COVID-19 Severity among Women of Reproductive Age with Symptomatic Laboratory-Confirmed SARS-CoV-2 by Pregnancy Status – United States, Jan 1, 2020 – Dec 25, 2021

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Running Title. Severe COVID-19 by pregnancy status

Abstract

Background. Information on the severity of COVID-19 attributable to the Delta variant in the United States among pregnant people is limited. We assessed the risk for severe COVID-19 by pregnancy status in the period of Delta variant predominance compared with the pre-Delta period.

Methods. Laboratory-confirmed SARS-CoV-2 infections among symptomatic women of reproductive age (WRA) were assessed. We calculated adjusted risk ratios for severe disease including intensive care unit (ICU) admission, receipt of invasive ventilation or extracorporeal membrane oxygenation (ECMO), and death comparing the pre-Delta period (January 1, 2020 – June 26, 2021) and the Delta period (June 27, 2021 – December 25, 2021) for pregnant and nonpregnant WRA.

Results. Compared with the pre-Delta period, the risk of ICU admission during the Delta period was 41% higher (adjusted risk ratio [aRR] 1.41; 95% CI, 1.17-1.69) for pregnant WRA and 9% higher (aRR 1.09; 95% CI, 1.00-1.18) for nonpregnant WRA. The risk of invasive ventilation or ECMO was higher for pregnant (aRR 1.83; 95% CI, 1.26-2.65) and nonpregnant WRA (aRR 1.34; 95% CI, 1.17-1.54) in the Delta period. During the Delta period, the risk of death was 3.33 (95% CI, 2.48-4.46) times the risk in the pre-Delta period among pregnant WRA and 1.62 (95% CI, 1.49-1.77) among nonpregnant WRA.

Conclusions. Compared with the pre-Delta period, pregnant and nonpregnant WRA were at increased risk for severe COVID-19 in the Delta period.

Keywords. pregnancy, COVID-19, SARS-CoV-2, Delta variant, women of reproductive age

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (1). During the period June 27 through December 25, 2021, SARS-CoV-2 infections in the United States were predominantly attributed to the highly transmissible Delta (B.1.617.2) variant (2,3). Reports have suggested the Delta variant was associated with more severe disease and death compared with the Alpha (B.1.1.7) variant in the general population (4,5). This was of particular concern for individuals already at increased risk for severe disease due to underlying medical conditions or pregnancy (6).

Data regarding Delta variant SARS-CoV-2 infections among pregnant people in the United States have been limited to studies at single institutions, healthcare systems, or states (7–10). It has been suggested that rates of severe-critical disease (7–9), death (9,10), and adverse perinatal outcomes (7,8) were increased in the period of Delta variant predominance compared with the pre-Delta period, though reports have been limited by study size. Larger studies are needed to determine the level of risk for severe outcomes among pregnant people during the period of Delta variant predominance in the United States, and to understand how the risk compared to nonpregnant people.

As of February 25, 2022, more than 45 million case reports of SARS-CoV-2 infections occurring between January 1, 2020 and December 25, 2021 have been reported to the US Centers for Disease Control and Prevention (CDC). In this study, we describe the risk for severe COVID-19 among symptomatic women of reproductive age (WRA) in the United States by pregnancy status in the period of Delta variant predominance compared with the pre-Delta period.

METHODS

We assessed the risk for intensive care unit (ICU) admission, receipt of invasive ventilation or extracorporeal membrane oxygenation (ECMO), and death among women aged 15-44 years. We included national case reports of laboratory-confirmed (11) SARS-CoV-2 infections reported to the CDC by February 25, 2022. Reports were collected through the National Notifiable Disease Surveillance System and data collection resources offered through CDC's COVID-19 emergency response (1). The study period includes reports with a clinical observance date, or CDC receipt date when clinical observance date was not available, of January 1, 2020 through December 25, 2021. We excluded reports with a death date before January 20, 2020. The pre-Delta period is defined as January 1, 2020 through June 26, 2021 while the Delta period is defined as June 27, 2021 through December 25, 2021, corresponding to Delta variant predominance in the United States (2). Pregnancy status information was supplemented with data from the Surveillance for Emerging Threats to Mothers and Babies Network (SET-NET), a population-based mother-baby linked longitudinal surveillance collaboration between CDC and state, local, and territorial health departments (12). All cases reported to SET-NET are laboratory-confirmed SARS-CoV-2 infections during pregnancy. Pregnancy status information was also supplemented using free-text searches of the other symptoms and the other underlying conditions fields of the COVID-19 case reports. This analysis was limited to symptomatic WRA with laboratory-confirmed SARS-CoV-2 infections with known pregnancy status. Symptomatic cases included reports where the 'symptomatic' field was selected or at least one specific symptom was marked "yes".

