Open Forum Infectious Diseases

MAJOR ARTICLE

Risk of Severe Maternal Morbidity Associated With Severe Acute Respiratory Syndrome Coronavirus 2 Infection During Pregnancy

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Background. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during pregnancy increases the risk of adverse fetal and neonatal outcomes, but the contribution to severe maternal morbidity (SMM) has been less frequently documented.

Methods. We conducted a national cohort study of 93 624 deliveries occurring between 11 March 2020 and 1 July 2021 using medical claims information from the OptumLabs Data Warehouse. SARS-CoV-2 infection was identified from diagnostic and laboratory testing claims records. We identified 21 SMM conditions using *International Classification of Diseases, Tenth Revision, Clinical Modification* and procedure codes and compared SMM conditions by SARS-CoV-2 status using Poisson regression with robust variance, adjusting for maternal sociodemographic and health factors, onset of labor, and week of conception.

Results. Approximately 5% of deliveries had a record of SARS-CoV-2 infection: 27.0% <7 days before delivery, 13.5% within 7–30 days of delivery, and 59.5% earlier in pregnancy. Compared to uninfected pregnancies, the adjusted risk of SMM was 2.22 times higher (95% confidence interval [CI], 1.97–2.48) among those infected <7 days before delivery and 1.66 times higher (95% CI, 1.23–2.08) among those infected 7–30 days before delivery. The highest risks were observed for acute respiratory distress syndrome (adjusted risk ratio [aRR], 13.24 [95% CI, 12.86–13.61]) and acute renal failure (aRR, 3.91 [95% CI, 3.32–4.50]).

Conclusions. COVID-19 is associated with increased rates of SMM.

Keywords. COVID-19; pregnancy outcomes; SARS-CoV-2; severe maternal morbidity.

Pregnancy is an immunologically vulnerable period, placing pregnant people at risk for more severe illness and complications from infections. It is now widely acknowledged that pregnant people are at higher risk due to coronavirus disease 2019 (COVID-19), the disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19–associated rates of admission to the intensive care unit, invasive ventilation, and need for extracorporeal membrane oxygenation are believed to be 2- to 3-fold higher among pregnant people compared to nonpregnant women of reproductive age [1–3].

While numerous studies have evaluated the impact of SARS-CoV-2 infection on pregnancy complications and conditions linked to severe maternal morbidity (SMM), the implications of SARS-CoV-2 for SMM have been less frequently evaluated. SMM is correlated with maternal mortality, since if left untreated, these conditions can lead to maternal death [4]. In addition to the severe direct health consequences of SMM to pregnant people, SMM additionally contributes to increased medical costs and extended hospitalization stays. Up to 60% of SMM conditions are preventable [5], and knowledge of the contribution of SARS-CoV-2 to these conditions is valuable for informing prevention efforts.

Most of the previous studies evaluating SARS-CoV-2 infection and SMM have not comprehensively evaluated SMM conditions [6–8], have been conducted in single US states or healthcare systems [9–12], or included a small number of cases and were not sufficiently powered to detect low incidence events contributing to SMM. Although larger, multicenter cohort studies have reported a 2- to 5-fold increase in the risk of acute respiratory distress syndrome, sepsis, acute renal failure, shock, obstetric hemorrhage, and acute cardiac events [12, 13], these studies did not report on each of the 21 indicators of SMM individually (as defined by the US Centers for Disease Control and Prevention [CDC]) [14]. Furthermore, some cohort studies have failed to identify any association between SARS-CoV-2 infection and SMM [9], indicating that further evaluation of the impact of COVID-19 on SMM is needed.

Received 30 August 2023; editorial decision 03 November 2023; accepted 01 December 2023; published online 7 December 2023

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Open Forum Infectious Diseases®

https://doi.org/10.1093/ofid/ofad613

To address this gap, we aimed to assess the risk of SMM following SARS-CoV-2 infection during pregnancy in a large, national claims-based pregnancy cohort.

METHODS

We conducted a national retrospective cohort study using deidentified medical claims data for commercially insured individuals from the OptumLabs Data Warehouse (OLDW). The OLDW includes longitudinal health information for enrollees, including medical and pharmacy claims, laboratory results, and insurance enrollment records. Individuals were included in the cohort if they had a record of delivery (*International Classification of Diseases, Tenth Revision, Clinical Modification* [*ICD-10-CM*] code Z37) between 11 March 2020 (ie, declaration of COVID-19 pandemic status) and 1 July 2021. Additional eligibility criteria included (1) enrollment in pharmacy coverage to ensure the most complete capture of medical information in the cohort; and (2) continuous enrollment in the commercial insurance plan for 294 days prior to the date of delivery (ie, to allow complete measurement of SARS-CoV-2 infection).

