

COVID-19 Severity among Women of Reproductive Age with Symptomatic Laboratory-Confirmed SARS-CoV-2 by Pregnancy Status – United States, Jan 1, 2020 – Sep 30, 2021

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Abstract

Importance: Pregnant people are at increased risk for severe COVID-19 compared with nonpregnant people. Limited information is available on the severity of COVID-19 attributable to the Delta variant, the predominant variant in the United States as of late June 2021, among pregnant persons.

Objective: To assess risk for severe COVID-19 by pregnancy status and time period relative to Delta variant predominance.

Design: Using a cross-sectional design, we describe characteristics of symptomatic women of reproductive age (WRA) with COVID-19 and calculate adjusted risk ratios for severe disease comparing pregnant with nonpregnant WRA during the pre-Delta period (January 1, 2020 – June 26, 2021) and the Delta period (June 27, 2021 – September 30, 2021). Additionally, we calculate adjusted risk ratios for severe disease comparing the Delta period with the pre-Delta period for pregnant and nonpregnant WRA.

Setting: Reports of COVID-19 in the United States occurring from January 1, 2020 – September 30, 2021, submitted to the CDC.

Participants: Pregnant and nonpregnant women aged 15-44 years.

Exposure(s): Laboratory-confirmed, symptomatic SARS-CoV-2 infection.

Main Outcome(s): Severe disease: (intensive care unit [ICU] admission, receipt of invasive ventilation or extracorporeal membrane oxygenation [ECMO], and death).

Results: Among 1,856,428 cases of symptomatic COVID-19 in WRA, the risk for severe disease was increased among pregnant compared with nonpregnant WRA during the pre-Delta and Delta periods. Compared with the pre-Delta period, the risk of ICU admission during the Delta period was 66% higher (adjusted risk ratio [aRR] 1.66, 95% CI: 1.34-2.06) for pregnant WRA and 23% higher (aRR 1.23, 95% CI: 1.12-1.35) for nonpregnant WRA. The risk of invasive ventilation or ECMO was higher for pregnant and nonpregnant WRA in the Delta period. During the Delta period, the risk of death was 3.40 (95% CI: 2.36-4.91) times the risk in the pre-Delta period among pregnant WRA and 1.96 (95% CI: 1.75-2.18) among nonpregnant WRA.

Conclusions and Relevance: The overall risk for severe COVID-19 among WRA remains low; however, symptomatic pregnant WRA remain at increased risk for severe outcomes compared with symptomatic nonpregnant WRA during Delta variant predominance. Compared with the pre-Delta period, pregnant and nonpregnant WRA are at increased risk for severe COVID-19 in the Delta period.

Key Points

Question: Does severity of COVID-19 among symptomatic women of reproductive age (WRA) differ by pregnancy status and time period relative to Delta variant predominance?

Findings: Pregnant WRA with symptomatic laboratory-confirmed SARS-CoV-2 infection are at increased risk for intensive care unit (ICU) admission and death compared with symptomatic nonpregnant WRA. Compared with pre-Delta predominance, the risk for ICU admission is increased among symptomatic pregnant and nonpregnant WRA during Delta predominance.

Meaning: The overall risk for severe disease from SARS-CoV-2 among WRA remains low; however, measures to prevent infection are especially important for groups at higher risk for severe illness, including pregnant people.

Introduction

Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).¹ Identified in 2019,² SARS-CoV-2 is now responsible for a global pandemic.³ Variants of SARS-CoV-2 have emerged since the start of the pandemic including the highly transmissible Delta (B.1.617.2) variant.⁴ Since June 27, 2021, SARS-CoV-2 infections in the United States were predominately attributed to the Delta variant.⁵ Reports suggest the Delta variant may be associated with more severe disease and death compared with the alpha (B.1.1.7) variant in the general population.^{6,7} This is of particular concern for individuals already at increased risk for severe disease due to underlying medical conditions or pregnancy.⁸

Data regarding Delta variant SARS-CoV-2 infections among pregnant people in the United States have been limited to studies at single institutions.⁹⁻¹¹ It has been suggested that rates of severe-critical disease^{10,11} and adverse perinatal outcomes appear to be increased in

the period of Delta variant predominance compared with the pre-Delta period, though reports have been limited by study size.¹¹ Larger studies are needed to determine level of risk for severe outcomes for pregnant people during the period of Delta variant predominance in the United States, and to understand how the risk compares to nonpregnant people.

