Incidence, Clinical Characteristics, and Risk Factors of SARS-CoV-2 Infection among Pregnant Individuals in the United States

Fatimah S. Dawood¹, Michael Varner², Alan Tita³, Gabriella Newes-Adeyi⁴, Cynthia Gyamfi-Bannerman^{5,6}, Ashley Battarbee³, Ann Bruno², Michael Daugherty¹, Lawrence Reichle⁴, Kelly Vorwaller², Celibell Vargas⁷, Mickey Parks³, Emily Powers², Miriam Lucca-Susana^{5,6}, Marie Gibson², Akila Subramaniam³, Yiling J. Cheng¹, Pei-Jean Feng¹, Sascha Ellington¹, Romeo R. Galang¹, Jennifer Meece⁸, Chris Flygare⁴, Melissa S. Stockwell^{6,7,9}

- (1) Centers for Disease Control and Prevention, Atlanta, GA, USA.
- (2) Department of Obstetrics and Gynecology, University of Utah Health Sciences Center, Salt Lake City, Utah, USA.
- (3) Center for Women's Reproductive Health and Department of Obstetrics and Gynecology, Division of Maternal-Fetal Medicine, University of Alabama at Birmingham, USA.
- (4) Abt Associates, Rockville, MD, USA.
- (5) Department of Obstetrics and Gynecology Division of Maternal-Fetal Medicine, Columbia University Irving Medical Center, USA.
- (6) New York-Presbyterian Hospital, New York, NY, USA.
- (7) Division of Child and Adolescent Health, Department of Pediatrics, Columbia University Irving Medical Center, New York, NY, USA.
- (8) Marshfield Virology Laboratory, Marshfield, WI, USA.
- (9) Department of Population and Family Health, Mailman School of Public Health, Columbia University Irving Medical Center, New York, NY, USA.

Corresponding Author: Fatimah S. 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: fdawood@cdc.gov.

Summary: During August 2020–March 2021, the incidence rate of SARS-CoV-2 infection among pregnant individuals at three United States sites was 10.0 per 1,000, equating to a 1% risk of infection per week. The asymptomatic fraction of infection was 35%.

Abstract

Background: Data about the risk of SARS-CoV-2 infection among pregnant individuals are needed

to inform infection prevention guidance and counseling for this population.

Methods: We prospectively followed a cohort of pregnant individuals during August 2020–March

2021 at three U.S. sites. The three primary outcomes were incidence rates of any SARS-CoV-2

infection, symptomatic infection, and asymptomatic infection, during pregnancy during periods of

SARS-CoV-2 circulation. Participants self-collected weekly mid-turbinate nasal swabs for SARS-

CoV-2 RT-PCR testing, completed weekly illness symptom questionnaires, and submitted additional

swabs with COVID-19-like symptoms. An overall SARS-CoV-2 infection incidence rate weighted by

population counts of women of reproductive age in each state was calculated.

Results: Among 1098 pregnant individuals followed for a mean of 10 weeks, nine percent (99/1098)

had SARS-CoV-2 infections during the study. Population weighted incidence rates of SARS-CoV-2

infection were 10.0 per 1,000 (95% confidence interval [CI] 5.7–14.3) person-weeks for any

infection, 5.7 per 1,000 (95% CI 1.7-9.7) for symptomatic infections, and 3.5 per 1,000 (95% CI 0-

7.1) for asymptomatic infections. Among 96 participants with SARS-CoV-2 infection and symptom

data, the most common symptoms were nasal congestion (72%), cough (64%), headache (59%), and

change in taste or smell (54%); 28% had measured or subjective fever. The median symptom

duration was 10 days (IQR6-16 days).

Conclusion: Pregnant individuals had a 1% risk of SARS-CoV-2 infection per week. Study findings

provide information about SARS-CoV-2 infection risk during pregnancy to inform counseling for

pregnant individuals about infection prevention practices, including COVID-19 vaccination.

Key Words: Pregnancy; Incidence rates; COVID-19

3

Introduction

Emerging data from the COVID-19 pandemic suggest that pregnant individuals might be at increased risks for critical illness¹ and some adverse pregnancy outcomes.²⁻⁵ While these data provide important information about risks to pregnant individuals once infected with SARS-CoV-2, data on community incidence of SARS-CoV-2 infection and risk factors for infection among pregnant individuals are needed to inform infection prevention counseling and guidance.⁶ In addition, data that quantify the risk of SARS-CoV-2 infection during pregnancy might inform decisions by pregnant individuals about whether to get the COVID-19 vaccine.

