Obstetric Hemorrhage Risk Associated with Novel COVID-19 Diagnosis from a Single-Institution Cohort in the United States

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Abstract

Objective The study aimed to compare the quantitative blood loss (QBL) and hemorrhage-related outcomes of pregnant women with and without a coronavirus disease 2019 (COVID-19) diagnosis.

Study Design This retrospective cohort study of all live deliveries at Boston Medical Center between April 1, 2020 and July 22, 2020 compares the outcomes of pregnant women with a laboratory-confirmed COVID-19 positive diagnosis and pregnant women without COVID-19. The primary outcomes are QBL and obstetric hemorrhage. The secondary outcomes analyzed were a maternal composite outcome that consisted of obstetric hemorrhage, telemetry-level (intermediate care unit) or intensive care unit, transfusion, length of stay greater than 5 days, or intraamniotic infection, and individual components of the maternal composite outcome. Groups were compared using Student's *t*-test, Chi-squared tests, or Fisher's exact. Logistic regression was used to adjust for confounding variables.

Results Of 813 women who delivered a live infant between April 1 and July 22, 2020, 53 women were diagnosed with COVID-19 on admission to the hospital. Women with a COVID-19 diagnosis at their time of delivery were significantly more likely to identify as a race other than white ($p = 0.01$), to deliver preterm ($p = 0.05$), to be diagnosed with preeclampsia with severe features ($p < 0.01$), and to require general anesthesia ($p < 0.01$). Women diagnosed with COVID-19 did not have a significantly higher QBL ($p = 0.64$). COVID-19 positive pregnant patients had no increased adjusted odds of obstetric hemorrhage (adjusted odds ratio [aOR]: 0.41, 95% confidence interval [CI]: 0.17–1.04) and no increased adjusted odds of the maternal morbidity composite (aOR: 0.98, 95% CI: 0.50–1.93) when compared with those without a diagnosis of COVID-19.

Conclusion Pregnant women with COVID-19 diagnosis do not have increased risk for obstetric hemorrhage, increased QBL or risk of maternal morbidity compared with pregnant women without a COVID-19 diagnosis. Further research is needed to describe the impact of a COVID-19 diagnosis on maternal hematologic physiology and pregnancy outcomes.

Keywords

- quantitative blood loss
- obstetric hemorrhage
- SARS-CoV-2
- Pregnancy

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Key Points

- Information about blood loss associated with peripartum COVID-19 is limited.
- COVID-19 diagnosis is not associated with increase in obstetric hemorrhage.
- COVID-19 diagnosis is not associated with increase in blood loss.

Early case reports in the general population have demonstrated severe morbidities from coagulopathies and bleeding disorders associated with novel coronavirus disease 2019 (COVID-19) infection.[1–3] Based on cases in pregnancy, it has been suggested that exacerbation of the immunologic shift of pregnancy combined with the cytokine storm provoked by COVID-19 infection could hasten consumptive coagulopathy.[4] However, with very few studies reporting the blood loss associated with COVID-19 deliveries, there is a void of robust data to direct clinical practice.[5,6]

Our institution has well-established practice utilizing quantitative blood loss (QBL) in delivery and operating rooms. We sought to assess whether QBL and rate of obstetric hemorrhage were different among pregnant women with and without COVID-19 infection.

Materials and Methods

This was a retrospective cohort study of all live deliveries at Boston Medical Center, an urban academic medical center and the largest safety-net hospital in New England, between April 1, 2020 and July 22, 2020. Demographic, obstetric, delivery, and COVID-19 status information were abstracted. Institutional review board approval was obtained from Boston University School of Medicine.

At our institution, QBL measurement is collected for all deliveries. Blood loss is quantified in cesarean with calibrated suction canisters and in vaginal deliveries with calibrated under-buttocks drapes along with weighing blood-soaked materials.[7] Information was gathered from department birth logs that are abstracted daily from the electronic medical record for all deliveries. This includes information about maternal demographics, maternal medical and obstetric history, antenatal course, intrapartum course, anesthesia type if any, and QBL. Additional information was abstracted by a trained chart abstractor (M.J.W.) into a standardized chart abstraction form using a secure database. Chart review was limited to the presenting symptoms and clinical course of COVID-19 infection among parturients.

Women were classified by COVID-19 status: positive or negative. Positive COVID-19 diagnosis was based on the result of a nasopharyngeal swab collected during that hospital admission. Our institution implemented universal testing on May 5, 2020. Prior to the implementation of universal testing, all patients were screened with questions recommended by the state department of public health and a temperature check but were only swabbed based on clinical suspicion.

Patients were also classified by presenting COVID-19 symptoms per national institutes of health guidelines as follows[8,9]:

- Asymptomatic or presymptomatic: Individuals who test positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by virologic testing using a molecular diagnostic (e.g., polymerase chain reaction) or antigen test, but have no symptoms.
- Mild illness: Individuals who have any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, and muscle pain) without shortness of breath, dyspnea, or abnormal chest imaging.
- Moderate Illness: Individuals who have evidence of lower respiratory disease by clinical assessment or imaging and a saturation of oxygen (SpO2) $\geq$94% on room air at sea level.
- Severe illness: Individuals who have respiratory frequency $>$30 breaths per minute, SpO2 $<$94% on room air at sea level, ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO2/FiO2) $<$300 mm Hg, or lung infiltrates $>$50%.
- Critical illness: Individuals who have respiratory failure, septic shock, and/or multiple organ dysfunction.

We chose to also include an additional stratification limited to two categories (asymptomatic or mild compared with moderate, severe, or critical) to stratify morbidity risks within the COVID-19 positive group.

