SARS-CoV-2 testing and detection during peripartum hospitalizations among a multi-center cohort of pregnant persons, March 2020–February 2021

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Abstract

Background: Identifying SARS-CoV-2 infections during peripartum hospitalizations is important to guide care, implement prevention measures, and understand infection burden.

Methods: This cross-sectional analysis used electronic health record data from hospitalizations during which pregnancies ended (peripartum hospitalizations) among a cohort of pregnant persons at 3 U.S. integrated healthcare networks (Sites 1–3). Maternal demographic, medical encounter, SARS-CoV-2 testing, and pregnancy and neonatal outcome information was extracted for persons with estimated delivery and pregnancy end dates during March 2020–February 2021 and ≥1 prenatal care record. Site-stratified multivariable logistic regression was used to identify factors associated with testing and compare pregnancy and neonatal outcomes among persons tested.

Results: Among 17,858 pregnant persons, 10,863 (60.8%) had peripartum SARS-CoV-2 testing; 222/10,683 (2.0%) had positive results. Testing prevalence varied by site and was lower during March–May 2020. Factors associated with higher peripartum SARS-CoV-2 testing odds were Asian race (adjusted odds ratio [aOR]: 1.36; 95% CI: 1.03–1.79; referent: White) (Site 1), Hispanic or Latina ethnicity (aOR: 1.33; 95% CI: 1.08–1.64) (Site 2), peripartum Medicaid coverage (aOR: 1.33; 95% CI: 1.06–1.66) (Site 1), and preterm hospitalization (aOR: 1.69; 95% CI: 1.19–2.39 [Site 1]; aOR: 1.39; 95% CI: 1.03–1.88 [Site 2]).

Conclusions: Findings highlight potential disparities in SARS-CoV-2 peripartum testing by demographic and pregnancy characteristics. Testing practice variations should be considered when interpreting studies relying on convenience samples of pregnant persons testing positive for SARS-CoV-2. Efforts to address testing differences between groups could improve equitable testing practices and care for pregnant persons with SARS-CoV-2 infections.

Keywords: COVID-19; pregnancy; neonate; SARS-CoV-2; SARS-CoV-2 testing

Introduction

Infections with SARS-CoV-2, the virus that causes COVID-19, often have asymptomatic presentation among peripartum persons and are detected incidentally by universal screening during hospitalizations [1–8]. Identifying peripartum SARS-CoV-2 infections is important for guiding care, implementing measures to prevent transmission to other patients, newborns, and hospital personnel, and understanding the burden of COVID-19 among pregnant persons. As testing guidelines [9,10], testing capacity, and SARS-CoV-2 infection prevalence changed during the COVID-19 pandemic, SARS-CoV-2 testing practices likely varied across facilities and over time. However, testing practices for SARS-CoV-2 during peripartum hospitalizations—defined as hospitalizations during which a pregnancy ends—have not been well characterized.

We used data from a large, diverse cohort of pregnant persons receiving antenatal and peripartum care in three integrated healthcare networks in the United States during the first year of the COVID-19 pandemic to identify individual and pregnancy characteristics associated with peripartum SARS-CoV-2 testing, describe SARS-CoV-2 testing and positivity rates over time, identify characteristics associated with positive SARS-CoV-2 test results, and compare pregnancy and neonatal outcomes by SARS-CoV-2 infection status during peripartum hospitalizations.

Methods

The Epidemiology of SARS-CoV-2 in Pregnancy and Infancy Network electronic cohort (eESPI) includes pregnant persons with ≥1 outpatient or telemedicine antenatal care visit within the included integrated healthcare networks during December 1, 2019–February 28, 2021, who had estimated delivery dates (EDD) and pregnancy end dates during March 1, 2020–February 28, 2021. Site personnel extracted data from electronic health records (EHRs) of cohort members based on International Classification of Diseases-10 (ICD-10) codes using a standardized data dictionary. Data extraction included maternal demographic characteristics, all medical encounters within the network including ambulatory care visits

and hospitalizations, SARS-CoV-2 testing, and pregnancy and neonatal outcomes. The three networks cover patients in Texas, Oregon, Washington, and California (Supplemental Methods); to maintain anonymity, networks are called Sites 1–3. Two sites extracted data on all eligible pregnancies and one extracted data for a random sample of eligible pregnancies.

SARS-CoV-2 testing policies differed by site (Supplemental Methods). Because site testing policies differed for hospitalized persons previously diagnosed with COVID-19, persons diagnosed with COVID-19 >3 days before peripartum hospitalization were excluded from this analysis, regardless of peripartum SARS-CoV-2 testing status. A previous COVID-19 diagnosis was defined by a positive SARS-CoV-2 real-time reverse transcription polymerase chain reaction assay (RT-PCR) test or a COVID-19 ICD-10 diagnostic code in the EHR. Because this analysis focused on peripartum hospitalizations, pregnancies that did not end during hospitalization were excluded. Induced abortions were also excluded because this analysis included an assessment of the association between peripartum SARS-CoV-2 infection status and pregnancy outcomes.

Peripartum hospitalizations were defined as hospitalizations during which a pregnancy ended, regardless of pregnancy outcome. Peripartum testing was defined as having a record of a SARS-CoV-2 RT-PCR test during or ≤3 days before peripartum hospitalization. Pregnant persons with ≥1 acute respiratory or febrile illness (ARFI) diagnosis code [11] recorded in the EHR ≤3 days before peripartum testing were defined as having a clinically-indicated test; others with peripartum testing were defined as having a routine screening test. ARFI discharge codes have been used previously to identify hospitalizations for acute illness likely to be associated with respiratory viral infection during pregnancy, as opposed to hospitalizations during which respiratory viral infection might have been identified incidentally by hospital screening practices [11,12]. To identify clinically-indicated tests, a modified version of the ARFI ICD-10 code cluster excluding respiratory syncytial virus, influenza, and COVID-19 diagnoses was used, since pathogen-specific codes were considered more likely to reflect test results rather than specific symptoms or testing indications (Supplemental Table 1).