Estimating SARS-CoV-2 infection incidence is challenging because it requires large-scale longitudinal community studies with systematic testing.⁶ In addition, a substantial fraction of SARS-CoV-2 infection is asymptomatic.⁷⁻¹¹ Serologic studies might not capture the true incidence and full burden of infections because asymptomatic infection might not consistently elicit antibodies to SARS-CoV-2 and detectable antibody titers after mild or asymptomatic infection might wane over time. 12,13 In addition, serologic studies are unable to precisely identify the timing of incident infections. Thus, studies designed to identify the true incidence and full burden of SARS-CoV-2 infection ideally should include systematic molecular testing for asymptomatic infections. The Epidemiology of SARS-CoV-2 in Pregnancy and Infancy Community cohort is a prospective multisite cohort study of pregnant individuals who participate in intensive surveillance for SARS-CoV-2 infection that includes weekly mid-turbinate nasal swab specimen collection regardless of symptoms and weekly surveillance for illness symptoms. Using data from this cohort, we aimed to estimate incidence rates of asymptomatic and symptomatic SARS-CoV-2 infections as a measure of the overall risk of infection during pregnancy and describe the clinical characteristics of infections. In addition, we conducted an exploratory analysis to examine selected exposures and practices as risk or protective factors of SARS-CoV-2 infection.

Methods

Participants and study setting

Participants were enrolled during August 2020–February 2021 at three U.S. medical centers in Salt Lake City, UT; New York City, NY; and Birmingham, AL. Individuals had to be pregnant at <28 weeks gestation to be eligible. See Supplemental Methods/Results for recruitment methods and additional eligibility criteria. During the study period from August 2020 through March 2021, local community mitigation measures varied by study location (see Supplemental Table 1).

Data Collection Procedures

Before data collection, individuals provided written informed consent to study participation. At enrollment, participants completed web-based or telephone surveys about their socio-demographic characteristics, past medical and obstetrical histories, prenatal care, whether they were told by a healthcare provider they had suspected or confirmed COVID-19 before enrollment and if they had a confirmatory laboratory test. Participants received an orientation about the study surveillance, including how to self-collect and mail mid-turbinate nasal swab specimens. Participants were asked to self-collect swab specimens every week during pregnancy; self-collection of nasal swabs has been previously validated for detection of SARS-CoV-2 infection. They were given prepared kits and materials to ship specimens on ice packs by overnight courier to a central laboratory. Participants were also asked to collect and ship additional swab specimens if they experienced onset of COVID-like illness (CLI) symptoms.

CLI was defined as one or more of measured or subjective fever, cough, shortness of breath, sore throat, diarrhea, muscle aches, chills, or change in taste or smell. Participants were contacted weekly until the end of pregnancy by text message, phone call, or email to ascertain whether they had CLI symptoms or any other illness symptoms during the preceding 7 days. Every fourth week, participants were asked "In the past month, when you left your home for activities that involved interacting with other people, how often did you use a mask or other covering over your nose and

mouth?" Response options were: always, sometimes, never. See Supplemental Methods/Results for additional surveillance methods.

Data about receipt of COVID-19 vaccines during pregnancy were collected at the end of pregnancy by survey and by data abstraction from medical records or participants' COVID-19 vaccination cards (see Supplemental Methods/Results).

Laboratory Methods

Respiratory swab specimens were tested by reverse transcription-polymerase chain reaction (RT-PCR) for SARS-CoV-2 using assays previously approved under Emergency Use Authorization: Quidel Lyra SARS-CoV-2 Assay or the ThermoFisher Combo Kit platform with ThermoFisher probes and primers (see Supplemental Methods/Results). 15

Sample size estimates

Sample size estimates were based on achieving precision around incidence rate estimates of SARS-CoV-2 infection by site. Sample size calculations indicated that 280 participants per site would be needed to estimate a cumulative incidence of SARS-CoV-2 infection of 10% with $\pm 4\%$ precision after accounting for 10% cohort attrition.

Outcomes and exposures of interest

The three primary incident outcomes of interest were any RT-PCR-confirmed SARS-CoV-2 infection, symptomatic infections, and asymptomatic infections. See Supplemental Methods/Results for outcome definitions. Clinical measurements of interest were frequencies of fever and other acute symptoms, duration of symptoms and SARS-CoV-2 viral RNA detection from nasal swabs, missed workdays, outpatient medically attended infection (including telemedicine and ambulatory care visits), and hospitalization.

In an exploratory analysis of risk and protective factors of SARS-CoV-2 infection, the primary outcome was any SARS-CoV-2 infection and exposures hypothesized to be possible risk or protective factors of SARS-CoV-2 infection included employment and telework status, residing in a household with a preschool aged child <5 years or with a school-aged child 5–17 years, and mask wearing when outside the house.

Analytic populations and statistical analysis

Individuals were considered enrolled if they met eligibility criteria, consented, and completed the enrollment questionnaire. Among enrolled participants, baseline characteristics were compared between participants who did and did not participate in surveillance to identify potential biases in the population available for analysis. All subsequent analyses were limited to enrolled individuals who participated in surveillance by submitting ≥1 weekly or acute illness swab specimen and did not report a diagnosis of laboratory-confirmed COVID-19 before enrollment. Among this analytic population, baseline characteristics were compared between participants who had incident SARS-CoV-2 infections versus those who did not. Underlying medical conditions were defined as those classified by CDC as conferring an increased risk for severe COVID-19.⁵ Chi-square, Fisher's exact test, or the Wilcoxon rank-sum test were used to test for statistical significance. A p-value <0.05 was considered statistically significant.

