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Epidemiology of COVID-19 in Pregnancy:

Risk Factors and Associations with Adverse Maternal and Neonatal Outcomes

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Condensation: Pregnant patients with severe/critical COVID-19 are at increased risk for adverse maternal and neonatal outcomes, whereas patients with mild disease appear to have similar outcomes compared to matched controls.

Short Title: Case-control study of COVID-19 in pregnancy

AJOG at a Glance

1. Why was the study conducted?

   The study was conducted to quantify the magnitude of risk of adverse maternal and neonatal outcomes associated with COVID-19 in pregnancy versus unaffected pregnant women and characterize the epidemiology and risk factors for adverse outcomes.

2. What are the key findings?

   COVID-19 in pregnancy is associated with adverse maternal and neonatal outcomes, and this association is primarily driven by morbidity associated with severe/critical disease. Black and Hispanic patients with obesity, advanced maternal age, medical comorbidities, and antepartum admissions related to COVID-19 have the greatest risk of associated complications.

3. What does this study add to what is already known?

   The study quantifies the magnitude of adverse maternal and neonatal outcomes associated with severe/critical COVID-19 compared to unaffected pregnant women during pregnancy.

Abstract

Background: COVID-19 may be associated with adverse maternal and neonatal outcomes in pregnancy, but there is little controlled data to quantify the magnitude of these risks or to characterize the epidemiology and risk factors.

Objective: To quantify the associations of COVID-19 with adverse maternal and neonatal outcomes in pregnancy and to characterize the epidemiology and risk factors.

Methods: We performed a matched case-control study of pregnant patients with confirmed COVID-19 (cases) who delivered between 16 and 41 weeks' gestation from March 11-June 11, 2020. Uninfected pregnant women (controls) were matched to COVID-19 cases on a 2:1 ratio based on delivery date. Maternal demographic characteristics, COVID-19 symptoms, laboratory evaluations, obstetrical and neonatal outcomes, and clinical management were chart abstracted. The primary outcomes included (i) a composite of adverse maternal outcome, defined as preeclampsia, venous thromboembolism, antepartum admission, maternal intensive care unit admission, need for mechanical ventilation, supplemental oxygen, or maternal death; and (ii) a composite of adverse neonatal outcome, defined as respiratory distress syndrome, intraventricular hemorrhage, necrotizing enterocolitis, five-minute Apgar score <5, persistent category 2 fetal heart rate tracing despite intrauterine resuscitation, or neonatal death. In order to quantify the associations between exposure to mild and severe/critical COVID-19 and adverse maternal and neonatal outcomes, unadjusted and adjusted analyses were performed using conditional logistic regression (to account for matching), with matched-pair odds ratio (OR) and 95% confidence interval (CI) based on 1000 bias-corrected bootstrap resampling as the effect measure. Associations were adjusted for potential confounders.

Results: 61 confirmed COVID-19 cases were enrolled during the study period (mild disease: n=54, 88.5%; severe disease: n=6, 9.8%; and critical disease: n=1, 1.6%). The odds of adverse composite maternal outcome were 3.4 times higher among cases compared to controls (18.0% versus 8.2%, adjusted OR 3.4, 95% CI 1.2-13.4). The odds of adverse composite neonatal outcome were 1.7 times higher in the case group compared to the control group (18.0% versus 13.9%, adjusted OR 1.7, 95% CI 0.8-4.8). Stratified analyses by disease severity indicated that the morbidity associated with COVID-19 in pregnancy was largely driven by the severe/critical disease phenotype. Major risk factors for associated morbidity were Black and Hispanic race, advanced maternal age, medical comorbidities, and antepartum admissions related to COVID-19.

Conclusions: COVID-19 during pregnancy is associated with increased risk for adverse maternal and neonatal outcomes, an association that is primarily driven by morbidity associated with severe/critical COVID-19. Black and Hispanic race, obesity, advanced maternal age, medical comorbidities, and antepartum admissions related to COVID-19 are risk factors for associated morbidity.

