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The Society for Obstetric Anesthesia and Perinatology (SOAP) COVID-19 Registry: An analysis of outcomes among pregnant women delivering during the initial SARS-CoV-2 outbreak in the United States

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GLOSSARY OF TERMS

aOR: adjusted odds ratio

ARDS: acute respiratory distress syndrome

BMI: body mass index

CDC: Center for Disease Control

CI: confidence interval

CPAP: continuous positive airway pressure

DTUA: data transfer and use agreement

GEE: generalized estimating equations

HELLP: hemolysis, elevated liver enzymes, low platelets

ICU: intensive care unit

IRB: institutional review board

ITP: idiopathic thrombocytopenic purpura

NICU: neonatal intensive care unit

PCR: polymerase chain reaction

SARS-CoV-2: severe acute respiratory syndrome coronavirus-2

SMD: standardized mean difference

SOAP: Society for Obstetric Anesthesia and Perinatology

ABSTRACT

Background: Early reports associating SARS-CoV-2 infection with adverse pregnancy outcomes were biased by including only women with severe disease without controls. The Society for Obstetric Anesthesia and Perinatology (SOAP) COVID Registry was created to compare peripartum outcomes and anesthetic utilization in women with and without SARS-CoV-2 infection delivering at institutions with widespread testing.

Methods: Deliveries from 14 U.S. medical centers, March 19-May 31, 2020, were included. Peripartum infection was defined as a positive SARS-CoV-2 polymerase chain reaction test within 14 days of delivery. Consecutive SARS-CoV-2 infected patients with randomly selected control patients were sampled (1:2 ratio) with controls delivering during the same day without a positive test. Outcomes were obstetric (e.g., delivery mode, hypertensive disorders of pregnancy, delivery < 37 weeks), an adverse neonatal outcome composite measure (primary), and anesthetic utilization (e.g., neuraxial labor analgesia and anesthesia). Outcomes were analyzed using generalized estimating equations to account for clustering within centers. Sensitivity analyses compared symptomatic and asymptomatic patients to controls.

Results: 1454 peripartum women were included: 490 with SARS-CoV-2 infection [176 (35.9%) symptomatic]; 964 controls. SARS-CoV-2 patients were slightly younger, more likely non-nulliparous, non-white, and Hispanic than controls. They were more likely to have diabetes, obesity, or cardiac disease and less likely to have autoimmune disease. After adjustment for confounders, individuals experiencing SARS-CoV-2 infection exhibited an increased risk for delivery < 37 weeks gestation compared to controls, 73 (14.8%) vs. 98 (10.2%) [adjusted odds ratio (aOR): 1.47 95% CI (1.03-2.09)]. Effect estimates for other obstetric outcomes and the neonatal composite outcome measure were not meaningfully different between SARS-CoV-2-patients versus controls. In sensitivity analyses, compared to controls, symptomatic SARS-CoV-

2 patients exhibited: increases in cesarean delivery [aOR: 1.57 95% CI (1.09-2.27)]; postpartum length of stay [aOR 1.89 95% CI (1.18-2.60)]; delivery < 37 weeks gestation [aOR 2.08 95% CI (1.29-3.36)]. These adverse outcomes were not found in asymptomatic women versus controls. SARS-CoV-2 patients (asymptomatic and symptomatic) were less likely to receive neuraxial labor analgesia [aOR: 0.52 95% CI (0.35–0.75)] and more likely to receive general anesthesia for cesarean delivery [aOR: 3.69 95% CI (1.40–9.74)] due to maternal respiratory failure.

Conclusions: In this large, multicenter U.S. cohort study of women with and without peripartum SARS-CoV-2 infection, differences in obstetric and neonatal outcomes seem to be mostly driven by symptomatic patients. Lower utilization of neuraxial analgesia in laboring patients with asymptomatic or symptomatic infection compared to patients without infection requires further investigation.

Key Points Summary

Question: Is SARS-CoV-2 infection associated with adverse peripartum outcomes?

Findings: Maternal and neonatal outcomes were less favorable in symptomatic pregnant women delivering with SARS-CoV-2 infection compared to controls but not in asymptomatic women, and women with SARS-CoV-2 in this cohort had lower utilization of neuraxial labor analgesia.

Meaning: The presence or absence of maternal SARS-CoV-2 symptoms at the time of delivery might help stratify risk and management, and provision of labor analgesia and potential barriers during a pandemic warrant further investigation.

INTRODUCTION

As of January 17, 2021, there were more than 93 million confirmed cases of COVID-19 and more than 2 million deaths globally.[1] In the obstetric population, initial reports from China seemed encouraging, documenting less morbidity with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during pregnancy than with SARS or MERS infections.[2] However, as the virus spread, it was difficult to formulate a consistent picture of the clinically relevant maternal and neonatal peripartum risks of SARS-CoV-2 infection. Initial reports cautioned that severe thrombocytopenia might be associated with COVID-19 infection[3-5] and that 'excessive' hypotension might be induced by neuraxial anesthesia during cesarean delivery.[6] Despite the growing body of literature on pregnancy and SARS-CoV-2 infection,[7-9] there has been little data comparing asymptomatic and symptomatic patients, and infected versus non-infected patients, with respect to obstetrical outcomes and anesthetic management.

Thrombotic complications and coagulopathy emerged along with evidence that SARS-CoV-2 induced a hypercoagulable state.[10,11] Pathological changes, such as intervillous thrombi, found in the placentas of patients infected with SARS-CoV-2, have been similar to those found in patients with hypertensive disorders of pregnancy, intrauterine growth restriction, and preterm delivery;[12,13] suggesting that pregnant patients with SARS-CoV-2 might be at risk for adverse pregnancy outcomes.[12] Although these associations are clinically plausible, our understanding of this disease has been limited by small cohorts, a lack of contemporary control groups, outcomes that are confounded by a focus on women with symptomatic and/or severe disease, and the aggregation of cases at different stages of pregnancy.[14-17] Over time, an increasing number of reports have suggested that a subset of obstetric patients become critically ill,[18-20] rendering case identification, risk stratification, and subsequent management crucial.

The Society for Obstetric Anesthesia and Perinatology (SOAP) COVID Registry was created with the primary goal of investigating peripartum outcomes and anesthetic management in women with and without SARS-CoV-2 infection during delivery hospitalizations in institutions with widespread testing, thus better representing the full spectrum of disease. Our hypothesis was that women with SARS-CoV-2 infection would have worse outcomes that those without SARS-CoV-2 infection.