For individuals selected into the cohort, we extracted all physician, facility, and laboratory claims records for 294 days preceding and 30 days following the date of delivery. We defined SMM from the delivery admission using *ICD-10-CM* and *ICD-10-PCS* codes (Supplementary Table 1) that identify the 21 SMM conditions as outlined by the US CDC [14]. We used *ICD-10-CM* code Z3A to identify gestational age at delivery. SARS-CoV-2 infection was identified based on the presence of either a diagnostic code in a facility or physician claim record consistent with a COVID-19 diagnosis (*ICD-10-CM* code U07.1) or a positive laboratory test for SARS-CoV-2 (Supplementary Table 2). We measured the interval (in days) between SARS-CoV-2 detection and delivery by subtracting the date of infection from the date of delivery. Intervals were grouped into 3 categories: <7 days prior to delivery, 7–30 days prior to delivery, or >30 days prior to delivery.

Maternal characteristics included age, race/ethnicity, educational attainment, insurance status, and US census region of residence. Maternal race and ethnicity information and educational attainment were imputed, using a proprietary algorithm supplied by an external vendor for the medical claims cohort. The algorithm uses a structured, rule-based system, drawing from personal information (first names, middle names, surnames) and residential information available from enrollees to impute race, ethnicity, and educational attainment. Race and ethnicity were defined as non-Hispanic Black, Hispanic, or non-Hispanic White. Other races not listed included Asian, American Indian, Alaskan Native, Pacific Islander, Native Hawaiian, and multiple races. Education was estimated based on the average level of education achieved among residents within the census block, and household income was derived using consumer data from the street address of the enrollee. We identified preexisting medical conditions associated with a higher risk of severe COVID-19 illness [15] using diagnoses from physician and facility medical claims records throughout the pregnancy. We similarly identified pregnancy complications from diagnostic codes present in all physician and facility medical claims records (Supplementary Table 3). Missing covariate information was imputed using expectation-maximization with bootstrapping procedures in the Amelia package in R software [16].

Because this study involved analysis of preexisting, deidentified data, it was considered exempt from Institutional Review Board approval. Access to study data was financially supported by OptumLabs and the University of California, Los Angeles. The funder had no influence in the design or implementation of the study or the decision to publish the study findings. The lead author (A. K. R.) affirms that this work is an honest, accurate, and transparent account of the study being reported; no important aspects of the study have been omitted; and any discrepancies from the study as originally planned have been explained.

Statistical Analysis

The incidence of SMM and individual SMM indicators was estimated by dividing the number of events by the total number of admissions. Where there were <11 events, these were suppressed in accordance with the data provider's suppression criteria. For these events, we report the maximum rate possible under suppression criteria (ie, <*X* events per 10 000 admissions). We used χ^2 statistics to examine the distribution of sociodemographic, health, and pregnancy factors associated with SARS-CoV-2 infection. To estimate the risk of SMM associated with SARS-CoV-2 infection, we used Poisson regression with a robust sandwich estimator for variance estimation to generate risk ratios (RRs) and 95% confidence intervals (CIs). Adjusted models controlled for maternal age, maternal race/ethnicity, household income, rural residence, educational attainment, presence of a preexisting health condition (yes/no), and onset of labor (spontaneous/clinician-indicated). To account for temporal variation in disease activity and maternal care over time, we additionally included the week of conception using a cubic B-spline. Because blood transfusion has been identified as an indicator of SMM with lower positive predictive values than other conditions [17], we considered SMM without blood transfusions as a separate outcome. Because Black and Hispanic pregnant people are more than twice as likely as White pregnant people to develop SMM [18], and SMM is more frequent for pregnant people with preexisting health conditions and pregnancies complicated by preeclampsia and other conditions [19], we estimated RRs for these groups separately. To inform the contribution of SARS-CoV-2 infection to SMM, we estimated the attributable risk and attributable

fractions. Attributable risks were estimated as the difference in incidence rates observed among pregnancies with and without SARS-CoV-2 infection. We estimated the attributable fraction (AF) and the population attributable fraction (PAF) based on the prevalence of the exposure and the adjusted RR using Levin's formula [20].

All analyses were performed in R version 4.0.2. To evaluate how unmeasured confounding could have influenced our results, we estimated E-values using the EValue package in R software [21] using the adjusted RRs and corresponding CIs.