Incidence rates per 1,000 person-weeks for each incident outcome were calculated with outcomes as the numerator and person-weeks at risk for events as the denominator. Person-weeks at risk for each outcome were calculated from the start of surveillance for each individual through the last week in which they participated in surveillance or through first incident case of SARS-CoV-2 infection (based on date of first positive test). To estimate incidences of any and asymptomatic SARS-CoV-2 infection, person-time was discounted for weeks in which participants did not submit a respiratory specimen. To estimate incidence of symptomatic SARS-CoV-2, person-time was discounted for weeks in which participants did not respond to weekly surveillance questionnaires or had symptomatic illness.

Incidence rates were calculated for the cohort overall and by site using data available through March 28, 2021. Age- and race/ethnicity-adjusted incidence rates by site were calculated using negative binomial models. To give a representative estimate for individuals of childbearing age in the United States, an aggregate age- and race/ethnicity-adjusted incidence rate across all sites was also calculated by weighting age- and race/ethnicity-adjusted estimates from each site by the U.S. 2019 census population count of women aged 15–49 years in each state. As a sensitivity analysis, incidence rates were calculated after restricting to periods of increased SARS-CoV-2 circulation at each site (see Supplemental Methods/Results). Additional sensitivity analyses were conducted to examine the impact on incidence rate estimates of including participants with COVID-19 infection before cohort enrollment and COVID-19 vaccination during the study period (see Supplemental Methods/Results).

The asymptomatic fraction of infection was calculated by dividing incidence rates of asymptomatic infection by rates of any infection. Ninety-five percent confidence intervals were calculated for selected frequencies and all incidence estimates assuming a binomial distribution.

To explore selected exposures as risk and protective factors for SARS-CoV-2 infection, discrete time-to-event proportional-hazards Cox models were used with a time scale of calendar weeks. Models compared the hazard of incident SARS-CoV-2 infection among participants with each exposure (Supplemental Methods/Results). The final base model included site and race and ethnicity. COVID-19 vaccination status was not included in the model because of incomplete data about vaccination for more than half of participants in the analysis due to ongoing cohort follow-up.

Descriptive statistics were used to characterize infections. Median duration of SARS-CoV-2 detection by RT-PCR was estimated for all infections using non-parametric survival analyses after accounting for interval censoring resulting from weekly swab specimen collection.

Analyses were conducted in SAS Version 9.4 (SAS Institute; Cary, NC).

Ethical review

The study protocol was reviewed and approved by the Columbia University Irving Medical Center Institutional Review Board (IRB) which served as the central IRB for all study sites. The Centers for Disease Control and Prevention (CDC) IRB relied on the review of the Columbia University Irving Medical Center IRB (See 45 C.F.R. part 46; 21 C.F.R. part 56.).

Results

Participant characteristics

Overall, 1,413 participants were enrolled in the cohort, of whom, 1619 (83%) participated in SARS-CoV-2 surveillance by submitting ≥1 weekly or acute illness specimen (Figure 1). See Supplemental Methods/Results and Supplemental Table 2 for additional recruitment and enrollment details. Of the 1,169 participants who participated in SARS-CoV-2 surveillance, 71 were excluded from subsequent analyses because they had a self-reported diagnosis of COVID-19 with laboratory-confirmation before enrollment. Of the remaining 1,098 participants, the median age was 30 years (interquartile range [IQR] 26–34 years), and 706 (64%) were employed, of whom 442 (62%) were not teleworking at enrollment (Table 1). Most participants (67%, 732/1098) enrolled during their second trimester (median gestational age 19 weeks, IQR 13–24). Among 400 participants with information available as of July 15, 2021 about COVID-19 vaccine receipt, 66 (17%) were fully vaccinated including three who had incident SARS-CoV-2 infections before vaccination. Among 808 (74% of 1,098) participants who responded at least once about mask use while outside the home, 551 (68%) reported always wearing masks for every month that they responded, 65 (8%) reported sometimes wearing masks for every month, 159 (20%) reported a mix of always or sometimes wearing masks, and 33 (4%) reported never wearing masks for at least some months.

The 1,098 participants in this analysis contributed 10,901 person-weeks of cohort observation time (mean per participant 10, standard deviation (SD) 6) and submitted 12,259 swab specimens for SARS-CoV-2 testing. County levels surveillance data indicate that the period of cohort follow-up included a defined wave of SARS-CoV-2 circulation at each site (Supplemental Figure 1).