METHODS

Sites and Case Ascertainment

The SOAP registry was created in March 2020. A registry Executive Committee was formed (6 members) and the SOAP President (LRL) made initial contact with SOAP leaders at 29 affiliated hospitals across the United States via e-mail. The 14 medical centers (including 17 hospitals) that agreed to participate included hospitals from the Northeast, South, Midwest, and Western regions of the United States. Each site obtained individual site IRB approval and written informed consent waivers and screened their own patients for inclusion. The sites had the option to either host a local REDCap database and then share data with the Massachusetts General Hospital (MGH) central database (after signing the Data Transfer and Use Agreement (DTUA)) or enter data directly into the central MGH database maintained in the Partners REDCap server after the DTUA was signed.

Consecutive sampling was used to identify all delivery hospitalizations occurring in participating centers between March 19 and May 31. Women were defined as infected in the peripartum period if they had a positive polymerase chain reaction (PCR) test for SARS-CoV-2 within 14 days of their delivery date. Over the course of the study period, testing evolved from symptoms-based in the early study period to universal screening at most participating institutions

in the later study period. For each patient added to the registry, it was documented whether or not they were admitted and tested under universal screening.

Initially, a single control patient without SARS-CoV-2 infection was identified using a convenience sampling method defined by investigators at each hospital for each day that an infected patient delivered and linked with all of the infected patients that delivered on that day (i.e., all selected deliveries on that day were considered as belonging to a cluster). This method resulted in a paucity of controls (215) that were considered to be limited by an unacceptable risk of selection bias given the lack of a standardized approach for their identification. As such, a new control group was created. Because data extraction involved manual record review, it was not feasible to include all delivering patients during the observation-period. Therefore, for each identified patient with SARS-CoV-2 infection two controls without a positive SARS-CoV-2 test were identified for inclusion. To best approximate a random sample, all potential controls who delivered on the same day and center as the case parturient were given case ID numbers in sequential order according to the timing of their deliveries. Using a random number generator from a uniform distribution ('runif' in R 3.6), two control IDs were randomly selected without replacement for each case by a statistician at the coordinating institution for each patient with infection. If insufficient control numbers existed, all available controls for that day were selected. A ratio of 1:2 was targeted to provide improved precision of our proposed exposure-outcome association. Assuming an event rate of 10%, an odds ratio of 1.5 was expected to have approximately 30% relative precision for a 95% CI if a 1 to 1.75 sampling ratio was achieved.

Data Elements

Pre-specified primary obstetric outcomes included cesarean delivery, hypertensive disorders of pregnancy [gestational hypertension, chronic hypertension with superimposed preeclampsia, preeclampsia with and without severe features, Hemolysis, Elevated Liver

Enzymes, Low platelets (HELLP) syndrome], preterm delivery, placental abruption, length of stay, estimated blood loss, and a composite adverse neonatal composite outcome measure, defined as experiencing any (i.e., one or more) of the following: positive by an Apgar score < 7 at 1 or 5 minutes, escalation of care in the delivery room with either usual or prolonged hospital stay or transfer to the NICU, or the need for respiratory support in the delivery room (e.g., transient mask ventilation, continuous positive airway support (CPAP) or intubation at delivery). Pre-specified (secondary) anesthetic outcomes included: for laboring patients, receipt of labor analgesia (neuraxial or other), and for cesarean delivery, anesthetic technique (i.e., neuraxial anesthesia or general anesthesia). Other secondary outcomes included maternal signs and symptoms of infection (e.g. fever, dyspnea), maternal vital signs and laboratory values on admission, and additional medical outcomes (e.g., supplemental oxygen, ICU status).

Data Analysis

The sampling plan allowed the comparison between locally and temporally similar deliveries but created clustering in the data structure. To account for the clustering within site-specific measurement occasions, the obstetric, neonatal, and anesthetic outcomes were analyzed using Generalized Estimating Equations (GEE; 'geepack' using R 3.6) with appropriate distribution and link functions, with robust standard error estimation. A sampling unit ID was specified for patients and controls according to the site and day of delivery, and an exchangeable covariance matrix was used to accommodate the covariance. Two versions of each model were conducted that considered both unadjusted and exposure-outcome associations adjusted for the prespecified confounders. The specified confounders were age, race, ethnicity, body mass index (BMI), and maternal comorbidities including diabetes, preexisting hypertension, cardiac, pulmonary or autoimmune disease for the obstetric, neonatal composite outcomes and the

anesthetic management. For some outcomes, the low observed event frequency precluded the use of a multivariable model to control for potential confounders.

The primary obstetric and anesthetic outcome analyses were repeated with predefined sensitivity analyses that redefined the exposure group as asymptomatic SARS-CoV-2 infected patients (excluding symptomatic patients) and asymptomatic SARS-CoV-2 infected patients (excluding symptomatic patients). Crude differences between background health characteristics of SARS-CoV-2 infected patients and controls were reported using standardized mean differences (SMD), and following the recommendations of Austin[21] interpreted as meaningful if SMD > 0.1 ($1.96 \times \sqrt{\frac{1}{964} + \frac{1}{490}}$). Contrasts were estimated along with 95% confidence intervals.

Results of all analyses are presented as contrasts with a reference group and are interpreted based on the magnitude of the point estimates, factoring the precision of each estimate as reflected in the width of its 95% confidence interval. Specifically, the following considerations were used in interpretation: 1) the strength of the adjusted effect size estimate (irrespective of whether or not the 95% confidence interval includes the null), 2) the degree to which the upper bound of the 95% CI excludes a large, clinically-relevant increased risk of the adverse event, and 3) the degree to which the effect estimates were consistent across sensitivity analyses.[22] Each analysis was conducted on the available data, with no attempts made to impute missing values. Missing data (%) are noted for all major primary and secondary data elements.

RESULTS

During the study period (March 19-May 31, 2020), 1454 peripartum women from 14 medical centers (17 hospitals) were included in the registry: 495 had SARS-CoV-2 infection and 964 were controls (Figure 1). Five identified SARS-CoV-2 were excluded due to a duplicate entry (n = 1), presumed SARS-CoV-2 positive on admission but later found to be CoV-2

negative (n = 2), and missing neonatal information (n = 2), for a final total of N= 490 COVID patients [176 (35.9%) were symptomatic]. The majority of patients (80.0%) were ascertained in the context of universal screening. 100% of the SARS-CoV-2 infected patients had a positive PCR test; 83.7% of controls had a negative PCR test, and the other negative controls were symptom-free and presumed negative. Baseline characteristics, demographic information, and comorbidities are reported in Table 1. Patients with SARS-CoV-2 infection were slightly younger (age 30.4 versus 32.0 years) and more likely to be non-nulliparous, non-white, and of Hispanic ethnicity than controls. They were also more likely to have co-morbid diabetes, obesity, or cardiac disease and less likely to have autoimmune disease than controls.