RESULTS

Of the 93 624 deliveries identified (Supplementary Figure 1), 4486 (4.8%) had a record of SARS-CoV-2 infection at any time during their pregnancy: 1211 (27.0%) within <7 days of delivery, 604 (13.5%) within 7–30 days prior to delivery, and 2671 (59.5%) earlier in pregnancy (Figure 1). Among the 4486 deliveries with a history of SARS-CoV-2 infection during pregnancy, 3644 (81.2%) were identified through clinical diagnosis alone, 397 (8.8%) by laboratory testing alone, and 445 (9.9%) through both clinical diagnosis and laboratory testing. Seven percent of infections detected during the 7 days prior to delivery, 17% of detections during the 7–30 days prior to delivery, and 24% of detections earlier in pregnancy were made by laboratory testing, indicating that more detections of SARS-CoV-2 were made by clinical diagnosis near delivery.

Those with SARS-CoV-2 infection within 7 days of delivery were more commonly younger (15–24 years old), Hispanic or non-Hispanic Black, resided in a rural area, had lower household income (<$40 000), and delivered after August 2020 compared to those without SARS-CoV-2 infection (Table 1). Lower household income (<$40 000) and a high school education or less were also more common among pregnancies with SARS-CoV-2 infection compared to those uninfected. Preexisting asthma was more common among those with SARS-CoV-2 infection during the 7–30 days prior to delivery (8.9%) or earlier in pregnancy (8.5%) compared to those uninfected (6.7%). Ninety-eight percent of deliveries with a SARS-CoV-2 infection during the week of delivery and 99% of uninfected deliveries resulted in a live birth ($P = .14$).

A total of 1983 deliveries had 1 or more conditions comprising the SMM composite, resulting in a rate of 212 (95% CI, 203–221) per 10 000 delivery admissions. When SMM admissions related to blood transfusion were excluded (n = 691), the rate of SMM was 138 (95% CI, 131–146) per 10 000 delivery admissions. The most common conditions identified were blood transfusion (85 per 10 000 admissions), eclampsia (<29 per 10 000 admissions), sepsis (24 per 10 000 admissions), pulmonary edema or acute heart failure (<24 per 10 000 admissions), disseminated intravascular coagulation (<22 per 10 000 admission), acute renal failure (17 per 10 000 admissions), and acute respiratory distress syndrome (ARDS; 17 per 10 000 admissions). All other events were less common. SMM at delivery admission was associated with lower (15–25 years) or advanced maternal age (≥35 years), non-Hispanic Black race, lower household income and educational attainment, preexisting medical conditions, and diagnosed pregnancy complications (Supplementary Table 5). We observed no variation in SMM over time ($P = .22$).

The risk of SMM was 2.22 times higher (95% CI, 1.97– 2.48) among those with SARS-CoV-2 infection within 7 days of delivery and 1.66 times higher (95% CI, 1.23–2.08) among those with infection 7–30 days prior to delivery compared to those who were uninfected (Table 2).

Based on estimated E-values, an unmeasured confounder would need to have a minimum strength of 3.87 with both SARS-CoV-2 infection and SMM to fully explain away the higher risk of SMM associated with SARS-CoV-2 infection <7 days prior to delivery (Supplementary Table 4). Among those with SARS-CoV-2 infection >30 days prior to delivery, we observed no association with SMM (aRR, 1.02 [95% CI, .76–1.28]). Stronger associations were observed after removing blood products transfusion from the definition of SMM, although with similar conclusions. Among those with SARS-CoV-2 infection during the 7 days prior to delivery, 55% of SMM cases could be attributed to infection (AF, 0.55 [95% CI, .43–.66]). At a population level, we estimate that 2% of SMM cases can be attributed to SARS-CoV-2 infection during the 7 days prior to delivery (PAF, 0.02 [95% CI, .00–.03]), or 3% if excluding blood products transfusion (PAF, 0.03 [95% CI, .00–.05]).

Among individual conditions of the SMM composite, we observed the highest risk associated with SARS-CoV-2 infection for ARDS (aRR, 13.24 [95% CI, 12.86–13.61]) (Supplementary Table 6). The risks of sepsis and acute renal failure were 3–4 times greater for deliveries following SARS-CoV-2 infection compared to uninfected (aRR, 3.15 [95% CI, 2.59–3.71] and aRR, 3.91 [95% CI, 3.32–4.50], respectively). An unobserved confounder would need to have an association greater than 26 or 5.7 with both SARS-CoV-2 infection and SMM to fully explain away the observed increased risk in ARDS and sepsis, respectively (Supplementary Table 4). We observed no difference in the risk of blood products transfusion associated with SARS-CoV-2 infection (aRR, 1.12 [95% CI, .65–1.59]).

