Risk factors for illness severity among pregnant women with confirmed SARS-CoV-2 infection – Surveillance for Emerging Threats to Mothers and Babies Network, 22 state, local, and territorial health departments, March 29, 2020 -March 5, 2021

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Summary: Among pregnant women with COVID-19, older age and underlying medical conditions were risk factors for increased illness severity. These findings can be used to inform pregnant women about their risk for severe COVID-19 illness and public health messaging.

Abstract

Background: Pregnant women with coronavirus disease 2019 (COVID-19) are at increased risk for severe illness compared with nonpregnant women. Data to assess risk factors for illness severity among pregnant women with COVID-19 are limited. This study aimed to determine risk factors associated with COVID-19 illness severity among pregnant women with SARS-CoV-2 infection.

Methods: Pregnant women with SARS-CoV-2 infection confirmed by molecular testing were reported during March 29, 2020–March 5, 2021 through the Surveillance for Emerging Threats to Mothers and Babies Network (SET-NET). Criteria for illness severity (asymptomatic, mild, moderate-to-severe, or critical) were adapted from National Institutes of Health and World Health Organization criteria. Crude and adjusted risk ratios for moderate-to-severe or critical COVID-19 illness were calculated for selected demographic and clinical characteristics.

Results: Among 7,950 pregnant women with SARS-CoV-2 infection, moderate-to-severe or critical COVID-19 illness was associated with age 25 years and older, healthcare occupation, pre-pregnancy obesity, chronic lung disease, chronic hypertension, and pregestational diabetes mellitus. Risk of moderate-to-severe or critical illness increased with the number of underlying medical or pregnancy-related conditions.

Conclusions: Older age and having underlying medical conditions were associated with increased risk of moderate-to-severe or critical COVID-19 illness among pregnant women. This information might help pregnant women understand their risk for moderate-to-severe or critical COVID-19 illness and inform targeted public health messaging.

Keywords: SARS-CoV-2, COVID-19, pregnancy, illness severity, risk factors

Introduction

Pregnant women with coronavirus disease 2019 (COVID-19) are at increased risk for severe illness compared with nonpregnant women [1]. A limited number of studies have suggested that risk factors for severe COVID-19 illness, such as older age and underlying medical conditions, might be similar between pregnant and non-pregnant people; however, individual studies have been limited in sample size, varied in sampling frame and inclusion criteria (e.g., inclusion of women with suspected COVID-19 and/or those with confirmed COVID-19), and primarily reported on pregnant women requiring hospitalization (including for childbirth) [2-4]. Additional information on risk factors for severe COVID-19 illness are needed to inform discussions about risk for severe illness, to guide public health messaging and to inform decision-making around resource allocation.

Public health jurisdictions report information, including pregnancy status, on confirmed and probable COVID-19 cases to CDC through the National Notifiable Diseases Surveillance System [5]. Through the Surveillance for Emerging Threats to Mothers and Babies Network (SET-NET), health departments from 22 jurisdictions collected supplementary information on pregnancy outcomes among women with SARS-CoV-2 infection confirmed by nucleic acid amplification testing and reported during March 29, 2020–March 5, 2021 [6]. To determine risk factors associated with COVID-19 illness severity, demographic and selected clinical characteristics were compared between pregnant women with moderate-to-severe or critical illness and those with asymptomatic infection or mild illness.

Materials and Methods

SET-NET is longitudinal surveillance of pregnant women and their infants to understand the effects of emerging and reemerging threats [6]. Supplementary pregnancy-related information is reported for women with laboratory confirmed SARS-CoV-2 infection (based on detection of SARS-CoV-2 in a clinical specimen by nucleic acid amplification testing) during pregnancy through the day of delivery in 2020 [7]. As of March 5, 2021, health departments from

22 jurisdictions (California [excluding Los Angeles County], Georgia, Houston, Kansas, Los Angeles County, Maryland, Massachusetts, Michigan, Minnesota, Nebraska, Nevada, New Jersey, New York [excluding New York City], North Dakota, Oklahoma, Pennsylvania [excluding Philadelphia], Philadelphia, Puerto Rico, Tennessee, U.S. Virgin Islands, Vermont, and Washington) have contributed data [6]. Pregnancy status was ascertained through routine COVID-19 case surveillance or through matching of reported cases with other sources (e.g., vital records, administrative data) to identify unreported pregnancy status or verify pregnancy status. Data were abstracted using standard data elements; sources include routine public health investigations, vital records, laboratory reports, and medical records. SET-NET methodology has been previously described [6]. Data submitted to SET-NET are reviewed for data quality errors (e.g., out of range dates), and feedback is shared with jurisdictions on cases that do not meet inclusion criteria and on cases with potential data issues for selected variables (e.g., date of first positive PCR test).