Of the 1,098 participants in the cohort, 99 (9%, 95% confidence interval [CI] 7%–11%) had RT-PCR–confirmed SARS-CoV-2 infection while in the cohort. The overall population weighted incidence of SARS-CoV-2 infection was 10.0 per 1,000 (95% CI 5.7–14.3) person-weeks (Supplemental Table 3, Figure 2) indicating a 1% risk of infection per week of pregnancy. Overall weighted incidences of asymptomatic and symptomatic SARS-CoV-2 were 3.5 per 1,000 (95% CI 0–7.1) and 5.7 per 1,000 (95% CI 1.7–9.7) person-weeks. The asymptomatic fraction of SARS-CoV-2 infections was 35%. Incidence rates at each site adjusted for participants' age and race/ethnicity ranged from 5.4 to 10.8 per 1,000 person-weeks (Figure 2, Supplemental Table 3). After restricting analyses to periods of increased SARS-CoV-2 circulation based on local surveillance data, the overall population weighted incidence of SARS-CoV-2 infection was 11.0 per 1,000 (95% CI 6.2-15.8) and site incidence rates adjusted for age and race/ethnicity ranged from 5.7 to 11.8 per 1,000 person-weeks (Supplemental Table 4). See Supplemental Methods/Results for additional sensitivity analyses.

Risk Factors of SARS-CoV-2 infection

After adjusting for site and race/ethnicity, being employed and either teleworking or not teleworking (adjusted hazard ratio (aHR) 1.1, 95% CI 0.6-2.0, and 1.4, 95% CI 0.9–2.3, respectively, p=0.35) and residing in a household with a child aged <5 years (aHR 0.8, 95% CI 0.5–1.2, p=0.32) were not associated with an increased risk of SARS-CoV-2 infection (Table 2). However, residing in a household with a child 5-17 years of age was associated with an increased risk of SARS-CoV-2 infection (aHR 1.6, 95% CI 1.0-2.4, p=0.046). Non-adherence to mask wearing when outside the home was not statistically associated with risk of infection (never versus always wearing a mask: aHR

1.7, 95% CI 0.2-13.0, sometimes versus always wearing a mask: aHR 0.6, 95% CI 0.2-1.8, p=0.60), although only 70% (721/1049) of individuals had available responses about mask-wearing practices.

Characteristics of SARS-CoV-2 infection episodes

Among the 99 participants with SARS-CoV-2 infections, 79 (80%) had symptomatic infection and 20 (20%) were asymptomatic throughout their infections. The median duration of viral RNA detection by RT-PCR was 14 days (IQR 8–16 days). Among participants with SARS-CoV-2 infection excluding 3 with symptomatic illness without detailed symptom data (n=96), the most common symptoms were nasal congestion (69, 72%), cough (61, 64%), headache (57, 59%), and change in taste or smell (52, 54%) (Figure 3). Twenty-eight percent (27/96) of participants had measured or subjective fever, of whom 14 of 21 (52%) who measured their temperatures had fever >100.4 degrees Fahrenheit.

Among 36 participants with symptomatic infection who completed illness follow-up surveys, the median symptom duration was 10 days (IQR 6–16), 19 participants (53%) reported missing work due to illness, and 14 (39%) reported seeking medical care for illness. One symptomatic infection was associated with a 2-day hospitalization for dehydration that did not require intensive care. There were no deaths.

Discussion:

Among a cohort of 1098 pregnant individuals at three U.S. sites, the overall age and race/ethnicity adjusted incidence rate of SARS-CoV-2 infection weighted for state populations of women of child-bearing age was 10.0 per 1,000 person-weeks indicating a 1% risk of infection per week during the study period. The cumulative incidence of infection during pregnancy was at least 9% based on infections during the study period. Incidence rate estimates in this cohort are similar to modelled estimates for US adults of childbearing age during February—December 2020 that adjust for case under-ascertainment (4.6-6.2 per 1,000 person-weeks). Incidence rates among this likely largely COVID-19 unvaccinated cohort are also similar to those among unvaccinated healthcare and frontline workers (9.7 per 1,000 person-weeks). And among adults aged 18-49 years (unpublished

data, F. Dawood, July 25, 2021) in other contemporaneous US cohorts with similar methods of SARS-CoV-2 surveillance.

In December 2020, the U.S. Advisory Committee on Immunization Practices stated that pregnant individuals should have the option to receive COVID-19 vaccine if they were in a group recommended for vaccination. ¹⁹ In July 2021, the American College of Obstetrics and Gynecology recommended that all pregnant individuals receive COVID-19 vaccine. ²⁰ As COVID-19 vaccine becomes more widely available to pregnant individuals, vaccine hesitancy will likely remain a factor in their decision-making about vaccination. An analysis of vaccine acceptance among this cohort during August-December 2020 prior to Emergency Use Authorization of COVID-19 vaccines in the United States found that only 41% of participants would get a COVID-19 vaccine during pregnancy if given the opportunity. 21 Our findings suggest that pregnant individuals have a similar risk of becoming infected with SARS-CoV-2 compared to the general population with almost one in ten individuals in the cohort becoming infected during the study period. Although the SARS-CoV-2 infections in this study were largely self-limited, the long-term effects of SARS-CoV-2 infection and associated symptoms during pregnancy on perinatal and infant outcomes remain unclear. 4,22,23 Information from this study adds to the growing evidence base about SARS-CoV-2 infection during pregnancy that can inform counseling and risk communication for pregnant individuals as they make decisions about infection prevention measures, including COVID-19 vaccination, amidst evolving local guidance and mandates.