Descriptive

In this study, we described the age, race and ethnicity, presence of symptoms, and underlying medical conditions of WRA by pregnancy status before and during the period of Delta variant predominance. Age was collapsed into three groups, 15-24, 25-34, and 35-44 years. Race and ethnicity were combined into a single variable. WRA of any ethnicity and a race of American Indian or Alaska Native (AI/AN), or

Native Hawaiian or Pacific Islander (NH/PI) were first identified. Then, WRA of Hispanic or Latino ethnicity and any race, except AI/AN and NH/PI were identified. Those with an ethnicity of non-Hispanic, unknown, or not reported, were grouped by reported race: Asian, Black, White, and multiple or other race (13,14). Finally, unknown was used to capture those with an unknown or not reported race without Hispanic ethnicity reported. Known status for symptoms and medical conditions was established by a "yes" or "no" in the COVID-19 case reports for at least one specific symptom or medical condition. Free-text fields were searched for individual symptoms and conditions. Symptoms included: headache, cough, muscle aches, fever (i.e., subjective or >100.4F), sore throat, runny nose, chills, new loss of taste or smell, shortness of breath, fatigue, diarrhea, nausea or vomiting, abdominal pain, chest pain, and wheezing. Medical conditions included: chronic lung disease, cardiovascular disease (including hypertension), diabetes, immunocompromised condition, severe obesity (i.e., body mass index ≥40 kg/m^2), autoimmune disorder, chronic renal disease, chronic liver disease, and other chronic disease.

Outcomes

We described three outcome categories to indicate severe disease: ICU admission, invasive ventilation or ECMO, and death. Cases with ECMO usage were assumed to have ICU admission. We described these outcomes by age, race and ethnicity, and presence of select underlying health conditions associated with more severe COVID-19 (15) (i.e., diabetes [15], cardiovascular disease [16], chronic lung disease (18), and severe obesity [14,18]), stratified by pregnancy status and time period relative to Delta variant predominance.

Models

Similar to methods previously described (20), we calculated risk ratios and their 95% confidence intervals (CI) using modified Poisson regression. When ICU admission, invasive ventilation or ECMO, and death were unknown or not reported, the outcome was assumed to have not occurred. For multivariable models, risk ratios were adjusted for age (continuous, in years), race and ethnicity, time

period (i.e., pre-Delta or Delta period), presence of diabetes, cardiovascular disease, chronic lung disease, and severe obesity, and an interaction term between time period and pregnancy status, unless otherwise specified. When an adjusted model did not converge due to small numbers, an exact Poisson regression was conducted. When examining risk by pregnancy status, pregnant WRA were compared with nonpregnant WRA as the referent group for the total study, pre-Delta, and Delta periods. When examining risk by time periods, the Delta period was compared with the pre-Delta period as the referent group. In overall adjusted models, non-Hispanic White and no underlying conditions were the referent groups.

SAS v9.4 (SAS Institute; Cary, NC) was used to conduct all analyses. Activities were reviewed by the CDC and conducted in accordance with applicable federal law and CDC policy (See: 45 C.F.R. part 46.102(l)(2), 21 C.F.R. part 56; 42 U.S.C. §241(d); 5 U.S.C. §552a; 44 U.S.C. §3501 et seq.).

RESULTS

More than 10.1 million reports of laboratory-confirmed SARS-CoV-2 infections among women aged 15-44 years had a clinical infection date or CDC receipt date of January 1, 2020 – December 25, 2021. Among 56 jurisdictions reporting, twelve jurisdictions had <1% completeness of pregnancy status among WRA, including seven jurisdictions that did not report pregnancy status. Overall, 25.0% of reports had a known pregnancy status (pregnant, n=164,344; nonpregnant, n=2,364,643). We linked 35,697 SET-NET cases from 17 participating jurisdictions to COVID-19 case reports by jurisdiction and a unique identifier. Pregnancy status was updated for 38.7% (n=13,826) of linked reports. Among linked reports, pregnancy status on the COVID-19 case report was misclassified for 3.6% (n=1,301) and unknown or not reported for 35.1% (n=12,525). Searching free-text fields, pregnancy status was updated to “yes” for 168 reports. After linkage and data cleaning, there were 178,338 pregnant WRA and 2,363,335 nonpregnant WRA

reports during the study period. Limiting to symptomatic COVID-19, our final analytic sample was 2,033,060 WRA. (Supplemental Figure)

Among 116,958 symptomatic pregnant WRA with laboratory-confirmed SARS-CoV-2 infection (Table 1), the majority were 25-34 years (57.8%) and non-Hispanic White (41.9%). Among the 17.5% (n=20,473) of pregnant WRA with known status for underlying medical conditions, the five most common conditions were chronic lung disease (9.3%), other chronic condition (6.9%), diabetes (5.9%), cardiovascular disease (5.8%), and severe obesity (5.6%). Among the 47.3% (n=55,310) of pregnant WRA with known status for any symptom, the five most common symptoms were cough (62.2%), headache (54.4%), muscle aches (44.9%), sore throat (36.6%), and fever (36.1%) (Figure 1). The pre-Delta period included 90,100 pregnant WRA and the Delta period included 26,858 pregnant WRA. The distributions of symptoms and underlying conditions in pregnant WRA were similar between periods.