Criteria for illness severity (asymptomatic, mild, moderate-to-severe, or critical) were adapted from National Institutes of Health and World Health Organization severity of illness categories (Figure) [8-9]. Women were considered asymptomatic if reported as having an absence of symptoms using a symptom status variable. Criteria were applied to classify severity using submitted data (including symptoms, intensive care unit (ICU) admission, invasive ventilation, use of COVID-19 therapies, complications associated with COVID-19, and death). If data were not reported for an outcome, the outcome was assumed not to have occurred. Crude risk ratios (RR) for moderate-to-severe or critical illness were calculated for selected demographic characteristics within age group, race/ethnicity, health insurance type, healthcare worker status and selected clinical characteristics, including diagnosis of underlying medical condition (pre-pregnancy obesity [body mass index ≥30 kg/m^2], chronic lung disease, chronic hypertension, pregestational diabetes mellitus, cardiovascular disease, and immunosuppression), trimester of SARS-CoV-2 infection, and diagnosis of pregnancy-related condition (gestational diabetes and

gestational hypertension) as reported through contact tracing, vital statistics, or medical records, compared to selected referent groups [6]. Calculations for gestational diabetes and gestational hypertension were restricted to women with SARS-CoV-2 infection at 20 weeks of gestation or later, as these pregnancy-related conditions are typically not diagnosed until later trimesters of pregnancy. We also calculated crude risk ratios comparing risk of moderate-to-severe or critical illness among pregnant women with any one condition (underlying medical or pregnancy-related condition), any two conditions, and three or more conditions compared to those without report of any condition. Adjusted risk ratios (aRR) and 95% CIs for moderate-to-severe or critical illness were estimated by binomial regression with the log link function, accounting for age (in years) as a continuous variable. Analyses were conducted using SAS (version 9.4; SAS Institute). This activity was reviewed by CDC, determined to be a non-research, public health surveillance activity, and was conducted consistent with applicable federal law and CDC policy [10].

Results

During March 29, 2020–March 5, 2021, data for 16,695 pregnant women with confirmed SARS-CoV-2 infection were submitted to SET-NET. Data for 8,745 (52.4%) women were insufficient for categorizing illness severity. The remainder of this report focuses on 7,950 (47.6%) pregnant women with SARS-CoV-2 infection and sufficient information to categorize illness severity.

Most women were aged 20-39 years (91.2%), 42.0% were Hispanic or Latina (Hispanic) ethnicity, and 54.5% had Medicaid (Table 1). At least one underlying medical condition was reported for 2,545 (36.4%) women, with pre-pregnancy obesity (28.2%) most commonly reported. Gestational diabetes was reported in 10.6% of women and gestational hypertension in 10.8%. Most women had SARS-CoV-2 infection identified in the third (57.9%) or second (29.0%) trimester (based on date of first positive test or symptom onset).

In crude analyses, pregnant women who were 25-29 years (RR=1.32, 95% CI: 1.02, 1.71), 30-34 years (RR=1.43, 95% CI: 1.10, 1.85), 35-39 years (RR=1.53, 95% CI: 1.16, 2.00), and 40

years of age and older (RR=1.66, 95% CI: 1.19, 2.32) were at an increased risk of moderate-to-severe or critical illness compared to pregnant women who were <20 years of age. Pregnant women who reported other health insurance (RR: 0.62, 95% CI: 0.42, 0.92) were at a decreased risk of moderate-to-severe or critical illness compared to pregnant women with private health insurance. Pregnant women reported as having a healthcare occupation (RR=1.25, 95% CI: 1.11, 1.41) were at an increased risk of moderate-to-severe or critical illness compared to pregnant women who were not reported as being in a healthcare occupation. Pregnant women with pre-pregnancy obesity (RR=1.36, 95% CI: 1.23, 1.51), chronic lung disease (RR=1.37, 95% CI: 1.18, 1.59), chronic hypertension (RR=1.45, 95% CI: 1.20, 1.76), and pregestational diabetes mellitus (RR=1.66, 95% CI: 1.35, 2.06) were at increased risk of moderate-to-severe or critical illness compared to pregnant women without these conditions.