Key words

Adverse maternal outcomes; Adverse neonatal outcomes; Case-control study; Coronavirus disease in pregnancy; COVID-19; Epidemiology; Morbidity; Novel coronavirus; Pandemic; SARS-CoV-2; Pregnancy; Risk factors; Virus

Introduction

Pregnant women are more susceptible to viral respiratory infections due to immunologic and physiologic adaptations of pregnancy (1). An early Chinese report of COVID-19, the disease caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), found that the risk of severe disease in pregnant patients was similar to the general population (2). This was also observed in initial studies in the United States (US), including a report from New York (3) and Washington (4).

Recent data from the National Notifiable Diseases Surveillance System, reported by the US Centers for Disease Control and Prevention (CDC) on June 25, 2020, compared outcomes of 8207 pregnant and 83205 non-pregnant women with COVID-19 (January 22-June 7, 2020) (5). The authors included all laboratory-confirmed infections with SARS-CoV-2 among women aged 15-44 years from all of the United States and Washington DC. The main findings were that pregnant women with COVID-19 were more likely to be hospitalized, require intubation and mechanical ventilation, and be admitted to an intensive care unit (ICU) compared to non-pregnant women. The authors concluded that pregnant women should be counseled about the potential for severe COVID-19 disease, despite a low absolute risk of ICU admissions and the need for mechanical ventilatory support. This report, which generated substantial press (6, 7), could not distinguish hospitalizations related to COVID-19 from obstetrical indications and could not ascertain if complications from COVID-19 or pregnancy resulted in escalation of medical care and increased morbidity (1).

To date, medical care and guidance from professional societies during the pandemic have been largely based on case reports and case series as well as epidemiologic studies that compared outcomes of pregnant women with COVID-19 to non-pregnant women. Most of these studies lacked an appropriate control group, a common limitation that has complicated our understanding of COVID-19's impact on pregnancy. Therefore, in order to quantify the maternal and neonatal risks associated with COVID-19 in pregnancy and to describe the epidemiology and risk factors for morbidity associated with COVID-19, we undertook a matched case-control study. Associations were evaluated for all COVID-19 patients, as well as for disease classified as mild versus severe/critical disease (2). We also characterized the epidemiology and identified risk factors for morbidity associated with COVID-19 in pregnancy.

Materials and Methods

We performed a matched case-control study at the Robert Wood Johnson University Hospital, a regional perinatal center in New Brunswick, NJ. The Institutional Review Board of the Rutgers Robert Wood Johnson Medical School, NJ granted ethics approval under a waiver of informed consent (PRO2020000854). The study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for case-control studies.

Consecutive pregnant patients with COVID-19 who were admitted to the hospital were enrolled from March 11 to June 11, 2020; this period corresponds to the first three months of the SARS-CoV-2 pandemic (8). COVID-19 testing to detect SARS-CoV-2 infection was performed by nasopharyngeal swab and quantitative polymerase-chain-reaction test. Prior to April 10, 2020,

patients admitted to labor and delivery were tested if they had symptoms of SARS-CoV-2 infection, had recent travel to high-risk countries with prevalent disease, or had direct contact with someone who traveled to high-risk countries or who had COVID-19 (e.g., considered to have a high-risk exposure). On April 10, 2020, we implemented universal COVID-19 testing for all pregnant patients at the time of hospital admission, regardless of symptoms or exposure history.

Consecutive patients with COVID-19 were prospectively identified in a clinical database. Patients were considered to be cases if they had positive COVID-19 testing and delivered between 16.0 and 41.6 weeks' gestation. Cases were categorized as mild, severe, or critical disease according to previously published criteria (9). Mild disease was defined as nonpneumonia and mild pneumonia; severe disease was defined as dyspnea, respiratory frequency ≥30/min, blood oxygen saturation ≤93%, partial pressure of arterial oxygen to fraction of inspired oxygen ratio <300, and lung infiltrates >50% on chest x-ray; and critical disease was defined as respiratory failure, septic shock, and multiple organ failure. Patients were eligible to be cases if initial COVID-19 testing was negative, but subsequent testing during the delivery hospitalization became positive. Patients were excluded if they were persons under investigation (PUI) without confirmatory testing or had negative COVID-19 testing or if they were hospitalized but discharged prior to delivery.