Among 1,916,102 symptomatic nonpregnant WRA with laboratory-confirmed SARS-CoV-2 infection (Table 1), the majority were 25-34 years (34.0%) and non-Hispanic White (46.9%). Among 20.1% (n=385,502) of nonpregnant WRA with known status for underlying medical conditions, the five most common conditions were chronic lung disease (8.7%), cardiovascular disease (7.1%), other chronic condition (7.0%), diabetes (4.8%), and immunocompromised condition (2.3%). Among the 44.6% (n=854,271) of nonpregnant WRA with known status for any symptom, the five most common symptoms were headache (62.6%), cough (58.9%), muscle aches (49.9%), fever (41.5%), and sore throat (39.3%) (Figure 1). The pre-Delta period included 1,478,747 nonpregnant WRA and the Delta period included 437,355 nonpregnant WRA. The distributions of symptoms and underlying conditions in nonpregnant WRA were similar between periods.

Among pregnant WRA, 0.46% (n=543) experienced ICU admission, 0.11% (n=128) experienced invasive ventilation or ECMO, and 0.15% (n=176) died. In the pre-Delta period, 0.10% (n=90) of pregnant WRA died, while 0.32% (n=86) of pregnant WRA in the Delta period died. Among nonpregnant WRA, 0.17% (n=3,266) experienced ICU admission, 0.05% (n=1,012) received invasive ventilation or ECMO, and 0.12% (n=2,212) died. In the pre-Delta period, 0.10% (n=1,494) of nonpregnant WRA died, while 0.16% (n=718) of nonpregnant WRA in the Delta period died. (Table 2)

For the total study period, the adjusted RRs (aRRs) for severe outcomes comparing pregnant WRA with nonpregnant WRA were the following: ICU admission (aRR 2.53; 95% CI, 2.26-2.83), receipt of invasive ventilation or ECMO (aRR 1.76; 95% CI, 1.39-2.22), and death (aRR 1.11; 95% CI, 0.90-1.38). The interaction term between pregnancy status and time period was significant at an alpha of 0.05 for ICU admission (p=0.0045) and death (p<0.0001), and not significant for receipt of invasive ventilation or ECMO (p=0.0613). The Supplemental Table describes the risk ratios for pregnant WRA compared with nonpregnant WRA by age, race and ethnicity, Delta period, underlying medical conditions, and interaction between pregnancy status and time period for the total study period.

Stratified by time period relative to Delta variant predominance, point estimates were higher during the Delta period compared with the pre-Delta period for each severe disease outcome. The aRR for ICU admission for pregnant compared with nonpregnant WRA during the pre-Delta period was 2.56 (95% CI, 2.29-2.87) versus 3.32 (95% CI, 2.77-3.98) in the Delta period. The aRR for invasive ventilation or ECMO in the pre-Delta period was 1.82 (95% CI, 1.44-2.30) and in the Delta period was 2.44 (95% CI, 1.74-3.43) for pregnant WRA compared with nonpregnant WRA. Comparing pregnant WRA to nonpregnant WRA the aRR for death in the pre-Delta period was 1.11 (95% CI, 0.90-1.38) and during the Delta period 2.36 (95% CI, 1.87-2.97). (Table 3)

Among pregnant WRA, the risk of ICU admission was 41% higher (aRR 1.41; 95% CI, 1.17-1.69) in the Delta period compared with the pre-Delta period for pregnant WRA and 9% higher (aRR 1.09; 95% CI, 1.00-1.18) for nonpregnant WRA. The risk of invasive ventilation or ECMO was 83% higher (aRR 1.83; 95% CI, 1.26-2.65) for pregnant WRA and 34% higher (aRR 1.34; 95% CI, 1.17 – 1.54) for nonpregnant WRA, in the Delta period. During the Delta period, the risk of death was 3.33 (95% CI; 2.48-4.46) times the risk in the pre-Delta period among pregnant WRA and 1.62 (95% CI, 1.49-1.77) among nonpregnant WRA. (Table 4)

DISCUSSION

Our analysis provides an overview of the severity of COVID-19 cases among symptomatic WRA in the United States before and during the period of Delta variant predominance. During our total study period, pregnant WRA were at higher risk for ICU admission and receipt of invasive ventilation or ECMO compared with nonpregnant WRA. Consistent with national case reports from the pre-Delta period (20,21), the absolute risk for severe illness from COVID-19 remained low among pregnant WRA during the Delta period. However, the aRRs for severe outcomes were higher in the Delta period than the pre-Delta period when comparing pregnant WRA with nonpregnant WRA.