The greatest burden of SARS-CoV-2 infection in terms of impact on SMM was observed among those with at least 1 preexisting medical condition. Among those with a preexisting medical condition, the risk of SMM was nearly 3 times higher following SARS-CoV-2 infection compared to no infection (aRR, 2.97 [95% CI, 2.64–3.29]), and among those infected, SARS-CoV-2 contributed to 66% of SMM cases (AF 0.66 [95% CI, .55–.78]) (Table 3). Among infected non-Hispanic Black pregnant people, 60% of SMM cases were attributed to SARS-CoV-2 (AF, 0.60 [95% CI, .38–.76]), and among infected

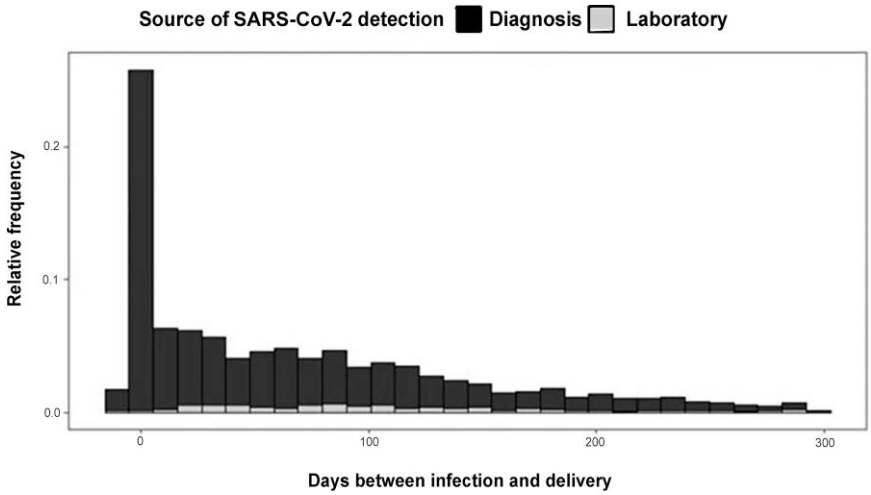

Figure 1. Time (in days) between severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and delivery, by mode of detection, March 2020 to July 2021. Some y-axis values have been suppressed in accordance with OptumLabs data release policy.

Hispanic pregnant people, 57% of SMM cases were attributed to SARS-CoV-2 (AF, 0.57 [95% CI, .41–.79]). We estimate that for all pregnant people in these higher risk groups, prevention of SARS-CoV-2 could have reduced the incidence of SMM by 3%–4%.

DISCUSSION

Among this large, national, commercially insured cohort of pregnant people who gave birth during a time when <24% of pregnant people had received a COVID-19 vaccine [22], we found that SARS-CoV-2 infection around the time of delivery was associated with increased risk of SMM, especially ARDS, and contributed to 2%–3% of total SMM cases. COVID-19 is preventable, and prevention of SARS-CoV-2 infection around the time of delivery could reduce the incidence of SMM and subsequent health burden, especially in high-risk groups.

Results in the Context of What Is Known

Our results align with those of previous studies evaluating SMM-related conditions, including ARDS, sepsis, and acute renal failure [13], and extend our understanding of how SARS-CoV-2 infection may impact SMM more broadly in the context of limited vaccination. Two large cohort studies in New York and California similarly found that SARS-CoV-2–infected patients who delivered between March 2020 and March 2021 were at a 2- to 2.5-fold greater risk of SMM compared to those who were uninfected [10, 12]. However, neither of these studies evaluated specific SMM conditions.

A previous analysis of data from 703 US hospitals between March and September 2020 that did evaluate individual SMM conditions showed that the risk of ARDS was 34-fold higher, the risk of sepsis was 14-fold higher, and acute renal failure was 3-fold higher for pregnant people infected with SARS-CoV-2 compared to uninfected pregnant people [13]. While our estimates are slightly more conservative (ARDS, 13.2; sepsis, 3.1; acute renal failure, 3.9), we similarly show elevated risks of SMM conditions due to infection occurring around the time of delivery. One important distinction between this study and ours is the identification of SARS-CoV-2 infection. We used both diagnostic coding and laboratory testing data, and we measured infection occurring at any stage in pregnancy; in contrast, Ko et al used diagnostic coding exclusively and only in the delivery hospitalization record [13].

