (%) (March 3, 2020 - June 26,2021)	Delta, n (%) (June 27-Dec. 25, 2021)
Death[e]	Yes	29 (0.51/1000 pregnant persons)	16 (0.41/1000 pregnant persons)	13 (0.72/1000 pregnant persons)
	No	39,080 (68.7)	27,523 (70.9)	11,557 (64.1)
	Unknown	17,747 (31.2)	11,289 (29.1)	6458 (35.8)

IQR, interquartile range.

[a]Row percent for total; remaining table includes column percent.;

[b]Trimester of prenatal care initiation was calculated from last menstrual period to first prenatal care visit.;

[c]Includes preeclampsia.;

[d]Last doses defined as last vaccination date greater than 14 days from infection. The majority of infections in the Delta cohort were vaccinated January to May of 2021 and were infected later in the Delta period (August-December 2021).;

[e]Death included deaths during pregnancy, at pregnancy outcome, and upto and including 42 days after outcome.

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TABLE 2

Pregnancy and infant outcomes by variant predominance period

		Total N (%)	Pre-delta, n (%) (March 3, 2020-June 26,2021)	Delta, n (%) (June 27-Dec. 25, 2021)	Unadjusted PR (95% CI)	Adjusted PR[a] (95% CI)
Total[b]		57,563 (100.0)	39,341 (68.3)	18,222 (31.7)		
Outcome	Live birth	57,188 (99.3)	39,121 (99.4)	18,067 (99.1)	ref	ref
	Stillbirth	310 (0.5)	177 (0.4)	133 (0.7)	1.62 (1.29–2.03)[c]	1.55 (1.14–2.09)[c]
	Spontaneous abortion	65 (0.1)	43 (0.1)	22 (0.1)		
Gestational age[d]	Term	42,449 (87.8)	28,757 (88.1)	13,692 (87.2)	ref	ref
	Preterm	5889 (12.2)	3877 (11.9)	2012 (12.8)	1.08 (1.02–1.14)[c]	1.14 (1.07–1.20)[c]
	Late preterm (34–37 wk)	4370 (9.0)	2886 (8.8)	1484 (9.4)		
	Moderate preterm (32–34 wk)	728 (1.5)	451 (1.4)	277 (1.8)		
	Early preterm (28–32 wk)	545 (1.1)	379 (1.2)	166 (1.1)		
	Very preterm (20–28 wk)	246 (0.5)	161 (0.5)	85 (0.5)		
	Unknown	0 (0.0)	0 (0.0)	0 (0.0)		
Preterm birth indication[e]	Spontaneous	980 (16.6)	605 (15.6)	375 (18.6)	N/A	N/A
	Indicated	1556 (26.4)	993 (25.6)	563 (28.0)	N/A	N/A
	Unknown	3353 (56.9)	2279 (58.8)	1074 (53.4)		
Small for gestational age	Yes	3145 (5.5)	2121 (5.4)	1024 (5.7)	1.04 (0.96–1.12)	1.07 (0.98–1.16)
	No	53,404 (93.4)	36,444 (93.2)	16,960 (93.9)	ref	ref
	Unknown	639 (1.1)	556 (1.4)	83 (0.5)		
Neonatal intensive care[f]	NICU admission	2476 (4.8)	1809 (5.1)	667 (4.2)	0.76 (0.70–0.83)[c]	0.74 (0.67–0.82)[c]
	None	45,593 (88.9)	30,562 (86.7)	15,031 (93.6)	ref	ref
	Unknown	3225 (6.3)	2870 (8.1)	355 (2.2)		

CI, confidence interval; *NICU,* neonatal intensive care unit; *PR,* prevalence ratio.

[a]Adjusted for continuous maternal age, race/ethnicity, and health insurance at delivery.;

[b]Row percent for total; remaining table includes column percent.;

[c]Indicates statistical significance.;

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[d] Among live-born infants with infection occurring at <37 weeks of gestation.;

[e] Among live-born infants with infection occurring at <37 weeks of gestation. Spontaneous preterm birth was reported if evidence existed of premature rupture of membranes, vaginal delivery, or labor was not induced and there was evidence of attempted use of forceps, vacuum, prolonged labor, precipitous labor, fetal intolerance to labor, or augmentation of labor. Indicated preterm birth was defined as no evidence of premature rupture of membranes, labor was induced, or evidence of cesarean delivery. Methodology adapted from Klebanoff, et al[20].;

[f] Among term, live-born infants.