As of October 26, 2021, more than 36 million cases of SARS-CoV-2 infections have been reported to the CDC through COVID-19 national case reports. 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 and time period relative to Delta variant predominance.

Methods

Using a cross-sectional design, 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, by pregnancy status. We included laboratory-confirmed¹² SARS-CoV-2 infections reported to the Centers for Disease Control and Prevention (CDC) by October 26, 2021 through the National Notifiable Disease Surveillance System or data collection resources offered through CDC's COVID-19 emergency response.¹ The study period includes reports with a clinical observance date or CDC report received date, when clinical observance date was not available, of January 1, 2020 to September 30, 2021, and excluded reports with a death date before January 20, 2020. The pre-Delta period is defined as January 1, 2020 to June 26, 2021 while the Delta period is defined as June 27, 2021 to September 30, 2021, corresponding to Delta variant predominance in the United States.⁵ Given the missingness of the pregnancy status variable on COVID-19 case reports, we supplemented information on pregnancy status 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.¹³ 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 fields and the other underlying conditions fields of the COVID-19 case reports. Our analysis was limited to symptomatic WRA with laboratory-confirmed SARS-CoV-2 infections with known pregnancy status. Symptomatic cases were those where the 'symptomatic' field was selected on the COVID-19 case reports or where any specific symptom was marked "Yes".

Descriptive

In this study, we described the age, race and ethnicity, presence of symptoms, and underlying medical conditions of included participants by pregnancy status and time period relative to Delta variant predominance. Age was collapsed into three groups, 15-24, 25-34, and 35-44 years. We combined race and ethnicity into a single variable. Persons 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, persons of Hispanic or Latino ethnicity and any race, except AI/AN and NH/PI were identified. Those with reported ethnicity of non-Hispanic, or unknown or no reported ethnicity, were grouped by reported race: Asian, Black, White, and multiple or other race.^{14,15} Finally, those with an unknown or not reported race and did not have Hispanic ethnicity reported were categorized as unknown. Known status for symptoms and medical conditions was established by a "Yes" or "No" in the COVID-19 case reports for any 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, chills, shortness of breath, fatigue, diarrhea, new loss of taste or smell, runny nose, 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/m²), autoimmune disorder, chronic renal disease, chronic liver disease, and other chronic disease.

Outcomes

We described three outcomes 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-19¹⁶ (i.e., diabetes,¹⁷ cardiovascular disease,¹⁸ chronic lung disease,¹⁹ and severe obesity^{16,20}), stratified by pregnancy status and time period relative to Delta variant predominance.

Models

Similar to methods previously described,²¹ we calculated risk ratios and their 95% confidence intervals 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 (in years), race and ethnicity, and presence of diabetes, cardiovascular disease, chronic lung disease, and severe obesity, unless otherwise specified. When an adjusted model did not converge due to small

numbers, an exact Poisson regression was performed to determine the covariate least associated with the outcome, and that covariate was removed from the model to achieve convergence. When examining risk by pregnancy status, pregnant WRA were compared with nonpregnant WRA as the referent group for the total study period, and for the 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 group.

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

As of October 26, 2021, the CDC received more than 8.2 million reports of laboratory-confirmed SARS-CoV-2 infections among women aged 15-44 years from 56 jurisdictions. More than 7.9 million had a clinical infection date or were reported during the study period (January 1, 2020 – September 30, 2021). Ten jurisdictions had <1% completeness of pregnancy status, including four jurisdictions that did not report pregnancy status. Overall, 26.6% of reports had a known pregnancy status (135,980 were pregnant and 1,980,239 were nonpregnant). We linked 27,619 SET-NET cases from 16 participating jurisdictions to COVID-19 case reports by jurisdiction and a unique identifier, updating pregnancy status for 10,769 (37.0%) linked cases. Pregnancy status on the COVID-19 case reports was misclassified for 3.4% of linked cases and unknown or not reported for 35.6% of linked cases. Searching free-text fields, pregnancy status was updated to “Yes” for 148 reports. After linkage and data cleaning, there were 146,897 pregnant WRA and 1,979,286 nonpregnant WRA reports during the study period. Limiting to symptomatic COVID-19, our final analytic sample was 1,856,428 WRA. (Supplemental Figure)

