Maternal and perinatal outcomes associated with SARS-CoV-2 infection during pregnancy, Florida, 2020–2021: A retrospective cohort study

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Running Title: Pregnancy outcomes in COVID-19 patients

Abstract

Background: The objective was to estimate risk of SARS-CoV-2 infection in pregnancy and assess adverse maternal and perinatal outcomes.

Methods: We used a population-based, retrospective cohort of all pregnancies with a live birth or fetal death in Florida from March 1, 2020 to April 30, 2021. COVID-19 case reports were matched to vital registries. Outcomes assessed were risk of infection in pregnancy, preterm birth, maternal or neonatal admission to an intensive care unit (ICU), perinatal or fetal death, and maternal death. Modified Poisson and multinomial logistic regression models were used to derive relative risk estimates.

Results: Of 234,492 women with a live birth or fetal death during the study period, 12,976 (5.5%) were identified with COVID-19 during pregnancy. Risk factors for COVID-19 in pregnancy included Hispanic ethnicity (relative risk [RR]=1.89), Black race (RR=1.34), being unmarried (RR=1.04), and being overweight or obese pre-pregnancy (RR=1.08-1.32). COVID-19 during pregnancy was associated with preterm birth (RR=1.31), Cesarean delivery (RR=1.04), and neonatal (RR=1.17) and maternal (RR=3.10) ICU admission; no association was found with increased risk of perinatal (RR=0.72) or fetal death (RR=0.86). Women infected during any trimester showed increased risk of preterm birth. Fourteen maternal deaths were identified among COVID-19 cases; of those who died 12 were obese. The death rate per 10,000 was 22.09 among obese and 1.22 among non-obese gravida with COVID-19 during pregnancy (RR=18.99, P=0.001).

Conclusions: Obesity is a risk factor for SARS-CoV-2 infection in pregnancy and for more severe COVID-19 illness among pregnant women. SARS-CoV-2 infection is associated with preterm birth.

Key words: COVID-19, maternal mortality, obesity, pregnancy outcomes, trimester

Introduction

Infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) during pregnancy can have adverse effects on maternal health and pregnancy outcomes.[1, 2] Early in the pandemic, deaths were reported in women with coronavirus disease 2019 (COVID-19) during pregnancy or the post-partum period.[3] Other reports have noted increased risk of miscarriage,[4] stillbirth,[5] and pre-term birth.[6] Obesity has been identified as an important risk factor for infection and severe outcomes from COVID-19, both in pregnant and non-pregnant persons.[1, 7, 8]

Florida is the third most populous state in the United States with an estimated population in 2019 of more than 21.2 million residents.[9] The first confirmed COVID-19 case in Florida was reported on March 1, 2020 and, as of early May 2021, more than 2.2 million COVID-19 cases have been reported in Florida residents. Serologic studies at the time estimated that 2.1 cumulative infections had occurred for each reported case.[10] Thus, as of May 2021, approximately 22% of Florida residents likely had current or past SARS-CoV-2 infection. Approximately 220,000 live births occur annually in Florida.[9]

The objectives of this study were to estimate risk for SARS-CoV-2 infection in pregnancy, as well as adverse maternal and perinatal outcomes associated with SARS-CoV-2 infection during pregnancy. To do this, we analyzed data from a retrospective population-based cohort of pregnant people with and without SARS-CoV-2 infection. Data were from all live births and fetal deaths among residents in Florida occurring during the first 14 months of the pandemic, supplemented with records on maternal deaths.

Methods

COVID-19 is a reportable disease in Florida, and all persons testing positive for acute SARS-CoV-2 infection by polymerase chain reaction (PCR), or antigen test are reported to the Florida Department of Health (FDOH). Most cases are reported via electronic laboratory reporting; data are maintained in the FDOH notifiable disease surveillance database.

The Florida birth and fetal death registries are maintained by the FDOH Bureau of Vital Statistics and include records on all live births and fetal deaths occurring in Florida. The fetal death registry contains records for death occurring in a fetus aged 20 or more weeks gestation. Records are submitted by hospitals and medical providers and contain information on the newborn or fetal death, as well as the mother and father. There are >330 variables contained in the comprehensive birth and fetal death record, including information on maternal and infant demographics, pre-pregnancy body mass index (BMI), pre-natal exposures such as tobacco use by the mother, obstetric history, medical care received during labor and delivery, and maternal and neonatal morbidity such as admission to an intensive care unit (ICU).

