Factors Associated with Hospitalization with Symptomatic COVID-19 Illness Among Pregnant Individuals: A Multi-Center Retrospective Cohort Study

Running Title: COVID-19 Hospitalization in Pregnancy

Carmen Sofia Arriola[1], De-Kun Li[2], Flor Muñoz[3], Michael Daugherty[1], Caroline Doughty-Skierski[3], Sascha Ellington[1], Jeannette Ferber[2], Nickolas Ferguson[4], Mara Greenberg[2], Louise Hadden[4], Jillian T. Henderson[5], Stephanie A. Irving[5], Mary Juergens[4], Venkatesh Kancharla[3], Allison L. Naleway[5], Gabriella Newes-Adeyi[4], Erin Nicholson[3], Roxana Odouli[1], Lawrence Reichle[4], Mo Sanyang[3], Fatimah S. Dawood[1]

(1) Centers for Disease Control and Prevention, Atlanta, Georgia, USA
(2) Kaiser Permanente Northern California, Oakland, California, USA
(3) Baylor College of Medicine, Houston, Texas, USA
(4) Abt Associates, Rockville, Maryland, USA
(5) Center for Health Research, Kaiser Permanente Northwest, Portland, Oregon, USA

Corresponding Author: Carmen Sofia Arriola, Influenza Division, Centers for Disease Control and Prevention, 1600 Clifton Rd MS A-32, Atlanta, GA 30329, United States; telephone: (404) 718-4589; fax (404) 639-3866; email: wus3@cdc.gov.

Alternate Corresponding Author: Fatimah Dawood, Influenza Division, Centers for Disease Control and Prevention, 1600 Clifton Rd MS A-32, Atlanta, GA 30329, United States; telephone: (404) 639-0431; fax (404) 639-3866; email: hgj0@cdc.gov.

Disclaimers: The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the US Centers for Disease Control and Prevention.

Potential Conflicts of Interest: Allison Naleway received research funding from Pfizer and Vir Biotechnology for unrelated studies. All other authors report no potential conflicts.

Abstract

Background: Pregnant individuals are at increased risk of COVID-19 hospitalization and death, and primary and booster COVID-19 vaccination is recommended for this population.

Methods: Among a cohort of pregnant individuals who received prenatal care at three healthcare systems in the United States, we estimated the cumulative incidence of hospitalization with symptomatic COVID-19 illness. We also identified factors associated with COVID-19 hospitalization using a multivariable Cox proportional-hazards model with pregnancy weeks as the timescale and a time-varying adjustor that accounted for SARS-CoV-2 circulation; model covariates included site, age, race, ethnicity, insurance status, pre-pregnancy weight status, and selected underlying medical conditions. Data were collected primarily through medical record extraction.

Results: Among 19,456 pregnant individuals with an estimated due date March 1, 2020-February 28, 2021, 75 (0.4%) were hospitalized with symptomatic COVID-19. Factors associated with hospitalization for symptomatic COVID-19 were Hispanic ethnicity (aHR: 2.7; 95% CI: 1.3,5.5), native Hawaiian or Pacific Islander race (aHR: 12; 95% CI: 3.2,45.5), age <25 years (aHR: 3.1; 95% CI: 1.3,7.6), pre-pregnancy obesity (aHR: 2.1; 95% CI: 1.1,3.9), diagnosis of a metabolic disorder (aHR: 2.2; 95% CI: 1.2,3.8), lung disease excluding asthma (aHR: 49; 95% CI: 28,84) and cardiovascular disease (aHR: 2.6; 95% CI: 1.5,4.7).

Conclusion: Although hospitalization with symptomatic COVID-19 was uncommon, pregnant individuals should be aware of risk factors associated with severe illness when considering COVID-19 vaccination.

Background

Accumulating data suggest that pregnant individuals are at increased risk for hospitalization, critical illness, and death associated with SARS-CoV-2 infection [1, 2]. SARS-CoV-2 infection during pregnancy may also increase the risk of selected adverse pregnancy outcomes [3-7]. The American College of Obstetricians and Gynecologists and the Centers for Disease Control and Prevention (CDC) recommend primary and booster COVID-19 vaccination for all pregnant individuals [8, 9]. Identifying risk factors for severe COVID-19 illness during pregnancy would provide valuable information to inform counseling and risk communication for pregnant individuals. To date, studies assessing risk factors for severe COVID-19 have largely been cross-sectional, and/or have been limited to single center studies. These studies used varying approaches to differentiate SARS-CoV-2-associated severe disease from incidental detection of SARS-CoV-2 infection identified by routine screening. They reported older maternal age, racial and ethnic minority groups, pre-pregnancy obesity, and pre-pregnancy chronic medical conditions including asthma as potential risk factors for severe SARS-CoV-2 infection [2, 10-15]. Using electronic medical record data from a retrospective cohort of nearly 20,000 pregnant individuals receiving prenatal care in three healthcare systems in the United States, we estimate the cumulative incidence of hospitalization with symptomatic COVID-19 among pregnant individuals. We also identify factors associated with COVID-19 hospitalizations among the hospitalized cohort.