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TABLE 3

Stillbirths by variant predominance period

		Total, N (%)	Pre-delta, n (%) (March 3,2020-June 26,2021)	Delta, n (%) (June 27, 2021-Dec. 25, 2021)
Stillbirth[a]	Total	310 (100.0)	177 (57.1)	133 (42.9)
Gestational age	(Median, IQR)	29.4 (23.0–34.9)	30.0 (23.5–35.6)	27.9 (22.5–33.4)
Days from maternal PCR+ to stillbirth	(Median, IQR)	18 (2–94)	29 (1–100)	13 (4–64)
Days from maternal PCR+ to stillbirth by trimester of infection	First (Median, IQR)	124 (95–164)	125 (94.3–170)	124 (97–146)
	Second (Median, IQR)	15 (2–57)	19 (2–67)	11 (3–33)
	Third (Median, IQR)	4 (1–12)	1 (0–12)	7 (1–12)
Trimester of infection	First	77 (24.8)	48 (27.1)	29 (21.8)
	Second	136 (43.9)	76 (42.9)	60 (45.1)
	Third	97 (31.3)	53 (29.9)	44 (33.1)
Delivery type	Vaginal	257 (82.9)	145 (81.9)	112 (84.2)
	Cesarean delivery	44 (14.2)	27 (15.3)	17 (12.8)
	Unknown	9 (2.9)	5 (2.8)	4 (3.0)
Induction	Induced	51 (16.5)	36 (20.3)	15 (11.3)
	Not induced	50 (16.1)	30 (16.9)	20 (15.0)
	Unknown	209 (67.4)	111 (62.7)	98 (73.7)
Pre-pregnancy obesity	Yes	106 (34.2)	64 (36.2)	42 (31.6)
	No	151 (48.7)	78 (44.1)	73 (54.9)
	Unknown	53 (17.1)	35 (19.8)	18 (13.5)
Gestational diabetes	Yes	25 (8.1)	14 (7.9)	11 (8.3)
	No	237 (76.5)	144 (81.4)	93 (69.9)
	Unknown	48 (15.5)	19 (10.7)	29 (21.8)
Pregnancy-induced hypertension	Yes	26 (8.4)	18 (10.2)	8 (6.0)
	No	215 (69.4)	117 (66.1)	98 (73.7)
	Unknown	69 (22.3)	42 (23.7)	27 (20.3)
Other underlying condition[b]	Yes	138 (44.5)	82 (46.3)	56 (42.1)
	No	154 (49.7)	89 (50.3)	65 (48.9)

		Total, N (%)	Pre-delta, n (%) (March 3,2020-June 26,2021)	Delta, n (%) (June 27, 2021-Dec. 25, 2021)
	Unknown	18 (5.8)	6 (3.4)	12 (9.0)

IQR, interquartile range; *PCR,* polymerase chain reaction.

[a]Row percent for total; remaining table includes column percent.;

[b]Includes pre-pregnancy diabetes, chronic hypertension, chronic lung disease, cardiovascular disease, renal disease, liver disease, autoimmune condition, immunosuppressive condition, and disability.

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TABLE 4

Pregnancy and infant outcomes by trimester of infection during delta variant predominance

		Total N (%)	First/second trimester, n (%)	Third trimester, n (%)	Unadjusted PR (95% CI)	Adjusted PR[a] (95% CI)
Total[b]		18,222 (100.0)	11,031 (60.5)	7191 (39.5)		
Outcome	Live birth	18,067 (99.1)	10,920 (99.0)	7147 (99.4)	ref	ref
	Stillbirth	133 (0.7)	89 (0.8)	44 (0.6)	0.76 (0.52–1.08)	0.69 (0.41–1.14)
	Spontaneous abortion	22 (0.1)	22 (0.2)	N/A		
Gestational age[c]	Term	13,692 (87.2)	9680 (88.6)	4012 (83.9)	ref	ref
	Preterm	2012 (12.8)	1240 (11.4)	772 (16.1)	1.42 (1.30–1.55)[d]	1.41 (1.28–1.56)[d]
	Late preterm (34–37 wk)	1484 (9.4)	893 (8.2)	591 (12.4)		
	Moderate preterm (32–34 wk)	277 (1.8)	153 (1.4)	124 (2.6)		
	Early preterm (28–32 wk)	167 (1.1)	110 (1.0)	57 (1.2)		
	Very preterm (20–28 wk)	84 (0.5)	84 (0.8)	N/A		
	Unknown	0 (0.0)	0 (0.0)	0 (0.0)		
Preterm birth indication[e]	Spontaneous	375 (18.6)	221 (17.8)	154 (19.9)	N/A	N/A
	Indicated	563 (28.0)	338 (27.3)	225 (29.1)	N/A	N/A
	Unknown	1074 (53.4)	681 (54.9)	393 (50.9)		
Small for gestational age	Yes	1024 (5.7)	596 (5.5)	428 (6.0)	1.10 (0.97–1.25)	1.10 (0.96–1.27)
	No	16,960 (93.9)	10,294 (94.3)	6666 (93.3)	ref	ref
	Unknown	83 (0.5)	30 (0.3)	53 (0.7)		
Neonatal intensive care[f]	NICU admission	667 (4.2)	367 (3.8)	300 (4.7)	1.29 (1.11–1.50)[d]	1.21 (1.01–1.45)[d]
	None	15,031 (93.6)	9239 (95.4)	5792 (90.9)	ref	ref
	Unknown	355 (2.2)	74 (0.8)	281 (4.4)		

CI, confidence interval; *NICU,* neonatal intensive care unit; *PCR,* polymerase chain reaction.

[a]Adjusted for continuous maternal age, race/ethnicity, and insurance at delivery.;

[b]Row percent for total; remaining table includes column percent.;

[c]Among live-born infants with maternal infection occurring at <37 weeks of gestation.;

[d]Indicates statistical significance.;

[e] Among live-born infants with maternal infection occurring at <37 weeks of gestation. Spontaneous preterm birth was reported if evidence existed of premature rupture of membranes, vaginal delivery, or labor was not induced and there was evidence of attempted use of forceps, vacuum, prolonged labor, precipitous labor, fetal intolerance to labor, or augmentation of labor. Indicated preterm birth was defined as no evidence of premature rupture of membranes, labor was induced, or evidence of cesarean delivery. Methodology adapted from Klebanoff, et al[20].;

[f] Among term, live-born infants.