Electronic records from the Florida birth and fetal death registries were cross-referenced to the state notifiable disease surveillance database to identify women with laboratory evidence by PCR or antigen test of SARS-CoV-2 infection during pregnancy and their newborn infants. Live births and fetal deaths occurring between March 1, 2020, and April 30, 2021, were used for the record linkage. The record matching utilized hierarchical, deterministic algorithms previously used in other vital statistics matching activities, combined with manual review, in an iterative process.[11] First level hierarchy matching variables included the mother's Social Security number, date of birth, or both. Second level hierarchy variables included mothers' first and last

name with application of probabilistic Jaro-Winkler functions to accommodate spelling variations.[12] Matched records were manually reviewed to ensure the accuracy of the match. Data on all live births and fetal deaths among Florida residents, occurring between March 1, 2020, and April 30, 2021, were compiled to generate two distinct cohorts: 1) pregnant women with a live birth or fetal death during the period; 2) all infants born during the period. Infection with SARS-CoV-2 during pregnancy was treated as the outcome variable when assessing disease risk in pregnant women and treated as the primary exposure variable for assessing risk of adverse maternal and perinatal outcomes. Women and newborns in the pregnancy and birth cohorts were categorized as with COVID-19 in pregnancy (i.e., 'ill' for the first analysis and 'exposed' for the second) if the vital statistics records matched to the COVID-19 notifiable disease surveillance database by the methods previously described.

Data on birth date or fetal death date and the gestational age at birth/fetal death, were used to estimate the conception date for women. Estimated conception date and SARS-CoV-2 laboratory test date were compared to classify all women with COVID-19 by trimester of pregnancy when infected with SARS-CoV-2. Trimester 1 was defined as the period from estimated conception through 13 weeks gestation, trimester 2 as gestational week 14-26, and trimester 3 as gestational week 27-44. Women and their newborns were excluded from all analyses if the date for their positive SARS-CoV-2 test occurred prior to the estimated conception date or after the birth date.

Pregnancy-associated deaths are ascertained by FDOH using standard methods previously described.[13, 14] These methods include periodic linkage between birth and death records, and a checkbox on the death certificate to indicate recent pregnancy. For this analysis, pregnancy-associated deaths with COVID-19 listed as a contributing cause were assessed for women with documented SARS-CoV-2 infection during, or within 42 days following pregnancy.

Relative risk (RR) estimates and 95% confidence intervals (95% CI) were computed using modified Poisson regression models with robust standard errors.[15, 16] Multinomial logistic regression was used for outcome variables with >2 categories to obtain RR estimates. Observations with missing data were excluded from regression analyses. We set statistical significance at $P < 0.05$. Multivariate models were estimated using variables identified during bivariate analyses or known risk factors for adverse maternal and perinatal outcomes. The log-likelihood ratio was used for a goodness of fit test and the Akaike Information Criteria (AIC) was applied to obtain model parsimony. The means for some continuous variables were compared using t-test and the Cochrane-Armitage test for trend was used to assess linear trends for increasing category of pre-pregnancy BMI. Data analysis was conducted using SAS, version 9.4 [SAS Institute; Cary NC].

BMI was expressed as weight in kilograms/(height in meters)^2 and pre-pregnancy BMI data were available on approximately 93% of records. Pre-pregnancy BMI data in the Florida birth registry have previously been found to be reliable and valid.[17] Nevertheless, the top and bottom 0.05% of BMI values were excluded as non-valid, resulting in the exclusion of values <14.1 or >62.0 kg/m^2. Based on pre-pregnancy BMI, standard adult cut-points were used to classify gravida into underweight, healthy weight, overweight, and obese.[18] Maternal age was classified into 3 groups (e.g., <18, 18-34, ≥35 years) and also used as a continuous variable. Birth weight and gestational age at birth were categorized using commonly recognized cut points to assess neonatal outcomes. Births were excluded from the regression analysis of preterm birth if SARS-CoV-2 infection occurred ≥37 weeks gestation. Admission to an intensive care unit (ICU) was used as an indicator of illness severity for both maternal and neonatal outcomes. Perinatal death

in an infant following live birth is indicated at the time birth records are submitted to the vital statistics system, usually within 2-3 days of birth.

COVID-19 vaccines approved for emergency use became available to Florida residents age 16-50 years, not covered by other risk categories, in March/April 2021, near the end of the analysis period.[19] Because vaccination status was only known for COVID-19 cases and not other cohort members, all cohort members were included in the analysis, regardless of vaccination status, and vaccination status was not assessed in the statistical analysis.

Ethics Statement

This activity was reviewed by the Ethics and Human Research Protection Program of FDOH and by the Centers for Disease Control and Prevention (CDC) and was determined by both institutions to be public health practice, exempt from further review by an institutional review board.

Results

Risk of COVID-19 in pregnancy

Of 234,492 women with a live birth or fetal death during the study period, 12,976 (5.5%) were identified with SARS-CoV-2 infection during pregnancy; 90% confirmed by PCR and 10% by antigen testing. Approximately 1.5% of pregnancies identified were multiple gestation, 198 among COVID-19 cases and 3,352 in women without COVID-19 in pregnancy. SARS-CoV-2 infection occurred during the third trimester in 57% of pregnancies with COVID-19. The mean age in COVID-19 cases was lower than in women without COVID-19 during pregnancy (29.1 vs. 29.5, $P<0.0001$). Unadjusted risk factors for SARS-CoV-2 in pregnancy included Hispanic or Haitian ethnicity, Black race, being foreign born, being unmarried, having less than high school education, being enrolled in Medicaid or other government insurance, being a participant in the

Special Supplemental Nutrition Program for Women, Infants, and Children (WIC), and being overweight or obese pre-pregnancy (Table 1). Risk of COVID-19 in pregnancy increased with severity of obesity in a dose response manner (Cochran-Armitage trend test, χ^2=12.55, P<0.0001). The mean pre-pregnancy BMI in COVID-19 cases was higher than in women without COVID-19 during pregnancy (28.0 vs. 27.2, P<0.001). Similar patterns persisted in multivariate analysis with the strongest associations observed for race, ethnicity, and increasing severity of obesity (Table 2).