Each COVID-19 case was matched to two controls by delivery date. Prior to April 10, controls were selected as the first two patients who delivered between 16.0 and 41.6 weeks' gestation

on the same date as cases if they were asymptomatic or had negative COVID-19 testing. After April 10, controls were selected if they had negative COVID-19 testing and delivered on the same date as the cases. On days with two or more cases, we identified the next two eligible controls as potential matches.

All patient data were abstracted from the electronic medical record. The primary outcomes were composites of adverse maternal outcomes and adverse neonatal outcomes. The maternal composite included preeclampsia (defined according to the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy (10)), venous thromboembolism, antepartum admission (defined as hospital admission for obstetrical or non-obstetrical indications for inpatient management for >48 hours), ICU admission, need for mechanical ventilation, supplemental oxygen, or maternal death. The neonatal composite included respiratory distress syndrome (RDS; defined as the need for supplemental oxygen and the presence of typical radiographic findings in the absence of other causes for respiratory distress), intraventricular hemorrhage (IVH; defined as grade 1-4 hemorrhages), necrotizing enterocolitis (defined as radiographic or operative findings consistent with perforation), five-minute Apgar score <5, persistent category 2 fetal heart rate tracing despite intrauterine resuscitation, or neonatal death. The primary maternal and neonatal outcomes were examined as a composite owing to small number of patients with the specific complication and, importantly, all of the individual outcomes were regarded as "competing risks."

Secondary maternal outcomes included components of the composite outcome as well as preterm delivery (defined as delivery prior to 37 weeks' gestation, <34 weeks' gestation, and <28 weeks' gestation), mode of delivery (cesarean or vaginal delivery), intrauterine fetal demise, length of hospital stay, and chorioamnionitis. Other neonatal outcomes included birthweight, neonatal intensive care unit (NICU) admission, one- and five-minute Apgar scores, and length of hospital stay. Per institutional policy, all babies born to COVID-19 positive mothers during the study period were considered PUI; these babies were admitted to the NICU until negative COVID-19 testing at 36 hours of life. Persistent category 2 fetal heart rate tracing despite intrauterine resuscitation, chorioamnionitis, and other clinical outcomes were defined by the providers managing each patient. If the provider believed that the patient met criteria for one of these diagnoses, it was noted in the medical record.

Gestational age was based on the best obstetrical estimate (11). Maternal demographics were abstracted from the electronic medical record, including age, gravidity, parity, body mass index (BMI) at delivery, race, and medical comorbidities. Renal disease was defined as baseline proteinuria >300 mg/24 hours or creatinine >1.1 mg/dL. Immunocompromised state was defined as human immunodeficiency virus or chronic steroid use. Anemia was defined as admission hemoglobin <10.5 mg/dL.

Data related to COVID-19 symptoms, laboratory evaluations, and clinical management were also abstracted. Maternal symptoms included fever (defined as temperature >100.4 deg F), cough, shortness of breath, chest pain, diarrhea, myalgias, and sore throat. Laboratory

evaluation included the results of routine complete blood counts and comprehensive metabolic panels (the latter when ordered for clinical purposes). Clinical management included supplemental oxygen, hydroxychloroquine, Remdesivir®, antibiotics, bronchodilators, mechanical ventilation, steroids, and ICU admission.

Statistical Analysis

Demographic characteristics of COVID-19 cases and controls were compared using descriptive statistics, including mean and standard deviation (SD) for normally distributed continuous variables, and median (interquartile range [IQR]) for non-normally distributed continuous variables. In order to quantify the associations between exposure to mild and severe/critical COVID-19 and adverse maternal and neonatal outcomes, we fit conditional logistic regression models from which we estimated matched-pair odds ratios (OR) and 95% confidence interval (CI). Analyses were adjusted for confounders, including advanced maternal age, obesity, maternal race, and comorbid medical problems (specifically diabetes, chronic hypertension, renal disease, immunocompromised state, asthma, and anemia). Owing to small study size, we estimated the variance of ORs (and by extension, 95% CIs) based on 1000 bias-corrected bootstrap resampling. All analyses were performed with Stata version 10.1 (StataCorp LP, College Station, TX).