Initial clinical presentation and laboratory tests

Most commonly, patients with SARS-CoV-2 infection were asymptomatic [314/490 (64.1%)] (Supplemental Table 1, Supplemental Digital Content, http://links.lww.com/AA/D542). Symptomatic patients with SARS-CoV-2 infection most often presented with cough 110/176 (62.5%) and low-grade fever 84/176 (47.7%). In contrast, temperature > 38°C on admission was extremely rare in both groups of patients (0.3-0.4%). Admission laboratory values were similar in patients with SARS-CoV-2 infection and in controls, except that lymphopenia was more common in infected patients. Thrombocytopenia, defined as a platelet count < 100 $x10^6$/L, was equally rare in infected and control patients (1-2%). Only 1 woman with asymptomatic SARS-CoV-2 infection had a platelet count < 70,000 x 10^6/L. Her platelet count of 49,000 x 10^6/L on admission increased to 63,000 x 10^6/L peripartum. She had immune thrombocytopenia (ITP), protein S deficiency, and delivered vaginally without neuraxial analgesia.

Obstetric and neonatal outcomes

Primary obstetric outcomes (adjusted and unadjusted) are displayed in Table 2. After adjustment for potential confounders, SARS-CoV-2 infection was associated with an increased risk for delivery at less than 37 weeks gestation compared to controls, 73 (14.8 %) vs. 98 (10.2%) [adjusted odds ratio (aOR): 1.47 (95% CI (1.03-2.09)]. Risk estimates for cesarean delivery and obstetric outcomes including hypertensive disorders of pregnancy, postpartum hemorrhage, and the neonatal composite outcome measure were not meaningfully different between groups, although CIs were wide and did not preclude clinically meaningful increases in risk. In a post-hoc sensitivity analysis model that adjusted for gestational age, the association between SARS-CoV-2 infection and the composite neonatal outcome was little changed [OR 1.29 (95% CI: 0.91-1.83)].

Table 3 displays the results of the subgroup (sensitivity) analysis comparing patients with asymptomatic or symptomatic SARS-CoV-2 infection with controls. In contrast to the analysis with SARS-CoV-2 infected patients in aggregate, there was an association between symptomatic SARS-CoV-2 infection and an increased risk for cesarean delivery compared to controls, 81/176 (46.0%) vs. 331/964 (34.4%) [aOR: 1.57 95% CI (1.09-2.27)] and increased postpartum length of stay compared to controls, 3.8 days vs 1.9 days [aOR: 1.89 95% CI (1.18-2.60)]. Symptomatic, SARS-CoV-2 patients also had a greater risk of delivery prior to 37 weeks than controls, 35/176 (19.9%) vs 98/964 (10.2%) [aOR: 2.08 95% CI (1.29 -3.36)].

Anesthetic Management

Anesthetic modalities differed between infected patients and non-infected controls. Although the majority of laboring patients received neuraxial labor analgesia in both groups (297/374 (79.4%) of SARS-CoV-2 patients and 656/738 (88.9%) of controls), patients with SARS-CoV-2 were less likely to receive neuraxial labor analgesia in both the unadjusted and adjusted models [OR 0.48 95% CI (0.34-0.70); aOR 0.52 95% CI (0.35-0.75)]. (Table 4) No

patients were recorded as having had nitrous oxide for labor analgesia during the study period. General anesthesia for cesarean delivery was utilized in 15/171 (8.7%) of patients with SARS-CoV-2 infection and 9/331 (2.6%) of controls [(OR 3.64 95% (1.45-9.12); aOR: 3.69 95% CI (1.40-9.74)]. Indications for general anesthesia in patients with SARS-CoV-2 infection were primarily related to maternal respiratory failure [12/15 (80.0%)] (Table 4). General anesthesia in patients without SARS-CoV-2 infection occurred more often in the setting of fetal indications [5/9 (55.6%)] or neuraxial failure [2/9 (22.2%)]. All patients who received general anesthesia had either tracheal intubation via videolaryngoscopy or already had an endotracheal tube in place at the time of cesarean delivery.

The subgroup (sensitivity) analysis showed that patients with either asymptomatic SARS-CoV-2 infection or symptomatic patients were less likely to receive neuraxial analgesia for labor than were patients without SARS-CoV-2 infection. (Table 5) In patients who had a cesarean delivery, symptomatic SARS-CoV-2 infection was associated with a marked increase in the utilization of general anesthesia 15/81 (18.5%) vs controls 9/331 (2.7%) [OR: 8.13 95% CI (3.26-20.26); aOR: 9.68 95% CI (3.48-26.91)].

Medical Outcomes of the SARS-CoV-2 Cohort

Among the 490 SARS-CoV-2 infected cases, 41 (8.4 %) required supplemental oxygen during their delivery hospitalization and 18/490 (3.7%) required intubation. Admission to an intensive level care unit (general or obstetric ICU) was required in 28/490 cases, which represents 5.7% of the total SARS-CoV-2 infected cohort and 15.9% (28/176) of the symptomatic SARS-CoV-2 infected patients. Nineteen out of the 28 critically ill patients (67.9%) had acute respiratory distress syndrome (ARDS), 10/28 (35.7%) had (Cr > 0.8 mg/dL), the normal upper limit for pregnancy, and 1/28 (3.6%) had acute cardiac injury (High Sensitivity Troponin =75 ng/L). None of the patients required extracorporeal membrane oxygenation

(ECMO) support. Most patients were discharged directly to home (487/490 [99.4%]), with 3 discharged to a rehabilitation facility. There were no maternal deaths, and 1 intrauterine fetal death that occurred at 23 weeks gestation in a SARS-CoV-2 patient.

DISCUSSION

In this large, multicenter U.S. cohort of women with peripartum SARS-CoV-2 infection during widespread universal testing, we analyzed obstetric outcomes, neonatal outcomes, and anesthetic management among patients with and without infection after controlling for confounders. Studies examining the full spectrum and impact of asymptomatic and symptomatic SARS-CoV-2 infection on pregnancy outcomes have been scarce. Our registry included some of the highest volume hospitals for COVID-19 cases (e.g., New York City and Boston) as well as those that were relatively spared during the study time period (e.g., in the South and West of the country). Our findings suggest that asymptomatic peripartum SARS-CoV-2 infection might not markedly increase either the rate of adverse pregnancy outcomes or the relative odds for cesarean delivery for most patients. This is in contrast to some prior international studies that reported very high cesarean delivery rates among women with SARS-CoV-2 infection: 76.9% in one case series from China[23] and 59%[24] and 47%[25] in cohort studies from the UK and Spain, respectively. These differences might reflect selection bias toward symptomatic pregnant patients with SARS-CoV-2 infection and those with severe illness, which would be consistent with our results, although we did not specifically compare symptomatic and asymptomatic women.