Presence of any health condition (underlying medical or pregnancy-related health condition) was associated with 39% increased risk (RR=1.39, 95% CI: 1.26, 1.53), two conditions was associated with a 59% increased risk (RR=1.59, 95% CI: 1.37, 1.84), and three or more conditions was associated with more than twice the risk (RR=2.31, 95% CI: 1.84, 2.90) of moderate-to-severe or critical illness compared to women without any reported conditions. Race/ethnicity, trimester of SARS-CoV-2 infection, cardiovascular disease, immunosuppression, gestational diabetes, and gestational hypertension were not associated with increased risk of moderate-to-severe or critical illness compared to the referent groups.

Adjusted risk ratios were similar to crude risk ratios with one exception. After adjustment for age as a continuous variable, other health insurance was not found to be associated with a decreased risk of moderate-to-severe or critical illness compared to the referent group (Private health insurance).

Discussion

In an analysis of a large cohort of pregnant women with SARS-CoV-2 infection reported from health departments from 22 jurisdictions through SET-NET, age 25 years and older, being a

healthcare worker, and presence of any underlying medical condition were associated with increased risk of moderate-to-severe or critical illness. The number of underlying medical or pregnancy-related conditions demonstrated an exposure-response relation with risk for moderate-to-severe or critical illness. Data collection is ongoing, and findings may change as additional data are collected and analyzed. Data are reported by health departments and can be updated as new information becomes available. Enhanced efforts to improve reporting of clinical data related to illness severity are ongoing.

These findings of association between older age, healthcare occupation, any underlying medical condition and increased risk of moderate-to-severe or critical COVID-19 illness are similar to those observed among nonpregnant adults. There have been few studies focused on risk factors for COVID-19 illness severity in pregnant women; those study findings suggest similar associations with older age and medical comorbidities as seen in the general adult population [2-4]. In this analysis, approximately half of pregnant women with moderate-to-severe or critical illness had no reported underlying medical conditions, which reinforces the importance of preventive measures, including vaccination, for pregnant women. An association was not found with trimester of SARS-CoV-2 infection, similar to findings from a recent systematic review and meta-analysis of SARS-CoV-2 infection in pregnancy [4]. An association of Hispanic or Latina race/ethnicity with moderate-to-severe or critical illness was not identified; however, Hispanic or Latina women represented half of all women with moderate-to-severe or critical illness in this analysis.

In this analysis an association was observed between occupation as a healthcare worker and increased risk of moderate-to-severe or critical COVID-19 illness. Data from a large cohort study demonstrated that relative to non-essential workers, healthcare workers had a higher risk of severe COVID-19 illness [11]. By contrast, at least two systematic reviews which included data from China, Italy, and the U.S. found that healthcare workers were at decreased risk of more severe illness [12-13]. Infection control training, PPE use, and handwashing were associated with

decreased risk. Certain exposures (such as involvement in intubations, direct patient contact, or contact with bodily secretions) were associated with increased infection risk. Considerations for assessing healthcare worker risk of severe disease include overall younger age of healthcare workers, lower prevalence of comorbidities, and potentially increased accessibility to healthcare systems and better knowledge of disease processes. Women of reproductive age make up a large portion of the healthcare workforce, especially in nursing and healthcare support roles, which have frequent, close contact with patients and work in settings that might increase their risk for acquiring SARS-CoV-2. A recent report noted that among healthcare workers with COVID-19, 79% of cases were in women. Health care support workers accounted for the largest overall group of occupation types (32%), and nurses constituted the largest single occupation type (30%) [14].

The findings in this report are subject to at least five limitations. First, this analysis was limited to pregnant women with SARS-CoV-2 infection confirmed by nucleic acid testing and does not include women diagnosed with non-PCR-based tests, such as antigen testing performed in an outpatient setting, and may lead to an under-ascertainment of milder cases. Second, the clinical criteria for classifying illness severity in this analysis were adapted for surveillance purposes from existing frameworks and used severity indicators that were captured systematically, while other criteria may not have been captured (e.g., respiratory rate and oxygen saturation on room air). Misclassification of illness severity is possible, particularly when data to classify cases into moderate-to-severe or critical illness categories are missing, which might bias towards a lower severity classification and attenuate associations [15]. Similarly, data cannot distinguish between asymptomatic, subclinical, or pre-symptomatic mild infection unless the individual subsequently reported for medical care and information was available in a medical record. Additionally, women who were tested upon hospital admission for delivery may have developed more severe symptoms later on that were not captured by SET-NET. Among women with date of testing and outcome available, 21% were identified within two days of delivery,