Among 104,345 symptomatic pregnant WRA with laboratory-confirmed SARS-CoV-2 infection (Table 1), the majority were 25-34 years (57.9%) and non-Hispanic White (40.2%). Among the 35.1% of pregnant WRA with known status for any symptom, the five most common symptoms were cough (61.1%), headache (53.2%), muscle aches (44.5%), sore throat (36.2%), and fever (34.3%). Among the 20.6% of pregnant WRA with known status for underlying medical conditions, the five most common conditions were chronic lung disease (9.7%), other chronic condition (8.5%), diabetes (5.9%), cardiovascular disease (5.3%), and severe obesity (4.9%). The pre-Delta period included 89,435 pregnant WRA and the Delta period included 14,910 pregnant WRA. The distributions of symptoms and underlying conditions in pregnant WRA were similar between periods.

Table 1

Symptomatic women aged 15-44 years with laboratory-confirmed SARS-CoV-2 infection by pregnancy status, total study period, and before and during the period of Delta variant predominance, United States, Jan 1, 2020 – Sep 30, 2021

Characteristic	No. (%)							
	Pregnant			Nonpregnant			All symptomatic women, 15-44 years	
	Total Study Period ^a	Pre-Delta Period ^b	Delta Period ^c	Total Study Period ^a	Pre-Delta Period ^b	Delta Period ^c		Total Study Period ^a
	(n=104,345)	(n=89,435)	(n=14,910)	(n=1,752,083)	(n=1,491,870)	(n=260,213)		(N=1,856,428)
Age group (years)								
15-24	25,789 (24.7)	22,025 (24.6)	3,764 (25.2)	589,284 (33.6)	505,789 (33.9)	83,495 (32.1)	615,073 (33.1)	
25-34	60,400 (57.9)	51,925 (58.1)	8,475 (56.8)	593,640 (33.9)	504,568 (33.8)	89,072 (34.2)	654,040 (35.2)	
35-44	18,156 (17.4)	15,485 (17.3)	2,671 (17.9)	569,159 (32.5)	481,513 (32.3)	87,646 (33.7)	587,315 (31.6)	
Race and Ethnicity^d								
Hispanic or Latino	34,498 (33.1)	31,012 (34.7)	3,486 (23.4)	472,031 (26.9)	420,015 (28.2)	52,016 (20.0)	506,529 (27.3)	
American Indian or Alaska Native	1,302 (1.2)	1,070 (1.2)	232 (1.6)	22,395 (1.3)	18,678 (1.3)	3,717 (1.4)	23,697 (1.3)	
Asian, non-Hispanic	3,109 (3.0)	2,765 (3.1)	344 (2.3)	49,456 (2.8)	43,454 (2.9)	6,002 (2.3)	52,565 (2.8)	
Black, non-Hispanic	12,507 (12.0)	10,305 (11.5)	2,202 (14.8)	219,679 (12.5)	178,851 (12.0)	40,828 (15.7)	232,186 (12.5)	
Native Hawaiian or Pacific Islander	582 (0.6)	510 (0.6)	72 (0.5)	7,828 (0.4)	6,635 (0.4)	1,193 (0.5)	8,410 (0.5)	
White, non-Hispanic	41,925 (40.2)	34,837 (39.0)	7,088 (47.5)	799,657 (45.6)	671,250 (45.0)	128,407 (49.3)	841,582 (45.3)	
Multiple or other race, non-Hispanic	5,978 (5.7)	5,127 (5.7)	851 (5.7)	101,615 (5.8)	87,976 (5.9)	13,639 (5.2)	107,593 (5.8)	
Unknown or not reported	4,444 (4.3)	3,809 (4.3)	635 (4.3)	79,422 (4.5)	65,011 (4.4)	14,411 (5.5)	83,866 (4.5)	
Symptoms reported								
Known status for symptoms	36,638 (35.1)	31,146 (34.8)	5,492 (36.8)	642,810 (36.7)	539,836 (36.2)	102,974 (39.6)	679,448 (36.6)	
Headache	19,493 (53.2)	16,166 (51.9)	3,327 (60.6)	379,203 (59.0)	319,035 (59.1)	60,168 (58.4)	398,696 (58.7)	
Cough	22,401 (61.1)	18,330 (58.9)	4,071 (74.1)	357,709 (55.6)	297,480 (55.1)	60,229 (58.5)	380,110 (55.9)	
Muscle aches	16,295 (44.5)	13,396 (43.0)	2,899 (52.8)	306,382 (47.7)	256,620 (47.5)	49,762 (48.3)	322,677 (47.5)	
Fever ^e	12,572 (34.3)	10,309 (33.1)	2,263 (41.2)	248,165 (38.6)	206,519 (38.3)	41,646 (40.4)	260,737 (38.4)	
Sore throat	13,246 (36.2)	10,947 (35.1)	2,299 (41.9)	240,253 (37.4)	202,048 (37.4)	38,205 (37.1)	253,499 (37.3)	
Chills	10,027 (27.4)	8,179 (26.3)	1,848 (33.6)	190,129 (29.6)	157,211 (29.1)	32,918 (32.0)	200,156 (29.5)	