Birth Outcomes

A total of 238,043 live births were reported during the 14-month birth cohort and 13,178 (5.5%) were among mothers with SARS-CoV-2 infection during pregnancy. The mean gestational age at birth was slightly lower for infants born to women with COVID-19 in pregnancy (38.2 vs 38.3 weeks, P<0.0001) as was mean birth weight (3216.1g vs 3236.6g, P<0.001). SARS-CoV-2 infection during pregnancy was associated with preterm birth <37 weeks gestation, increased rate of Cesarean delivery, and admission to neonatal ICU (Table 3). No increased risk was observed for perinatal death, fetal death, or birth anomalies. When trimester of infection was accounted for, women infected during any trimester showed increased risk of preterm, very preterm, and extremely preterm birth compared to women without COVID-19 during pregnancy, and the point estimates were significant in all but two instances (Figure 1).

Maternal outcomes

COVID-19 during pregnancy was strongly associated with maternal admission to an ICU. The point estimates for this association increased by trimester of infection, with the highest risk in women with SARS-CoV-2 infection during the third trimester compared to women without infection (Table 4). The observed association was statistically significant for women with SARS-

CoV-2 infection during the second or third trimester, but not significant for the first trimester. Risk of ICU admission increased with increasing levels of pre-pregnancy obesity, after adjusting for other factors, with an approximately two-fold greater risk for women with class 3 obesity compared to those with healthy weight.

A total of 14 women were identified who died of COVID-19 during pregnancy or in the post-partum period; none were vaccinated against COVID-19, including the 7 patients whose illness onset was after December 2020 when vaccines were authorized (Table 5). Four of the deaths occurred in women age 40 or over and obesity was noted in 12 of the 14 women. Four deaths occurred in women with COVID-19 symptom onset in the post-partum period and these pregnancies were, therefore, excluded from the previous pregnancy and birth cohort analysis. Of the ten women with COVID-19 during pregnancy, nine were obese and one was not obese. The death rate was 23.09 per 10,000 among obese and 1.22 per 10,000 among non-obese gravida with COVID-19 during pregnancy (RR=18.99; 95% CI: 2.41-149.84; P=0.001). Among the 14 pregnancies with a maternal death, there was 1 spontaneous abortion, 2 fetal death, and 11 live births -- 9 by Cesarean and 2 by vaginal delivery. The 14 deaths represent 5.88 COVID-19-related maternal deaths per 100,000 live births during the period.

Discussion

Among pregnant women, we found increased risk of SARS-CoV-2 infection during pregnancy associated with increasing levels of pre-pregnancy obesity and factors related to lower socio-economic status. Women with COVID-19 during pregnancy were more than three times as likely to be admitted to an ICU compared to pregnant women without COVID-19 and this risk was highest when infection occurred in the third trimester. Among the maternal deaths identified, obesity was a co-morbid condition in most deaths, and 29% of deaths involved SARS-CoV-2

infection following birth. This may be attributable to immunological changes during pregnancy that can continue in the post-partum period.

SARS-CoV-2 infection in pregnancy was associated with an increased risk of preterm birth, and this was observed for infection occurring in all trimesters of pregnancy. Preterm birth can have wide-ranging adverse impacts on the long-term health and development of the newborn, including effects on pulmonary, cardiovascular, renal, and neurologic development. [20] We also noted a slight increased risk of Cesarean delivery associated with COVID-19 in pregnancy. However, we did not observe an association with increased risk of perinatal or fetal death.

Our findings are generally consistent with previous reports. Others have reported higher rates of COVID-19 during pregnancy associated with non-white race, Medicaid as the primary payer, and higher maternal BMI.[21, 22] Our results extend previous findings with additional details on risk by race/ethnicity to include Haitian ethnicity, and by demonstrating a dose response relationship between increasing pre-pregnancy BMI and risk of COVID-19 in pregnancy.

Previous studies have also reported associations between COVID-19 in pregnancy with preterm birth, increased rate of Cesarean delivery, and neonatal admission to ICU.[6, 22-25] Our study adds additional details regarding risk of preterm birth by trimester of infection. Several studies have noted more severe COVID-19 illness in pregnant women with obesity.[24, 26, 27] Our study adds new details by presenting data by trimester of infection and class of obesity.