Supplemental Methods include ICD-10 codes used to define pregnancy complications, labor or delivery complications, neonatal respiratory or cardiovascular disorder, and neonatal disturbances or malformations at birth. Maternal and neonatal deaths were captured in the data only if they occurred during a peripartum hospitalization.

Multivariable logistic regression was used to assess factors associated with peripartum SARS-CoV-2 testing, factors associated with SARS-CoV-2 positivity among persons tested, and the association between SARS-CoV-2 positivity (stratified by infections identified by clinically-indicated vs. routine screening testing) and pregnancy and neonatal outcomes. For each analysis, data were first analyzed by site to assess effect modification. If evidence of effect modification was identified, site-specific results were presented; otherwise, results were aggregated. Adjusted odds ratios (aORs) and 95% confidence intervals (CIs) were calculated, adjusting for specific variables in each model.

The model assessing factors associated with peripartum SARS-CoV-2 testing included peripartum hospitalization month (3-month increments), maternal age group at conception, race and ethnicity, peripartum Medicaid coverage, number of routine antenatal visits, any complications during the current pregnancy, peripartum hospitalization at <37 weeks gestational age, and pregnancy loss during peripartum hospitalization. Variables were selected *a priori* to evaluate hypotheses that testing may vary by demographic group, level of antenatal care, and perceived risk level of the pregnancy. Site was found to be an effect modifier of the association between multiple predictors and peripartum testing, thus site-stratified models are presented. We hypothesized that peripartum SARS-CoV-2 testing practices may have differed by demographic or pregnancy characteristics during months when testing was performed at the discretion of healthcare professionals and patients but testing practices may have been more homogeneous when universal testing protocols were in place. To assess whether differences in testing practices persisted during universal SARS-CoV-2 testing, we conducted a sensitivity analysis restricting the multivariable model for each site to peripartum hospitalizations occurring when the site had a universal SARS-CoV-2 testing protocol for hospitalized pregnant persons (Supplemental Methods).

The model assessing factors associated with SARS-CoV-2 positivity among persons with peripartum testing included site, maternal age group at conception, race and ethnicity, peripartum Medicaid coverage, pre-pregnancy obesity, gestational diabetes, and having an ARFI diagnosis code during peripartum hospitalization. Variables were selected *a priori* based on previously identified associations with SARS-CoV-2 infection or severity during pregnancy [2,13,14].

Models assessing pregnancy or neonatal outcomes (pregnancy loss, preterm birth, Cesarean delivery, having a labor or delivery complication, maternal intensive care unit [ICU] admission, fetal distress, neonatal respiratory or cardiovascular disorders, neonatal disturbances or malformations at birth, neonatal ICU admission, and neonatal death) had SARS-CoV-2 positivity as the primary predictor (with positivity via clinically-indicated vs. routine screening test assessed separately, each compared to a referent of all persons testing negative for SARS-CoV-2) and were adjusted for variables associated with SARS-CoV-2 positivity that may be associated with pregnancy or neonatal outcomes: site, peripartum Medicaid coverage, and maternal age group at conception.

Data were analyzed in SAS 9.4. This activity was reviewed by the Centers for Disease Control and Prevention (CDC) and was conducted consistent with applicable federal law and CDC policy (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.).

Results

Overall, 19,456 pregnancies were captured in the eESPI cohort; of these, 1,130 (5.8%) were excluded because the pregnancy did not end during hospitalization, or the pregnancy outcome was induced abortion (Figure 1). Of 18,326 remaining pregnancies, 468 (2.6%) had a history of COVID-19 during pregnancy >3 days before peripartum hospitalization and were excluded. Of the remaining 17,858 pregnant persons included in the analysis, the majority (58.7%) were aged 25–34 years at conception (Table 1). The most common race and ethnicity groups were White (42.5%), Hispanic or Latina (27.3%), and Asian (15.5%); 22.3% of persons had peripartum Medicaid coverage.

Among the 17,858 pregnant persons included, 10,863 (60.8%) had SARS-CoV-2 RT-PCR testing performed during or ≤3 days before peripartum hospitalization. Of those, 403 (3.7%) had an ARFI diagnosis code suggesting a clinical indication for testing; the other 10,460 (96.3%) had routine screening tests. Among persons tested, 222 (2.0%) had positive SARS-CoV-2 results, including 27 of 403 (6.7%) with clinically-indicated tests and 195 of 10,460 (1.9%) with routine screening tests (Figure 1).

Proportions with peripartum SARS-CoV-2 testing varied by site and over time (Figure 2). During months when sites conducted SARS-CoV-2 testing for most peripartum hospitalizations (Site 1: May 2020–February 2021, Site 2: December 2020–February 2021, Site 3: April 2020–February 2021), 0.2–5.0% of persons with peripartum testing had positive test results each month, with timing of peak positivity mirroring peaks in case counts nationally and in states where sites were located (Supplemental Figure 1) [15].