Results

During the three-month study period, there were 61 pregnant patients diagnosed with COVID-19 who delivered at our institution and met the inclusion criteria (cases). Each case was

matched to two controls by delivery date. Eleven (18%) cases were enrolled in the first month, 28 (45.9%) were enrolled in the second, and 22 (36.1%) were enrolled in the third. Among the cases, disease severity was mild (n=54, 88.5%), severe (n=6, 9.8%), and critical (n=1, 1.6%). Demographic characteristics for cases and controls are described in **Table 1**. Overall, the groups were well matched, but there were more white women with COVID-19 (58.3% versus 42.7%). 142 (77.6%) patients were healthy and without medical comorbidities. Compared to controls, however, patients with severe/critical disease had higher rates of medical comorbidities (42.9% versus 24.6%), such as a diabetes (28.6% versus 16.4%), chronic hypertension (28.6% versus 4.9%), renal disease (14.4% versus 0%), and anemia (14.3% versus 3.3%). Also, cases with severe/critical disease were more likely to be Hispanic (57.1% versus 26.2%) and Black (14.1% versus 6.6%).

Overall 61.1% of patients with mild COVID-19 were asymptomatic. Of the 11 patients who were enrolled during the first month of the study period, 1 (9.1%) patient was asymptomatic; testing of the asymptomatic patient was due to a high-risk exposure. During the latter two months of the study period, 32 (64%) patients were asymptomatic. The most common symptoms for mild disease were cough, fever, and myalgias (**Table 2**). In contrast, all patients with severe/critical disease reported symptoms, with cough, shortness of breath, and fever being the most common symptoms. All patients with severe/critical disease required supplemental oxygen, and some also received other interventions such as hydroxychloroquine (n=4, 57.1%) in the early part of the study period and corticosteroids (n=4, 57.1%) in the latter part. In contrast,

only one patient with mild disease received treatment; the patient was treated with antibiotics for a bacterial pneumonia.

Laboratory results are described in **Table 3**. Patients with mild disease had similar mean white blood cell and platelet counts and median lymphocyte counts and transaminases. In contrast, cases with severe/critical COVID-19 had higher risks of white blood cell count <9.5 cells/L, platelets <150,000/mm^3, lymphocytes <10^9 cells/L, and elevated alanine aminotransferase >45 units/L or aspartate transaminase >35 units/L, compared to controls.

Obstetrical and neonatal outcomes are described in **Table 4**. Cases with mild disease had similar obstetrical outcomes compared to controls. However, cases with severe/critical disease had more adverse obstetrical outcomes, including earlier gestational age of delivery (34.0 versus 38.7 weeks; mean difference 4.8 weeks, 95% CI 2.6, 6.9). Cases were more likely to deliver preterm <37, <34, and <28 weeks' gestation, compared to controls. Patients with severe/critical COVID-19 also had higher risks of antepartum admissions, cesarean delivery, chorioamnionitis, preeclampsia, and persistent category 2 fetal heart rate tracing despite intrauterine resuscitation, and required longer hospital stays, compared to controls.

Four patients with severe/critical disease required antepartum admissions compared to one control patient. All four cases were admitted for management of COVID-19 and required delivery during their admissions. One was admitted at 38 weeks' gestation with COVID-19 symptoms and severe disease. After a period of maternal stabilization, she required cesarean

delivery at 39 weeks for worsening respiratory status. The other three patients had clinician-initiated preterm deliveries at 26 weeks' gestation (critical disease with emergent cesarean delivery in the ICU for refractory hypotension and persistent category 2 fetal heart rate tracing despite intrauterine resuscitation), at 29.3 weeks (repeat cesarean delivery for severe COVID-19 in the context of superimposed PEC with severe features), and at 34.6 weeks (induction of labor for severe COVID-19 with worsening respiratory status). The control patient was admitted with preeclampsia with severe features and HELLP syndrome at 28 weeks' gestation. She underwent inpatient expectant monitoring for 48 hours and then had a successful induction of labor.