A recent study has reported an increased risk of stillbirth associated with COVID-19 diagnosis and the risk was much higher during the period of Delta variant predominance in the U.S.[28] We found no association with stillbirth, however, our data reflect the period prior to Delta variant predominance. In addition, we matched surveillance data using laboratory evidence of

SARS-CoV-2 infection to the fetal death registry, as opposed to utilizing hospital diagnostic codes, which may also account for the differences observed.

Past studies have consistently shown that obese individuals are at increased risk of COVID-19, likely through hormone and nutrient dysregulation that can impair the response to infection.[8] Our data show that the risks associated with COVID-19 during pregnancy are strongly influenced by obesity. These risks continued in the post-partum period. Both pregnancy and obesity are underlying medical conditions associated with higher risk for severe COVID-19.[29] Therefore, our findings underscore the importance of monitoring obese obstetric patients testing positive for SARS-CoV-2, for possible respiratory decompensation and rapid decline, in the setting of acute COVID-19 illness. CDC recommends COVID-19 vaccination for all people 5 years and older, including people who are pregnant, breastfeeding, trying to get pregnant now, or might become pregnant in the future.[30]

While our findings are generally consistent with past reports, many previous studies were unable to fully adjust for pre-pregnancy BMI or account for trimester of infection when assessing birth outcomes for women with SARS-CoV-2 infection. In addition, many previous studies were based on data from hospital networks and were not population based.[21, 22, 26] Thus, the main value of the present study may be in validating, through population-based data, findings previously reported in network-based studies.

Many previous studies have required PCR confirmation when classifying SARS-CoV-2 infection during pregnancy.[1] Data from these studies may reflect patients who were more likely to seek medical care for COVID-19-like illness. In our study, we included both PCR and antigen testing and 10% of COVID-19 cases included in our study relied on antigen testing. Thus, our findings may reflect a broader spectrum of SARS-CoV-2 infected patients to include those for whom

antigen testing alone may be more common, such as patients with asymptomatic infection or milder illness who did not seek care for their illness, or those tested outside a clinical setting. This may partially explain point estimates closer to the null observed in our study, when compared to other studies relying exclusively on PCR testing.

Strengths of this study include robust laboratory-based ascertainment of COVID-19 cases across a large, diverse population, with efficient linkage of COVID-19 cases to population-based registries to include a comparison group. This permitted extensive control for potential confounding factors and consideration of timing of infection for the maternal and birth outcomes assessed. Limitations include limited clinical data on severity of illness or treatment measures and missing data on pre-pregnancy BMI for approximately 7% of participants. Impact of COVID-19 vaccination on outcomes was not assessed. Pregnant women with COVID-19 who were never tested for SARS-CoV-2 would have been misclassified as non-infected; such misclassification could attenuate the magnitude of the associations assessed. In addition, there is no comprehensive pregnancy registry in Florida. Thus, the analysis did not account for pregnancies that ended in miscarriage or were not otherwise recorded in the birth or fetal death registry.

Conclusions

Obesity is a risk factor for COVID-19 in pregnancy and a risk factor for more severe COVID-19 illness among pregnant women. SARS-CoV-2 infection is associated with preterm birth, but no association was found with increased risk of fetal or perinatal death.

NOTES

Contribution to authorship

Conceptualization: TD

Data curation: TD, ES, RP, AT

Formal analysis: TD, GK

Methodology: TD, GK, GP

Project administration: TD

Writing-original draft: TD, GK

Writing-review & editing: TD, GK, ES, RP, AT, GP

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Disclosure of Interests

The authors report no conflict of interest.

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Table 1. Frequencies and relative risk estimates of demographic and other characteristics of cases and non-cases of COVID-19 during pregnancy, Florida, March 1, 2020–April 30, 2021

Characteristics of women	Women with COVID-19 during pregnancy, n (%)	Women without COVID-19 during pregnancy, n (%)	Unadjusted RR[a] (95% CI)
Total pregnant women[b]	12,976 (5.5)	221,516 (94.5)	
Trimester of pregnancy when infected			
Trimester 1	1,912 (15)	N/A	N/A
Trimester 2	3,710 (29)	N/A	N/A
Trimester 3	7,354 (57)	N/A	N/A
Race/ Ethnicity			
Hispanic/Latino	5,693 (44)	67,563 (31)	1.97 (1.90-2.06)
Haitian	578 (5)	8,034 (4)	1.71 (1.57-1.86)
Non-Hispanic/Non-Haitian			
White	3,777 (29)	92,372 (42)	1.0 (ref)
Black	2,345 (18)	37,589 (17)	1.50 (1.42-1.57)
Asian	148 (1.1)	6,614 (3)	0.56 (0.47-0.66)
Other races	247 (2)	6,476 (2)	0.94 (0.82-1.06)
Missing	188 (1.5)	2,868 (1.3)	N/A
Foreign born			
Yes	5,117 (39)	71,000 (32)	1.36 (1.31-1.40)