In this study, the risks of ICU admission, receipt of invasive ventilation or ECMO, and death were increased for both pregnant and nonpregnant WRA in the Delta period compared with the pre-Delta period. A small cohort study in Alabama described an increased risk for ICU admission (aRR 3.42; 95% CI, 1.91-6.11) and for intubation (aRR 4.18; 95% CI, 2.06-8.48) in pregnant WRA during Delta predominance compared with a pre-Delta period (8). Adhikari et al. described a significant increase in the proportion of

severe or critical illnesses among pregnant patients with COVID-19 during a period of Delta predominance (9).

The strength of this analysis is the use of national COVID-19 case report data which enabled the description of multijurisdictional trends over time. However, these data have several important limitations. National reporting for COVID-19 is voluntary. Most cases are reported to CDC within 10 days of clinical observance (interquartile range 4-49 days), although longer lag times have been observed. Over time, some jurisdictions have stopped reporting certain variables such as pregnancy status and severe outcomes, only providing minimal case information. A study by Manning et al. (22) found the sensitivity of the COVID-19 case report form pregnancy field as 45.3% and 42.1% for Illinois and Tennessee, respectively. As seen with our linkage to SET-NET, pregnancy status may be misclassified. COVID-19 national case report data are subject to data entry errors, reporting errors, and lack confirmation of data. For example, death status is not confirmed by a death record. Furthermore, information is not available to indicate if a report has been updated over time. Mild cases of COVID-19 are likely underreported, and some outcomes such as death may experience longer lags in reporting (23). Our report does not include hospitalizations as an indicator for severe disease as the national case report does not differentiate reason for hospitalization (i.e., solely for COVID-19 versus pregnancy related care). Reporting of race and ethnicity is not consistent across jurisdictions. We stratified this analysis by period respective to Delta variant predominance using date as a proxy because the COVID-19 national case report data does not include genomic information. Therefore, our results may underestimate the risk during the Delta period as the Delta variant was circulating prior to nationwide Delta predominance, and at the end of our study period circulation of the Omicron variant (BA.1.1, B.1.1.529, BA.2) was rapidly increasing (2). This analysis would benefit from greater completeness of the pregnancy status field on the case report form and knowledge of vaccination status, to understand how

severe disease varied by pregnancy status and vaccination status for symptomatic WRA. Despite the availability of a vaccination status field on the case report form, only 14 jurisdictions have reported this variable.

Precautions should be taken to prevent exposure to SARS-CoV-2, especially among groups at increased risk for severe COVID-19 such as pregnant WRA. Preventing exposure can limit the transmission of COVID-19 which may slow the emergence of new variants (24). To reduce the risk for acquiring SARS-CoV-2, the CDC recommends pregnant people receive COVID-19 vaccination, practice hand hygiene, wear a mask at public indoor spaces, and practice physical distancing behaviors, particularly when indoors in crowded spaces and when near individuals who are sick (25). The greatest risk for COVID-19 is currently among those who are unvaccinated (26). Vaccination can prevent infection and reduces the likelihood of severe disease if infection occurs. The CDC, the American College of Obstetricians and Gynecologists, and the Society for Maternal-Fetal Medicine recommend COVID-19 vaccination for all eligible individuals, including those who are pregnant, lactating, trying to get pregnant now, or might become pregnant in the future (27,28). Evidence suggests individuals not fully vaccinated have more than 10 times higher COVID-19 mortality risk (26). Accumulating data provide evidence of both the safety (29–32) and effectiveness (33,34) of COVID-19 vaccination during pregnancy.

National case surveillance is an important public health resource to understand national trends in disease. This study utilized national COVID-19 case report data to understand the severity of disease during the pre-Delta and Delta periods for symptomatic WRA. The absolute risk for severe COVID-19 remained low among symptomatic WRA; however, pregnant WRA were at increased risk for severe disease compared with nonpregnant WRA and the risk of severe illness in pregnant and nonpregnant WRA was increased during Delta variant predominance in the United States.