Driven primarily by the gestational age at delivery, the offspring of pregnant patients with severe/critical COVID-19 had lower birthweights, and higher rates of NICU admission, RDS, and IVH compared to controls (**Table 4**). Neonatal outcomes were similar for pregnant patients with mild COVID-19 versus controls.

Associations of COVID-19 and composites of adverse maternal and neonatal outcomes are described in **Table 5**. Comparing all COVID-19 cases to controls, the unadjusted odds ratios of adverse maternal and neonatal outcome were 2.7 (95% CI 1.0-10.0) and 1.4 (95% CI 0.6-3.6) respectively. After adjusting for advanced maternal age, obesity, race, and comorbid medical problems, the adjusted odds of adverse maternal and neonatal outcomes were 3.4 (95% CI 1.2-13.4) and 1.7 (95% CI 0.8-4.8), respectively. In analyses stratified by disease severity, the odds of adverse maternal and neonatal outcome were similar for mild COVID-19 cases versus

299 controls (**Table 5**). These results suggest that the morbidity associated with COVID-19 in
300 pregnancy is largely driven by the severe/critical phenotype.
301
302 **Comment**
303 *Principal Findings*
304 We evaluated the risk factors that drive the associations between COVID-19 and adverse
305 maternal and neonatal outcomes. In this matched case-control study, we demonstrated that
306 pregnant women with mild COVID-19 have similar outcomes compared to pregnant controls
307 matched by delivery date whereas pregnant patients with severe/critical disease have worse
308 outcomes. Black and Hispanic race, advanced maternal age, obesity, medical comorbidities,
309 such as diabetes and chronic hypertension, and antepartum admission related to COVID-19 are
310 risk factors for adverse maternal and neonatal outcomes.
311
312 *Results of the Study in Context*
313 The main finding of this study is that severe/critical disease drive morbidity associated with
314 COVID-19 in pregnancy. As broader testing for COVID-19 becomes available, the prevalence of
315 asymptomatic and mild disease has increased. The results of this study can provide some
316 reassurance for most pregnant patients.
317
318 After implementation of universal testing, we found that 64% of cases were asymptomatic. Our
319 rate of asymptomatic disease was lower than other reports of asymptomatic presentation on
320 labor and delivery. For example, in the initial experience of Columbia with universal testing,

87.9% of labor and delivery admissions with COVID-19 were asymptomatic (12). Although the reason for higher rates of self-reported symptoms is uncertain in this study, there is still a large burden of asymptomatic positive patients with COVID-19. The public health threat that this poses – both for transmission in the greater community and for risk to healthcare providers – underscores the importance of access to universal testing for COVID-19 on labor and delivery.

Among the COVID-19 cases, disease severity was mild (n=54, 88.5%), severe (n=6, 9.8%), and critical (n=1, 1.6%). These proportions are comparable to what has been observed in non-pregnant patients (2).

Clinical Implications

The results of this study provide a risk profile associated with maternal and neonatal complications associated with COVID-19 in pregnancy. Although limited by small numbers, patients with severe/critical disease were more likely to be older (advanced maternal age), obese, Black and Hispanic, and have medical comorbidities. Although young and healthy patients may have manifestations of severe COVID-19, the results of this study suggest that specific risk factors are the driver of risk.

CDC surveillance data suggests that pregnancy is associated with increased risk for hospitalization, ICU admission, and mechanical ventilation (5). The CDC study found low absolute rates of ICU admission and mechanical ventilation, but was limited by incomplete data. The study could not explain whether COVID-19 or obstetrical complications were

responsible for higher rates of ICU and mechanical ventilation. In this context, the results presented in this case-control study shed light on the risk factors and associations that drive morbidity associated with COVID-19. Pregnant patients who require ICU admission and mechanical ventilation are more likely to have severe/critical COVID-19.