Our approach offers several advantages. First, previous research has shown that restriction to diagnostic coding alone may miss up to 30% of COVID-19 cases [23]. Second, because we were able to identify infections occurring throughout the pregnancy, we were able to show that even when diagnosed outside the week of delivery, an elevated risk of SMM associated with SARS-CoV-2 infection can still be observed.

We identified several groups of pregnant people where SARS-CoV-2 infection may be of particular concern for SMM, including Black and Hispanic pregnant people and those with preexisting medical conditions. These findings align with those from previous investigations, suggesting that pregnant people with preexisting health conditions and Black and Hispanic pregnant people are more likely to experience severe COVID-19 and downstream health consequences compared to their White counterparts. An ongoing living systematic review of 435 observational studies (at the time of writing) indicates that preexisting medical conditions were associated with an 48% increase in the odds of severe COVID-19 during pregnancy [24]. Furthermore, prior surveillance data have consistently documented higher rates of severe COVID-19 among

Table 1. Characteristics of Pregnant People Aged 15–49 Years Delivering Between March 2020 and July 2021, by Severe Acute Respiratory Syndrome Coronavirus 2 Infection Status—United States

Characteristic	Infection Within 7 Days of Delivery (n = 1211)	Infection 7–30 Days Prior to Delivery (n = 604)	Infection >30 Days Prior to Delivery (n = 2671)	No SARS-CoV-2 Infection (n = 89 138)	χ^2 *P* Value
Maternal age					<.001
15–24 y	159 (13.1)	72 (11.9)	312 (11.7)	8364 (9.4)	
25–29 y	295 (24.3)	179 (29.6)	732 (27.4)	20 043 (22.5)	
30–34 y	421 (34.8)	230 (38.1)	969 (36.3)	34 447 (38.6)	
35–39 y	273 (22.5)	102 (16.9)	524 (19.6)	21 324 (23.9)	
≥40 y	63 (5.2)	21 (3.5)	134 (5.0)	4960 (5.6)	
Maternal race and ethnicity					<.001
Hispanic	231 (19.1)	127 (21.0)	561 (21.0)	14 155 (15.9)	
Non-Hispanic White	722 (59.6)	355 (58.8)	1559 (58.4)	56 746 (63.7)	
Non-Hispanic Black	161 (13.3)	83 (13.7)	376 (14.1)	10 224 (11.5)	
Races not listed here[a]	97 (8.0)	39 (6.5)	175 (6.5)	8013 (9.0)	
Household income					<.001
<$40 000	269 (22.2)	107 (17.7)	601 (22.5)	17 378 (19.5)	
$40 000–$74 999	284 (23.5)	160 (26.5)	558 (20.9)	19 480 (21.8)	
$75 000–$124 999	327 (27.0)	172 (28.5)	744 (27.8)	24 851 (27.9)	
$125 000–$199 999	205 (16.9)	97 (16.1)	446 (16.7)	16 097 (18.1)	
≥$200 000	126 (10.4)	68 (11.3)	322 (12.1)	11 332 (12.7)	
Rurality of residence					.001
Metropolitan	1077 (88.9)	531 (87.9)	2340 (87.6)	80 266 (90.0)	
Micropolitan	62 (5.1)	42 (6.9)	181 (6.8)	4816 (5.4)	
Small town	45 (3.7)	17 (2.8)	99 (3.7)	2622 (2.9)	
Rural	27 (2.2)	14 (2.3)	51 (1.9)	1434 (1.6)	
Education[b]					<.001
High school or less	330 (27.2)	137 (22.7)	696 (26.1)	18 476 (20.7)	
Some college or technical	586 (28.4)	314 (52.0)	1360 (50.9)	45 664 (51.2)	
College graduate or more	295 (24.4)	153 (25.3)	615 (23.0)	24 998 (28.0)	
Preexisting medical conditions					
Any condition[c]	147 (12.1)	83 (13.7)	346 (12.9)	10 010 (11.2)	.006
Asthma	80 (6.6)	54 (8.9)	228 (8.5)	6006 (6.7)	<.001
Hypertension	59 (4.9)	27 (4.5)	110 (4.1)	3711 (4.1)	.65
Delivery date					<.001
Jan–Aug 2020	247 (20.4)	80 (13.2)	61 (2.3)	32 582 (36.5)	
Aug–Dec 2020	545 (45.0)	289 (47.8)	764 (28.6)	33 892 (38.0)	
Jan–Jul 2021	419 (34.6)	235 (38.9)	1846 (69.1)	22 664 (25.4)	
Pregnancy complications					
Any complication	534 (44.1)	269 (44.5)	1235 (46.2)	39 346 (44.1)	.20
Plural pregnancy	21 (1.7)	…[d]	…[d]	1567 (1.7)	.74
Preeclampsia	61 (5.0)	40 (6.6)	131 (4.9)	4541 (5.1)	.37
Gestational diabetes	156 (12.9)	61 (10.1)	319 (11.9)	10 530 (11.8)	.38
Premature rupture of membranes	136 (11.2)	72 (11.9)	333 (12.5)	11 500 (12.9)	.29
Antepartum hemorrhage	79 (6.5)	44 (7.3)	196 (7.3)	5599 (6.3)	.11
Premature onset of labor	86 (7.1)	43 (7.1)	157 (5.9)	4982 (5.6)	.04
Induction of labor	316 (26.1)	159 (26.3)	764 (28.6)	23 544 (26.4)	.09
Cesarean delivery	232 (19.1)	104 (17.2)	437 (16.4)	15 859 (17.8)	.15
Postpartum hemorrhage	64 (5.3)	32 (5.3)	141 (5.3)	4747 (5.3)	.99
Pregnancy ended in live birth	1192 (98.4)	>593 (>98.2)[d]	>2600 (>99.6)[d]	88 330 (99.1)	.14