At Site 1, among 4,692 pregnant persons, odds of peripartum SARS-CoV-2 testing were significantly higher among persons with peripartum hospitalizations during June 2020–February 2021 (aOR range: 8.72–11.3 for 3-month increments in this period relative to March–May 2020), Asian persons (aOR: 1.36; 95% CI: 1.03–1.79; referent: White), persons with peripartum Medicaid coverage (aOR: 1.33; 95% CI: 1.06–1.66), and persons admitted for peripartum hospitalizations preterm (before 37 weeks gestation) (aOR: 1.69; 95% CI: 1.19–2.39). At Site 2, among 6,912 pregnant persons, odds of peripartum SARS-CoV-2 testing were

significantly higher among persons with peripartum hospitalizations during September 2020–February 2021 (aOR range: 6.72–142), Hispanic or Latina persons (aOR: 1.33; 95% CI: 1.08–1.64), and persons admitted for peripartum hospitalizations preterm (aOR: 1.39; 95% CI: 1.03–1.88). At Site 3, among 5,153 pregnant persons, odds of peripartum SARS-CoV-2 testing were significantly higher among persons with peripartum hospitalizations during June 2020–February 2021 (aOR range: 30.4–70.3) (Table 2). Results were generally similar in a sensitivity analysis restricted to peripartum hospitalizations that occurred when sites had universal SARS-CoV-2 testing protocols for hospitalized pregnant persons (Supplemental Table 2).

Among 8,278 persons with peripartum testing and complete data on predictors for SARS-CoV-2 positivity, higher odds of a positive test result were observed among persons aged <25 years at conception (aOR: 3.14; 95% CI: 1.87–5.28; referent: 35–50 years), of Hispanic or Latina ethnicity (aOR: 2.46; 95% CI: 1.55–3.89; referent: White), with peripartum Medicaid coverage (aOR: 1.66; 95% CI: 1.14–2.42), and with an ARFI diagnosis code during peripartum hospitalization (aOR: 6.64; 95% CI: 4.18–10.6) (Table 1).

Among 27 persons positive for SARS-CoV-2 by clinically-indicated testing, four required intensive care, eight received bilevel positive airway pressure or continuous positive airway pressure support, and one required invasive mechanical ventilation; percentages with these interventions were lower among persons positive for SARS-CoV-2 by routine screening test or negative for SARS-CoV-2 (Supplemental Table 3). No pregnant persons died during peripartum hospitalizations.

Compared with all persons who tested negative for SARS-CoV-2 regardless of testing indication (N=10,641), persons who tested positive by clinically-indicated testing (N=27) had higher odds of preterm birth (37.0% vs. 8.4%; aOR: 6.82; 95% CI: 2.97–15.6) and ICU admission (14.8% vs. 4.5%; aOR: 8.03; 95% CI: 2.19–29.4); their newborns had higher odds of respiratory or cardiovascular disorder (39.3% vs. 13.6%; aOR: 3.96; 95% CI: 1.80–8.71) and neonatal ICU admission (25.0% vs. 10.8%; aOR: 2.79; 95% CI: 1.09–7.16). Odds of Cesarean delivery, labor or delivery complication, diagnosis of fetal distress, and neonatal disturbances or malformations at birth did not differ between these groups. Differences in pregnancy loss and neonatal deaths

by maternal peripartum SARS-CoV-2 infection status were not evaluated due to sample size. Compared with the 10,641 persons who tested negative for SARS-CoV-2, persons who tested positive by routine screening testing (N=195) had higher odds of a labor or delivery complication (11.8% vs. 10.2%; aOR: 2.17; 95% CI: 1.30–3.64) and ICU admission (12.3% vs. 4.5%; aOR: 1.98; 95% CI: 1.26–3.13) (Table 3).

Discussion

Among a cohort of >17,000 persons with peripartum hospitalizations during March 2020–February 2021 within three U.S. integrated healthcare networks, nearly 2 out of 3 persons were tested for SARS-CoV-2 during or within 3 days before their peripartum hospital stays, but testing rates varied substantially during the analytic period. Persons of certain racial and ethnic backgrounds, persons with peripartum Medicaid coverage, and persons admitted for peripartum hospitalization preterm were more likely to be tested at two sites. Findings highlight potential disparities in SARS-CoV-2 infection screening which may impact infection identification and subsequent care. Findings also suggest that analyses of characteristics and outcomes among convenience samples of persons with positive peripartum SARS-CoV-2 tests should be interpreted with caution because of potentially unidentified testing biases. During periods with high testing rates, up to 1 in 20 pregnant persons had peripartum SARS-CoV-2 infections, underscoring the importance of infection screening and control practices during peripartum hospitalizations.

This analysis identified differences in SARS-CoV-2 testing by hospitalization month, race and ethnicity, Medicaid coverage, and gestational age at hospitalization, including during time periods with universal testing protocols. Testing differences by month and site are not surprising given that testing resources, capacity, and institutional testing protocols evolved during the COVID-19 pandemic. However, findings related to testing variation by patient demographic and clinical factors highlight two important considerations. First, studies inferring differences in risk of infection or outcomes based on convenience samples of pregnant persons who test positive for SARS-CoV-2 may incorrectly attribute increased risk to characteristics associated with being tested for SARS-CoV-2. Making comparisons among persons who

were tested for SARS-CoV-2 can mitigate the effect of potential variations in testing [16]. Second, distinguishing between SARS-CoV-2 infections associated with clinical illness versus those incidentally identified by routine screening may be important for studies examining the effect of SARS-CoV-2 infection on pregnancy and perinatal outcomes. While we found that peripartum SARS-CoV-2 infection identified by clinically-indicated testing was associated with multiple adverse pregnancy and neonatal outcomes, SARS-CoV-2 infection identified by routine screening tests was only associated with having a labor or delivery complication and ICU admission. These findings are consistent with results from a study in Spain in which pregnant persons with symptomatic COVID-19 had higher preterm birth rates than persons without COVID-19, but persons with asymptomatic SARS-CoV-2 infections did not [3]. Results are also consistent with another study's findings of similar peripartum outcomes between persons with asymptomatic SARS-CoV-2 infections and persons negative for SARS-CoV-2 [17]. However, further research on the impact of asymptomatic SARS-CoV-2 infections during pregnancy should be considered.