Methods

Retrospective Cohort Design and Data Collection

A retrospective cohort of pregnant individuals was identified using electronic medical records (EMR) from three health systems in the United States: Kaiser Permanente Northern California (KPNC) in California, Kaiser Permanente Northwest (KPNW) in Oregon and Washington, and Baylor in Texas (see Supplemental Methods for additional details about study sites). Pregnant individuals aged 12 to 50 years were included in the cohort if they had an estimated delivery date (EDD) between March 1, 2020 and February 28, 2021 and at least one prenatal care outpatient or telemedicine visit within the health system from December 1, 2019, through February 28, 2021.

A standardized data dictionary was used to capture EMR data about individuals' demographic and social characteristics, pre-pregnancy body mass index (BMI (kg/m2), by categories: underweight BMI<18.5 or healthy weight BMI 18.5-24.9, overweight BMI 25-29.9, obese BMI ≥30), underlying medical conditions, prenatal care, hospitalizations, pregnancy complications, SARS-CoV-2 testing, and birth outcomes. Race and ethnicity were extracted from electronic medical records based on individuals' self-report. ICD-10 discharge diagnosis codes were also captured from hospitalizations to identify those associated with acute respiratory infection or febrile illness (ARFI). ARFI discharge codes (appendix 2) have been used in previous studies assessing influenza vaccine effectiveness against influenza-associated hospitalizations during pregnancy to identify hospitalizations for acute illness likely to be associated with respiratory viral infection, as opposed to those in which respiratory viral infection might have been identified incidentally based on hospital screening practices [16, 17]. SARS-CoV-2 infections were identified from results of clinician-ordered real-time reverse transcriptase-polymerase chain reaction assay (rRT-PCR) up to 3 days prior to admission. Data about the clinical course of hospitalization were abstracted for any individual hospitalized with an ARFI code.

Analytic Definitions and Methods

A hospitalization with symptomatic COVID-19 was defined as a hospitalization with a positive SARS-CoV-2 test and an ARFI ICD-10 discharge code. Hospitalizations with symptomatic COVID-19 may or may not include delivery hospitalizations. We calculated the risk of being hospitalized with symptomatic COVID-19 (cumulative incidence) by dividing the number of symptomatic COVID-19 hospitalizations by the total number of individuals captured in the cohort. We also calculated the frequency of symptomatic COVID-19 hospitalizations among the cohort stratified by selected demographic (race/ethnicity, age) and social characteristics (smoking, alcohol use during pregnancy), underlying medical conditions (having at least one medical condition from list on appendix 1, diabetes, metabolic disorders diagnosis not obesity, asthma, lung disease diagnosis excluding asthma, cardiovascular disorders (acute or chronic heart failure diagnosis, cardiac arrest diagnosis, and acute and non-acute heart disease diagnosis), immunosuppressive conditions, neurologic disorders and other chronic disease including cancer,

chronic renal and liver disease (See appendix 1 for ICD-10 codes), and factors associated with the course of pregnancy.

To identify factors associated with symptomatic COVID-19 hospitalization during pregnancy, we developed a Cox proportional-hazards regression model with a timescale of pregnancy weeks. Age, site, pre-pregnancy BMI, and metabolic, respiratory and cardiovascular disorders were chosen *a priori* for inclusion in the model based on data from the published literature suggesting a possible association between these factors and severe COVID-19 illness [2, 10, 11, 14, 18, 19]. Other potential risk factors were identified from univariate comparisons between individuals with and without symptomatic COVID-19 hospitalization with a significant association (p-value<0.05). Individuals with unknown/missing data for race, Medicaid coverage and pre-pregnancy BMI were excluded from this analysis. The model also included a time-varying covariate for high versus low SARS-CoV-2 circulation to adjust for risk of exposure during each week of pregnancy. High circulation weeks were those in which the weekly case count for a given health system's service areas was greater than the median number of cases per week during the study period. Service area case counts were derived from Health and Human Services (HHS) county-level surveillance data for the counties in each health system's service area [20]. Crude and adjusted Hazards Ratios (HR) with 95% confidence intervals (CIs) were estimated for associations between variables of interest and symptomatic COVID-19 hospitalization.