It remains debated whether vertical transmission of SARS-CoV-2 occurs, and current CDC guidelines call for treating offspring of COVID-19 patients as PUI, which typically involves isolation precautions and COVID-19 testing (13). The guidelines further suggest that shared decision-making should be utilized to determine the extent of social distancing between the patient and the neonate. All neonates of COVID-19 patients in the study had testing at 36 hours of life, and all results were negative.

We found increased risk of preterm delivery among severe/critical patients affected by COVID-19 compared to controls. These findings are similar to other studies that suggests the preterm birth risk is primarily clinician-initiated rather than spontaneous (14, 15). This observation is notable during the pandemic lockdown, when some countries have noted a reduction in spontaneous preterm birth rates (16).

Strengths and Limitations

Our study has several strengths. As a matched case-control study, maternal and neonatal outcomes of patients with COVID-19 could be compared with matched controls. Other influential studies that have informed our knowledge of COVID-19 in pregnancy have lacked

365 control groups, including case reports (17, 18), case series (19-21), and epidemiologic studies
366 (5, 15).
367
368 Although the study was robust and included maternal and neonatal outcomes that were
369 rigorously abstracted, the data was abstracted from delivery hospitalizations. We recognize
370 that some patients with COVID-19 in the community may not have required hospitalization or
371 were hospitalized, but remained undelivered over the course of this project. These patients
372 were not included in this study. As such, the current analysis may bias towards more severe
373 phenotype for patients with severe/critical COVID-19 during the first three months of the
374 pandemic.
375
376 The study's sample size was relative small, leading to imprecision in the effect measure
377 estimates. We included two matched controls per COVID-19 case (which may have resulted in
378 improved power), but the small sample size limited conclusions about rare outcomes. For
379 example, a large retrospective cohort study that included 3309 births found higher rates of
380 intrauterine fetal demise during the pandemic compared to a pre-pandemic period (22), but we
381 were underpowered for rare outcomes such as this. There is great need for robust research on
382 this topic, which is why have presented this data at this time, but we intend to continue data
383 collection for the purposes of larger studies in the future.
384

Finally, whether the findings reported in this study permits generalizability remains uncertain. Hospital-based studies are guided by referrals to the institution and may not reflect the prevailing landscape of patients seen in other hospital settings or the general population.

Conclusions

The CDC recommends that pregnant patients take steps to minimize acquisition of the infection that causes COVID-19 due to potential for severe disease compared to non-pregnant patients (5). Most pregnant patients with COVID-19 have mild disease, and this is not associated with substantial risk of adverse maternal and neonatal outcomes. However, the results of this matched case-control study show the driver for risk in pregnancy is severe/critical disease. Moreover, specific risk factors are associated with the severe/critical disease phenotype, including Black and Hispanic race, advanced maternal age, obesity, medical comorbidities, and antepartum admission related to COVID-19. While the results of this study support the CDC's conclusion, the main findings suggest disease severity and specific risk factors drive risk associated with COVID-19 during pregnancy.

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463 **Table 1**
464 **Demographic characteristics of COVID-19 cases versus matched controls**
465