Data are presented as No. (%).

Abbreviation: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

[a]Races not listed here included Asian, American Indian, Alaskan Native, Pacific Islander, Native Hawaiian, and multiple races.

[b]Education represents the average educational attainment for the census block of the enrollee's household.

[c]Any preexisting health condition included a diagnosis of asthma, diabetes, chronic hypertension, chronic heart disease, metabolic disorders, immunosuppression, blood disorders, neurological disease, and renal disease. Frequencies for individual conditions are presented where data suppression criteria were not met.

[d]Data suppressed in accordance with the data provider's suppression policy.

Table 2. Risk of Severe Maternal Morbidity Associated With Severe Acute Respiratory Syndrome Coronavirus 2 Infection Among Pregnant People Delivering Between March 2020 and July 2021—United States

Condition	Infection Within <7 Days of Delivery (n = 1211)	Infection 7–30 Days Prior to Delivery (n = 604)	Infection >30 Days Prior to Delivery (n = 2671)	No SARS-CoV-2 Infection (n = 89 138)
SMM				
Cases per 10 000 admissions (95% CI)	479 (372–614)	348 (229–526)	213 (165–275)	207 (198–217)
RR (95% CI)	2.31 (2.06–2.57)	1.68 (1.25–2.10)	1.03 (.77–1.29)	Reference
aRR[a] (95% CI)	2.22 (1.97–2.48)	1.66 (1.23–2.08)	1.02 (.76–1.28)	Reference
Attributable risk (95% CI)	272 (190–353)	141 (26–255)	6 (−48 to 61)	Reference
AF in exposed (95% CI)[b]	0.55 (.43–.66)	0.40 (.14–.65)	0.02 (.00–.27)	Reference
PAF (95% CI)[b]	0.02 (.0–.03)	0.00 (−.02 to .03)	0.00 (−.01 to .01)	Reference
SMM excluding blood products transfusion				
Cases per 10 000 admissions (95% CI)	413 (315–540)	282 (177–446)	153 (113–208)	133 (125–141)
RR (95% CI)	3.11 (2.83–3.39)	2.12 (1.65–2.59)	1.15 (.85–1.46)	Reference
aRR[a] (95% CI)	3.01 (2.73–3.29)	2.13 (1.66–2.60)	1.16 (.85–2.60)	Reference
Attributable risk (95% CI)	280 (214–346)	149 (57–241)	20 (−23 to 65)	Reference
AF in exposed (95% CI)[b]	0.67 (.58–.76)	0.53 (.31–.75)	0.14 (.00–.40)	Reference
PAF (95% CI)[b]	0.03 (.00–.05)	0.01 (−.01 to .03)	0.00 (−.02 to .03)	Reference

Abbreviations: AF, attributable fraction; aRR, adjusted risk ratio; CI, confidence interval; PAF, population attributable fraction; RR, risk ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SMM, severe maternal morbidity.

[a]Risk ratios adjusted for maternal age, race/ethnicity, household income, educational attainment, rurality of residence, preexisting health condition (yes/no), onset of labor (spontaneous/clinician-indicated), and week of conception (cubic spline).