To characterize the clinical course of symptomatic COVID-19 hospitalizations, frequencies/descriptive statistics were calculated for hospital length of stay, gestational age at admission, pneumonia diagnosis (ICD-10 codes J12-J18 listed in discharge codes), receipt of remdesivir treatment, ICU admission, mechanical ventilation or extracorporeal membrane oxygenation, pregnancy complications/outcomes, and death. We performed all analyses in R (4.1.0 version).

Patient Consent Statement

This protocol was reviewed and approved by the Institutional Review Boards of participating sites; sites were granted waivers of informed consent. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.[§]

Results

The study population included 19,456 pregnant individuals with an EDD between March 1, 2020 and February 28, 2021. Demographic characteristics of the population are depicted in Table 1. The median gestational age at first prenatal care visit was 8 weeks (interquartile range (IQR) 6–12 weeks gestation) and 39 weeks at delivery or end of pregnancy (IQR 38–40 weeks). 55% of the study population had at least one underlying medical condition other than anemia. The most common medical conditions were metabolic disorders excluding obesity (14%), asthma (13%), and cardiovascular disorders (8%).

Among the 19,456 individuals in the study population, 10,067 (52%) had at least one hospitalization during pregnancy with testing for SARS-CoV-2; among them, 434 (4%) had a hospitalization with an ARFI discharge diagnosis code, of which 75 (17%) hospitalizations in 75 individuals included a positive test for SARS-CoV-2 and were thus identified as symptomatic COVID-19 hospitalizations. Among the 19,456 individuals in the study population, the cumulative incidence of symptomatic COVID-19 hospitalization was 0.4% (range by site 0.1-0.6%).

In the adjusted Cox proportional-hazard model (n=15,726), factors associated with symptomatic COVID-19 hospitalization included Hispanic ethnicity (aHR: 2.7; 95% CI: 1.3,5.7) or native Hawaiian or Pacific Islander race (aHR: 11; 95% CI: 2.2,50.4), age 18-24 years (aHR: 3.2; 95% CI: 1.3,7.8), pre-pregnancy obesity (aHR: 1.9; 95% CI: 1.002,3.5), metabolic disorders other than obesity (aHR: 1.9; 95% CI: 1.03,3.3), lung disease excluding asthma (aHR: 41.7; 95% CI: 23.5,73.9), and chronic cardiovascular disorders (aHR: 2.3; 95% CI: 1.2,4.4) (Table 2).

[§] See e.g., 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.

Among the 75 individuals hospitalized with symptomatic COVID-19 illness during pregnancy, the median gestational age at admission was 37 weeks (IQR 33-39 weeks) and all of these hospitalizations occurred during the third trimester (Table 3). Five hospitalizations occurred in individuals with a diagnosis of gestational diabetes and five in those with a pre-pregnancy diagnosis of arterial hypertension. During hospitalization, forty individuals had pneumonia, sixteen were admitted to the intensive care unit, one needed mechanical ventilation, and none needed extracorporeal membrane oxygenation. Twelve individuals received Remdesivir during the hospitalization. The median length of hospital stay was 3 days (IQR 2-5). Forty-nine of the 75 hospitalizations resulted in end of pregnancy during the hospitalization, including 36 (73%) term deliveries and 13 (27%) preterm deliveries at <37 weeks gestation (median gestational age of preterm deliveries 35.5, IQR 34-36.5). There were no stillbirths and no maternal deaths.

Discussion

Among 19,456 pregnant individuals, the cumulative incidence of symptomatic COVID-19 hospitalization was 0.4% indicating that roughly 1 in 250 pregnant individuals had a COVID-19 hospitalization. Estimates of the true community risk of COVID-19 hospitalization among pregnant individuals are scarce, but our findings are consistent with the few available published studies indicating that overall risk of hospitalization is low [15, 21, 22]. Nevertheless, we found that certain underlying medical conditions and pre-pregnancy obesity were strongly associated with an increased risk of COVID-19 hospitalization underscoring the added importance of COVID-19 vaccination. In addition, we found that Hispanic ethnicity and Native Hawaiian or Pacific Islander race were also associated with an increased risk of COVID-19 hospitalization even after adjustment for other factors in the multivariable analysis providing additional evidence of racial and ethnic disparities in COVID-19 health outcomes consistent with many previous reports [22-24].