Consistent with previous studies [18–20], we found peripartum SARS-CoV-2 infection was associated with adverse outcomes for both peripartum persons and their neonates, particularly among persons positive by clinically-indicated testing. Compared with pregnant persons testing negative for SARS-CoV-2, persons with SARS-CoV-2 infection identified by clinically-indicated testing had higher odds of preterm birth, maternal and neonatal ICU admission, and neonatal respiratory and cardiovascular disorders. These findings provide additional evidence that SARS-CoV-2 infection can result in serious sequelae for pregnant persons and their newborns. SARS-CoV-2 prevention practices such as COVID-19 vaccination during pregnancy, which was not widely available during the study period, can reduce risk of infection and thus subsequent sequelae [21,22]. In addition, findings that certain demographic characteristics (Hispanic or Latina ethnicity and peripartum Medicaid coverage) were associated with peripartum SARS-CoV-2 infection underscore inequities that place some populations at increased risk of SARS-CoV-2 infection and morbidity [23,24].

Even during peak SARS-CoV-2 testing and detection months, approximately 10–20% of peripartum persons were not tested, likely resulting in missed infections and missed opportunities to implement

procedures to reduce transmission to others in the hospital [5]. During periods when sites had universal SARS-CoV-2 testing protocols for peripartum hospitalizations, testing differences by demographic or pregnancy characteristics were observed at all sites. However, the specific characteristics associated with lower testing odds differed by site, highlighting potential challenges in interpreting and generalizing findings from single-center studies that estimate peripartum SARS-CoV-2 prevalence or report risk factors for peripartum SARS-CoV-2 infection during periods of reported universal testing. Further research on reasons underlying testing differences between demographic groups could improve equitable testing practices and care for pregnant persons with SARS-CoV-2 infections. Additionally, further research on peripartum SARS-CoV-2 testing practices should be conducted during the era of widespread COVID-19 vaccination and should consider the association between vaccination status and testing.

This analysis examined detailed SARS-CoV-2 testing, pregnancy, and clinical data from a large and diverse multi-site cohort. However, several limitations should be considered. First, available data were restricted to what was included in EHRs at the discretion of healthcare professionals. Second, ARFI diagnosis codes were used to identify clinically-indicated SARS-CoV-2 testing and presumed symptomatic SARS-CoV-2 infections. This approach is likely imperfect, and some tests and infections may have been misclassified. Third, persons tested for SARS-CoV-2 >3 days before peripartum hospitalization were not classified as having a peripartum SARS-CoV-2 test, although they may have had tests scheduled and conducted proximate to EDDs or scheduled deliveries. The decision to define peripartum SARS-CoV-2 testing as occurring during or ≤3 days before peripartum hospitalization was based on preliminary data from this cohort showing that most tests conducted within the week before peripartum hospitalization occurred ≤3 days before hospitalization and few additional tests would be captured if including testing 4–7 days before hospitalization. Last, this analysis was restricted to pregnancies ending during hospitalizations, limiting assessment of the effect of peripartum SARS-CoV-2 infection on miscarriages, which may not result in hospitalization, and other adverse pregnancy outcomes occurring before or after peripartum hospitalization. Furthermore, the restrictions on pregnancy end dates and EDDs in the cohort (pregnancies must have both ended and had EDDs during March 2020–February

2021) restricted the analytic period for detecting miscarriages and preterm births, reducing sample size available for analyzing these outcomes.

Within this cohort, up to 5% of peripartum persons were positive for SARS-CoV-2 during peak testing and SARS-CoV-2 detection months, with most infections identified by routine screening. Overall SARS-CoV-2 infection prevalence during peripartum hospitalizations may have been higher because persons with COVID-19 diagnoses >3 days before peripartum hospitalization were excluded but may have had SARS-CoV-2 infections when hospitalized. We found differential SARS-CoV-2 testing practices by selected demographic and pregnancy characteristics, despite protocols for universal SARS-CoV-2 screening implemented at all sites for portions of the analytic period. Peripartum SARS-CoV-2 infection identified by clinically-indicated testing was associated with increased odds of adverse pregnancy and neonatal outcomes. Findings support the importance of SARS-CoV-2 prevention practices during pregnancy to reduce infection and associated adverse health outcomes. Findings also support universal SARS-CoV-2 testing on labor and delivery wards during high circulation periods to promptly identify infections and reduce transmission risk to others in the hospital, with efforts to limit possible bias introduced when identifying patients for testing. Lastly, our findings can inform the design and interpretation of analyses assessing the effect of peripartum SARS-CoV-2 infection on pregnancy and perinatal outcomes.

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Table 1. Demographic, clinical, and pregnancy characteristics, by SARS-CoV-2 positivity status during peripartum hospitalization, Epidemiology of SARS-CoV-2 in Pregnancy and Infancy Network electronic cohort — March 2020–February 2021