NOTES

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Table 1. Characteristics of women 15-44 years with symptomatic, laboratory-confirmed SARS-CoV-2 infection by pregnancy status, Jan 1, 2020 – Dec 25, 2021

Characteristic	Pregnant			Nonpregnant		
	Total Study Period[a]	Pre-Delta Period[b]	Delta Period[c]	Total Study Period[a]	Pre-Delta Period[b]	Delta Perio
	(n=116,958)	(n=90,100)	(n=26,858)	(n=1,916,102)	(n=1,478,747)	(n=437,35
Age group (years)						
15-24	28,962 (24.8)	22,241 (24.7)	6,721 (25.0)	637,752 (33.3)	500,636 (33.9)	137,116 (31
25-34	67,640 (57.8)	52,308 (58.1)	15,332 (57.1)	650,970 (34.0)	500,732 (33.9)	150,238 (34
35-44	20,356 (17.4)	15,551 (17.3)	4,805 (17.9)	627,380 (32.7)	477,379 (32.3)	150,001 (34
Race and Ethnicity[d]						
Hispanic or Latino	37,017 (31.6)	30,838 (34.2)	6,179 (23.0)	506,633 (26.4)	414,786 (28.0)	91,847 (21
American Indian or Alaska Native	1,231 (1.1)	909 (1.0)	322 (1.2)	20,116 (1.0)	14,929 (1.0)	5,187 (1
Asian, non-Hispanic	3,710 (3.2)	2,995 (3.3)	715 (2.7)	60,786 (3.2)	48,501 (3.3)	12,285 (2
Black, non-Hispanic	15,090 (12.9)	11,270 (12.5)	3,820 (14.2)	258,101 (13.5)	192,612 (13.0)	65,489 (15
Native Hawaiian or Pacific Islander	646 (0.6)	496 (0.6)	150 (0.6)	8,159 (0.4)	6,256 (0.4)	1,903 (0
White, non-Hispanic	49,046 (41.9)	35,558 (39.5)	13,488 (50.2)	899,294 (46.9)	675,562 (45.7)	223,732 (51
Multiple or other race, non-Hispanic	4,453 (3.8)	3,433 (3.8)	1,020 (3.8)	70,742 (3.7)	53,452 (3.6)	17,290 (4
Unknown or not reported	5,765 (4.9)	4,601 (5.1)	1,164 (4.3)	92,271 (4.8)	72,649 (4.9)	19,622 (4
Underlying medical condition						
Known underlying medical condition status	20,473 (17.5)	15,875 (17.6)	4,598 (17.1)	385,502 (20.1)	299,320 (20.2)	86,182 (19
Chronic lung disease	1,904 (9.3)	1,453 (9.2)	451 (9.8)	33,701 (8.7)	26,397 (8.8)	7,304 (8
Cardiovascular disease[e]	1,186 (5.8)	896 (5.6)	290 (6.3)	27,217 (7.1)	21,166 (7.1)	6,051 (7
Diabetes	1,210 (5.9)	978 (6.2)	232 (5.0)	18,693 (4.8)	14,955 (5.0)	3,738 (4
Immunocompromised condition	470 (2.3)	366 (2.3)	104 (2.3)	9,023 (2.3)	6,989 (2.3)	2,034 (2
Severe obesity (BMI ≥40 kg/m^2)	1,155 (5.6)	971 (6.1)	184 (4.0)	4,569 (1.2)	3,550 (1.2)	1,019 (1
Autoimmune disorder	184 (0.9)	126 (0.8)	58 (1.3)	4,237 (1.1)	2,984 (1.0)	1,253 (1

Chronic renal disease	88 (0.4)	65 (0.4)	23 (0.5)	2,342 (0.6)	1,810 (0.6)	532 (0
Chronic liver disease	72 (0.4)	48 (0.3)	24 (0.5)	1,313 (0.3)	1,018 (0.3)	295 (0
Other chronic disease	1,406 (6.9)	1,136 (7.2)	270 (5.9)	26,832 (7.0)	20,722 (6.9)	6,110 (7

Abbreviation: BMI, body mass index

Note: Percentages for individual symptoms and underlying medical conditions use known status for individual symptoms and known status for underlying medical conditions for denominators, respectively. All other percentages use column total as denominator.

[a]Total study period includes cases with a clinical observance date, or Centers for Disease Control and Prevention receipt date when clinical observance date was not available, of January 1, 2020 through December 25, 2021.

[b]Pre-Delta period includes cases with a clinical observance date or Centers for Disease Control and Prevention report received date, when clinical observance date was not available, of January 1, 2020 through June 26, 2021.

[c]Delta period includes cases with a clinical observance date or Centers for Disease Control and Prevention report received date, when clinical observance date was not available, of June 27, 2021 through December 25, 2021.

[d]Non-Hispanic includes unknown and not reported ethnicity.

[e]Cardiovascular disease includes hypertension.