which could reflect universal screening on admission. Third, a large portion of women could not be categorized for illness severity due to insufficient information, and testing and reporting might be more frequent among women with more severe illness. Differences in case ascertainment (e.g., asymptomatic infection detected via universal screening vs testing and reporting of more severe cases of illness) challenge interpretation of the overall distribution of illness severity. The ability to detect differences in demographic characteristics between included and excluded women were limited by a large portion of missing demographic information among excluded cases due to the large surge of cases and limited capacity for complete data collection. Additionally, obtaining accurate data to distinguish underlying medical conditions from pregnancy-related medical conditions (e.g., diabetes vs gestational diabetes) depends on medical record abstraction. Potential misclassification of underlying medical conditions and pregnancy-related medical conditions might limit detection of an association with moderate-to-severe or critical illness. Medical record abstraction of clinical information are ongoing, and statistical comparisons by illness severity should be interpreted with caution. Fourth, while these data are population-based for the jurisdictions included, they are not nationally representative and include a higher frequency of Hispanic and Latina women compared with all women of reproductive age in national case surveillance data and with provisional national 2020 data on births among women with COVID-19 during pregnancy [1, 16-17]. Fifth, relative to the proportion of women with SARS-CoV-2 infection in the second and third trimesters of pregnancy, few women with first trimester infection have been reported to date. This limits our ability to understand whether trimester of infection is associated with severity of COVID-19 illness.

Despite these limitations, this report has several strengths, including the large size of the population-based cohort, inclusion of both hospitalized and non-hospitalized pregnant women, restriction of the study population to pregnant women with confirmed COVID-19, information to describe risk factors for illness severity among pregnant women with COVID-19, and uniform application of illness severity criteria.

Future research could further focus on clinical relevance of maternal COVID-19 illness severity and outcomes among newborns, infants, and children. Additional follow-up data on SARS-CoV-2 infection are needed to increase certainty of findings related to severity of COVID-19 illness and timing of infection during pregnancy.

These data can help counsel pregnant women about their risk for moderate-to-severe or critical COVID-19 illness and guide their choice of prevention strategies, target public health messaging, and inform decisions around resource allocation. It is important that pregnant women are informed of their increased risk for severe COVID-19 illness, the signs of severe COVID-19 illness, and strategies for prevention, including vaccination [18-20].

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References

1. Zambrano LD, Ellington S, Strid P, et al. Update: Characteristics of Symptomatic Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status — United States, January 22–October 3, 2020. MMWR Morb Mortal Wkly Rep, **2020**; 69:1641–1647.
2. Di Martino D, Chiaffarino F, Patanè L, et al. Assessing risk factors for severe forms of COVID-19 in a pregnant population: A clinical series from Lombardy, Italy. Int J Gynaecol Obstet. Epub ahead of print. October 24, 2020 [cited 2021 Feb 16] Available from: doi: 10.1002/ijgo.13435.
3. Brandt JS, Hill J, Reddy A, et al. Epidemiology of coronavirus disease 2019 in pregnancy: risk factors and associations with adverse maternal and neonatal outcomes. Am J Obstet Gynecol. Epub ahead of print. September 25, 2020 [cited 2021 Feb 16] Available from: doi: 10.1016/j.ajog.2020.09.043.
4. Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. BMJ, **2020**; 370:m3320.
5. Centers for Disease Control and Prevention – National Center for Immunization and Respiratory Diseases – Information for Health Departments on Reporting Cases of COVID-19. Available from: https://www.cdc.gov/coronavirus/2019-ncov/php/reporting-pui.html. Accessed December 21, 2020.
6. Woodworth KR, Reynolds MR, Burkel V, et al. A Preparedness Model for Mother–Baby Linked Longitudinal Surveillance for Emerging Threats. Matern Child Health J, **2021** Jan 4:1–9.
7. Centers for Disease Control and Prevention – Office of Public Health Scientific Services – Coronavirus Disease 2019 (COVID-19) 2020 Interim Case Definition, Approved

August 5, 2020; Available from: https://wwwn.cdc.gov/nndss/conditions/coronavirus-disease-2019-covid-19/case-definition/2020/08/05/. Accessed February 4, 2021.