	Overall[a] (N = 17,858)	SARS-CoV-2 positive[b] (N =222)	SARS-CoV-2 negative[b] (N =10,641)	aOR (95% CI)[c] (N = 8,278)[d]
Site				
Site 1	4,983/17,858 (27.9%)	35/222 (15.8%)	3,803/10,641 (35.7%)	ref.
Site 2	7,144/17,858 (40.0%)	44/222 (19.8%)	1,931/10,641 (18.1%)	**2.30 (1.31–4.04)**
Site 3	5,731/17,858 (32.1%)	143/222 (64.4%)	4,907/10,641 (46.1%)	**2.61 (1.55–4.40)**
Age at conception				
< 25 years	2,747/17,858 (15.4%)	87/222 (39.2%)	1,755/10,641 (16.5%)	**3.14 (1.87–5.28)**
25–34 years	10,487/17,858 (58.7%)	106/222 (47.7%)	6,270/10,641 (58.9%)	1.46 (0.91–2.36)
35–50 years	4,624/17,858 (25.9%)	29/222 (13.1%)	2,616/10,641 (24.6%)	ref.
Race and ethnicity[e]				
White	7,585/17,858 (42.5%)	41/222 (18.5%)	4,742/10,641 (44.6%)	ref.
Hispanic or Latina	4,882/17,858 (27.3%)	128/222 (57.7%)	2,980/10,641 (28.0%)	**2.46 (1.55–3.89)**
Black	1,822/17,858 (10.2%)	32/222 (14.4%)	1,271/10,641 (11.9%)	1.63 (0.91–2.92)
Asian	2,763/17,858 (15.5%)	13/222 (5.9%)	1,287/10,641 (12.1%)	1.23 (0.63–2.41)
Other	500/17,858 (2.8%)	7/222 (3.2%)	219/10,641 (2.1%)	2.10 (0.71–6.20)
Unknown	306/17,858 (1.7%)	1/222 (0.5%)	142/10,641 (1.3%)	n/a
Peripartum Medicaid coverage[f]	3946/17,705 (22.3%)	122/220 (55.5%)	2,904/10,554 (27.5%)	**1.66 (1.14–2.42)**
Underlying conditions				
Pre-pregnancy obesity[g]	4,407/14,927 (29.5%)	65/175 (37.1%)	2,540/8,262 (30.7%)	1.08 (0.78–1.50)
Gestational diabetes	2,192/17,858 (12.3%)	13/222 (5.9%)	1,330/10,641 (12.5%)	0.59 (0.30–1.14)
ARFI diagnostic code during peripartum hospitalization[h]	654/17,858 (3.7%)	34/222 (15.3%)	295/10,641 (2.8%)	**6.64 (4.18–10.6)**

Abbreviations: aOR, adjusted odds ratio; ARFI, acute respiratory or febrile illness; CI, confidence interval; n/a, not applicable; ref., referent; RT-PCR, real-time reverse transcription polymerase chain reaction assay; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

a.) Includes SARS-CoV-2 positive and SARS-CoV-2 negative persons, and persons not tested.

b.) SARS-CoV-2 positive or negative by RT-PCR test during or ≤ 3 days before peripartum hospitalization.

c.) Adjusted odds ratios control for all variables in the model. Confidence intervals that do not overlap with the null value of 1 are shown in bold.

d.) Number of persons included in the model after exclusions for missing data.

e.) To standardize race and ethnicity categories across the three sites that had differing methods of data collection for race and ethnicity, if a person's ethnicity was recorded as Hispanic or Latina in the electronic health record, that person's race and ethnicity was categorized as Hispanic or Latina in this analysis. If ethnicity was non-Hispanic or Latina or unknown, and race was White, Black, or Asian, the person's race and ethnicity was categorized as White, Black, or Asian, respectively. If a person's ethnicity was non-Hispanic or Latina or unknown and race was American Indian or Alaska Native, Native Hawaiian/Pacific Islander, or multiracial, the person's race and ethnicity was categorized as Other. If ethnicity was non-Hispanic or unknown and race was unknown, the race and ethnicity was categorized as unknown. Persons with unknown race and ethnicity were considered to have missing race and ethnicity and were not included in the multivariable model.
f.) Medicaid status was captured at the time of peripartum hospitalization. Ref.: did not have peripartum Medicaid coverage.
g.) Obesity was defined as body mass index ≥ 30 kg/m^2.
h.) ARFI diagnostic code at any time during the peripartum hospitalization (not restricted to ≤ 3 days before peripartum SARS-CoV-2 testing).

Table 2. Associations between demographic, clinical, and pregnancy characteristics and peripartum SARS-CoV-2 testing, hospitalized pregnant persons, Epidemiology of SARS-CoV-2 in Pregnancy and Infancy Network electronic cohort — March 2020–February 2021

	Site 1 aOR (95% CI)[a] N = 4,692[b]	**Site 2** aOR (95% CI)[a] N = 6,912[b]	**Site 3** aOR (95% CI)[a] N = 5,153[b]
Month of peripartum hospital admission			
March–May 2020	ref.	ref.	ref.
June–August 2020	**8.72 (7.15–10.7)**	0.70 (0.46–1.06)	**70.3 (41.1–121)**
September–November 2020	**11.3 (8.98–14.2)**	**6.72 (4.99–9.06)**	**88.4 (47.0–166)**
December 2020–February 2021	**8.98 (7.15–11.3)**	**142 (105–192)**	**30.4 (20.0–46.4)**
Age at conception			
< 25 years	0.91 (0.70–1.16)	0.87 (0.64–1.19)	0.77 (0.55–1.06)
25–34 years	1.17 (0.96–1.42)	0.90 (0.76–1.08)	1.00 (0.78–1.27)
35–50 years	Ref.	ref.	ref.
Race and ethnicity[c]			
White	ref.	ref.	ref.
Hispanic or Latina	1.00 (0.79–1.26)	**1.33 (1.08–1.64)**	1.24 (0.95–1.61)
Black	1.16 (0.80–1.70)	0.77 (0.54–1.10)	1.09 (0.80–1.47)
Asian	**1.36 (1.03–1.79)**	1.22 (0.99–1.50)	0.94 (0.63–1.39)
Other	0.86 (0.58–1.27)	0.85 (0.57–1.28)	0.93 (0.07–11.8)
Peripartum Medicaid coverage[d]	**1.33 (1.06–1.66)**	1.11 (0.85–1.44)	1.24 (0.96–1.60)
Number of routine antenatal visits[e]			
< 5 visits	ref.	ref.	ref.
5–11 visits	1.29 (0.87–1.93)	0.66 (0.30–1.45)	1.16 (0.93–1.45)
≥ 12 visits	0.95 (0.60–1.51)	0.97 (0.44–2.12)	1.22 (0.70–2.14)