Smaller case series[15] and studies[26] reported rates of preterm delivery of up to 20%, including a large multinational meta-analysis of over 10,996 cases in which the preterm birth was 21%.[27] These findings are comparable to our results (14.8 %) which may have been primarily driven by symptomatic patients. Although our study did not allow us to separate spontaneous versus medically indicated preterm birth, the predominance of symptomatic patients

delivering between 34-37 weeks may suggest medically indicated deliveries are driving this finding.

Our study suggests that non-white race and minority ethnicity are overrepresented among pregnant SARS-CoV-2 infected cohorts. This result is corroborated by other studies in pregnant and non-pregnant patients with SARS-CoV-2 infection in the U.S.[27], including a recent CDC report of over 460,000 SARS-CoV-2 cases in which 29.7% of pregnant patients versus 22.6% of non-pregnant were Hispanic.[20] This finding is likely influenced by other factors such as population density, the inability to socially isolate and other social determinants of health,[28] which were not investigated in our or most others' studies.

Among our symptomatic patients with SARS-CoV-2 infection, presenting signs and symptoms, primarily respiratory, were also consistent with other reports.[24,27] Interestingly, the rate of maternal temperature above 38°C on admission to the labor and delivery units was not different between SARS-CoV-2 infected patients and controls. A lower rate of fever in pregnant compared to non-pregnant SARS-CoV-2 patients has been demonstrated,[29] as well as a lack of difference in temperature between symptomatic and asymptomatic infected pregnant patients.[30] This finding may compromise the benefit of temperature screening, which is a common practice prior to entry to public spaces during the COVID-19 pandemic.

The finding of less neuraxial labor analgesia use in asymptomatic and symptomatic SARS-CoV-2 patients compared to controls was unexpected, given the lack of apparent contraindications and the strong recommendations for proactive use of these techniques by SOAP and other major national professional organizations to avoid unnecessary general anesthesia.[31] All participating institutions reported seeking guidance from these recommendations and none reported explicit policies that discouraged or delayed neuraxial anesthesia. This discrepancy persisted despite controlling for some potential confounders that are

known to impact neuraxial anesthetic use such ethnicity.[32] The use of general anesthesia for cesarean delivery was conversely increased, although case numbers were small and the cited reason was most often "maternal respiratory failure." Reasons for not choosing neuraxial labor techniques were not recorded in the Registry, but might have included delays awaiting laboratory results (e.g., platelet counts), the burden of the required additional personal protective equipment, or provider concern about performing procedures on infected patients, particularly during this first wave of the COVID-19 pandemic. It is possible that these outcomes would be different if assessed during the later waves of the pandemic (June 2020-present) due to a better understanding of the disease, more international experience with neuraxial anesthesia in the setting of COVID-19, and more liberal use of non-invasive respiratory assist devices. A recent investigation across 6 hospitals found a significant reduction (7.7% to 3.7%, $p< 0.001$) in general anesthesia rates for cesarean delivery (risk ratio; 0.50 95% CI (0.39-0.93) during the pandemic (April-July 2020) compared to 2019 and a decline in conversion from regional to general anesthesia.[9] However, this downward trend was preexisting, prior to the pandemic, and the investigators did not compare the use of these anesthetic techniques in contemporaneous patients with and without SARS-CoV-2 infection, or those with asymptomatic and symptomatic disease.[9]

Fortunately, neither transmission of SARS-CoV-2 infection to the anesthesiologist nor central nervous system transmission of virus to the patient specifically during obstetric neuraxial procedures have been reported. Although thrombocytopenia has been reported in cases of SARS-CoV-2,[33] severe thrombocytopenia precluding the use of neuraxial anesthesia in obstetric patients is extremely rare.[34] When severe thrombocytopenia is present,[35] it is often in the context of critical illness with concomitant systemic disease and multi-organ dysfunction. The only patient in our cohort with severe thrombocytopenia had a known alternative etiology: ITP. Although the precise etiology of SARS-CoV-2-related thrombocytopenia is unknown, the

current hypothesis is of an immune mediated mechanism with preserved platelet function.[33] Furthermore, other changes in hemostasis related to SARS-CoV-2 infection including enhanced clot formation, hyperfibrinogenemia, and hypofibrinolysis, are procoagulant and may be protective against neuraxial bleeding in the absence of disseminated intravascular coagulation (DIC).[36] Finally, concern for respiratory challenges associated with neuraxial anesthesia for cesarean delivery in patients with symptomatic SARS-CoV-2 infection could include the loss of accessory respiratory muscle function, the supine position, and a reluctance to use adjunct respiratory aids (e.g., hi-flow nasal cannula) which appears to be changing. It is worth noting, however, that in our cohort, it appears that most (80%) general anesthetics for cesarean delivery were due to maternal respiratory failure.

In our large cohort, 5.7% of all cases and 15.9% of the symptomatic cases required ICU admission, highlighting the impact of the subgroup of patients studied. Published ICU admission rates for obstetric patients with SARS-CoV-2 infection range from 1.5% when both ambulatory and inpatient patients are included[20] to 13.5% in a subset of patients with significant comorbidities.[37] The CDC recently reported for symptomatic women, after adjusting for confounders, a higher risk of being admitted to the ICU (10.5 versus 3.9 per 1,000 cases; adjusted risk ratio [aRR] 3.0; 95% CI (2.6–3.4)], receiving invasive ventilation [2.9 versus 1.1 per 1,000 cases; aRR 2.9; 95% CI (2.2–3.8)] and maternal death [1.5 versus 1.2 per 1,000 cases; aRR 1.7 95% CI (1.2-2.4)], although reason for ICU admission was not identified.[20] Similarly, a multicenter case-control study with propensity score matching concluded that admission to the hospital and ICU was increased for pregnant versus for non-pregnant women, although the investigators acknowledged that the threshold for admission of pregnant patients with SARS-CoV-2 to the hospital and the ICU may be lower.[38]

Strengths of this study include the focus on a large cohort of hospitalized peripartum patients from geographically diverse U.S. locations with varied SARS-CoV-2 status and a contemporaneous control cohort that were selected by a random process to maximize representation. Our study does have important limitations. Inter- and intra- institution ascertainment of SARS-CoV-2 status differed over time evolving from testing for symptoms to universal testing. Whereas all included "positive" patients and more than 79% of control patients were tested for SARS-CoV-2 infection, not all the control patients were tested. In some centers, this may mean that a control patient could have been an asymptomatic carrier. Asymptomatic carrier status is currently not well understood, and in some women, PCR positive testing appears to persist for several weeks beyond the initial infection.[39] Whereas we adjusted outcomes for several identifiable confounders, there is always the potential for unmeasured confounders. Also, findings with large confidence intervals for some outcomes suggest that our study may have been underpowered to find clinically significant differences that might exist between groups. Finally, we acknowledge that some patients in our cohort have been included in previous reports,[20,30,40] however, to our knowledge these reports lack anesthetic management or a robust a control population against which to compare.