The findings of this study related to underlying conditions are consistent with previous studies assessing risk factors for severe COVID-19 among pregnant individuals [1, 2, 11-13, 15, 25, 26]. Obesity is a condition widely recognized to be associated with severe COVID-19 in the general population [18], and this association also seems to be present among pregnant individuals [2, 10-

14]. Galang et al., in a study with a large population of pregnant individuals in the United States had similar findings, where women with obesity and chronic conditions including chronic cardiovascular and respiratory disorders were at higher risk of severe COVID-19 illness [14]. These findings support additional counseling about the importance of infection prevention measures, including COVID-19 vaccination, for pregnant individuals with these conditions.

The findings regarding race disparities may reflect an increased risk of SARS-CoV-2 infection and/or an increased risk of severe illness because of inequities in social determinants of health [27]. Multiple other studies have documented disproportionately higher rates of infection, hospitalization, and adverse outcomes among Hispanic populations in the United States [15, 28-30]. These findings highlight the importance of studies to identify social determinants that may increase risks for COVID-19 exposure and the risk for severe disease to further outreach to communities that have been disproportionately affected by COVID-19 to provide information about disease prevention.

Strengths of this study include the use of a large and defined multi-site study with standardized data captured from first antenatal visit to the end of pregnancy, and the use of acute respiratory and febrile illness ICD-10 codes [16, 17] to distinguish symptomatic COVID-19 hospitalizations from hospitalizations with incidental detection of SARS-CoV-2 by routine screening. However, this study also has several limitations. By limiting to EMR data, we may have missed information that was not collected in EMRs. Likewise, some demographic variables were not well captured by EMRs, resulting in high numbers of missing data. For instance, maternal education was missing in ~90% of the cohort. Missing data for variables such as race and ethnicity also pose a limitation for some comparisons. Furthermore, by using ICD-10 codes, this study may be subject to coding errors or missed information not provided by codes. We also acknowledge that SARS-CoV-2 infections were ascertained by clinical testing; however, from our data, 68% of symptomatic hospitalizations were tested for SARS-CoV-2. Factors associated with higher risk of symptomatic COVID-19-associated hospitalization identified in this analysis could reflect increased risk for infection itself and/or for having infection severe enough to

warrant testing and/or hospitalization. In addition, vaccination was not available for most of the study period so we were not able to include it in the analysis.

In conclusion, this study adds to the literature on risk factors for severe COVID-19 among pregnant individuals. Pregnant individuals living with chronic conditions such as obesity or chronic respiratory conditions other than asthma should be aware of the increased risk for more severe presentation of the disease if infected with SARS-CoV-2. This analysis also underscores the importance of COVID-19 vaccination to prevent severe COVID-19 disease among pregnant individuals.

Acknowledgments: The authors at KPNC thank Andrew K. Hirst for his help with programming and technical support. The authors thank Elizabeth Shuster (KPNW), Jan Van Marter (KPNW), Nanette Bond (Baylor), Patricia Santarcangelo (Baylor), Sarah Sharkey (CDC), Michael Duckworth (Abt), Peiyi Zhang (Abt).

Funding: This study was funded by the US Centers for Disease Control and Prevention through Contract # 75D30120C08150 with Abt Associates.

Table 1. Baseline characteristics of pregnant individuals enrolled and those hospitalized with symptomatic COVID-19, eESPI[ǂ] network