[b]AF in exposed and PAF were estimated based on the observed prevalence of coronavirus disease 2019 and the aRR, using Levin's formula [20].

minority populations, both in the US [2] and abroad [25]. Racial disparities in SMM and maternal mortality continue to be documented in the US [5, 26], with mortality rates 3–4 times higher among Black pregnant people compared to White pregnant people. Surveillance-based investigations and cohort studies have both identified a 30%–50% higher rate of SMM among Black pregnant people and a 14% higher rate of SMM among Hispanic pregnant people compared to White pregnant people [7, 11, 27]. Several researchers have suggested that the quality and completeness of prenatal care and experiences with racism contribute to these disparities [5, 26, 28]. From our results, it appears that Black and Hispanic pregnant people are not only at higher risk of severe COVID-19 and SMM but are also at higher risk of SMM when diagnosed with SARS-CoV-2 infection during the month of delivery. While overall, prevention of SARS-CoV-2 infection could result in a 2.1% decrease in the incidence of SMM, we estimate that prevention of COVID-19 could result in a 3.5% decrease in SMM cases among Black and Hispanic mothers, and a 4.2% decrease in SMM among those with preexisting medical conditions.

Given the benefits of COVID-19 prevention, additional efforts to vaccinate Black and Hispanic pregnant people remain needed. The coverage of COVID-19 vaccine is 13% lower among Black pregnant people and 12% lower among Hispanic pregnant people compared to non-Hispanic White pregnant people [29, 30]. Tailored vaccine promotion efforts that incorporate community-driven strategies may be effective in increasing the uptake of COVID-19 vaccines and reducing racial and ethnic gaps in COVID-19 immunization coverage [31], thereby protecting pregnant people at greatest risk of SMM.

Clinical and Research Implications

Our results further highlight the importance of preventing SARS-CoV-2 infection during pregnancy. Since the roll-out of effective COVID-19 vaccines in December 2020 in the US [32, 33], the US and most other countries now prioritize COVID-19 vaccination during pregnancy. As of February 2023, 121 countries actively recommend COVID-19 vaccines during pregnancy, and another 64 countries permit vaccination of pregnant people [34]. Given the growing evidence supporting the safety and effectiveness of COVID-19 vaccines during pregnancy [35–39], COVID-19 vaccination before or during pregnancy could prevent cases of SMM.

Our study offers evidence from one of the few national studies of SARS-CoV-2 infection and SMM during the emergence of the SARS-CoV-2 Delta variant. However, with the more recent emergence of Omicron and subsequent variants, future research should evaluate whether results vary by SARS-CoV-2 variant. Furthermore, to inform preventive efforts, additional research should consider whether COVID-19 vaccination and recommended treatment measures (ie, antiviral medication) prevent severe maternal health consequences, such as SMM.

Strengths and Limitations

Our study had several strengths and limitations. First, we analyzed national data from a large cohort of pregnancies with commercial health insurance. While this reduced our ability to generalize our findings to Medicaid enrollees and the uninsured population, there were several advantages of this approach. Since individuals were insured for the entirety of their

Table 3. Proportion of Severe Maternal Morbidity Cases Attributable to Severe Acute Respiratory Syndrome Coronavirus 2 Infection, by Maternal Race/Ethnicity and Health Conditions Diagnosed Prior to and During Pregnancy

Maternal Characteristic	Infection ≤30 Days Prior to Delivery Cases per 10 000 Admissions (95% CI)	No SARS-CoV-2 Infection Cases per 10 000 Admissions (95% CI)	Adjusted RR[a] (95% CI)	Attributable Risk (95% CI)	AF in Exposed (95% CI)[b]	PAF (95% CI)[b]
All pregnancies	435 (351–539)	207 (198–217)	2.04 (1.82–2.26)	228 (161–295)	0.51 (.40–.62)	0.02 (.01–.03)
By race/ethnicity						
Hispanic	531 (342–814)	217 (194–242)	2.33 (1.88–2.79)	314 (158–469)	0.57 (.41–.79)	0.03 (.02–.05)
Non-Hispanic White	>297	192 (181–204)	1.82 (1.51–2.14)	>105	0.51 (.39–.63)	0.02 (.01–.03)
Non-Hispanic Black	697 (439–1087)	279 (249–313)	2.50 (2.04–2.97)	418 (204–630)	0.60 (.38–.76)	0.03 (.00–.05)
By maternal age						
<25 y	476 (268–832)	242 (211–277)	1.87 (1.29–2.45)	234 (31–438)	0.46 (.14–.78)	0.02 (.00–.04)
25–34 y	418 (316–551)	182 (171–194)	2.21 (1.93–2.50)	236 (156–315)	0.55 (.42–.68)	0.02 (.01–.03)
≥35 y	458 (301–689)	248 (230–268)	1.81 (1.40–2.23)	210 (65–354)	0.45 (.21–.68)	0.01 (.00–.03)
Diagnosed pregnancy complication						
No pregnancy complication	296 (208–420)	117 (108–127)	2.37 (2.01–2.74)	179 (112–247)	0.58 (.43–.73)	0.03 (.02–.03)
≥1 pregnancy complication	610 (465–798)	321 (305–339)	1.89 (1.61–2.17)	289 (164–413)	0.47 (.32–.62)	0.02 (.01–.03)
Preexisting medical condition						
None	303 (229–399)	176 (167–185)	1.68 (1.40–1.97)	127 (61–193)	0.40 (.24–.57)	0.01 (.01–.02)
≥1 medical condition	1348 (966–1850)	457 (417–499)	2.97 (2.64–3.29)	891 (613–1170)	0.66 (.55–.78)	0.04 (.00–.08)