No	7,859 (61)	150,516 (68)	1.0 (ref)
Maternal age in years			
<18	125 (1)	2,235 (1)	0.94 (0.79-1.11)
18-34	10,445 (81)	174,157 (79)	1.0 (ref)
≥35	2,403 (18)	45,027 (20)	0.90 (0.86-0.94)
Marital status			
Not married	6,731 (52)	103,463 (47)	1.22 (1.18-1.26)
Married	6,242 (48)	118,011 (53)	1.0 (ref)
Education			
< High school	1,569 (12)	22,694 (10)	1.07 (1.02-1.14)
High school graduate	4,358 (34)	68,049 (31)	1.0 (ref)
> High school education	6,952 (54)	129,103 (59)	0.85 (0.82-0.88)
Pre-pregnancy BMI			
Underweight, <18.5	311 (2.6)	6,982 (3.4)	0.85 (0.76-0.96)
Normal, 18.5-24.9	4,456 (37.3)	84,804 (42)	1.0 (ref)
Overweight, 25.0-29.9	3,455 (29)	57,014 (28)	1.15 (1.10-1.20)
Obesity Class 1, 30.0-34.9	2,079 (17.4)	31,923 (17)	1.23 (1.16-1.28)
Obesity Class 2, 35.0-39.9	1,048 (9)	15,175 (7)	1.29 (1.21-1.38)
Obesity Class 3, ≥ 40.0	762 (6.3)	10,300 (5)	1.38 (1.28-1.47)
Principle source of payment			
Medicaid	6,577 (51)	102,246 (46)	1.21 (1.16-1.25)
Private insurance	5,343 (41)	101,252 (46)	1.0 (ref)
Self-pay	692 (5)	10,869 (5)	0.97 (0.87-1.08)

Other government insurance	323 (2.5)	6,327 (3)	1.19 (1.11-1.29)
Missing	41 (<1)	822 (< 1)	N/A
WIC participant			
Yes	5,853 (46)	84,515 (39)	1.32 (1.28-1.37)
No	6,910 (54)	133,889 (61)	1.0 (ref)

Abbreviation: RR, relative risk; CI, confidence interval; ref, reference category; BMI, body mass index; WIC, the Special Supplemental Nutrition Program for Women, Infants, and Children.

[a]Relative risk estimates obtained using the modified Poisson regression model.

[b]Pregnant women from live birth and fetal death registry. Numbers in some categories may not add to total, due to missing data for some variables.

Table 2. Relative risk estimates from multivariate regression model of selected characteristics and factors associated with COVID-19 during pregnancy, Florida, March 1, 2020–April 30, 2021

Characteristics	Adjusted RR[a] (95% CI)
Race/ Ethnicity	
Hispanic/Latino	1.89 (1.82-1.98)
Haitian	1.59 (1.45-1.74)
Non-Hispanic/Non-Haitian	
White	1.00 (ref)
Black	1.34 (1.27-1.42)
Asian	0.59 (0.50-0.70)
Other or more than one race	0.94 (0.83-1.07)
Maternal age (years)	
<18	0.83 (0.69-1.00)
18-34	1.00 (ref)
≥35	0.91 (0.87-0.95)
Marital status	
Not married	1.04 (1.00-1.08)
Married	1.00 (ref)
WIC participant	
Yes	1.12 (1.08-1.16)
No	1.00 (ref)
Pre-pregnancy BMI	

Underweight, <18.5	0.85 (0.76-0.96)
Normal, 18.5-24.9	1.00 (ref)
Overweight, 25.0-29.9	1.08 (1.03-1.13)
Obesity Class 1, 30.0-34.9	1.14 (1.09-1.20)
Obesity Class 2, 35.0-39.9	1.23 (1.15-1.31)
Obesity Class 3, ≥ 40.0	1.32 (1.23-1.43)

Abbreviation: RR, relative risk; CI, confidence interval; ref, reference category; WIC, the Special Supplemental Nutrition Program for Women, Infants, and Children; BMI, body mass index.

[a]RRs estimated using the modified Poisson regression model. Model includes all variables listed. Includes 11,775 cases and 201,459 non-cases with available data for all variables (n = 213,234).

Table 3. Frequencies and relative risk estimates of neonatal and fetal outcomes associated with COVID-19 during pregnancy, Florida, March 1, 2020–April 30, 2021