In conclusion, our study demonstrates that in this multicenter cohort of peripartum patients with and without SARS-CoV-2 infection, differences between obstetric and neonatal outcomes seem to be mostly driven by symptomatic patients. The lower utilization of neuraxial analgesia in laboring patients with asymptomatic or symptomatic infection compared to patients without infection warrants further investigation.

REFERENCES

1. WHO Coronavirus Disease (COVID-19) Dashboard. 2020; https://covid19.who.int/. Accessed August 4, 2020.
2. Di Mascio D, Khalil A, Saccone G, et al. Outcome of Coronavirus spectrum infections (SARS, MERS, COVID 1 -19) during pregnancy: a systematic review and meta-analysis. *American journal of obstetrics & gynecology MFM.* 2020:100107.
3. Lippi G, Plebani M, Henry BM. Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A meta-analysis. *Clinica chimica acta; international journal of clinical chemistry.* 2020;506:145-148.
4. Liu Y, Sun W, Guo Y, et al. Association between platelet parameters and mortality in coronavirus disease 2019: Retrospective cohort study. *Platelets.* 2020;31(4):490-496.
5. Bauer ME, Chiware R, Pancaro C. Neuraxial procedures in COVID-19 positive parturients: a review of current reports. *Anesthesia and analgesia.* 2020.
6. Chen R, Zhang Y, Huang L, Cheng BH, Xia ZY, Meng QT. Safety and efficacy of different anesthetic regimens for parturients with COVID-19 undergoing Cesarean delivery: a case series of 17 patients. *Canadian journal of anaesthesia = Journal canadien d'anesthesie.* 2020.
7. Bamber JH, Lucas DN. COVID-19 and access to labour epidural analgesia in UK hospitals. *Anaesthesia.* 2020;75(8):1119-1120.
8. Savasi VM, Parisi F, Patanè L, et al. Clinical Findings and Disease Severity in Hospitalized Pregnant Women With Coronavirus Disease 2019 (COVID-19). *Obstetrics & Gynecology.* 2020;136(2):252-258.

9. Bhatia K, Columb M, Bewlay A, et al. The effect of COVID-19 on general anaesthesia rates for caesarean section. A cross-sectional analysis of six hospitals in the north-west of England. *Anaesthesia.* 2020.

10. Görlinger K, Dirkmann D, Gandhi A, Simioni P. COVID-19 associated coagulopathy and inflammatory response: what do we know already and what are the knowledge gaps? *Anesthesia and analgesia.* 2020.

11. Connors JM, Levy JH. COVID-19 and its implications for thrombosis and anticoagulation. *Blood.* 2020;135(23):2033-2040.

12. Shanes ED, Mithal LB, Otero S, Azad HA, Miller ES, Goldstein JA. Placental Pathology in COVID-19. *American journal of clinical pathology.* 2020;154(1):23-32.

13. Ernst LM. Maternal vascular malperfusion of the placental bed. *APMIS : acta pathologica, microbiologica, et immunologica Scandinavica.* 2018;126(7):551-560.

14. Mendoza M, Garcia-Ruiz I, Maiz N, et al. Pre-eclampsia-like syndrome induced by severe COVID-19: a prospective observational study. *BJOG : an international journal of obstetrics and gynaecology.* 2020.

15. Chen H, Guo J, Wang C, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *Lancet (London, England).* 2020;395(10226):809-815.

16. Li Y, Zhao R, Zheng S, et al. Lack of Vertical Transmission of Severe Acute Respiratory Syndrome Coronavirus 2, China. *Emerging infectious diseases.* 2020;26(6):1335-1336.

17. Liu Y, Chen H, Tang K, Guo Y. Clinical manifestations and outcome of SARS-CoV-2 infection during pregnancy. *The Journal of infection.* 2020.

18. Breslin N, Baptiste C, Gyamfi-Bannerman C, et al. COVID-19 infection among asymptomatic and symptomatic pregnant women: Two weeks of confirmed presentations

to an affiliated pair of New York City hospitals. *American journal of obstetrics & gynecology MFM.* 2020:100118.

19. Collin J, Byström E, Carnahan A, Ahrne M. Public Health Agency of Sweden's Brief Report: Pregnant and postpartum women with severe acute respiratory syndrome coronavirus 2 infection in intensive care in Sweden. *Acta obstetricia et gynecologica Scandinavica.* 2020;99(7):819-822.

20. Zambrano LD ES, Strid P, Galang RR, Oduyebo T, Tong VT, Woodworth KR, Nahabedian JF, Azziz-Baumgartner E, Gilboa SM, Meaney-Delman, D. Characteristics of symptomatic women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status - United States, January 22-October 3, 2020. *MMWR Morb Mortal Wkly Rep.* 2020;69:1641-1647.

21. Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. *Statistics in medicine.* 2009;28(25):3083-3107.

22. Wasserstein RL LN. The ASA's Statement on p-Values: Context, Process, and Purpose. *Am Stat.* 2016;70(2):129-133.

23. Yu N, Li W, Kang Q, et al. Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19 in Wuhan, China: a retrospective, single-centre, descriptive study. *The Lancet Infectious diseases.* 2020;20(5):559-564.

24. Knight M, Bunch K, Vousden N, et al. Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population based cohort study. *BMJ (Clinical research ed).* 2020;369:m2107.

25. Martínez-Perez O, Vouga M, Cruz Melguizo S, et al. Association Between Mode of Delivery Among Pregnant Women With COVID-19 and Maternal and Neonatal Outcomes in Spain. *Jama.* 2020.

26. Juan J, Gil MM, Rong Z, Zhang Y, Yang H, Poon LC. Effects of coronavirus disease 2019 (COVID-19) on maternal, perinatal and neonatal outcomes: a systematic review. *Ultrasound in Obstetrics & Gynecology.* 2020;n/a(n/a).

27. Figueiro-Filho EA, Yudin M, Farine D. COVID-19 during pregnancy: an overview of maternal characteristics, clinical symptoms, maternal and neonatal outcomes of 10,996 cases described in 15 countries. *Journal of perinatal medicine.* 2020;48(9):900-911.

28. Emeruwa UN, Ona S, Shaman JL, et al. Associations Between Built Environment, Neighborhood Socioeconomic Status, and SARS-CoV-2 Infection Among Pregnant Women in New York City. *Jama.* 2020;324(4):390-392.

29. Gao YJ, Ye L, Zhang JS, et al. Clinical features and outcomes of pregnant women with COVID-19: a systematic review and meta-analysis. *BMC infectious diseases.* 2020;20(1):564.

30. Prabhu M, Cagino K, Matthews KC, et al. Pregnancy and postpartum outcomes in a universally tested population for SARS-CoV-2 in New York City: a prospective cohort study. *BJOG : an international journal of obstetrics and gynaecology.* 2020.