Table 2. Prevalence of severe COVID-19 outcomes among symptomatic women aged 15-44 years with laboratory-confirmed SARS-CoV-2 infection by pregnancy status, Jan 1, 2020 – Dec 25, 2021

	Pregnant			Nonpregnant	
	Total Study Period[a]	Pre-Delta Period[b]	Delta Period[c]	Total Study Period[a]	Pre-Delta Period
	(n=116,958)	(n=90,100)	(n=26,858)	(n=1,916,102)	(n=1,478,747
ICU Admission					
All	543 (0.46)	392 (0.44)	151 (0.56)	3,266 (0.17)	2,506 (0.17
Age group (years)					
15-24	84 (15.47)	65 (16.58)	19 (12.58)	552 (16.90)	417 (16.64
25-34	309 (56.91)	221 (56.38)	88 (58.28)	1,004 (30.74)	762 (30.41
35-44	150 (27.62)	106 (27.04)	44 (29.14)	1,710 (52.36)	1,327 (52.95
Race and Ethnicity[d]					
Hispanic or Latino, any race	196 (36.10)	162 (41.33)	34 (22.52)	1,034 (31.66)	846 (33.76
American Indian or Alaska Native	3 (0.55)	NR	NR	73 (2.24)	57 (2.27
Asian, non-Hispanic	53 (9.76)	40 (10.20)	13 (8.61)	136 (4.16)	114 (4.55
Black, non-Hispanic	95 (17.50)	66 (16.84)	29 (19.21)	681 (20.85)	518 (20.67
Native Hawaiian or Pacific Islander	14 (2.58)	NR	NR	59 (1.81)	41 (1.64
White, non-Hispanic	142 (26.15)	86 (21.94)	56 (37.09)	1,112 (34.05)	807 (32.20
Multiple or other race, non-Hispanic	23 (4.24)	14 (3.57)	9 (5.96)	89 (2.73)	63 (2.51
Unknown or not reported	17 (3.13)	12 (3.06)	5 (3.31)	82 (2.51)	60 (2.39
Underlying medical condition					
Chronic lung disease	32 (5.89)	22 (5.61)	10 (6.62)	330 (10.10)	266 (10.61
Cardiovascular disease[e]	32 (5.89)	21 (5.36)	11 (7.28)	439 (13.44)	348 (13.89
Diabetes	53 (9.76)	39 (9.95)	14 (9.27)	512 (15.68)	413 (16.48
Severe obesity (BMI ≥40 kg/m^2)	27 (4.97)	21 (5.36)	6 (3.97)	183 (5.60)	136 (5.43
Invasive Ventilation or ECMO					
All	128 (0.11)	86 (0.10)	42 (0.16)	1,012 (0.05)	739 (0.05
Age group (years)					

15-24	25 (19.53)	14 (16.28)	11 (26.19)	180 (17.79)	139 (18.8
25-34	61 (47.66)	41 (47.67)	20 (47.62)	307 (30.34)	213 (28.8
35-44	42 (32.81)	31 (36.05)	11 (26.19)	525 (51.88)	387 (52.3
Race and Ethnicity[d]					
Hispanic or Latino, any race	43 (33.59)	33 (38.37)	10 (23.81)	308 (30.43)	242 (32.7
American Indian or Alaska Native	2 (1.56)	NR	NR	22 (2.17)	N
Asian, non-Hispanic	7 (5.47)	NR	NR	35 (3.46)	29 (3.9
Black, non-Hispanic	26 (20.31)	20 (23.26)	6 (14.29)	201 (19.86)	130 (17.5
Native Hawaiian or Pacific Islander	5 (3.91)	NR	NR	25 (2.47)	17 (2.3
White, non-Hispanic	34 (26.56)	19 (22.09)	15 (35.71)	355 (35.08)	254 (34.3
Multiple or other race, non-Hispanic	6 (4.69)	NR	NR	21 (2.08)	14 (1.8
Unknown or not reported	5 (3.91)	NR	NR	45 (4.45)	33 (4.4
Underlying medical condition					
Chronic lung disease	11 (8.59)	NR	NR	128 (12.65)	97 (13.1
Cardiovascular disease[e]	15 (11.72)	NR	NR	172 (17.00)	121 (16.3
Diabetes	23 (17.97)	17 (19.77)	6 (14.29)	189 (18.68)	138 (18.6
Severe obesity (BMI ≥40 kg/m^2)	12 (9.38)	NR	NR	86 (8.50)	54 (7.3
Death					
All	176 (0.15)	90 (0.10)	86 (0.32)	2,212 (0.12)	1,494 (0.1
Age group (years)					
15-24	19 (10.80)	10 (11.11)	9 (10.47)	299 (13.52)	229 (15.3
25-34	94 (53.41)	51 (56.67)	43 (50.00)	612 (27.67)	417 (27.9
35-44	63 (35.80)	29 (32.22)	34 (39.53)	1,301 (58.82)	848 (56.7
Race and Ethnicity[d]					
Hispanic or Latino, any race	55 (31.25)	40 (44.44)	15 (17.44)	509 (23.01)	384 (25.7
American Indian or Alaska Native	6 (3.41)	NR	NR	62 (2.80)	44 (2.9
Asian, non-Hispanic	10 (5.68)	NR	NR	50 (2.26)	35 (2.3
Black, non-	36 (20.45)	18 (20.00)	18 (20.93)	611 (27.62)	406 (27.1