	Total cohort members (n=19,456)	Pregnant individuals hospitalized with symptomatic COVID-19 (n=75)
	n (col %)	n (row %)
Site		
A	5,460 (28)	8 (0.15)
B	5,996 (31)	35 (0.58)
C	8,000 (41)	32 (0.4)
Race/Ethnicity (mutually exclusive)		
Hispanic	5,380 (28)	44 (0.82)
White, Non-Hispanic	8,206 (42)	13 (0.16)
Black or African American, Non-Hispanic	1,974 (10)	6 (0.30)
American Indian or Alaska Native, Non-Hispanic	62 (0)	0 (0)
Asian, Non-Hispanic	3,010 (15)	9 (0.30)
Native Hawaiian or Pacific Islander, Non-Hispanic	148 (1)	3 (2)
Multi-race	316 (2)	0 (0)
Other	10 (0)	0 (0)
Unknown	350 (2)	0 (0)
Age at start of pregnancy (years)		
12 - 24	2,986(15)	22 (0.74)
25 - 34	11,344 (58)	44 (0.39)
>=35	5,126 (26)	9 (0.18)
Medicaid Coverage		
Yes	4,247 (22)	30 (0.71)
No	15,008 (77)	44 (0.29)
Unknown	201 (1)	1 (0.50)
Pregnancy singleton or multiple		
Singleton	18,300 (94)	72 (0.39)
Multiple	300 (2)	3 (1)
Unknown	856 (5)	0 (0)
Pre-pregnancy BMI[ǂ]		
Underweight, Normal or healthy weight	6,842 (35)	19 (0.28)
Overweight	4,588 (24)	17 (0.37)
Obese	4,584 (25)	29 (0.63)
Unknown	3,172 (16)	10 (0.32)
First pregnancy		
Yes	7,996 (41)	25 (0.31)
No	10,958 (56)	49 (.45)
Unknown	502 (3)	1 (0.20)
Gestational age at first antenatal care visit (weeks)		
Median (IQR)	8 (6-12)	8 (6-12)

Smoking during pregnancy		
Yes	1,200 (6)	4 (0.33)
No	17,975 (92)	70 (0.39)
Unknown	281 (1)	1 (0.36)
Alcohol use during pregnancy		
Yes	4,126 (21)	11 (0.27)
No	13,387 (69)	53 (0.40)
Unknown	1,943 (10)	11 (0.57)
Underlying medical conditions (at least one)*	10,750 (55)	55 (0.51)
Diabetes	431 (2)	2 (0.46)
Metabolic disorder diagnosis not obesity**	2,723 (14)	18 (0.66)
Asthma	2,602 (13)	15 (0.58)
Lung disease diagnosis excluding asthma***	250 (1)	24 (9.6)
Chronic cardiovascular disorders[§]	1,501 (8)	16 (1.07)
Immunosuppressive conditions	370 (2)	2 (0.54)
Neurologic disorders	530 (3)	0 (0)
Other chronic conditions[¥]	336 (2)	2 (0.60)

Note: [ŧ]Underweight/Normal or healthy weight (BMI <25), Overweight (BMI 25-29.9), Obese (BMI ≥30); *At least one condition identified from the following list: blood disorder diagnosis other than anemia, diabetes diagnosis, acute heart failure diagnosis, (acute or chronic) heart failure diagnosis, cardiac arrest diagnosis, acute heart disease diagnosis, non-acute heart disease diagnosis, cancer diagnosis, immune disorder diagnosis, acute renal failure diagnosis, (non-acute) renal failure diagnosis, acute liver failure diagnosis, (non0acute) liver failure diagnosis, (acute or chronic) liver disease diagnosis, asthma diagnosis, other chronic respiratory conditions excluding asthma, obesity diagnosis, severe (morbid) obesity diagnosis, other metabolic disorder diagnosis, altered mental status diagnosis, encephalopathy diagnosis, meningitis diagnosis, anoxic brain damage diagnosis, encephalitis or myelitis diagnosis, coma diagnosis, critical illness polyneuropathy diagnosis, cerebral infarction diagnosis, cerebral hemorrhage diagnosis, cerebral edema diagnosis, acute or chronic neurologic disease diagnosis, only acute neurologic disease diagnosis, arterial or venous embolism diagnosis, arterial or venous embolism diagnosis, acute gastrointestinal complications, acute hematological complications, pulmonary embolism diagnosis, carditis diagnosis, defibrination syndrome diagnosis, ketoacidosis diagnosis, hyperosmolarity diagnosis, diabetic coma diagnosis, thyroid storm diagnosis, rhabdomyolisis diagnosis, myositis diagnosis, critical illness myopathy diagnosis, history of gestational diabetes, pregnancy complicated by preexisting hypertension with or without preeclampsia, preeclampsia diagnosis during pregnancy or postpartum, with or without severe features, and including superimposed preeclampsia, preeclampsia with severe features, hellp syndrome, gestational hypertension (new onset) without proteinuria (Appendix 1);**ICD-10: E03-E07, E22, E23, E32, E27, E40-E46, E50-E56, E70-E72, E74, E78, E88, M10, E83, E75.2, E76, E77, E79, E80, E85, E89.1, E89.6, E01, E20, E21, E24, E25, E26, E28, E31, E34;*** ICD-10: A15, A17, A18, A19, A31, D86, E84, J40, J41, J42, J43, J47, J60, J61, J62.0, J62.8, J63.6, J64, J67, J68, J69.0, J69.1, J69.8, J70.9, J85, J93, J98, M34, M35, Q34, R09.1, A31.0, B39, B40,, B41, B44, B45, B46.0, D86.0, E88.01, J62, J63, J65, J66, J69, J70, J82, J84, J86, J95.0, J96, J98.1, J99, P25, P26, P27, P28, Q33, T86.8, J44; [§]Cardiovascular disorders include acute or chronic heart failure diagnosis, cardiac arrest diagnosis, and acute and non-acute heart disease diagnosis; [¥]Cancer, Chronic renal disease, Chronic liver disease; [ŧ]The Epidemiology of SARS-CoV-2 in Pregnancy and Infancy (ESPI) Network