Characteristic	No. (%)						
	Pregnant			Nonpregnant			All symptomatic women, 15-44 years
	Total Study Period ^a	Pre-Delta Period ^b	Delta Period ^c	Total Study Period ^a	Pre-Delta Period ^b	Delta Period ^c	
	(n=104,345)	(n=89,435)	(n=14,910)	(n=1,752,083)	(n=1,491,870)	(n=260,213)	(N=1,856,428)
Shortness of breath	10,056 (27.4)	8,507 (27.3)	1,549 (28.2)	154,153 (24.0)	133,779 (24.8)	20,374 (19.8)	164,209 (24.2)
Fatigue	8,997 (24.6)	7,208 (23.1)	1,789 (32.6)	155,042 (24.1)	127,265 (23.6)	27,777 (27.0)	164,039 (24.1)
Runny nose	9,201 (25.1)	7,439 (23.9)	1,762 (32.1)	142,933 (22.2)	116,701 (21.6)	26,232 (25.5)	152,134 (22.4)
Diarrhea	6,105 (16.7)	5,034 (16.2)	1,071 (19.5)	137,095 (21.3)	115,917 (21.5)	21,178 (20.6)	143,200 (21.1)
New loss of taste or smell	8,292 (22.6)	6,858 (22.0)	1,434 (26.1)	134,006 (20.8)	112,985 (20.9)	21,021 (20.4)	142,298 (20.9)
Nausea or vomiting	9,097 (24.8)	7,497 (24.1)	1,600 (29.1)	124,954 (19.4)	103,631 (19.2)	21,323 (20.7)	134,051 (19.7)
Abdominal pain	3,098 (8.5)	2,584 (8.3)	514 (9.4)	59,599 (9.3)	50,750 (9.4)	8,849 (8.6)	62,697 (9.2)
Chest pain	1,699 (4.6)	1,381 (4.4)	318 (5.8)	32,146 (5.0)	26,373 (4.9)	5,773 (5.6)	33,845 (5.0)
Wheezing	841 (2.3)	666 (2.1)	175 (3.2)	17,150 (2.7)	13,714 (2.5)	3,436 (3.3)	17,991 (2.6)
Underlying medical condition							
Known underlying medical condition status	21,497 (20.6)	18,348 (20.5)	3,149 (21.1)	435,874 (24.9)	363,021 (24.3)	72,853 (28.0)	457,371 (24.6)
Chronic lung disease	2,082 (9.7)	1,774 (9.7)	308 (9.8)	38,780 (8.9)	33,655 (9.3)	5,125 (7.0)	40,862 (8.9)
Cardiovascular disease ^f	1,143 (5.3)	995 (5.4)	148 (4.7)	27,597 (6.3)	23,670 (6.5)	3,927 (5.4)	28,740 (6.3)
Diabetes	1,261 (5.9)	1,113 (6.1)	148 (4.7)	20,144 (4.6)	17,664 (4.9)	2,480 (3.4)	21,405 (4.7)
Immunocompromised condition	496 (2.3)	416 (2.3)	80 (2.5)	9,935 (2.3)	8,480 (2.3)	1,455 (2.0)	10,431 (2.3)
Severe obesity (BMI \geq 40 kg/m ²)	1,049 (4.9)	935 (5.1)	114 (3.6)	5,566 (1.3)	4,891 (1.3)	675 (0.9)	6,615 (1.4)
Autoimmune disorder	198 (0.9)	157 (0.9)	41 (1.3)	4,557 (1.0)	3,671 (1.0)	886 (1.2)	4,755 (1.0)
Chronic renal disease	87 (0.4)	78 (0.4)	9 (0.3)	2,633 (0.6)	2,240 (0.6)	393 (0.5)	2,720 (0.6)
Chronic liver disease	77 (0.4)	55 (0.3)	22 (0.7)	1,526 (0.4)	1,305 (0.4)	221 (0.3)	1,603 (0.4)
Other chronic disease	1,831 (8.5)	1,608 (8.8)	223 (7.1)	29,403 (6.7)	24,659 (6.8)	4,744 (6.5)	31,234 (6.8)

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.