Any complication during pregnancy[f]	1.19 (0.88–1.61)	0.93 (0.65–1.35)	1.18 (0.95–1.45)
Peripartum hospitalization at < 37 weeks gestation	**1.69 (1.19–2.39)**	**1.39 (1.03–1.88)**	0.83 (0.62–1.13)
Pregnancy loss[g]	0.54 (0.17–1.73)	0.65 (0.11–3.80)	2.99 (0.82–10.9)

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; ref., referent; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
a.) Adjusted odds ratios control for all variables in the model. Confidence intervals that do not overlap with the null value of 1 are shown in bold.
b.) Number of persons included in the model after exclusions for missing data.
c.) To standardize race and ethnicity categories across the three sites that had differing methods of data collection for race and ethnicity, if a person's ethnicity was recorded as Hispanic or Latina in the electronic health record, that person's race and ethnicity was categorized as Hispanic or Latina in this analysis. If ethnicity was non-Hispanic or Latina or unknown, and race was White, Black, or Asian, the person's race and ethnicity was categorized as White, Black, or Asian, respectively. If a person's ethnicity was non-Hispanic or Latina or unknown and race was American Indian or Alaska Native, Native Hawaiian/Pacific Islander, or multiracial, the person's race and ethnicity was categorized as Other. If ethnicity was non-Hispanic or unknown and race was unknown, the race and ethnicity was categorized as unknown.
d.) Medicaid status was captured at the time of peripartum hospitalization. Ref.: did not have peripartum Medicaid coverage.
e.) In the cohort, the median number of routine antenatal visits was 9; interquartile range: was 5–11.
f.) Data on the following pregnancy complications were extracted from the electronic health record: hemorrhage during pregnancy, bleeding in pregnancy, hypertension complicating pregnancy (by diagnostic codes), excessive vomiting during pregnancy, renal disease during pregnancy, infectious and parasitic diseases complicating pregnancy (by diagnostic codes), diabetes during pregnancy, gestational diabetes arising in pregnancy, thyroid dysfunction in pregnancy (by diagnostic codes), drug dependence during pregnancy, congenital cardiovascular disorders complicating pregnancy, epilepsy complicating pregnancy, malposition of fetus, cephalopelvic disproportion, abnormalities of organs and soft tissues of pelvis, suspected damage to fetus due to maternal drug use, fetal growth restriction, and early or threatened labor.
g.) Refers to pregnancy loss during the peripartum hospitalization. Ref.: live birth.

Table 3. Pregnancy and neonatal outcomes, by SARS-CoV-2 positivity status during peripartum hospitalization, Epidemiology of SARS-CoV-2 in Pregnancy and Infancy Network electronic cohort — March 2020–February 2021

	SARS-CoV-2 negative (N = 10,641)[a]	SARS-CoV-2 positive via clinically-indicated test (N = 27)[a]	SARS-CoV-2 positive via clinically-indicated test vs SARS-CoV-2 negative aOR (95% CI)[b]	SARS-CoV-2 positive via routine screening test[a] (N = 195)	SARS-CoV-2 positive via routine screening test vs SARS-CoV-2 negative aOR (95% CI)[c]
Pregnancy outcome					
Live birth	10,573/10,641 (99.4%)	27/27 (100.0%)	ref.	193/195 (99.0%)	ref.
Term live birth (≥ 37 weeks gestation)[d]	9,684/10,573 (91.6%)	17/27 (63.0%)	ref.	179/193 (92.7%)	ref.
Pre-term live birth (< 37 weeks gestation)[d]	889/10,573 (8.4%)	10/27 (37.0%)	**6.82 (2.97–15.6)**	14/193 (7.3%)	0.73 (0.42–1.28)
Pregnancy loss (referent: live birth)	68/10,641 (0.6%)	0	NR[e]	2/195 (1.0%)	1.52 (0.36–6.37)
Pregnancy loss at < 20 weeks gestation	19/10,641 (0.2%)	0	--	0	--
Pregnancy loss at ≥ 20 weeks gestation	47/10,641 (0.4%)	0	--	2/195 (1.0%)	--
Mode of delivery					
Vaginal	7,159/10,522 (68.0%)	17/27 (63.0%)	ref.	143/193 (74.1%)	ref.
Induced (among vaginal deliveries)	1,115/7,159 (15.6%)	4/17 (23.5%)	--	15/143 (10.5%)	--