	COVID-19 cases (n=61)	Controls (n=122)
Maternal age (years)[†]	30.3 (6.4)	30.9 (6.3)
Maternal age ≥35 years	17 (27.9)	37 (30.3)
Gravidity[‡]	3 (2-4)	2 (2-4)
Parity[‡]	2 (1-3)	1 (1-3)
Pre-pregnancy BMI (kg/m^2)[†]	31.5 (7.3)	30.1 (5.7)
Normal BMI (<25.0)	10 (16.4)	15 (12.3)
Overweight (25.0-29.0)	23 (37.7)	59 (48.4)
Obese	28 (45.9)	48 (39.3)
Class 1 obese (30.0-34.9)	11 (18.0)	27 (22.1)
Class 2 obese (35.0-39.9)	8 (13.1)	12 (9.8)
Class 3 obese (≥40)	9 (14.8)	9 (7.4)
Maternal race		
White	35 (58.3)	47 (42.7)
Black	2 (3.3)	8 (7.3)
Hispanic	21 (35.0)	32 (29.1)
Asian/Indian	2 (3.3)	23 (20.9)
No past medical history	50 (82.0)	92 (75.4)
Comorbid medical condition	11 (18.0)	30 (24.6)
Diabetes	7 (11.5)	20 (16.4)
Chronic hypertension	2 (3.3)	6 (4.9)
Renal disorder	1 (1.6)	0
Immuno-compromised	2 (3.3)	1 (0.8)
Asthma	2 (3.3)	4 (3.3)
Anemia	2 (3.3)	4 (3.3)
Twins	0	1 (0.8)

Data presented as n (percent). [†]Data presented as mean (standard deviation). [‡]Data presented as median (interquartile range).

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Table 2
Characteristics of COVID-19 symptoms among cases and controls matched by delivery date, stratified by disease severity

	COVID-19 cases (n=61)	
	Mild (n=54)	**Severe/critical (n=7)**
COVID-19 disease		
Mild disease	54 (100)	0
Severe disease	0	6 (85.7)
Critical disease	0	1 (14.3)
COVID-19 symptoms		
None	33 (61.1)	0
Fever	13 (24.1)	5 (71.4)
Cough	14 (25.9)	7 (100)
Shortness of breath	2 (3.7)	6 (85.7)
Chest pain	0	1 (14.3)
Diarrhea	0	1 (14.3)
Myalgias	5 (9.3)	1 (14.3)
Sore throat	1 (1.9)	0
COVID-19 treatment		
Any treatment	1 (1.9)	7 (100)
Supplemental O_2	0	7 (100)
Hydroxychloroquine	0	4 (57.1)
Remdesivir®	0	2 (28.6)
Antibiotics	1 (1.9)	3 (42.9)
Bronchodilators	0	3 (42.9)
Mechanical ventilation	0	1 (14.3)
Steroid use	0	4 (57.1)
ICU admission	0	1 (14.3)

Data presented as n (percent).

Table 3

Laboratory findings of patients with COVID-19 stratified by disease severity versus controls matched by delivery date

Laboratory Findings	COVID-19 cases (n=61)		Controls (n=122)	Severe/critical vs controls: OR (95% CI)
	Mild (n=54)	Severe/critical (n=7)		
WBC, cells/L[†]	10.4 (3.3)	7.9 (3.6)	10.0 (2.7)	–
WBC <9.5 cells/L	24 (44.4)	5 (71.4)	54 (44.3)	2.5 (0.3, ∞)
Platelets, 10^3/mm^{3†}	212.8 (56.8)	214.6 (75.3)	209.5 (55.6)	–
Platelets <150,000, mm^3	3 (5.6)	2 (28.6)	14 (11.5)	4.0 (0.5, ∞)
Lymphocytes, [‡] cells/L[†] (n=54)	195 (171-242)	230 (147-294)	204 (163-241)	–
Lymphocytes <10^9, cells/L	1 (3.0)	2 (40.0)	2 (4.1)	–
AST, units/L,[‡] (n=35)	22 (19-26)	34 (21-54)	23 (17-25)	–
ALT, units/L,[‡] (n=35)	14 (12-20)	17 (13-45)	34 (21-54)	–
Elevated ALT >45 units/L or AST >35 units/L	2 (13.3)	2 (33.3)	3 (10.3)	–

Data presented as n (percent). [†]Data presented as mean (standard deviation). [‡]Data presented as median (interquartile range).
WBC, white blood count; AST, aspartate aminotransferase; ALT, alanine aminotransferase.