31. Society for Obstetric Anesthesia and Perinatology. www.SOAP.org. Accessed January 18, 2020.

32. Butwick AJ, Blumenfeld YJ, Brookfield KF, Nelson LM, Weiniger CF. Racial and Ethnic Disparities in Mode of Anesthesia for Cesarean Delivery. *Anesthesia and analgesia.* 2016;122(2):472-479.

33. Tang MW, Nur E, Biemond BJ. Immune thrombocytopenia due to COVID-19 during pregnancy. *American journal of hematology.* 2020;95(8):E191-e192.

34. Bauer M, Bernstein K, Dinges E, et al. Obstetric Anesthesia During the COVID-19 Pandemic. *Anesthesia and analgesia.* 2020.

35. Liao D ZF, Luo L, Xu M, Wang H, Xia J, Gao Y, Cai L, Wang Z, Yin P, Wang Y, Tang L, Deng J, Mei H, Hu Y. Haematological characteristics and risk factors in the classification and prognosis evaluation of COVID-19: a retrospective cohort study. *Lancet Haematol.* 2020.

36. Nougier C, Benoit R, Simon M, et al. Hypofibrinolytic state and high thrombin generation may play a major role in SARS-COV2 associated thrombosis. *Journal of Thrombosis and Haemostasis.*n/a(n/a).

37. Guan WJ, Liang WH, Zhao Y, et al. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. *The European respiratory journal.* 2020;55(5).

38. Badr DA, Mattern J, Carlin A, et al. Are clinical outcomes worse for pregnant women at ≥20 weeks' gestation infected with coronavirus disease 2019? A multicenter case-control study with propensity score matching. *American journal of obstetrics and gynecology.* 2020;223(5):764-768.

39. Sohn Y, Jeong SJ, Chung WS, et al. Assessing Viral Shedding and Infectivity of Asymptomatic or Mildly Symptomatic Patients with COVID-19 in a Later Phase. *Journal of clinical medicine.* 2020;9(9).

40. Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ (Clinical research ed).* 2020;370:m3320.

FIGURE LEGENDS

Figure 1. Distribution of patients included in the Registry by geography, symptom status, and critical illness.

Table 1. Baseline Characteristics of Obstetric Patients with and without SARS-CoV-2 infection in the peripartum period

TABLE 2. Analysis of obstetric outcomes for peripartum patients with and without SARS-CoV-2 infection

Table 3. Sensitivity Analysis of Primary Obstetrical Outcomes of Asymptomatic SARS-CoV-2 Patients versus Controls, and Symptomatic SARS-CoV-2 Patients versus Controls

Table 4. Analysis of anesthetic outcomes for peripartum patients with and without SARS-CoV-2 infection.

Table 5. Sensitivity Analysis of Primary Anesthetic Outcomes of Asymptomatic SARS-CoV-2 Patients versus Controls, and Symptomatic SARS-CoV-2 Patients versus Controls

Supplemental Table 1. Initial Clinical Presentation and Laboratory Findings of Obstetric Patients with and without SARS CoV-2 infection in the peripartum period

Table 1. Baseline Characteristics of Obstetric Patients with and without SARS-CoV-2 infection in the peripartum period

	SARS-CoV-2 N=490	Control N=964	SMD	% Missing
Age (mean (SD))	30.4 (6.2)	32.0 (5.6)	0.268	0.2
Parity (n(%))			0.329	0.1
0	183 (37.5)	470 (48.8)		
1	138 (28.3)	300 (31.1)		
2+	167 (34.2)	194 (20.1)		
Singleton or multiple pregnancy (n(%))			0.079	0.6
Singleton	478 (98.4)	933 (97.2)		
Multiple pregnancy	8 (1.6)	27 (2.8)		
BMI, kg/m^3 (mean (SD))	31.4 (6.1)	30.2 (5.9)	0.199	5.6
Obese (n(%))	258 (56.6)	410 (44.8)	0.261	5.6
Race (n(%))			0.365	0.0
White	171 (34.9)	432 (44.8)		
Black or African American	80 (16.3)	133 (13.8)		
Asian	24 (4.9)	100 (10.4)		
Multiple or Other	181 (36.9)	226 (23.4)		
Unknown	34 (6.9)	73 (7.6)		
Ethnicity			0.394	0.0
Hispanic	191 (39.0)	205 (21.3)		
Non-Hispanic	299 (61.0)	759 (78.7)		
Comorbidities (n(%))				
Total number of patients with any comorbidities	111 (22.7)	244 (25.3)	0.058	0.1
Diabetes			0.267	0.0
Preexisting	10 (2.0)	14 (1.5)		
Gestational	33 (6.7)	67 (7.0)		
Hypertension - Preexisting	26 (5.3)	48 (5.0)	0.026	0.0
Cardiac Disease	4 (0.8)	15 (1.6)	0.220	0.0
Pulmonary Disease			0.062	0.0
Asthma	40 (8.2)	95 (9.9)		
Other	2 (0.4)	5 (0.5)		
Autoimmune Disease	17 (3.4)	47 (4.9)	0.424	0.1

BMI = Body Mass Index, SD = standard deviation, SMD = standardized mean difference

% missing data are provided for all variable categories with expected values for all patients

Note: Crude differences between SARS-CoV-2 infected patients and controls were reported using standardized mean differences (SMD), and following the recommendations of Austin (2009) interpreted as meaningful if: SMD > 0.1 ($1.96 \times \sqrt{\frac{1}{964} + \frac{1}{490}}$*).*

TABLE 2. Analysis of obstetric outcomes for peripartum patients with and without SARS-CoV-2 infection

Obstetrical Outcome	SARS-CoV-2 N=490	Controls N = 964	Unadjusted Effect Estimate (95% CI) p-value	Adjusted Effect Estimate (95%CI) p-value	% Missing
Mode of Delivery-Cesarean (n(%))	171 (34.9)	331 (34.4)	1.07 (0.84 to 1.38) 0.587	1.02 (0.79 to 1.32) 0.866	5.9
Hypertensive Disorders of Pregnancy (n(%))	75 (15.3)	123 (12.8)	1.31 (0.84 to 1.38) 0.587	1.12 (0.75 to 1.67) 0.584	6.1
Gestational Age at Delivery, weeks	38.1 (2.6)	38.4 (2.4)	-0.32 † (0.90 to 1.92) 0.163	-0.28 † (-0.56 to 0.00) 0.051	6.4
Delivery < 37 week (n(%))	72 (14.8)	98 (10.2)	1.56 (1.11 to 2.19) 0.011	1.47 (1.03 to 2.09) 0.035	
Delivery < 34 weeks (n(%))	25 (5.1)	43 (4.5)	1.07 (0.63 to 1.82) 0.789	0.96 (0.57 to 1.61) 0.873	
Placental Abruption (n(%))	6 (1.2)	10 (1.0)	1.42 (0.45 to 4.47) 0.552	NA NA NA	6.2
Postpartum Length of Stay, days	2.7 (3.5)	1.9 (1.2)	0.80 † (0.45 to 1.16) < 0.001	0.77 † (0.44 to 1.11) < 0.001	5.9
Estimated Blood Loss, mL	466.8 (359.6)	468.7 (473.7)	-11.4 † (-61.31 to 38.51) 0.654	-22.10 † (-69.46 to 25.27) 0.361	7.6