8. National Institutes of Health – COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. Available from: https://www.covid19treatmentguidelines.nih.gov/. Accessed December 21, 2020.
9. World Health Organization – Clinical management of COVID-19: interim guidance. Available from: https://apps.who.int/iris/handle/10665/332196. Accessed December 21, 2020.
10. Department of Health and Human Services – 45 C.F.R. part 46, 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq. Available from: https://www.hhs.gov/ohrp/sites/default/files/ohrp/policy/ohrpregulations.pdf. Accessed February 4, 2021.
11. Mutambudzi M, Niedwiedz C, Macdonald EB, et al. Occupation and risk of severe COVID-19: prospective cohort study of 120 075 UK Biobank participants. Occup Environ Med, **2020** Dec 9:oemed-2020-106731. doi: 10.1136/oemed-2020-106731. Epub ahead of print. PMID: 33298533.
12. Chou R, Dana T, Buckley DI, Selph S, Fu R, Totten AM. Epidemiology of and Risk Factors for Coronavirus Infection in Health Care Workers: A Living Rapid Review. Ann Intern Med, **2020** Jul 21; 173(2):120-136. doi: 10.7326/M20-1632. Epub 2020 May 5. PMID: 32369541; PMCID: PMC7240841.
13. Sahu AK, Amrithanand VT, Mathew R, Aggarwal P, Nayer J, Bhoi S. COVID-19 in health care workers - A systematic review and meta-analysis. Am J Emerg Med, **2020** Sep; 38(9):1727-1731. doi: 10.1016/j.ajem.2020.05.113. Epub 2020 Jun 6. PMID: 32738467; PMCID: PMC7837172.
14. Hughes MM, Groenewold MR, Lessem SE, et al. Update: Characteristics of Health Care Personnel with COVID-19 — United States, February 12–July 16, 2020. MMWR Morb

Mortal Wkly Rep, **2020**; 69:1364–1368.

DOI: http://dx.doi.org/10.15585/mmwr.mm6938a3external icon.

15. Lipsitch M, Donnelly CA, Fraser C, et al. Potential biases in estimating absolute and relative case-fatality risks during outbreaks. PLoS Negl Trop Dis, **2015**; 9:e0003846.
16. Centers for Disease Control and Prevention – National Center for Health Statistics – Maternal and Infant Characteristics Among Women with Confirmed or Presumed Cases of Coronavirus Disease (COVID-19) During Pregnancy. Available from: https://www.cdc.gov/nchs/covid19/technical-linkage.htm. Accessed December 21, 2020.
17. Ellington S, Strid P, Tong VT, et al. Characteristics of women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status—United States, January 22–June 7, 2020. MMWR Morb Mortal Wkly Rep, **2020**; 69:769–75.
18. Centers for Disease Control and Prevention – National Center for Immunization and Respiratory Diseases – Symptoms of Coronavirus. Available from: https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html. Accessed December 21, 2020.
19. Centers for Disease Control and Prevention – National Center for Immunization and Respiratory Diseases – Pregnancy, Breastfeeding, and Caring for Newborns. Available from: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/pregnancy-breastfeeding.html/. Accessed February 8, 2021.
20. Centers for Disease Control and Prevention – National Center for Immunization and Respiratory Diseases – Interim Clinical Considerations for Use of mRNA COVID-19 Vaccines Currently Authorized in the United States. Available from: https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fvaccines%

2Fcovid-19%2Finfo-by-product%2Fpfizer%2Fclinical-considerations.html. Accessed February 1, 2020.

Table 1. Risk ratios for moderate-to-severe or critical illness among pregnant women with SARS-CoV-2 infection during pregnancy compared to asymptomatic infection or mild illness for selected demographic and clinical characteristics, Surveillance for Emerging Threats to Mothers and Babies Network, 22 state, local, and territorial health departments, March 29, 2020 -March 5, 2021 (n=7,950)[a]