Hispanic					
Native Hawaiian or Pacific Islander	4 (2.27)	NR	NR	22 (0.99)	11 (0.74
White, non-Hispanic	54 (30.68)	20 (22.22)	34 (39.53)	781 (35.31)	483 (32.33
Multiple or other race, non-Hispanic	7 (3.98)	NR	NR	56 (2.53)	39 (2.61
Unknown or not reported	4 (2.27)	NR	NR	121 (5.47)	92 (6.16
Underlying medical condition					
Chronic lung disease	9 (5.11)	NR	NR	89 (4.02)	65 (4.35
Cardiovascular disease[e]	13 (7.39)	8 (8.89)	5 (5.81)	203 (9.18)	134 (8.97
Diabetes	17 (9.66)	10 (11.11)	7 (8.14)	181 (8.18)	115 (7.70
Severe obesity (BMI ≥40 kg/m^2)	3 (1.70)	NR	NR	71 (3.21)	40 (2.68

Abbreviations: BMI, body mass index; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit admission; NR, not reported.

Note: The percentages for the 'All' row for each outcome were calculated using the total number of symptomatic women of reproductive age in the corresponding column as the denominator. The percentages for the age, race and ethnicity, and underlying health conditions rows were calculated using the total number in the 'All' row in the corresponding column as the denominator. Categories with <5 reports in the pre-Delta or Delta periods are not reported by period.

[a]Total study period includes cases with a clinical observance date, or Centers for Disease Control and Prevention receipt date when clinical observance date was not available, of January 1, 2020 through December 25, 2021.

[b]Pre-Delta period includes cases with a clinical observance date or Centers for Disease Control and Prevention report received date, when clinical observance date was not available, of January 1, 2020 through June 26, 2021.

[c]Delta period includes cases with a clinical observance date or Centers for Disease Control and Prevention report received date, when clinical observance date was not available, of June 27, 2021 through December 25, 2021.

[d]Non-Hispanic includes unknown and not reported ethnicity.

[e]Cardiovascular disease includes hypertension.

Table 3. Risk ratios for severe COVID-19 comparing pregnant with nonpregnant women during the total study period, and before and during the period of Delta variant predominance, Jan 1, 2020 – Dec 25, 2021

	Risk Ratio (95					
	Total Study Period[b]		p-value of interaction term[c]	Pre-Delta Period[d]		Delta Perio
	Unadjusted	Adjusted[f]		Unadjusted	Adjusted[g]	Unadjusted
ICU Admission	2.72 (2.49-2.98)	2.53 (2.26-2.83)	0.0045	2.57 (2.31-2.86)	2.56 (2.29-2.87)	3.24 (2.72-3
Invasive Ventilation or ECMO	2.07 (1.72-2.49)	1.76 (1.39-2.22)	0.0613	1.91 (1.53-2.39)	1.82 (1.44-2.30)	2.51 (1.81-3
Death	1.30 (1.12-1.52)	1.11 (0.90-1.38)	<0.0001	0.99 (0.80-1.22)	1.10 (0.89-1.37)	1.95 (1.56-2

Abbreviations: ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit admission.

[a]Pregnant compared with nonpregnant referent group.

[b]Total study period includes cases with a clinical observance date, or Centers for Disease Control and Prevention receipt date when clinical observance date was not available, of January 1, 2020 through December 25, 2021.

[c]Interaction term between pregnancy status and time period (i.e., pre-Delta or Delta).

[d]Pre-Delta period includes cases with a clinical observance date or Centers for Disease Control and Prevention report received date, when clinical observance date was not available, of January 1, 2020 through June 26, 2021.

[e]Delta period includes cases with a clinical observance date or Centers for Disease Control and Prevention report received date, when clinical observance date was not available, of June 27, 2021 through December 25, 2021.

[f]Adjusted for age (in years), race and ethnicity, Delta period, presence of chronic lung disease, cardiovascular disease, diabetes, and severe obesity, and interaction term between pregnancy and Delta period.

[g]Adjusted for age (in years), race and ethnicity, and presence of chronic lung disease, cardiovascular disease (including hypertension), diabetes, and severe obesity (body mass index ≥40 kg/m^2).