>500 mL for Vaginal Delivery (n(%))	35 (11.4)	66 (10.5)	1.10 (0.70 to 1.73) 0.694	1.10 (0.70 to 1.75) 0.676	
>1 Liter for Cesarean Delivery (n(%))	18 (10.8)	40 (12.2)	0.74 (0.38 to 1.42) 0.365	0.66 (0.33 to 1.30) 0.228	
Neonatal Composite Outcome (n(%))	97 (19.6)	164 (16.5)	1.24 (0.90 to 1.71) 0.193	1.21 (0.86 to 1.70) 0.266	3.7

CI = confidence interval, mL = milliliters

NA indicates that the model was not conducted.

% missing data are provided for all variable categories with expected values for all patients

All effect estimates are odds ratios except where noted by †, which indicates effect estimates in the original units.
Neonatal composite outcome includes 1- and 5-minute APGAR scores as well as the need for respiratory support or an escalation of care in the delivery room.

Adjusted for confounding variables: age, race, ethnicity, BMI, and maternal morbidities (including diabetes, preexisting hypertension, and cardiac, pulmonary, or autoimmune disease)

Table 3: Sensitivity Analysis of Primary Obstetrical Outcomes of Asymptomatic SARS-CoV-2 Patients versus Controls, and Symptomatic SARS-CoV-2 Patients versus Controls

	Asymptomatic SARS-CoV-2+	Asymptomatic SARS-CoV-2+	Symptomatic SARS-CoV-2+	Symptomatic SARS-CoV-2+	
Obstetrical Outcome	Unadjusted Effect Estimate 95% CI p-value	Adjusted Effect Estimate 95% CI p-value	Unadjusted Effect Estimate 95% CI p-value	Adjusted Effect Estimate 95% CI p-value	% Missing
Mode of Delivery - Cesarean	0.80 (0.60 to 1.07) 0.129	0.79 (0.58 to 1.07) 0.128	1.74 (1.24 to 2.45) 0.001	1.57 (1.09 to 2.27) 0.016	5.9
Hypertensive Disorders of Pregnancy	1.01 (0.67 to 1.53) 0.948	0.91 (0.59 to 1.40) 0.656	1.88 (1.11 to 3.19) 0.019	1.51 (0.86 to 2.64) 0.150	6.1
Gestational Age at Delivery, weeks	-0.15 † (-0.47 to 0.17) 0.361	-0.13 † (-0.44 to 0.18) 0.412	-0.65 † (-1.13 to -0.18) 0.007	-0.56 † (-1.03 to -0.10) 0.018	6.4
Delivery < 37 week	1.20 (0.80 to 1.81) 0.382	1.16 (0.76 to 1.79) 0.49	2.30 (1.47 to 3.62) <0.001	2.08 (1.29 to 3.36) 0.003	
Delivery < 34 weeks	0.75 (0.38 to 1.48) 0.400	0.68 (0.35 to 1.31) 0.248	1.70 (0.84 to 3.45) 0.138	1.50 (0.74 to 3.08) 0.262	
Placental Abruption	1.73 (0.50 to 5.94) 0.386	NA NA NA	0.83 (0.10 to 6.65) 0.859	NA NA NA	6.2
Postpartum Length of Stay, days	0.17 † (-0.11to 0.45) 0.232	0.18 † (-0.10 to 0.46) 0.206	1.98 † (1.24 to 2.72) <0.001	1.89 † (1.18 to 2.60) <0.001	5.9
Estimated Blood Loss, mL	-38.40 † (-92.87 to 16.07) 0.167	-38.51 † (-91.61 to 14.59) 0.155	38.08 † (-33.04 to 109.21) 0.294	8.26 † (-57.58 to 74.1) 0.806	7.6
>500 mL for Vaginal Delivery	1.01 (0.59 to 1.73) 0.969	1.03 (0.6 to 1.78) 0.912	1.31 (0.66 to 2.62) 0.438	1.29 (0.64 to 2.61) 0.484	

>1 Liter for Cesarean Delivery	0.64 (0.27 to 1.50) 0.300	0.58 (0.24 to 1.42) 0.235	0.86 (0.38 to 1.96) 0.718	0.75 (0.32 to 1.74) 0.505	
Neonatal Composite Outcome	0.82 (0.55 to 1.23) 0.345	0.82 (0.54 to 1.24) 0.339	2.17 (1.45 to 3.26) <0.001	2.09 (1.35 to 3.25) 0.001	3.7

mL= milliliters

All effect estimates are odds ratios except where noted by †, which indicates effect estimates in the original units.

Adjusted for confounding variables: age, race, ethnicity, BMI, and maternal morbidities (including diabetes, preexisting hypertension, and cardiac, pulmonary, or autoimmune disease)

NA indicates that the model was not conducted.

% missing data are provided for all variable categories with expected values for all patients

Table 4. Analysis of anesthetic management for peripartum patients with and without SARS-CoV-2 infection

Anesthetic Outcome	SARS-CoV-2 N=490	Controls N=964	Unadjusted Effect Estimate (95%CI) p-value	Adjusted Effect Estimate (95%CI) p-value	% Missing
Primary Neuraxial Labor Analgesia	297 (79.4)	656 (88.9)	0.48 (0.34 to 0.70) < 0.001	0.52 (0.35 to 0.75) 0.001	6.1
Epidural (n, %)	117 (31.3)	299 (40.5)	NA	NA	
CSE/DPE (n, %)	180 (48.1)	357 (48.4)	NA	NA	
Intravenous Opioids (n, %)	2 (0.5)	2 (0.3)	NA	NA	
Nitrous Oxide (n, %)	0 (0.0)	0 (0.0)	NA	NA	
None (n, %);	75 (20.1)	80 (10.8)	NA	NA	
Primary Anesthesia for Cesarean Delivery					5.8
New Neuraxial – Spinal or CSE (n, %)	122 (74.4)	237 (68.5)	1.22 (0.83 to 1.81) 0.311	1.09 (0.70 to 1.68) 0.699	
General Anesthesia (n, %)	15 (8.7)	9 (2.6)	3.64 (1.45 to 9.12) 0.006	3.69 (1.40 to 9.74) 0.008	
Indications for General Anesthesia					12.5
Maternal Indications (n, %)	13 (86.7)	2 (22.2)	16.50 (1.67 to 162.92) 0.016	NA NA NA	
Maternal Respiratory Failure (n, %)	12 (80.0)	0 (0.0)	NA	NA	