	No. of women (%) [Total no. of women with available information]						
	Total	Moderate-to-severe or critical illness	Asymptomatic infection or mild illness	Crude Risk Ratio	95% CI	Adjusted Risk Ratio	95% CI
Total	7,950 [6273]	1,659 (20.9) [1316]	6,291 (79.1) [4957]				
Age							
<20	348 (5.6)	55 (4.2)	293 (5.9)	1	ref.	-	-
20-24	1271 (20.3)	222 (16.9)	1049 (21.2)	1.11	(0.84, 1.45)	-	-
25-29	1898 (30.3)	396 (30.1)	1502 (30.3)	**1.32**	**(1.02, 1.71)**	-	-
30-34	1683 (26.8)	380 (28.9)	1303 (26.3)	**1.43**	**(1.10, 1.85)**	**-**	**-**
35-39	867 (13.8)	209 (15.9)	658 (13.3)	**1.53**	**(1.16, 2.00)**	**-**	**-**
40 +	206 (3.3)	54 (4.1)	152 (3.1)	**1.66**	**(1.19, 2.32)**	-	-
Race/ethnicity	[6891]	[1452]	[5439]				

White, Non-Hispanic	2355 (34.2)	513 (35.3)	1842 (33.9)	1	ref.	1	ref.
Asian, Non-Hispanic	257 (3.7)	62 (4.3)	195 (3.6)	1.11	(0.88, 1.39)	1.07	(0.83, 1.39)
Black, Non-Hispanic	1157 (16.8)	235 (16.2)	922 (17.0)	0.93	(0.81, 1.07)	1.00	(0.86, 1.17)
Hispanic or Latina	2893 (42.0)	601 (41.4)	2292 (42.1)	0.95	(0.86, 1.06)	0.91	(0.81, 1.02)
Multiple or other, Non-Hispanic	229 (3.3)	41 (2.8)	188 (3.5)	0.82	(0.62, 1.10)	1.04	(0.77, 1.40)
Health insurance	[5012]	[1132]	[3880]				
Private	2035 (40.6)	465 (41.1)	1570 (40.5)	1	ref.	1	ref.
Medicaid	2730 (54.5)	625 (55.2)	2105 (54.3)	1.00	(0.90, 1.11)	1.05	(0.93, 1.19)
Other	156 (3.1)	22 (1.9)	134 (3.5)	**0.62**	**(0.42, 0.92)**	0.70	(0.47, 1.05)
Self-pay/none	91 (1.8)	20 (1.8)	71 (1.8)	0.96	(0.65, 1.43)	0.97	(0.65, 1.46)
Healthcare occupation	[4206]	[985]	[3221]				
No	3188 (75.8)	704 (71.5)	2484 (77.1)	1	ref.	1	ref.
Yes	1018 (24.2	281 (28.5)	737 (22.9)	**1.25**	**(1.11, 1.41)**	**1.23**	**(1.08,**

	)						**1.39)**
Trimester of SARS-CoV-2 infection[c]	[7394]	[1578]	[5816]				
First	967 (13.1)	206 (13.1)	761 (13.1)	1	ref.	1	ref.
Second	2145 (29.0)	523 (33.1)	1622 (27.9)	1.14	(0.99, 1.32)	1.16	(0.98, 1.38)
Third	4282 (57.9)	849 (53.8)	3433 (59.0)	0.93	(0.81, 1.07)	1.00	(0.85, 1.17)
Underlying medical condition[d]	[6998]	[1469]	[5529]				
Any underlying medical condition	2545 (36.4)	684 (46.6)	1861 (33.7)	**1.52**	**(1.39, 1.67)**	**1.57**	**(1.42, 1.74)**
Obesity[e]	1974 (28.2)	512 (34.9)	1462 (26.4)	**1.36**	**(1.23, 1.51)**	**1.33**	**(1.19, 1.49)**
Chronic lung disease	443 (6.3)	144 (9.8)	299 (5.4)	**1.37**	**(1.18, 1.59)**	**1.41**	**(1.20, 1.65)**
Chronic hypertension	247 (3.5)	78 (5.3)	169 (3.1)	**1.45**	**(1.20, 1.76)**	**1.40**	**(1.14, 1.71)**
Diabetes mellitus (type 1 or type 2)	161 (2.3)	58 (4.0)	103 (1.9)	**1.66**	**(1.35, 2.06)**	**1.57**	**(1.25, 1.97)**
Cardiovascular disease	125 (1.8)	38 (2.6)	87 (1.6)	1.29	(0.98, 1.69)	1.21	(0.91,