^aTotal study 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 Jan 1, 2020 through Sep 30, 2021.

^bPre-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 Jan 1, 2020 through Jun 26, 2021.

^cDelta 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 Jun 27, 2021 through Sep 30, 2021.

^dNon-Hispanic includes unknown and not reported ethnicity.

^eFever includes subjective or >100.4F.

^fCardiovascular disease includes hypertension.

Among 1,752,083 symptomatic nonpregnant WRA with laboratory-confirmed SARS-CoV-2 infection, the majority were 25-34 years (33.9%) and non-Hispanic White (45.6%). Among the 36.7% of nonpregnant WRA with known status for any symptom, the five most common symptoms were headache (59.0%), cough (55.6%), muscle aches (47.7%), fever (38.6%), and sore throat (37.4%). Among 24.9% of nonpregnant WRA with known status for underlying medical conditions, the five most common conditions were chronic lung disease (8.9%), other chronic condition (6.7%), cardiovascular disease (6.3%), diabetes (4.6%), and immunocompromised condition (2.3%). The pre-Delta period included 1,491,870 nonpregnant WRA and the Delta period included 260,213 nonpregnant WRA. The distributions of symptoms and underlying conditions in nonpregnant WRA were similar between periods. (Table 1)

Among pregnant WRA, 0.55% (n=570) experienced ICU admission, 0.13% (n=138) experienced invasive ventilation or ECMO, and 0.14% (n=144) died. In the pre-Delta period, 0.11% (n=94) of pregnant WRA died, while 0.34% (n=50) of pregnant WRA in the Delta period died. Among nonpregnant WRA, 0.21% (n=3,737) experienced ICU admission (n=3,737), 0.07% (n=1,245) received invasive ventilation or ECMO, and 0.11% (n=1,878) died. In the pre-Delta period, 0.09% (n=1,400) of nonpregnant WRA died, while 0.18% (n=478) of nonpregnant WRA in the Delta period died. (Table 2)

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, total study period, and before and during the period of Delta variant predominance, overall and by select characteristics, United States, Jan 1, 2020 – Sep 30, 2021

	No. (%)					
	Pregnant			Nonpregnant		
	Total Study Period ^a	Pre-Delta Period ^b	Delta Period ^c	Total Study Period ^a	Pre-Delta Period ^b	Delta Period ^c
	(n=104,345)	(n=89,435)	(n=14,910)	(n=1,752,083)	(n=1,491,870)	(n=260,213)
ICU Admission						
All	570 (0.55)	455 (0.51)	115 (0.77)	3,737 (0.21)	3,115 (0.21)	622 (0.24)
Age group (years)						
15-24	96 (16.84)	83 (18.24)	13 (11.30)	609 (16.30)	510 (16.37)	99 (15.92)
25-34	317 (55.61)	252 (55.38)	65 (56.52)	1,134 (30.35)	936 (30.05)	198 (31.83)
35-44	157 (27.54)	120 (26.37)	37 (32.17)	1,994 (53.36)	1,669 (53.58)	325 (52.25)
Race and Ethnicity						
Hispanic or Latino, any race	221 (38.77)	200 (43.96)	21 (18.26)	1,146 (30.67)	1,021 (32.78)	125 (20.10)
American Indian or Alaska Native	3 (0.53)	NR	NR	78 (2.09)	69 (2.22)	9 (1.45)
Asian, non-Hispanic	50 (8.77)	39 (8.57)	11 (9.57)	145 (3.88)	128 (4.11)	17 (2.73)
Black, non-Hispanic	99 (17.37)	74 (16.26)	25 (21.74)	801 (21.43)	653 (20.96)	148 (23.79)
Native Hawaiian or Pacific Islander	14 (2.46)	NR	NR	66 (1.77)	50 (1.61)	16 (2.57)
White, non-Hispanic	135 (23.68)	95 (20.88)	40 (34.78)	1,246 (33.34)	989 (31.75)	257 (41.32)
Multiple or other race, non-Hispanic	33 (5.79)	22 (4.84)	11 (9.57)	156 (4.17)	123 (3.95)	33 (5.31)
Unknown or not reported	15 (2.63)	NR	NR	99 (2.65)	82 (2.63)	17 (2.73)
Underlying health conditions						
Diabetes	59 (10.35)	47 (10.33)	12 (10.43)	620 (16.59)	547 (17.56)	73 (11.74)
Cardiovascular disease ^f	32 (5.61)	25 (5.49)	7 (6.09)	501 (13.41)	438 (14.06)	63 (10.13)
Chronic lung disease	41 (7.19)	32 (7.03)	9 (7.83)	406 (10.86)	362 (11.62)	44 (7.07)
Severe obesity (BMI \geq 40 kg/m ²)	28 (4.91)	23 (5.05)	5 (4.35)	237 (6.34)	201 (6.45)	36 (5.79)
Invasive Ventilation or ECMO						
All	138 (0.13)	111 (0.12)	27 (0.18)	1,245 (0.07)	1,013 (0.07)	232 (0.09)
Age group (years)						
15-24	27 (19.57)	20 (18.02)	7 (25.93)	200 (16.06)	176 (17.37)	24 (10.34)
25-34	64 (46.38)	53 (47.75)	11 (40.74)	365 (29.32)	282 (27.84)	83 (35.78)
35-44	47 (34.06)	38 (34.23)	9 (33.33)	680 (54.62)	555 (54.79)	125 (53.88)
Race and Ethnicity						