Neonatal outcome	COVID-19 during pregnancy, No. (%)	No COVID-19 during pregnancy, No. (%)	Unadjusted RR (95% CI)	Adjusted RR (95% CI)[b]	Adjusted RR (95% CI)[c]
Number of live births[a]	13,178 (5.5)	224,865 (94.5)			
Preterm birth					
≥37 weeks	11,663[d] (88.5)	201,540 (89.7)	1.0 (ref)[d]	1.0 (ref)[d]	1.0 (ref)[d]
Preterm, <37 weeks	1,513 (11.5)	23,226 (10.3)	1.38 (1.31-1.44)	1.34 (1.28-1.40)	1.31 (1.24-1.37)
≥37 weeks	11,663[d] (88)	201,540 (89)	1.0 (ref)[d,e]	1.0 (ref)[d,e]	1.0 (ref)[d,e]
Moderate to late preterm, ≥32 to <37 weeks	1,286 (10)	19,657 (9)	1.39 (1.32-1.46)	1.36 (1.29-1.43)	1.32 (1.26-1.40)
Very preterm, ≥28 to <32 weeks	152 (1)	1,996 (1)	1.67 (1.42-1.97)	1.65 (1.40-1.94)	1.60 (1.34-1.91)
Extremely preterm, <28 weeks	75 (<1)	1,573 (<1)	1.05 (0.84-1.33)	1.07 (0.85-1.35)	0.99 (0.77-1.27)
Low birth weight					
≥2500g	11,994 (91)	205,558 (91.4)	1.0 (ref)	1.0 (ref)	1.0 (ref)
<2500g	1,184 (9)	19,307 (8.6)	1.05 (0.99-1.11)	1.05 (0.99-1.10)	1.06 (1.00-1.12)
≥2500g	11,994 (91)	205,558 (91)	1.0 (ref)[e]	1.0 (ref)[e]	1.0 (ref)[e]

≥1500 to <2500g	986 (7)	16,025 (7)	1.06 (0.99-1.13)	1.04 (0.99-1.10)	1.06 (1.00-1.12)
≥1000 to <1500g	111 (1)	1,676 (<1)	1.14 (0.94-1.38)	1.12 (0.91-1.34)	1.11 (0.88-1.32)
<1000g	87 (<1)	1,606 (<1)	0.93 (0.745-1.15)	0.92 (0.72-1.12)	0.86 (0.66-1.06)
5-minute Apgar score					
<9	1,959 (15)	32,347 (15)	1.03 (0.99-1.08)	1.04 (0.99-1.08)	1.03 (0.98-1.07)
9 or greater	11,165 (85)	191,391 (85)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Birth anomaly					
yes	129 (1)	2,138 (1)	1.03 (0.86-1.22)	1.04 (0.87-1.24)	1.01 (0.84-1.22)
no	12,955 (99)	221,278 (99)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Admitted to Neonatal ICU					
yes	1,451 (11)	21,006 (9)	1.18 (1.12-1.24)	1.18 (1.13-1.24)	1.17 (1.11-1.23)
no	11,687 (89)	203,064 (91)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Mechanical ventilation needed >6 hours					
yes	89 (<1)	1,281 (<1)	1.19 (0.96-1.47)	1.21 (0.98-1.50)	1.17 (0.94-1.45)
no	13,049 (>99)	222,790 (>99)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Perinatal death[f]					
yes	47 (<1)	1,177 (<1)	0.74 (0.55-0.98)	0.73 (0.54-0.98)	0.72 (0.53-0.98)
no	13,131 (>99)	223,790 (>99)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Cesarean delivery					
yes	4,943 (38)	80,082 (36)	1.05 (1.03-1.08)	1.06 (1.04-1.09)	1.04 (1.02-1.07)

no	8,226 (62)	144,538 (64)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Fetal death[g]					
yes	69 (1)	1,366 (1)	0.83 (0.66-1.05)	0.86 (0.69-1.08)	0.86 (0.67-1.10)
no	13,178 (99)	224,865 (99)	1.0 (ref)	1.0 (ref)	1.0 (ref)

Abbreviation: RR, relative risk; CI, confidence interval; ref, reference category; ICU, intensive care unit.

[a]Numbers in some categories may not add to total, due to missing data for some variables.

[b]Adjusted for maternal age and age-squared, mother married (y/n), plurality (y/n), infant sex, tobacco use during pregnancy (y/n), previous poor pregnancy outcome (y/n), pre-gestational diabetes mellitus (y/n).

[c]Adjusted for same variables in model a, with additional adjustment for pre-pregnancy BMI treated as a continuous variable. Approximately 7% of records were excluded due to missing data for pre-pregnancy BMI.

[d]N=9,121 after excluding 2,542 births from analysis with SARS-CoV-2 infection ≥37 weeks gestation.

[e]RR estimates from multinomial logistic regression.

[f]Infant non-living at time birth certificate was submitted, usually within 2-3 days of birth.

[g]Data includes all pregnancies that resulted in a live birth or fetal death.

Table 4. Relative risk estimates of factors associated with maternal admission to intensive care unit, Florida, March 2020–April 2021