Abbreviations: AF, attributable fraction; CI, confidence interval; PAF, population attributable fraction; RR, risk ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

[a]Risk ratios adjusted for maternal age, race/ethnicity, household income, educational attainment, rurality of residence, preexisting health condition diagnosis (yes/no), onset of labor (spontaneous/clinician-indicated), and week of conception (cubic spline). Analyses by race/ethnicity did not adjust for race/ethnicity, and analyses by preexisting medical condition did not adjust for pre-existing medical conditions.

[b]AF in exposed and PAF were estimated based on the observed prevalence of COVID-19 and the adjusted risk ratio, using Levin's formula [20].

pregnancy, we can assume participants had access to clinical care, including testing for SARS-CoV-2. Additionally, because they were insured, this was a well-defined cohort on which we were able to extract comprehensive information on all health encounters throughout the pregnancy and at time of delivery. Despite this, we did not have individual-level information on race and ethnicity, nor did we have information on COVID-19 symptoms. It is therefore possible that some individuals were misclassified by race and/or ethnicity, that some asymptomatic individuals were included through routine screening, and that some asymptomatic cases were misclassified as not having a SARS-CoV-2 infection (resulting in some exposure misclassification). Although we employed the CDC algorithm for identifying SMM and previous studies support the validity of using *ICD* codes for measuring SMM [40], measurement is restricted to the delivery admission and the inclusion of certain conditions (ie, blood transfusion) may reduce the validity [17]. For this reason, we considered SMM with and without blood transfusion included as a SMM condition, and the exclusion of blood transfusion did not change the interpretation of our findings. Finally, this is an observational study, and although we adjusted for important sociodemographic and health information, we cannot entirely rule out the possible influence of uncontrolled or residual confounding. However, based on our E-value estimation, very strong unmeasured confounding would be needed to explain away our results, particularly for the observed increase in the risk of sepsis and ARDS.

CONCLUSIONS

SARS-CoV-2 infection during the month prior to delivery, and particularly during the week of delivery, was associated with a 2-fold increase in the risk of SMM. We estimate that 2%–3% of SMM cases could have been avoided through infection prevention during pregnancy. These findings support global guidelines recommending COVID-19 vaccination prior to or during pregnancy and other COVID-19 prevention measures to prevent SARS-CoV-2 infection among pregnant people.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Acknowledgments. The authors acknowledge the technical guidance and support related to accessing and analyzing OptumLabs data provided by the OptumLabs team.

Author contributions. A. K. R.: conceptualization, methodology, formal analysis, data curation, writing—original draft, project administration, funding acquisition. O. A. A.: methodology, writing—review and editing, funding acquisition. D. B. F.: methodology, writing—review and editing. S. G. S.: methodology, validation, data curation, writing—review and editing, funding acquisition.

Data sharing. During the conduct of the study, the first author had full access to the study data and takes responsibility for the integrity of the data and the accuracy of the data analysis; however, the authors do not have

ongoing access to the data analyzed in this study, nor do they have permission to share the study data with other researchers.

Patient consent statement. This research relied on existing administrative health data and did not involve any work with human subjects.

Disclaimer. The funder had no influence in the design or implementation of the study or the decision to publish the study findings.

Financial support. This work received no direct financial support; however, access to study data was financially supported by OptumLabs and the University of California, Los Angeles. The World Health Organization Collaborating Centre for Reference and Research on Influenza is supported by the Australian Government Department of Health.

Potential conflicts of interest. All authors: No reported conflicts.

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