Table 2. Risk factors associated with symptomatic COVID-19 hospitalization during pregnancy, n=15,726

	HR (95%CI)	aHR (95%CI)
Race/Ethnicity		
Hispanic	**5.3 (2.9, 9.9)**	**2.7 (1.3,5.7)**
White, Non-Hispanic	*Ref*	*Ref*
Black or African American, Non-Hispanic	2.3 (0.9, 6)	1.04 (0.4,2.9)
American Indian or Alaska Native, Non-Hispanic	NA	NA
Asian, Non-Hispanic	1.7 (0.7,4)	2.1 (0.9,5.4)
Native Hawaiian or Pacific Islander, Non-Hispanic	**13.0 (3.7,46)**	**11.0 (2.2,50.4)**
Multi-race	NA	NA
Other	NA	NA
Age at start of pregnancy (years)		
<18 - 24	**5 (2.3,11)**	**3.2 (1.3,7.8)**
25 - 34	2 (1, 4.2)	2.0 (0.9,4.3)
>=35	*Ref*	*Ref*
Medicaid Coverage		
Yes	**3.2 (2,5.1)**	1.4 (0.8,2.6)
No	*Ref*	*Ref*
Pre-pregnancy BMI[ǂ]		
Underweight /Normal or healthy weight	*Ref*	*Ref*
Overweight	1.4 (0.72,2.7)	1.2 (0.6,2.4)
Obese	**2.4 (1.3,4.3)**	**1.9 (1.002,3.5)**
Underlying medical conditions (at least one)**	**2.7 (1.3,5.6)**	1.8 (0.7,4.7)
Diabetes	1.5 (0.37,6.2)	0.5 (0.06,3.5)
Metabolic disorder diagnosis not obesity*	**1.8 (1.1,3.1)**	**1.9 (1.03,3.3)**
Asthma	1.4 (0.8,2.5)	1.3 (0.7,2.3)
Lung disease diagnosis excluding asthma*	**37.0 (23,61)**	**41.7 (23.5,73.9)**
Chronic cardiovascular disorders[§]	**3.3 (1.9,5.7)**	**2.3 (1.2,4.4)**

HR=hazard ratio; aHR=adjusted hazard ratio from Cox proportional hazard model using pregnancy weeks as the timescale. Model adjusted by race/ethnicity, age at start of pregnancy, Medicaid coverage, pre-pregnancy BMI, underlying medical conditions (at least one, diabetes, other metabolic disorders, asthma, other chronic respiratory conditions excluding asthma, chronic cardiovascular disorders), site and period of high and low SARS-CoV-2 circulation.

Note: *See Appendix 1; **At least one condition identified from list on Appendix 1 excluding anemia; [ǂ]Underweight/Normal or healthy weight (BMI <25), Overweight (BMI 25-29.9), Obese (BMI ≥30); [§]Cardiovascular disorders include acute or chronic heart failure diagnosis, cardiac arrest diagnosis, and acute and non-acute heart disease diagnosis.