Factors	COVID-19 during any trimester			By trimester of infection		
				Trimester 1	Trimester 2	Trimester 3
	RR[a] (95% CI)	aRR[b] (95% CI)	aRR[c] (95% CI)	aRR[d] (95% CI)	aRR[d] (95% CI)	aRR[d] (95% CI)
COVID-19 (Y vs N)	3.07 (2.26-4.17)	3.01 (2.19-4.11)	3.10 (2.20-4.37)	1.61 (0.52-5.02)	3.33 (1.88-5.92)	3.43 (2.24-5.27)
Plurality		4.22 (2.68-6.65)	4.23 (2.54-7.03)	3.70 (2.06-6.64)	3.79 (2.16-6.64)	3.69 (2.10-6.48)
Pre-gestational diabetes		2.67 (1.37-5.20)	2.60 (1.27-5.30)	2.84 (1.31-6.15)	3.03 (1.49-6.18)	2.49 (1.15-5.39)
Previous preterm delivery		2.56 (1.57-4.19)	2.84 (1.68-4.81)	2.67 (1.47-4.84)	2.99 (1.73-5.17)	2.63 (1.48-4.65)
Maternal age (<18 vs 18-34)		0.79 (0.20-3.20)	1.03 (0.26-4.12)	1.07 (0.29-4.65)	1.13 (0.28-4.50)	1.06 (0.27-4.24)
Maternal age (≥35 vs 18-34)		1.59 (1.24-2.04)	1.45 (1.09-1.92)	1.49 (1.10-2.02)	1.48 (1.10-1.99)	1.45 (1.09-1.94)
Infant Sex (F vs M)		1.26 (1.00-1.57)	1.42 (1.10-1.82)	1.46 (1.11-1.92)	1.50 (1.15-1.97)	1.41 (1.08-1.83)
Maternal tobacco use		2.35 (1.55-3.57)	2.07 (1.26-3.38)	2.25 (1.37-3.69)	2.19 (1.33-3.58)	2.14 (1.31-3.51)
Pre-pregnancy BMI (vs Normal)						
Underweight, <18.5			1.67 (0.90-3.11)	1.61 (0.84-3.09)	1.77 (0.95-3.30)	1.56 (0.82-2.98)
Overweight, 25.0-29.9			1.15 (0.87-1.59)	1.11 (0.79-1.56)	1.11 (0.79-1.55)	1.16 (0.83-1.61)

Obesity Class 1, 30.0-34.9	1.16 (0.79-1.70)	1.13 (0.75-1.70)	1.14 (0.76-2.07)	1.20 (0.81-1.76)
Obesity Class 2, 35.0-39.9	1.27 (0.79-2.04)	1.09 (0.63-1.87)	1.25 (0.76-2.07)	1.16 (0.70-1.94)
Obesity Class 3, ≥ 40.0	2.30 (1.49-3.55)	1.86 (1.11-3.09)	1.97 (1.21-3.20)	2.11 (1.32-3.37)

Abbreviation: RR, relative risk; CI, confidence interval; vs, versus; Y, yes; N, no; F, female; M, male; BMI, body mass index; ICU, intensive care unit.

[a]Bivariate analysis includes 234,492 pregnant women, 315 of whom were admitted to ICU. Of the 315 ICU patients, 48 were COVID-19 cases and 267 were non-COVID-19 cases.

[b]RR estimated using modified Poisson regression models adjusting for COVID-19 illness, maternal age (<18, 18-34, ≥35), plurality (y/n), infant sex, tobacco use during pregnancy (y/n), previous preterm delivery (y/n), pre-gestational diabetes (y/n). A total n = 233,543 pregnant women were included in the analysis.

[c]Adjusted for same variables in model b, with additional adjustment for pre-pregnancy BMI (6 categories: underweight, normal, overweight, obese 1-3). The total number of pregnant women included in this analysis is n= 217,680.

[d]RRs for trimester of SARS-CoV-2 infection adjusted for same factors listed for model c above, and stratified by trimester of infection.

Table 5. Maternal deaths among women with COVID-19, Florida, March 2020 – May 2021

No.	Age	Race-Ethnicity	Illness Onset	Gestational age at onset (weeks)	Days between onset & birth	Days between onset & death	Pre-pregnancy BMI	Comorbidities	Delivery/birth outcome, birth weight, Apgar scores	Obstetric history[a], prenatal care, misc.
1	40	Black Non-Hispanic	March 2020	37	7	12	33.2	Obesity, CAD, asthma, previous gastric bypass, thymus gland cancer, glaucoma, depression, bipolar disorder, sleep apnea	CS at 38 weeks. 3330g. Breech. Apgar5=8	G1P1; 12 prenatal visits. Perforated bowel due to intussusception. Gained 84lbs during pregnancy.
2	24	Other Hispanic	June 2020	33	3	8	41	Obesity, hypertension	CS at 33 weeks. 2948g.	G1P1; no prenatal care. Uninsured. Pre-eclampsia. Cerebral edema, PREC syndrome.
3	33	White Hispanic	June 2020	Post-partum (day 5)	NA	34	32.9[b]	Obesity, asthma	Vaginal at 37 weeks. 3345g. Apgar5=9	G4P4; 2 prenatal visits. Gestational diabetes. Bilateral tubal ligation on day 2 post-partum.
4	24	Other Hispanic	July 2020	36	6	15	34.2	Obesity, anemia	Vaginal at 36 weeks. 3620g. Apgar5=8	G1P1; 8 prenatal visits. Pre-eclampsia.
5	46	White Hispanic	August 2020	Post-partum (day 18)	NA	21	18.2	Infertility, ART	CS at 34 weeks. 2580g. Apgar5=9	G3P2; more than 7 prenatal visits. HELLP syndrome, pre-eclampsia.
6	32	Black	August	32	2	16	49.8[b]	Obesity, myomectomy,	CS at 33 weeks. 2438g	G2P1; 9 prenatal visits. Gestational diabetes.