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

	No. (%)					
Hispanic or Latino, any race	52 (37.68)	NR	NR	345 (27.71)	306 (30.21)	39 (16.81)
American Indian or Alaska Native	1 (0.72)	NR	NR	27 (2.17)	NR	NR
Asian, non-Hispanic	8 (5.80)	NR	NR	37 (2.97)	NR	NR
Black, non-Hispanic	26 (18.84)	NR	NR	267 (21.45)	206 (20.34)	61 (26.29)
Native Hawaiian or Pacific Islander	5 (3.62)	NR	NR	32 (2.57)	23 (2.27)	9 (3.88)
White, non-Hispanic	34 (24.64)	24 (21.62)	10 (37.04)	435 (34.94)	339 (33.46)	96 (41.38)
Multiple or other race, non-Hispanic	7 (5.07)	NR	NR	42 (3.37)	30 (2.96)	12 (5.17)
Unknown or not reported	5 (3.62)	NR	NR	60 (4.82)	49 (4.84)	11 (4.74)
Underlying health conditions						
Diabetes	24 (17.39)	18 (16.22)	6 (22.22)	238 (19.12)	202 (19.94)	36 (15.52)
Cardiovascular disease ^d	13 (9.42)	NR	NR	209 (16.79)	172 (16.98)	37 (15.95)
Chronic lung disease	14 (10.14)	NR	NR	170 (13.65)	141 (13.92)	29 (12.50)
Severe obesity (BMI \geq 40 kg/m ²)	11 (7.97)	NR	NR	114 (9.16)	88 (8.69)	26 (11.21)
Death						
All	144 (0.14)	94 (0.11)	50 (0.34)	1,878 (0.11)	1,400 (0.09)	478 (0.18)
Age group (years)						
15-24	15 (10.42)	10 (10.64)	5 (10.00)	231 (12.30)	194 (13.86)	37 (7.74)
25-34	78 (54.17)	51 (54.26)	27 (54.00)	515 (27.42)	378 (27.00)	137 (28.66)
35-44	51 (35.42)	33 (35.11)	18 (36.00)	1,132 (60.28)	828 (59.14)	304 (63.60)
Race and Ethnicity						
Hispanic or Latino, any race	50 (34.72)	43 (45.74)	7 (14.00)	405 (21.57)	343 (24.50)	62 (12.97)
American Indian or Alaska Native	4 (2.78)	NR	NR	70 (3.73)	56 (4.00)	14 (2.93)
Asian, non-Hispanic	9 (6.25)	NR	NR	42 (2.24)	33 (2.36)	9 (1.88)
Black, non-Hispanic	29 (20.14)	20 (21.28)	9 (18.00)	545 (29.02)	394 (28.14)	151 (31.59)
Native Hawaiian or Pacific Islander	5 (3.47)	NR	NR	25 (1.33)	15 (1.07)	10 (2.09)
White, non-Hispanic	35 (24.31)	16 (17.02)	19 (38.00)	678 (36.10)	467 (33.36)	211 (44.14)
Multiple or other race, non-Hispanic	8 (5.56)	NR	NR	75 (3.99)	61 (4.36)	14 (2.93)
Unknown or not reported	4 (2.78)	NR	NR	38 (2.02)	31 (2.21)	7 (1.46)
Underlying health conditions						
Diabetes	17 (11.81)	11 (11.70)	6 (12.00)	210 (11.18)	158 (11.29)	52 (10.88)
Cardiovascular disease ^d	13 (9.03)	NR	NR	225 (11.98)	172 (12.29)	53 (11.09)