Patient already intubated (n, %)	0 (0.0)	1 (11.1)	NA	NA	
Postpartum Hemorrhage (n, %)	1 (6.7)	1 (11.1)	NA	NA	
Neuraxial Failure (n, %)	0 (0.0)	2 (22.2)	NA	NA	
Fetal Indications (n, %)	2 (13.3)	5 (55.6)	0.18 (0 to 26.90) 0.504	NA NA NA	

CI= confidence interval, CSE = combined spinal epidural, DPE = dural puncture epidural

All effect estimates are odds ratios except where noted by †, which indicates effect estimates in the original units.
Adjusted for confounding variables: age, race, ethnicity, BMI, and maternal morbidities (including diabetes, preexisting hypertension, and cardiac, pulmonary, or autoimmune disease)

NA indicates that the model was not conducted.

% missing data are provided for all variable categories with expected values for all patients

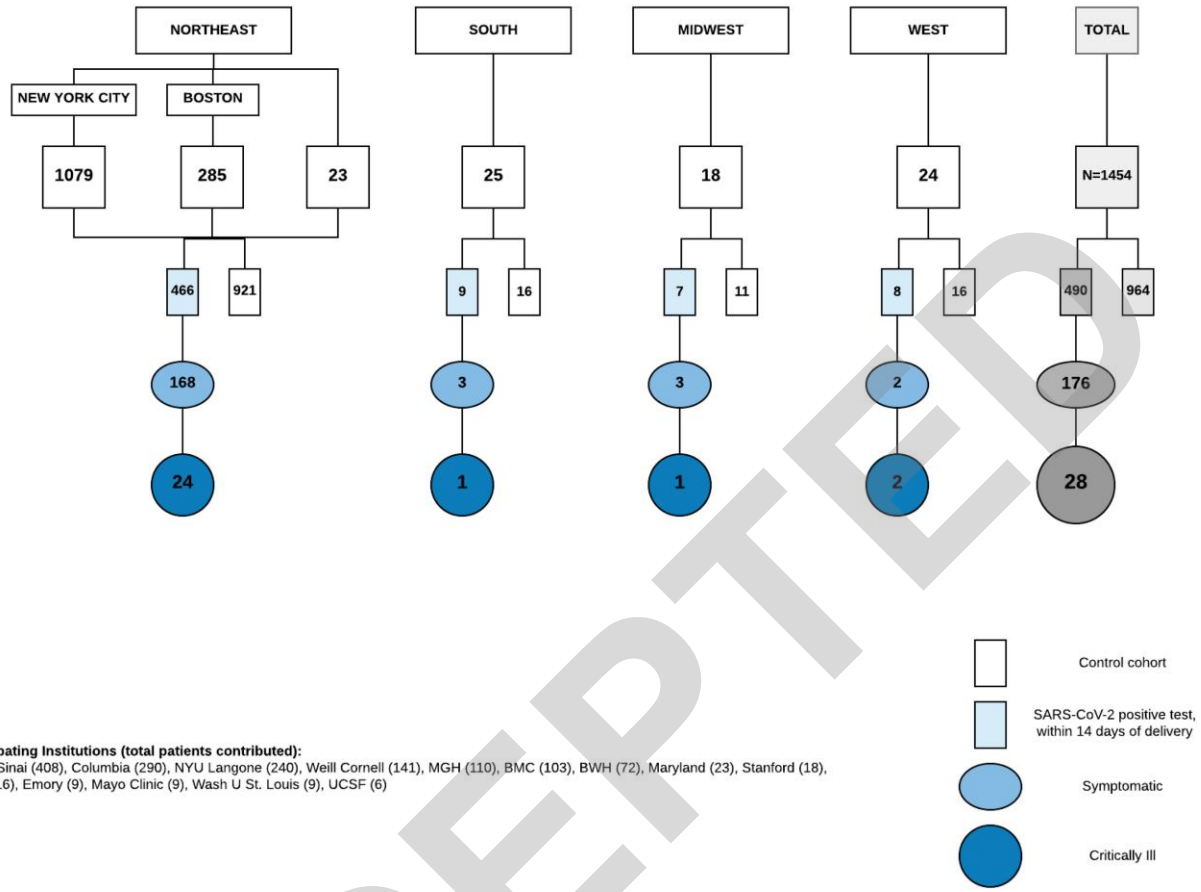
Table 5: Sensitivity Analysis of Primary Anesthetic Outcomes of Asymptomatic SARS-CoV-2 Patients versus Controls, and Symptomatic SARS-CoV-2 Patients versus Controls

	Asymptomatic SARS-CoV-2+	Asymptomatic SARS-CoV-2+	Symptomatic SARS-CoV-2+	Symptomatic SARS-CoV-2+	
Anesthetic Technique	Unadjusted Effect Estimate 95% CI p-value	Adjusted Effect Estimate 95% CI p-value	Unadjusted Effect Estimate 95% CI p-value	Adjusted Effect Estimate 95% CI p-value	% Missing
Primary Neuraxial Labor Analgesia	0.52 (0.34 to 0.80) 0.003	0.56 (0.36 to 0.88) 0.011	0.43 (0.26 to 0.71) 0.001	0.44 (0.26 to 0.74) 0.002	6.1
Anesthesia for Cesarean Delivery					
New Neuraxial	1.87 (1.15 to 3.06) 0.012	1.69 (0.99 to 2.88) 0.055	0.83 (0.49 to 1.42) 0.494	0.73 (0.41 to 1.29) 0.274	5.8
General Anesthesia	0.48 (0.06 to 3.95) 0.499	0.45 (0.06 to 3.47) 0.442	8.13 (3.26 to 20.26) <0.001	9.68 (3.48 to 26.91) <0.001	

All effect estimates are odds ratios except where noted by †, which indicates effect estimates in the original units.
Adjusted for confounding variables: age, race, ethnicity, BMI, and maternal morbidities (including diabetes, preexisting hypertension, and cardiac, pulmonary, or autoimmune disease)

% missing data are provided for all variable categories with expected values for all patients

Figure 1. Distribution of patients included in the Registry by geography, symptom status, and critical illness.



Participating Institutions (total patients contributed):
Mount Sinai (408), Columbia (290), NYU Langone (240), Weill Cornell (141), MGH (110), BMC (103), BWH (72), Maryland (23), Stanford (18), Duke (16), Emory (9), Mayo Clinic (9), Wash U St. Louis (9), UCSF (6)