							1.61)
Immunosuppression	60 (.9)	17 (1.2)	43 (.8)	1.36	(0.90, 2.04)	1.32	(0.87, 1.99)
Pregnancy-related condition[d]	[3168]	[689]	[2479]				
Gestational diabetes	336 (10.6)	78 (11.3)	258 (10.4)	1.08	(0.88, 1.33)	0.95	(0.76, 1.20)
Gestational hypertension	341 (10.8)	84 (12.2)	257 (10.4)	1.15	(0.94, 1.40)	1.05	(0.84, 1.31)
Number of conditions[f]	[7074]	[1487]	[5587]				
None	4224 (59.7)	748 (50.3)	3476 (62.2)	1	ref.	1	ref.
Any 1 condition	2181 (30.8)	536 (36.1)	1645 (29.4)	**1.39**	**(1.26, 1.53)**	**1.41**	**(1.27, 1.58)**
Any 2 conditions	554 (7.8)	156 (10.5)	398 (7.1)	**1.59**	**(1.37, 1.84)**	**1.51**	**(1.28, 1.78)**
Any 3 or more conditions	115 (1.6)	47 (3.2)	68 (1.2)	**2.31**	**(1.84, 2.90)**	**2.11**	**(1.63, 2.73)**

[a]During March 29, 2020–March 5, 2021, data for 16,695 pregnant women with SARS-CoV-2 infection were submitted to SET-NET. Data for 8,745 (52.4%) women were insufficient for categorizing severity of illness.

[b]Adjusted for age as a continuous variable.

[c]Trimester of SARS-CoV-2 infection based on date of first positive test or symptom onset.

[d]Referent group: pregnant women without report of underlying medical condition or pregnancy-related condition, respectively.

[e]Pregestational obesity defined as body mass index ≥30 kg/m^2.

[f]Includes underlying medical conditions (pre-pregnancy obesity, chronic lung disease, chronic hypertension, diabetes mellitus (type 1 or type 2), cardiovascular disease and immunosuppression) and pregnancy-related conditions (gestational diabetes and gestational hypertension).

Figure Legend

Criteria for categorizing severity of illness among pregnant women with SARS-CoV-2 infection, Surveillance for Emerging Threats to Mothers and Babies Network (SET-NET) Abbreviations: ARDS = acute respiratory distress syndrome, ECMO = extracorporeal membrane oxygenation, ICU= intensive care unit

[a]Adapted from National Institutes of Health https://www.covid19treatmentguidelines.nih.gov/overview/clinical-spectrum/ and World Health Organization https://www.who.int/publications/i/item/clinical-management-of-covid-19.

[b]Data considered in classification included systematically collected indicators of illness severity. A search was performed to identify informative clinical data in free text notes; however, free text notes are not routinely collected and are often missing. Ability to distinguish moderate and severe illness is limited by data which are not routinely collected and highly likely to be missing from free text notes: respiratory rate, blood oxygen saturation on room air.

[c]Limitations: persons with mild symptoms may not seek medical care. Unless a case interview was performed, we will not have information on mild symptoms.

[d]Limitations include inability to distinguish between asymptomatic or pre-symptomatic mild infection unless the individual reported for medical care and information was available in a medical record.

[e]Response options for symptom status include (symptomatic, asymptomatic, and unknown). https://www.cdc.gov/coronavirus/2019-ncov/downloads/pui-form.pdf.

Figure 1

Severity of Illness	Description of the surveillance categorization of severity of COVID-19 illness among pregnant women[a]
Critical	Defined as reported with complication of COVID-19: mechanical ventilation/intubation, ECMO, ICU admission, ARDS, respiratory failure, septic shock, or multiple organ dysfunction; COVID-19 listed as a cause of death
Moderate-to-Severe[b]	Defined as reported with any of the following, and not meeting criteria for critical illness: • Symptoms of dyspnea/shortness of breath AND at least one of the following: fever or cough. • Receipt of oxygen therapy by nasal cannula or a high-flow oxygen device, pneumonia • Treatment for COVID-19 with remdesivir, convalescent plasma, hydroxychloroquine + azithromycin, hydroxychloroquine alone. Additional treatments may be included as evidence of disease severity, referring to NIH treatment guidelines.
Mild[c]	Defined as symptomatic illness with at least one of the individual symptoms reported, and not meeting criteria for moderate-to-severe or critical illness
Asymptomatic infection[d]	Defined as reported as asymptomatic[e] (not just absence of reported symptoms) and not meeting criteria for mild, moderate-to-severe, or critical illness
Insufficient information	Defined as missing information needed to categorize into asymptomatic infection, mild, moderate-to-severe, or critical illness