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

	No. (%)					
Chronic lung disease	7 (4.86)	NR	NR	104 (5.54)	86 (6.14)	18 (3.77)
Severe obesity (BMI \geq 40 kg/m ²)	2 (1.39)	NR	NR	89 (4.74)	63 (4.50)	26 (5.44)
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.

^aTotal study 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 Jan 1, 2020 through Sep 30, 2021.

^bPre-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 Jan 1, 2020 through Jun 26, 2021.

^cDelta 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 Jun 27, 2021 through Sep 30, 2021.

^dCardiovascular disease includes hypertension.

For the total study period, the adjusted RRs (aRRs) for severe outcomes comparing pregnant WRA with nonpregnant WRA were the following: ICU admission (aRR 2.60 [95% CI: 2.35-2.88]), receipt of invasive ventilation or ECMO (aRR 1.86 [95% CI: 1.51-2.30]), and death (aRR 1.51 [95% CI: 1.25-1.82]). The supplemental table describes the risk ratios for pregnant WRA compared with nonpregnant WRA by age, race and ethnicity, and underlying medical conditions 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 2.46 (95% CI 2.19-2.76) versus 3.35 (95% CI 2.69-4.17) 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 2.06 (95% CI: 1.31-3.23) for pregnant WRA compared with nonpregnant WRA. Comparing pregnant WRA to nonpregnant WRA the aRR for death in the pre-Delta period was 1.28 (95% CI: 1.02-1.63) and during the Delta period 2.21 (95% CI: 1.61-3.04). (Table 3)

Table 3

Risk ratios for severe COVID-19 outcomes among symptomatic women aged 15-44 years with laboratory-confirmed SARS-CoV-2 infection comparing pregnant with nonpregnant women during the total study period, and before and during the period of Delta variant predominance, United States, Jan 1, 2020 – Sep 30, 2021

Risk Ratio (95% Confidence Interval) ^a						
	Total Study Period ^b		Pre-Delta Period ^c		Delta Period ^d	
	Unadjusted	Adjusted ^e	Unadjusted	Adjusted ^e	Unadjusted	Adjusted ^e
ICU Admission	2.56 (2.32-2.83)	2.60 (2.35-2.88)	2.44 (2.18-2.72)	2.46 (2.19-2.76)	3.23 (2.61-3.99)	3.35 (2.69-4.17)
Invasive Ventilation or ECMO	1.86 (1.52-2.28)	1.86 (1.51-2.30)	1.83 (1.45-2.30)	1.82 (1.44-2.30)	2.03 (1.32-3.12)	2.06 (1.31-3.23)
Death	1.29 (1.07-1.55)	1.51 (1.25-1.82)	1.12 (0.89-1.41)	1.28 (1.02-1.63)	1.83 (1.34-2.48)	2.21 (1.61-3.04)
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 report received date, when clinical observance date was not available, of Jan 1, 2020 through Sep 30, 2021.						
^c 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 Jan 1, 2020 through Jun 26, 2021.						
^d 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 Jun 27, 2021 through Sep 30, 2021.						
^e Adjusted for age (in years), race and ethnicity, and presence of diabetes, cardiovascular disease, chronic lung disease, and severe obesity.						