Table 3. Clinical presentation of hospitalized pregnant individuals with symptomatic COVID-19 (n=75)

	All (n=75)
	n (%)
Gestational age of fetus at admission (weeks)	
Median (IQR)	37 (33-39)
Length of hospital stay (days)	
Median (IQR)	3 (2-5)
Pneumonia diagnosis	40 (53)
Remdesivir treatment	12 (16)
ICU admission	16 (21)
Mechanical ventilation	1 (1)
ECMO	0 (0)
Existing conditions during current pregnancy at time of hospitalization	
Hypertension*	5 (7)
Gestational diabetes	5 (7)
Early or threatened labor	30 (40)
Death	0 (0)
Hospitalization resulted in end of pregnancy	49 (65)
Miscarriage	0 (0)
Still birth	0 (0)
Live birth -Term infant	36/49 (73)
Live birth -Preterm infant	13/49 (27)

IQR: interquartile range; ICU: intensive care unit, ECMO: extracorporeal membrane oxygenation. * Pre-existing hypertension complicating pregnancy, pre-existing hypertension with preeclampsia, gestational hypertension, preeclampsia, eclampsia.

References

1. Zambrano, L.D., S. Ellington, P. Strid, R.R. Galang, 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**(44): p. 1641-1647.

2. Allotey, J., E. Stallings, M. Bonet, M. Yap, 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**: p. m3320.

3. Woodworth, K.R., E.O. Olsen, V. Neelam, E.L. Lewis, et al., *Birth and Infant Outcomes Following Laboratory-Confirmed SARS-CoV-2 Infection in Pregnancy - SET-NET, 16 Jurisdictions, March 29-October 14, 2020.* MMWR Morb Mortal Wkly Rep, 2020. **69**(44): p. 1635-1640.

4. Wang, C.L., Y.Y. Liu, C.H. Wu, C.Y. Wang, et al., *Impact of COVID-19 on Pregnancy.* Int J Med Sci, 2021. **18**(3): p. 763-767.

5. Ko, J.Y., C.L. DeSisto, R.M. Simeone, S. Ellington, et al., *Adverse Pregnancy Outcomes, Maternal Complications, and Severe Illness Among US Delivery Hospitalizations With and Without a Coronavirus Disease 2019 (COVID-19) Diagnosis.* Clin Infect Dis, 2021. **73**(Suppl 1): p. S24-S31.

6. DeSisto, C.L., B. Wallace, R.M. Simeone, K. Polen, et al., *Risk for Stillbirth Among Women With and Without COVID-19 at Delivery Hospitalization - United States, March 2020-September 2021.* MMWR Morb Mortal Wkly Rep, 2021. **70**(47): p. 1640-1645.

7. Vouga, M., G. Favre, O. Martinez-Perez, L. Pomar, et al., *Maternal outcomes and risk factors for COVID-19 severity among pregnant women.* Sci Rep, 2021. **11**(1): p. 13898.

8. Centers for Disease Control and Prevention. *COVID-19 Vaccines While Pregnant or Breastfeeding*. 2021 [cited 2021 May 24]; Available from: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/pregnancy.html.

9. The American College of Obstetricians and Gynecologists (ACOG). 2021 [cited 2021 December 12]; Available from: https://www.acog.org/news/news-releases/2021/07/acog-smfm-recommend-covid-19-vaccination-for-pregnant-individuals.

10. Tutiya, C., F. Mello, G. Chaccur, C. Almeida, et al., *Risk factors for severe and critical Covid-19 in pregnant women in a single center in Brazil.* J Matern Fetal Neonatal Med, 2021: p. 1-4.

11. Mattar, C.N., S. Kalimuddin, S.P. Sadarangani, S. Tagore, et al., *Pregnancy Outcomes in COVID-19: A Prospective Cohort Study in Singapore.* Ann Acad Med Singap, 2020. **49**(11): p. 857-869.

12. Petrakis, D., D. Margina, K. Tsarouhas, F. Tekos, et al., *Obesity a risk factor for increased COVID19 prevalence, severity and lethality (Review).* Mol Med Rep, 2020. **22**(1): p. 9-19.

13. Savasi, V.M., F. Parisi, L. Patane, E. Ferrazzi, et al., *Clinical Findings and Disease Severity in Hospitalized Pregnant Women With Coronavirus Disease 2019 (COVID-19).* Obstet Gynecol, 2020. **136**(2): p. 252-258.

14. Galang, R.R., S.M. Newton, K.R. Woodworth, I. Griffin, et al., *Risk Factors for Illness Severity Among Pregnant Women With Confirmed Severe Acute Respiratory Syndrome Coronavirus 2 Infection-Surveillance for Emerging Threats to Mothers and Babies Network, 22 State, Local, and Territorial Health Departments, 29 March 2020-5 March 2021.* Clin Infect Dis, 2021. **73**(Suppl 1): p. S17-S23.