We estimated that 35% of SARS-CoV-2 infections during pregnancy are asymptomatic which is consistent with findings from a meta-analysis of studies among adults of childbearing age with longitudinal follow-up (31%, 95% CI 26–37%). This finding underscores the potential risks of SARS-CoV-2 transmission from pregnant individuals with asymptomatic infection to others in their households and community and the potential risks for horizontal transmission to their newborns. In addition, in this study, pregnant individuals residing in households with children aged 5-17 years had a higher risk of SARS-CoV-2 infection than those who did not which may reflect an increased risk of

infection from children in the home or differences in community social mixing patterns among individuals with school-aged children.

Strengths of this study include enrollment of a large, demographically diverse community cohort of pregnant individuals, systematic surveillance and testing for asymptomatic and symptomatic SARS-CoV-2 infections, and a follow-up period that included periods of increased SARS-CoV-2 circulation at each study site. Cohort follow-up is ongoing and pregnancy outcomes will be reported once follow-up is complete. However, several study limitations should be considered. First, adherence rates to weekly swab specimen collection varied by site, and individuals who participated in surveillance differed from those who did not with respect to baseline characteristics and potential exposures that might influence risk of SARS-CoV-2 infection. Thus, estimates of cumulative SARS-CoV-2 infection incidence should be considered minimum estimates, and some infections may have been missed. Second, the study sample size was selected to estimate infection incidence, and the analysis of risk factors for infection might have been underpowered to detect small effect sizes. In addition, 30 percent of participants were not included in the analysis examining the association between mask-wearing and infection risk because they did not receive the monthly surveillance question about mask wearing due to a surveillance messaging error or did not respond to monthly surveillance contacts when the question was asked. Thus, the absence of association between potential risk and protective factors and SARS-CoV-2 infection should be interpreted with caution.

Pregnant individuals in this study had a 1 percent risk of SARS-CoV-2 infection per week. Estimates of SARS-CoV-2 infection incidence among pregnant individuals in this study are similar to estimates among adults of child-bearing age in the general population. These findings, coupled with emerging data that pregnant individuals have an increased risk of some severe outcomes if infected with SARS-CoV-2 ¹⁻⁴, provide information to inform counseling and risk communication for pregnant individuals making decisions about SARS-CoV-2 infection prevention measures during the ongoing COVID-19 pandemic.

NOTES

Acknowledgments: The authors wish to acknowledge Kristina Wielgosz at the Centers for Disease Control and Prevention for analytic support; Raul Silverio, Sabine Bousleiman, Liqun Wang, Nataly Beltre, Zoilo Castillo, Rebecca Santiago, Haley Manchon, Laura Staeheli, Katherine Matos, Luis Alba, Catia Neves, Angela Cameron, Michelle Vanegas, Chelsea Wynn, Luiza Kalemi, and Fiorcelys Bueno all from Columbia University Irving Medical Center; and Louise Hadden, Elizabeth Axelrod, Amanda Grittner, Isaiah Gerber, Jenna Spirt, Lauren Scarpati, Michael Duckworth, Marci Schalk, Tana Brummer, Brandon Poe, Andrea Bronaugh, Rajbansi Raorane, and Lillian Boyer all from the Abt data team. Study data were collected and managed using REDCap electronic data capture tools hosted at Vanderbilt University Medical Center with grant support UL1 TR000445 from NCATS/NIH. REDCap (Research Electronic Data Capture) is a secure, web-based software platform designed to support data capture for research studies, providing 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for data integration and interoperability with external sources.

Disclaimers: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention. Any references to specific commercial products are for identification purposes only and do not constitute an endorsement by CDC. CDC funded this study. CDC-affiliated authors were involved in study design, data collection, analysis and interpretation, report writing, and the decision to submit the paper for publication. The corresponding author had full access to all data used in the analysis and had final responsibility for the decision to submit for publication.

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

Conflicts of Interest: The authors have no conflicts of interest to declare.