Among pregnant WRA, the risk of ICU admission was 66% higher (aRR 1.66, 95% CI: 1.34-2.06) in the Delta period compared with the pre-Delta period for pregnant WRA and 23% higher (aRR 1.23, 95% CI: 1.12-1.35) for nonpregnant WRA. The risk of invasive ventilation or ECMO was 63% higher (aRR 1.63, 95% CI: 1.03-2.59) for pregnant WRA and 41% higher (aRR 1.41, 95% CI: 1.20 – 1.67) for nonpregnant WRA, in the Delta period. During the Delta period, the risk of death was 3.40 (95% CI: 2.36-4.91) times the risk in the pre-Delta period among pregnant WRA and 1.96 (95% CI: 1.75-2.18) among nonpregnant WRA. (Table 4)

Table 4

Risk ratios for severe COVID-19 outcomes among symptomatic women aged 15-44 years with laboratory-confirmed SARS-CoV-2 infection comparing the period of Delta variant predominance with the period before Delta variant predominance, by pregnancy status, United States, Jan 1, 2020 – Sep 30, 2021

	Risk Ratio (95% Confidence Interval) ^a			
	Pregnant		Nonpregnant	
	Unadjusted	Adjusted ^b	Unadjusted	Adjusted ^b
ICU Admission	1.51 (1.22-1.89)	1.66 (1.34-2.06)	1.14 (1.04-1.26)	1.23 (1.12-1.35)
Invasive Ventilation or ECMO	1.46 (0.92-2.31)	1.63 (1.03-2.59)	1.31 (1.11-1.55)	1.41 (1.20-1.67)
Death	3.19 (2.21-4.61)	3.40 (2.36-4.91)	1.96 (1.76-2.18)	1.96 (1.75-2.18)
Abbreviations: ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit admission.				
^a Delta period compared with pre-Delta referent period. The 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 Jun 27, 2021 through Sep 30, 2021. 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 Jan 1, 2020 through Jun 26, 2021.				
^b Adjusted for age (in years), race and ethnicity, and presence of diabetes, cardiovascular disease, chronic lung disease, and severe obesity.				

Discussion

Our analysis provides an overview of the severity of COVID-19 cases among symptomatic WRA in the United States before and after Delta variant predominance. During our total study period, pregnant WRA were at higher risk for ICU admission, receipt of invasive ventilation or ECMO, and death compared with nonpregnant WRA. Consistent with case surveillance reports from the pre-Delta period,^{21,22} the absolute risk for severe illness from COVID-19 remains low among pregnant WRA. The aRRs for severe outcomes were higher in the Delta period than the pre-Delta period when comparing pregnant WRA with nonpregnant WRA, however the confidence intervals overlapped.

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.¹¹ 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.¹⁰

This analysis benefits from use of the COVID-19 national case surveillance data providing a large sample size of individual COVID-19 reports including symptomatic pregnant WRA. These data are useful to describe overall trends observed. However, national reporting for COVID-19 is voluntary, and the data have limitations. Most cases are reported to CDC within 8 days of clinical observance (interquartile range 4-22), 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 al²³ 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 and removal of reports with an unknown or not reported pregnancy status from this analysis may result in greater statistical imprecision. COVID-19 national case surveillance data is subject to data entry errors, reporting errors, and lacks 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.²⁴ Our report does not include hospitalizations as an indicator for severe disease as the national case surveillance report does not differentiate hospitalizations solely for COVID-19 and hospitalizations solely for pregnancy related care. Reporting of race and ethnicity is not consistent across jurisdictions. We stratify this analysis by period respective to Delta variant predominance using date as a proxy because the COVID-19 national case surveillance data does not include genomic information. Therefore, our results may underestimate the risk in the Delta period as Delta cases, prior to nationwide Delta predominance, are captured in the pre-Delta period. 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 9 jurisdictions have reported this variable, and

among all WRA reported since April 2021, missingness is >93%, and among symptomatic WRA >88%. We were therefore unable to assess the role of vaccination in this analysis.

Precautions should be taken to prevent exposure to SARS-CoV-2, especially among groups at increased risk for severe COVID-19 such as symptomatic pregnant WRA. Preventing exposure can limit the transmission of COVID-19 which may slow the emergence of new variants.²⁵ 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.²⁶ The greatest risk for COVID-19 is currently among those unvaccinated. 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.²⁹ Accumulating data provide evidence of both the safety³⁰⁻³³ and effectiveness^{34,35} 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 surveillance data to understand the severity of disease during the pre-Delta and Delta periods for symptomatic WRA. The absolute risk for severe COVID-19 remains low among symptomatic WRA; however, pregnant WRA are at increased risk for severe disease compared with nonpregnant WRA and the risk of severe illness in pregnant and nonpregnant WRA has increased since June 27, 2021, when Delta became the predominant variant in the United States.

Declarations

Competing interests:

The authors declare no competing interests.

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