		Non-Hispanic	2020					PCOS	Apgar5=7	
7	37	Black Non-Hispanic	August 2020	34	1	57	30.5	Obesity, hypertension	CS at 34 weeks. 2631g. Apgar5=9.	G3P2; more than 6 prenatal visits. Pre-eclampsia, gestational diabetes. Placental abruption. Bilateral tubal ligation on day 2 post-partum.
8	40	White Hispanic	January 2021	Post spontaneous abortion (day 3)	NA	30	54	Obesity	Spontaneous abortion 3 days prior to symptom onset	DVT, stroke.
9	35	White Non-Hispanic	February 2021	36	10	50	38	Obesity, depression, anxiety, HSV	CS at 37 weeks. 3645g. Apgar5=9	10 prenatal visits. Gestational diabetes. Stroke in ER.
10	33	White Non-Hispanic	February 2021	27	18	22	44.4[b]	Obesity, hypertension, asthma, HPV.	CS at 30 weeks. Breech. 1945g. Apgar5=8	G2P1; 10 prenatal visits
11	26	White Hispanic	March 2021	22	NA	2	26		Intrauterine fetal demise at 22 weeks	G1P0; 3 prenatal visits.
12	34	White Hispanic	March 2021	27	12	30	37.5[b]	Obesity	CS at 27 weeks. 1400g. Apgar5=3	Pneumothorax, ARDS
13	40	Black Non-Hispanic	April 2021	Post-partum (day 11)	NA	26	45	Obesity, hypertension	CS at 36 weeks. 2665g. Apgar5=9	14 prenatal visits. ARDS.
14	23	Black Non-	April	17	30	40	48[b]	Obesity	Fetal death at 21	G3P2; 4 prenatal visits

	Hispanic	2021		weeks

Abbreviations: DOB, date of birth; BMI, Pre-pregnancy body mass index; CS, Cesarean section delivery; g, grams; G, gravidity; P, parity; ER, emergency room; ARDS, Acute Respiratory Distress Syndrome; CAD, coronary artery disease; PCOS, polycystic ovarian syndrome; ART, assisted reproductive technology; HELLP, Hypertension, preeclampsia/eclampsia/hemolysis, elevated liver enzymes, and low platelet count; HPV, human papillomavirus infection; PREC, posterior reversible encephalopathy syndrome; DVT, deep vein thrombosis; Apgar5, 5-minute Apgar score.

[a]Obstetric history includes current pregnancy and birth outcome referenced in the table.

[b]BMI at labor and delivery, not pre-pregnancy BMI.

Figure legend

Figure 1. Adjusted relative risk estimates of selected birth outcomes among women with SARS-CoV-2 infection during pregnancy, compared to women without infection, by trimester of infection. The dot shows the point estimate, and the horizontal line shows the 95% confidence interval. SARS-CoV-2 infection was the primary exposure variable, stratified by trimester of infection, compared to uninfected. Models were adjusted for maternal age and age-squared, mother married (yes/no), multiple gestation pregnancy (yes/no), infant sex, tobacco use during pregnancy (yes/no), previous poor pregnancy outcome (yes/no), pre-gestational diabetes mellitus (yes/no), and pre-pregnancy BMI treated as a continuous variable. 2,542 births were excluded from the pre-term birth analysis with SARS-CoV-2 infection ≥37 weeks gestation.

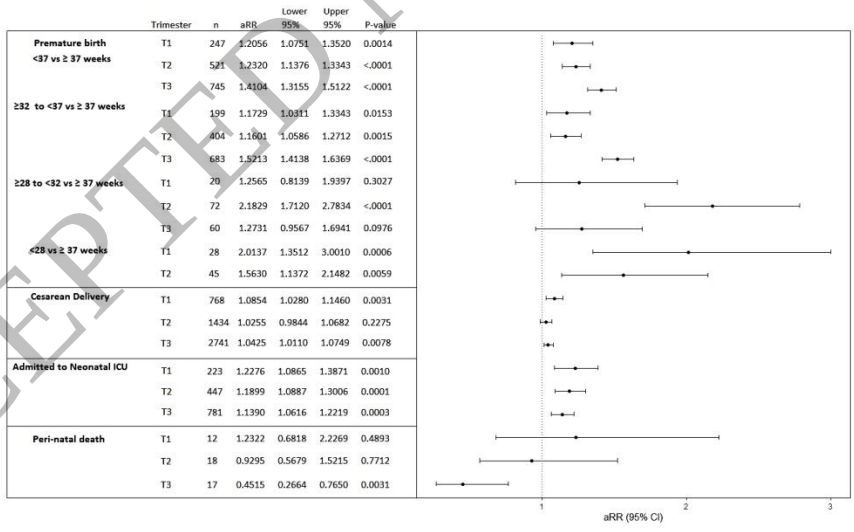

Figure 1
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