Cesarean delivery (referent: vaginal delivery)	3,363/10,522 (32.0%)	10/27 (37.0%)	1.32 (0.58–2.99)	50/193 (25.9%)	0.74 (0.53–1.03)
Any labor or delivery complication[f]	1,083/10,641 (10.2%)	4/27 (14.8%)	0.72 (0.21–2.52)	23/195 (11.8%)	**2.17 (1.30–3.64)**
Post-partum hemorrhage	621/10,641 (5.8%)	2/27 (7.4%)	--	11/195 (5.6%)	--
Chorioamnionitis during labor	496/10,641 (4.7%)	2/27 (7.4%)	--	14/195 (7.2%)	--
Placental abruption during delivery	69/10,641 (0.6%)	0	--	2/195 (1.0%)	--
Pulmonary embolism during labor	5/10,641 (<0.1%)	0	--	0	--
Mother admitted to ICU	478/10,641 (4.5%)	4/27 (14.8%)	**8.03 (2.19–29.4)**	24/195 (12.3%)	**1.98 (1.26–3.13)**
Fetal distress	1,488/10,641 (14.0%)	3/27 (11.1%)	0.60 (0.18–2.03)	24/195 (12.3%)	0.90 (0.58–1.39)
Neonates (n)	10,756	28		196	
Neonatal clinical characteristics[g]					
Respiratory or cardiovascular disorder	1,466/10,756 (13.6%)	11/28 (39.3%)	**3.96 (1.80–8.71)**	22/196 (11.2%)	0.75 (0.48–1.18)
Disturbances or malformations at birth	1,511/10,756 (14.0%)	6/28 (21.4%)	0.80 (0.28–2.26)	23/196 (11.7%)	1.26 (0.76–2.09)
Admitted to neonatal ICU	1,167/10,756 (10.8%)	7/28 (25.0%)	**2.79 (1.09–7.16)**	24/196 (12.2%)	0.86 (0.56–1.34)
Neonatal death during birth hospitalization[h]	25/9,712 (0.3%)	0	NR[e]	1/181 (0.6%)	2.14 (0.28–16.2)

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; ICU, intensive care unit; NR, not reported; ref., referent; RT-PCR, real-time reverse transcription polymerase chain reaction assay; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

a.) Includes pregnant persons tested by RT-PCR during or ≤ 3 days prior to the peripartum hospitalization. Pregnant persons who had ≥ 1 acute respiratory or febrile illness diagnosis code recorded in the electronic health record ≤ 3 days before peripartum testing were defined as having had a clinically-indicated test; others with peripartum testing were considered to have had a routine screening test. Persons negative for SARS-CoV-2 include persons who tested negative either via a clinically-indicated or routine screening test.

b.) Odds ratios are adjusted for site, Medicaid coverage at the end of pregnancy, and maternal age group at conception. Confidence intervals that do not overlap with the null value of 1 are shown in bold. The total number of observations in each model varied by outcome, after excluding those with missing data. For this column: N = 10,513 for preterm birth, N = 10,461 for Cesarean delivery, N = 10,580 for labor or delivery complication, N = 10,580 for fetal distress, N = 10,580 for maternal ICU admission, N = 10,696 for neonatal respiratory or cardiovascular disorder, N = 10,696 for neonatal disturbances or malformations at birth, and N = 10,697 for neonatal ICU admission.

c.) Odds ratios are adjusted for site, Medicaid coverage at the end of pregnancy, and maternal age group at conception. Confidence intervals that do not overlap with the null value of 1 are shown in bold. The total number of observations in each model varied by outcome, after excluding those with missing data. For this column: N = 10,679 for preterm birth, N = 10,748 for pregnancy loss, N = 10,627 for Cesarean delivery, N = 10,748 for labor or delivery complication, N = 10,748 for fetal distress, N = 10,748 for maternal ICU admission, N = 10,864 for neonatal respiratory or cardiovascular disorder, N = 10,864 for neonatal disturbances or malformations at birth, N = 10,865 for neonatal ICU admission, and N = 9,813 for neonatal death.

d.) Denominator is the number of pregnancies resulting in live birth for which the gestational age at delivery was available.

e.) Model results are not reported if no persons had the outcome of interest within one of the comparison groups, or if the multivariable model did not converge.

f.) Data on the following labor or delivery complications were extracted from the electronic health record: post-partum hemorrhage, chorioamnionitis during labor identified by diagnostic codes, placental abruption during delivery, pulmonary embolism during labor by diagnostic codes, and maternal seizure during delivery. No persons in the cohort experienced maternal seizures during delivery. Persons may have experienced more than one of the listed labor or delivery complications.

g.) Denominator is the number of liveborn neonates.

h.) Among liveborn neonates with known status at mother's hospital discharge.

Figure 1. Inclusion and peripartum SARS-CoV-2 testing, hospitalized pregnant persons, Epidemiology of SARS-CoV-2 in Pregnancy and Infancy Network electronic cohort — March 2020–February 2021

Figure 2. Peripartum SARS-CoV-2 testing and positive tests, hospitalized pregnant persons, Epidemiology of SARS-CoV-2 in Pregnancy and Infancy Network electronic cohort — March 2020–February 2021