475 **Table 4**
476 **Obstetrical and neonatal outcomes stratified by disease severity versus controls matched by delivery date**
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	COVID-19 cases (n=61)		Controls (n=122)	Severe/critical vs controls: OR (95% CI)
	Mild (n=54)	Severe/critical (n=7)		
Obstetrical Outcomes				
Length of stay (days)‡	3 (2-3)	6 (5-17)	3 (3-3)	–
Antepartum admission	0	4 (57.1)	1 (0.8)	–
Cesarean delivery	9 (16.7)	5 (71.4)	40 (32.8)	4.6 (0.7, ∞)
Gestational age at testing (weeks)†	38.8 (2.8)	33.6 (5.8)	38.8 (2.5)	–
Gestational age at delivery (weeks)†	39.0 (2.7)	34.0 (5.8)	38.7 (2.5)	–
Preterm delivery				
<37 weeks	3 (5.6)	4 (57.1)	10 (8.2)	4.6 (0.4, ∞)
<34 weeks	1 (1.9)	3 (42.9)	4 (3.3)	6.0 (0.7, ∞)
<28 weeks	1 (1.9)	1 (14.3)	1 (0.8)	2.0 (0.5, 4.0)
Chorioamnionitis	1 (1.9)	1 (14.3)	2 (1.6)	–
Venous thromboembolism	0	0	0	–
Persistent category 2 fetal heart rate tracing	3 (5.6)	3 (42.9)	9 (7.4)	–
Preeclampsia	4 (7.4)	2 (28.6)	10 (8.2)	–
Intrauterine fetal demise	0	0	0	–
Neonatal Outcomes				
Birth weight (grams)†	3230 (549)	2293 (1104)	3246 (605)	
Apgar, 1-minute‡	9 (9-9)	9 (1-9)	9 (9-9)	–
Apgar, 5-minute‡	9 (9-9)	9 (5-9)	9 (9-9)	–

NICU admission	46 (85.2)	7 (100.0)	14 (11.5)	–
NICU length of stay (days)[‡]	2 (2-3)	9 (5-49)	0-0	–
Respiratory distress syndrome (RDS)	1 (1.9)	4 (57.1)	6 (4.9)	–
Intraventricular hemorrhage (IVH)	0	2 (28.6)	1 (0.8)	–
Necrotizing enterocolitis	0	0	0	–
Neonatal death	1 (1.9)	0	1 (0.8)	–

Data presented as n (percent). [†]Data presented as mean (standard deviation). [‡]Data presented as median (interquartile range).
NICU: neonatal intensive care unit

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Table 5
Associations of COVID-19 and composites of adverse maternal and neonatal outcomes

	COVID-19 cases (n=61)			Controls (n=122)	Odds ratio (95% confidence interval)	
	All cases (n=61)	Mild (n=54)	Severe/ Critical (n=7)		Unadjusted	Adjusted
					All cases vs controls	
Maternal composite	11 (18.0)	–	–	10 (8.2)	2.7 (1, 10)	3.4 (1.2, 13.4)
Neonatal composite	11 (18.0)	–	–	17 (13.9)	1.4 (0.6, 3.6)	1.7 (0.8, 4.8)
					Mild cases vs controls	
Maternal composite	–	4 (7.4)	7 (100)	10 (8.2)	0.7 (<0.01, 3.3)	1.1 (<0.01, 6.0)
Neonatal composite	–	5 (9.3)	6 (85.7)	17 (13.9)	1.0 (0.1, 7.7)	1.0 (0.1, 7.7)

Composite maternal outcome includes venous thromboembolism, preeclampsia, intensive care unit admission, mechanical ventilation, antepartum admission, supplemental oxygen, and death.
Composite neonatal outcome includes respiratory distress syndrome, intraventricular hemorrhage, necrotizing enterocolitis, five-minute Apgar score <5, persistent category 2 fetal heart rate tracing, and neonatal death
ORs were adjusted for advanced maternal age, obesity, race, and comorbid medical problem; 95% CIs were based on 1000 bias-corrected bootstrap resampling method.
Note: The analyses for severe/critical cases vs controls were not estimable due to small numbers and the lack of convergence of the conditional logistic regression model.