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(44):1641-1647. DOI: 10.15585/mmwr.mm6944e3.
- 2. Adhikari EH, Moreno W, Zofkie AC, et al. Pregnancy Outcomes Among Women With and Without Severe Acute Respiratory Syndrome Coronavirus 2 Infection. JAMA Netw Open 2020;3(11):e2029256. DOI: 10.1001/jamanetworkopen.2020.29256.
- 3. Woodworth KR, Olsen EO, Neelam V, 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):1635-1640. DOI: 10.15585/mmwr.mm6944e2.
- 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. DOI: 10.1136/bmj.m3320.
- 5. Centers for Disease Control and Prevention. People with Certain Medical Conditions. (https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html).
- 6. Hu YJ, Wake M, Saffery R. Clarifying the Sweeping Consequences of COVID-19 in Pregnant Women, Newborns, and Children With Existing Cohorts. JAMA Pediatr 2021;175(2):117-118. DOI: 10.1001/jamapediatrics.2020.2395.
- 7. Oran DP, Topol EJ. The Proportion of SARS-CoV-2 Infections That Are Asymptomatic : A Systematic Review. Ann Intern Med 2021. DOI: 10.7326/M20-6976.
- 8. Sakurai A, Sasaki T, Kato S, et al. Natural History of Asymptomatic SARS-CoV-2 Infection. N Engl J Med 2020;383(9):885-886. DOI: 10.1056/NEJMc2013020.
- 9. Sutton D, Fuchs K, D'Alton M, Goffman D. Universal Screening for SARS-CoV-2 in Women Admitted for Delivery. N Engl J Med 2020;382(22):2163-2164. DOI: 10.1056/NEJMc2009316.
- 10. Menachemi N, Yiannoutsos CT, Dixon BE, et al. Population Point Prevalence of SARS-CoV-2 Infection Based on a Statewide Random Sample Indiana, April 25-29, 2020. MMWR Morb Mortal Wkly Rep 2020;69(29):960-964. DOI: 10.15585/mmwr.mm6929e1.
- 11. Petersen I, Phillips A. Three Quarters of People with SARS-CoV-2 Infection are Asymptomatic: Analysis of English Household Survey Data. Clin Epidemiol 2020;12:1039-1043. DOI: 10.2147/CLEP.S276825.
- 12. Long QX, Tang XJ, Shi QL, et al. Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. Nat Med 2020;26(8):1200-1204. DOI: 10.1038/s41591-020-0965-6.
- 13. Lei Q, Li Y, Hou HY, et al. Antibody dynamics to SARS-CoV-2 in asymptomatic COVID-19 infections. Allergy 2021;76(2):551-561. DOI: 10.1111/all.14622.
- 14. Tu YP, Jennings R, Hart B, et al. Swabs Collected by Patients or Health Care Workers for SARS-CoV-2 Testing. N Engl J Med 2020;383(5):494-496. DOI: 10.1056/NEJMc2016321.
- 15. US Food and Drug Administration. Emergency Use Authorization, TaqPath COVID-19 Combo Kit. (https://www.fda.gov/media/136113/download).
- 16. Bureau UC. Annual Estimates of the Resident Population by Single Year of Age and Sex: April 1, 2010 to July 1, 2019. (https://www.census.gov/data/tables/time-series/demo/popest/2010s-state-detail.html).
- 17. Centers for Disease Control and Prevention. Estimated Disease Burden of COVID-19. (https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/burden.html).
- 18. MG T, JL B, AL N, et al. Interim Estimates of Vaccine Effectiveness of BNT162b2 and mRNA-1273 COVID-19 Vaccines in Preventing SARS-CoV-2 Infection Among Health Care Personnel, First Responders, and Other Essential and Frontline Workers Eight U.S. Locations, December 2020–March 2021. MMWR Morb Mortal Wkly Rep 2021. DOI: http://dx.doi.org/10.15585/mmwr.mm7013e3external icon.

- 19. Dooling K, Marin M, Wallace M, et al. The Advisory Committee on Immunization Practices' Updated Interim Recommendation for Allocation of COVID-19 Vaccine United States, December 2020. MMWR Morb Mortal Wkly Rep 2021;69(5152):1657-1660. DOI: 10.15585/mmwr.mm695152e2.
- 20. American College of Obstetrics and Gynecology. ACOG and SMFM Recommend COVID-19 Vaccination for Pregnant Individuals. 2021. https://www.acog.org/news/news-releases/2021/07/acog-smfm-recommend-covid-19-vaccination-for-pregnant-individuals. Accessed August 10, 2021.
- 21. Battarbee A, Stockweel M, Varner M, Newes-Adeyi G, Daugherty M, Gyamfi-Bannerman C. Attitudes toward COVID-19 illness and COVID-19 vaccination among pregnant women: a cross-sectional multicenter study during August-December 2020. medRxiv 2021. DOI: https://doi.org/10.1101/2021.03.26.21254402.
- 22. Norman M, Naver L, Soderling J, et al. Association of Maternal SARS-CoV-2 Infection in Pregnancy With Neonatal Outcomes. JAMA 2021. DOI: 10.1001/jama.2021.5775.
- 23. Dumitriu D, Gyamfi-Bannerman C. Understanding Risk for Newborns Born to SARS-CoV-2-Positive Mothers. JAMA 2021. DOI: 10.1001/jama.2021.6210.
- 24. Buitrago-Garcia D, Egli-Gany D, Counotte MJ, et al. Occurrence and transmission potential of asymptomatic and presymptomatic SARS-CoV-2 infections: A living systematic review and meta-analysis. PLoS Med 2020;17(9):e1003346. DOI: 10.1371/journal.pmed.1003346.