Table 4. Risk ratios for severe COVID-19 outcomes comparing the period of Delta variant predominance with the period before Delta variant predominance, by pregnancy status

	Risk Ratio (95% Confidence Interval)[a]			
	Pregnant		Nonpregnant	
	Unadjusted	Adjusted[b]	Unadjusted	Adjusted[b]
ICU Admission	1.29 (1.07-1.56)	1.41 (1.17-1.69)	1.03 (0.95-1.11)	1.09 (1.00-1.18)
Invasive Ventilation or ECMO	1.64 (1.13-2.37)	1.83 (1.26-2.65)	1.25 (1.09-1.44)	1.34 (1.17-1.54)
Death	3.21 (2.39-4.31)	3.33 (2.48-4.46)	1.62 (1.49-1.78)	1.62 (1.49-1.77)

Abbreviations: ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit admission.

[a]Delta period compared with pre-Delta referent period. The pre-Delta period includes cases with a clinical observance date or Centers for Disease Control and Prevention report received date, when clinical observance date was not available, of January 1, 2020 through June 26, 2021. The Delta period includes cases with a clinical observance date or Centers for Disease Control and Prevention report received date of June 27, 2021 through December 25, 2021.

[b]Adjusted for age (in years), race and ethnicity, and presence of chronic lung disease, cardiovascular disease (including hypertension), diabetes, and severe obesity (body mass index ≥40 kg/m^2).

FIGURE LEGENDS

Figure 1. Symptoms of women 15-44 years with laboratory-confirmed SARS-CoV-2 infection by pregnancy status, Jan 1, 2020 – Dec 25, 2021

Note. Fever includes subjective or >100.4^{o}F. Pre-Delta period includes cases with a clinical observance date or Centers for Disease Control and Prevention report received date, when clinical observance date was not available, of January 1, 2020 through June 26, 2021. Delta period includes cases with a clinical observance date or Centers for Disease Control and Prevention report received date, when clinical observance date was not available, of June 27, 2021 through December 25, 2021.

Supplemental Figure. Flow chart describing inclusion of symptomatic women aged 15-44 with laboratory-confirmed SARS-CoV-2 infections by pregnancy status, United States, Jan 1, 2020 – Dec 25, 2021

[a]SET-NET, Surveillance for Emerging Threats to Mothers and Babies Network

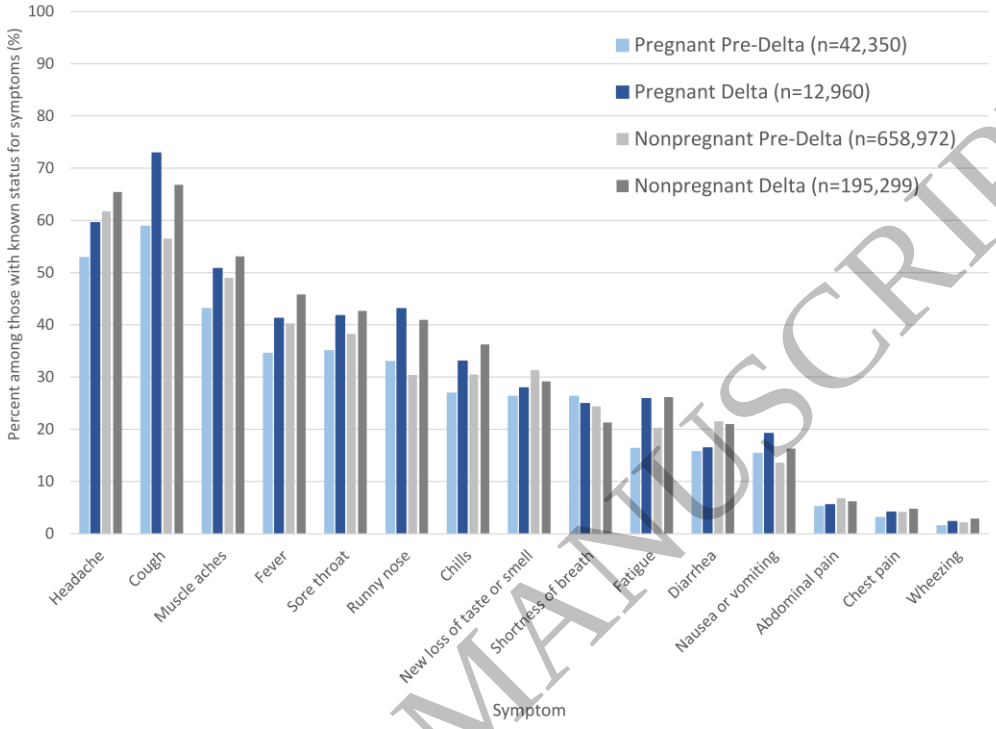

Figure 1
165x128 mm (.62 x DPI)