15. Ferrara, A., M.M. Hedderson, Y. Zhu, L.A. Avalos, et al., *Perinatal Complications in Individuals in California With or Without SARS-CoV-2 Infection During Pregnancy.* JAMA Intern Med, 2022.

16. Naleway, A.L., S. Ball, J.C. Kwong, B.E. Wyant, et al., *Estimating Vaccine Effectiveness Against Hospitalized Influenza During Pregnancy: Multicountry Protocol for a Retrospective Cohort Study.* JMIR Res Protoc, 2019. **8**(1): p. e11333.

17. Thompson, M.G., J.C. Kwong, A.K. Regan, M.A. Katz, et al., *Influenza Vaccine Effectiveness in Preventing Influenza-associated Hospitalizations During Pregnancy: A*

Multi-country Retrospective Test Negative Design Study, 2010-2016. Clin Infect Dis, 2019. **68**(9): p. 1444-1453.

18. Yang, J., J. Hu, and C. Zhu, *Obesity aggravates COVID-19: A systematic review and meta-analysis.* J Med Virol, 2021. **93**(1): p. 257-261.

19. Sentilhes, L., F. De Marcillac, C. Jouffrieau, P. Kuhn, et al., *Coronavirus disease 2019 in pregnancy was associated with maternal morbidity and preterm birth.* Am J Obstet Gynecol, 2020. **223**(6): p. 914 e1-914 e15.

20. Health and Human Services. *Number of COVID-19 cases confirmed by U.S. county & State Health Departments by Report Week*. Protect Public Data Hub 2021 [cited 2021 April 8]; Available from: www.protect.hhs.gov.

21. Molteni, E., C.M. Astley, W. Ma, C.H. Sudre, et al., *SARS-CoV-2 (COVID-19) infection in pregnant women: characterization of symptoms and syndromes predictive of disease and severity through real-time, remote participatory epidemiology.* medRxiv, 2020.

22. Ames, J.L., A. Ferrara, L.A. Avalos, S.E. Badon, et al., *COVID-19 prevalence, symptoms, and sociodemographic disparities in infection among insured pregnant women in Northern California.* PLoS One, 2021. **16**(9): p. e0256891.

23. Lokken, E.M., E.M. Huebner, G.G. Taylor, S. Hendrickson, et al., *Disease severity, pregnancy outcomes, and maternal deaths among pregnant patients with severe acute respiratory syndrome coronavirus 2 infection in Washington State.* Am J Obstet Gynecol, 2021.

24. Mackey, K., C.K. Ayers, K.K. Kondo, S. Saha, et al., *Racial and Ethnic Disparities in COVID-19-Related Infections, Hospitalizations, and Deaths : A Systematic Review.* Ann Intern Med, 2021. **174**(3): p. 362-373.

25. Eskenazi, B., S. Rauch, E. Iurlaro, R.B. Gunier, et al., *Diabetes mellitus, maternal adiposity, and insulin-dependent gestational diabetes are associated with COVID-19 in pregnancy: the INTERCOVID study.* Am J Obstet Gynecol, 2021.

26. Radan, A.P., M.M. Fluri, K. Nirgianakis, B. Mosimann, et al., *Gestational diabetes is associated with SARS-CoV-2 infection during pregnancy: A case-control study.* Diabetes Metab, 2022. **48**(4): p. 101351.

27. Webb Hooper, M., A.M. Napoles, and E.J. Perez-Stable, *COVID-19 and Racial/Ethnic Disparities.* JAMA, 2020. **323**(24): p. 2466-2467.

28. Yehia, B.R., A. Winegar, R. Fogel, M. Fakih, et al., *Association of Race With Mortality Among Patients Hospitalized With Coronavirus Disease 2019 (COVID-19) at 92 US Hospitals.* JAMA Netw Open, 2020. **3**(8): p. e2018039.

29. Jacobson, M., T.Y. Chang, M. Shah, R. Pramanik, et al., *Racial and Ethnic Disparities in SARS-CoV-2 Testing and COVID-19 Outcomes in a Medicaid Managed Care Cohort.* Am J Prev Med, 2021. **61**(5): p. 644-651.

30. Centers for Disease Control and Prevention. *Risk for COVID-19 Infection, Hospitalization, and Death By Race/Ethnicity*. 2022 [cited 2022 Feb 11]; Available from: https://www.cdc.gov/coronavirus/2019-ncov/covid-data/investigations-discovery/hospitalization-death-by-race-ethnicity.html.