Table 1 Baseline characteristics of pregnant individuals enrolled and participating in surveillance for SARS-CoV-2 infection in the Epidemiology of SARS-CoV-2 in Pregnancy and Infancy community cohort^a, n=1,098 individuals

	All participan ts	SARS-CoV-2 Infection	No SARS-CoV-2 Infection	
	n (col%) ^b	n (row %)	n	p- value
Baseline characteristics				
All	1098	99	999	
Site				
Salt Lake City, UT	470 (43)	35 (7)	435 (9)	
Birmingham, AL	274 (25)	17 (6)	257 (94)	0.003
New York City, NY	354 (32)	47 (13)	307 (87)	0.003
Age, median (interquartile range)	30 (26-34)	31 (26-33)	30 (26-34)	0.87
	4 (7			
Age group	1/1/6			
18-24 years	182 (17)	13 (7)	169 (93)	
25-34 years	688 (63)	67 (10)	621 (90)	0.51
≥35 years	228 (21)	19 (8)	209 (92)	
Highest educational level				
Less than college	561/1091	56 (10)	505 (90)	
Some college or college graduate	(51) 530/1091 (49)	42 (8)	488 (92)	0.23
Race/ethnicity	220/1010	42 (12)	206 (07)	
Hispanic/Latina	339/1049 (32)	43 (13)	296 (87)	
White, Non-Hispanic	501/1049 (48)	41 (8)	460 (92)	
Black, Non-Hispanic	166/1049 (16)	7 (4)	159 (96)	0.008
Other, Non-Hispanic	43/1049 (4)	2 (5)	41 (95)	
Employment and telework status				
Employed, teleworking	264/1080 (24)	21 (8)	243 (92)	
Employed, not teleworking	442/1080 (41)	45 (10)	397 (90)	0.46
Not employed	374/1080 (35)	30 (8)	344 (92)	

Underlying medical conditions ^d				
None	849 (77)	83 (10)	766 (90)	
At least 1	249 (23)	16 (6)	233 (94)	0.1
Household with child aged <5 years				
Yes	413/1086 (38)	33 (8)	380 (92)	
No	673/1086 (62)	65 (10)	608 (90)	0.35
Household with child aged 5-17 years				
Yes	337/1086 (31)	40 (12)	297 (88)	
No	749/1086 (69)	58 (8)	691 (92)	0.028
Current pregnancy characteristics			U'	
Trimester at enrollment		19		
First (0 to 13 6/7 weeks gestation)	366 (33)	45 (12)	321 (88)	0.005
Second (14 to 27 6/7 weeks gestation)	732 (67)	54 (7)	678 (93)	0.007
	1,7	P		
Trimester at first prenatal visit				
First (0 to 13 6/7 weeks gestation)	958/1042 (92)	90 (9)	868 (91)	
Second (13 6/7 to 27 6/7 weeks gestation)	83/1042 (8)	3 (4)	80 (96)	0.18
Third (>=28 weeks gestation)	1/1042 (<1)	0 (0)	1 (100)	
Multiple gestation pregnancy				
Yes	26/1093 (2)	2 (8)	24 (92)	
No	5/1093 (<1)	0 (0)	5 (100)	1.00
First pregnancy				
Yes	327/1096	27 (8)	300 (92)	
	(30)		, ,	0.56
No	769/1096 (70)	72 (9)	697 (91)	
Self-reported receipt of COVID-19 vaccination during pregnancy ^e				
Partially vaccinated	25/400 (6)	0 (0)	25 (100)	0.09
Fully vaccinated	66/400 (17)	3 (5)	63 (95)	
Not vaccinated	309/400 (77)	32 (10)	277 (90)	

Month full vaccination was attained among fully-vaccinated participants ^e				0.37
January 2021	27/66 (41)	0 (0)	27 (100)	
February 2021	29/66 (44)	2 (7)	27 (93)	
March 2021	10/66 (15)	1 (10)	9 (90)	

- a Excluding 71 participants with self-reported diagnosis of COVID-19 with laboratory-confirmed before cohort enrollment.
- b Column percentages are calculated out of participants with available data for each variable. Denominators indicate number of participants with available data if different from n=1098.
- c P-values comparing the frequency of baseline characteristics among individuals with and without SARS-CoV-2 infection.
- d Underlying medical conditions classified by the Centers for Disease Control and Prevention as conferring an increased risk for severe COVID-19, including cancer, chronic kidney disease, chronic lung disease, dementia or neurological conditions, diabetes (types 1 or 2), down syndrome, heart conditions including hypertension, HIV infection, immunocompromised state, liver disease, sickle cell disease or thalassemia, solid organ or blood stem cell transplant, and stroke or cerebrovascular disease. Centers for Disease Control and Prevention list available here: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html.
- e COVID-19 vaccination status was based on participant report as the primary data source for information about receipt, vaccine type, number of doses and dates of vaccination using data available for the cohort as of July 15, 2021. If dates of vaccination were not available from participant report, abstracted information from electronic medical records or COVID-19 vaccination cards was used to determine timing of vaccination. Data from electronic medical records or COVID-19 vaccination cards was also prioritized if vaccine type was discordant from these sources compared to participant self-report. Fully vaccinated was defined as receipt of two doses of vaccines with a recommended two-dose series or one dose of a vaccine for which only a single dose is recommended. Partially vaccinated was defined as receipt of one dose of vaccines with a recommended two-dose series. Of the 99 participants with SARS-CoV-2 infection, 35 had information about receipt of COVID-19 vaccination during the study period. Of these 35 participants, 3 reported receipt of COVID-19 vaccine, all after their SARS-CoV-2 infections.