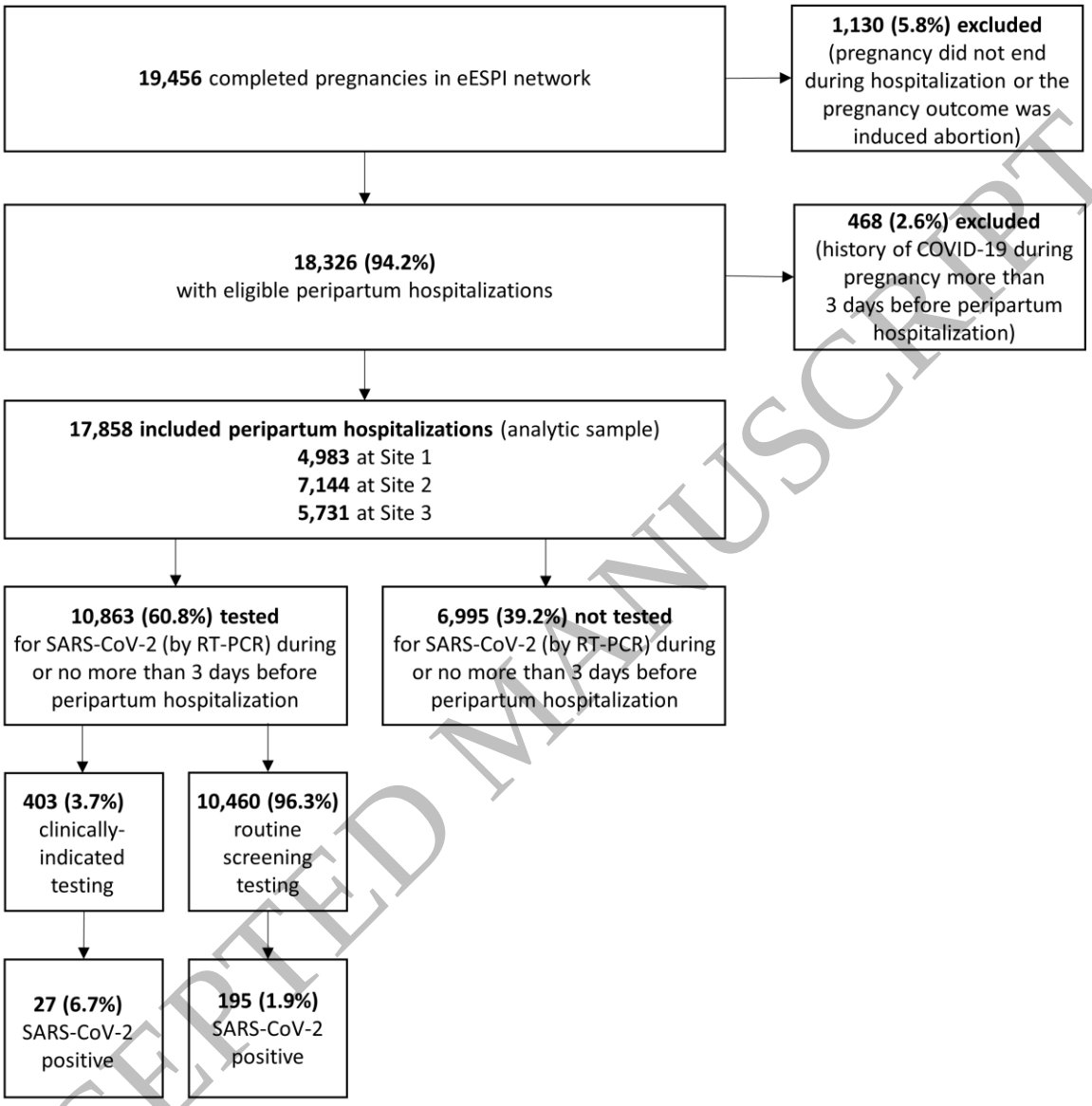

Figure 1
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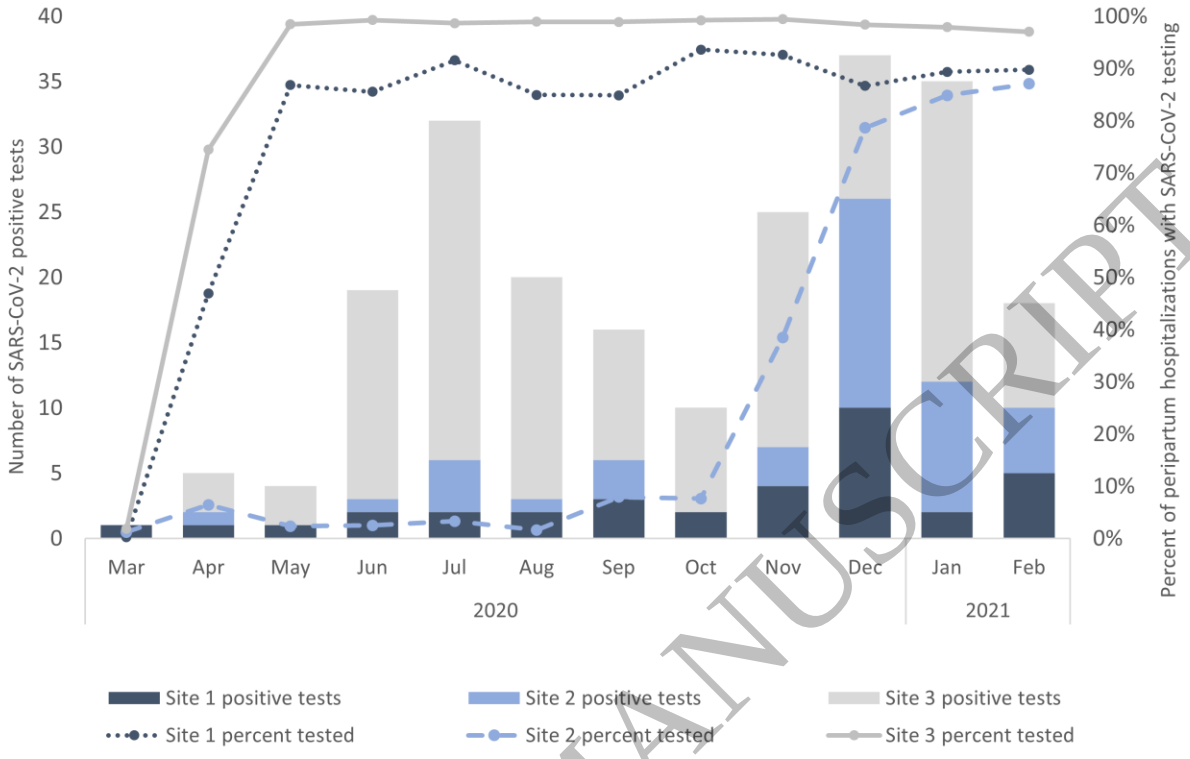

Figure 2
165x117 mm (x DPI)