Table 2 Adjusted risk of SARS-CoV-2 infection among pregnant individuals enrolled and participating in the Epidemiology of SARS-CoV-2 in Pregnancy and Infancy community cohort, by selected exposures and preventive practices, n=1049 individuals^a

selected exposures and preventive practices, n=10	N^b	# of SARS- CoV-2 Infecti ons	Adjusted Hazard Ratio (95% CI)		p- val ue	
Base model						
Site	104 9	93		0		
Salt Lake City, UT			Ref	1/1	0.0	
Birmingham, AL			2.0	(1.0, 3.8)	0.0	
New York City, NY			2.1	(1.0, 4.3)	71	
Race/ethnicity	104	93	19			
White, Non-Hispanic			Ref			
Hispanic/Latina			1.3	(0.6, 2.6)	0.5	
Black, Non-Hispanic		7	0.7	(0.3, 1.7)	4	
Other, Non-Hispanic			0.6	(0.1, 2.5)		
Variables in base model adjusting for site and race/ethnicity plus ^c Employment and telework status	103	90				
	2					
Employed, teleworking			1.1	(0.6, 2.0)	0.3	
Employed, not teleworking			1.4	(0.9, 2.3)	5	
Not employed			Ref			
Household with child aged 5-17 years	104	93				
Yes			1.6	(1.0, 2.4)	0.0	
No			Ref	1	46	
Household with child aged <5 years	104	93				
Yes	1		0.8	(0.5, 1.2)	0.3	
No			Ref	· -	2	
Mask use when outside the home	670 5 ^d	38				
Always			Ref			
Sometimes			0.6	(0.2, 1.8)	0.6	
Never			1.7	(0.2, 13.0)	7 0	

a Base models exclude participants with missing data on race/ethnicity (n=49).

b n corresponds to number of participants included in each model for time invariant factors (site, race/ethnicity, employment and telework status, and households with children aged 5-17 years or <5 years) and person-weeks for time varying factors (mask use when outside the home). Participants with missing data for variables were excluded. Person-weeks with missing swab submission were also excluded.

c Base model includes site and race/ethnicity plus the variables listed in the table added individually to the base model.

d Denotes person-weeks of observation among a total of 721 participants included in the model.



FIGURE LEGENDS

Figure 1 Cohort recruitment, screening, consent, and surveillance participation, Epidemiology of SARS-CoV-2 in Pregnancy and Infancy community cohort, Utah, New York, and Alabama, August 2020–March 2021

a Prescreened includes all individuals who study staff screened for selected eligibility criteria such as age before formal eligibility screening. $\$ b Ineligible because individual was not planning to deliver at the study site (n=29), not willing to self-collect and mail respiratory specimens (n=49), had unknown gestational age (n=1), or was currently enrolled in an influenza or COVID-19 vaccine trial (n=3).

Figure 2 SARS-CoV-2 infection incidences per 1,000 person-weeks among pregnant individuals enrolled and participating in the Epidemiology of SARS-CoV-2 in Pregnancy and Infancy community cohort, adjusted for age and race/ethnicity by site and symptom status, September 2020–March 2021, n=1,098 individuals

[See separate TIF file]

Error bars denote 95% confidence intervals.

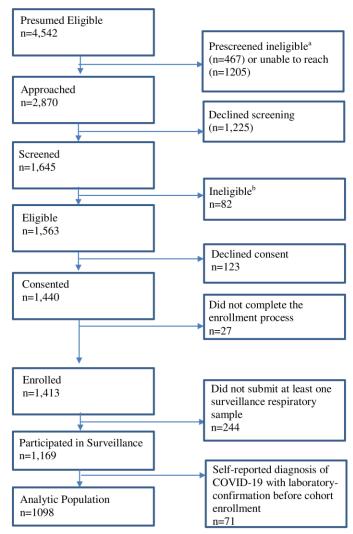
*Weighted for population counts of women aged 15–49 years in each state using U.S. Census Bureau population estimates for 2019 by age and state (Annual Estimates of the Resident Population by Single Year of Age and Sex: April 1, 2010 to July 1, 2019. (Accessed at https://www.census.gov/data/tables/time-series/demo/popest/2010s-state-detail.html.)

Figure 3 Symptom frequencies among pregnant individuals with incident SARS-CoV-2 infections in the Epidemiology of SARS-CoV-2 in Pregnancy and Infancy community cohort, September 2020–March 2021, n=96 infections^a

[See separate TIF file]

Error bars denote 95% confidence intervals assuming a binomial distribution. a Excluding 3 symptomatic infections without detailed information about individual symptoms.

Figure 1 Cohort recruitment, screening, consent, and surveillance participation, Epidemiology of SARS-CoV-2 in Pregnancy and Infancy community cohort, Utah, New York, and Alabama, August 2020–March 2021



a Prescreened includes all individuals who study staff screened for selected eligibility criteria such as age before formal eligibility screening. \
b Ineligible because individual was not planning to deliver at the study site (n=29), not willing to self-collect and mail respiratory specimens (n=49), had unknown gestational age (n=1), or was currently enrolled in an influenza or COVID-19 vaccine trial (n=3).