The primary outcomes were QBL and obstetric hemorrhage. Obstetric hemorrhage was defined as any QBL greater than 1,000 mL. The secondary outcome was a maternal morbidity composite based on existing maternal composites in the literature.[10,11] This maternal composite consists of physiologic antecedents and consequences of obstetric hemorrhage and includes obstetric hemorrhage, telemetry-level (intermediate care unit) or intensive care unit stay, transfusion, length of stay greater than 5 days, or intraamniotic infection.

Exposure groups were compared with descriptive and bivariate statistics using Student's *t*-test for continuous variables, Chi-squared test, or Fisher's exact for categorical variables. Multiple logistic regression models for the primary and secondary outcomes were developed to estimate the effect of COVID-19 status on blood loss, hemorrhage, and other obstetric outcomes. Clinically relevant covariates for initial inclusion in multivariable statistical models were selected using results of the stratified analyses, and factors were removed in a backward stepwise fashion, based on significant changes in the exposure adjusted odds ratio. All analyses were completed using STATA MP, version 16 (College Station, TX).

Results

Of 813 women who delivered a live infant between April 1 and July 22, 2020, 53 women were diagnosed with COVID-19

with a nasopharyngeal swab on admission to the hospital. Maternal and obstetric characteristics according to COVID-19 status are shown in ►Table 1. Exposure groups were not significantly different with regards to age, insurance type (private vs. public), body mass index (BMI), parity, delivery mode, or percentage of inductions. Women with a COVID-19 diagnosis were, however, more likely to be delivered preterm (<37 weeks' gestation) ($p = 0.05$), more likely to identify as Hispanic race ($p < 0.01$), less likely to identify as White race ($p = 0.01$), and more likely to have a diagnosis of preeclampsia with severe features ($p < 0.01$) compared with women without a diagnosis of COVID-19. Despite no differences in delivery mode, women with COVID-19 were also more likely to receive general anesthesia ($p < 0.01$) and less likely to receive epidural anesthesia ($p = 0.02$) compared with women without a COVID-19 diagnosis.

Table 1 Maternal and obstetric characteristics by COVID-19 status

	COVID positive deliveries ($n = 53$)	COVID negative deliveries ($n = 760$)	*p*-Value
Age	29.8 ± 5.9	30.2 ± 6.0	0.63
Race			
Hispanic	−19 (73.1)	−119 (39.8)	<0.01
Black	−8 (26.9)	−111 (37.1)	0.61
White	−0 (0)	−56 (18.7)	0.01
Asian	−0 (0)	−4 (1.3)	0.29
Middle Eastern	−0 (0)	−9 (3.0)	0.36
Government insurance	45 (84.9)	555 (73.0)	0.06
BMI ($n = 812$)	33.1 ± 7.2 ($n = 53$)	32.4 ± 6.3 ($n = 758$)	0.42
BMI > 30	−36 (67.9)	−479 (63.0)	−0.47
BMI > 40	−8 (15.1)	−86 (11.3)	−0.41
COVID severity			
Asymptomatic or mild	−45 (84.9)		
Moderate or severe or critical	−8 (15.1)		
COVID severity (NIH)[a]			
Asymptomatic/presymptomatic	−38 (71.7)		
Mild illness	−7 (13.2)		
Moderate illness	−2 (3.8)		
Severe illness	−4 (7.6)		
Critical illness	−2 (3.8)		
Gestational age	38.1 ± 2.9	38.9 ± 2.1	<0.01
Preterm	9 (17.0)	66 (8.7)	0.05
Parity	2.9 ± 1.6	2.8 ± 1.8	0.53
Induction	17 (32.1)	255 (33.6)	0.83
Delivery mode			
Vaginal	−30 (56.6)	−503 (66.2)	0.16
Cesarean	−23 (43.4)	−257 (33.8)	
Preeclampsia with severe features	10 (18.9)	59 (7.8)	<0.01
Anesthesia type			
None	−14 (26.4)	−189 (24.9)	0.80
Epidural	−19 (35.9)	−400 (52.6)	0.02
Spinal	−10 (18.9)	−85 (11.2)	0.09
Combined	−8 (15.1)	−82 (10.8)	0.33
General	−2 (3.8)	−4 (0.5)	<0.01

Abbreviations: BMI, body mass ; COVID, coronavirus disease; NIH, national institutes of health.
Note: Percent of patients in that delivery mode category with the associated outcome or as mean ± standard deviation.
[a]COVID severity defined per National Institutes of Health guidelines: https://www.covid19treatmentguidelines.nih.gov/overview/management-of-covid-19/.

Table 2 Maternal outcomes by COVID-19 status

	COVID positive deliveries ($n = 53$)	COVID negative deliveries ($n = 760$)	aOR (95% CI)	*p*-Value
Quantitative blood loss	551 ± 332.2	584.7 ± 509.3		0.64
Obstetric hemorrhage	6 (11.3)	140 (18.4)	0.41 (0.17–1.04)[c]	
Maternal composite[a]	17 (32.1)	205 (27.0)	0.98 (0.50–1.93)[b]	
Intraamniotic infection	2 (3.8)	46 (6.1)	0.61 (0.14–2.57)	
Any transfusion	0 (0)	14 (1.8)		0.32
Maternal LOS	4.4 ± 4.0	3.4 ± 1.8		<0.01
LOS > 5 d	12 (22.6)	74 (9.7)	1.8 (0.73–4.61)[d]	
ICU or IMCU	6 (11.3)	5 (0.7)	28.5 (6.73–120.19)[e]	

Abbreviations: aOR, adjusted odds ratio; BMI, body mass values; COVID, coronavirus disease; CI, confidence interval; ICU, intensive care unit; IMCU, intermediate care unit; LOS, length of stay.
[a]Maternal composite outcome is considered categorically positive for maternal morbidity if the mother experienced any of the following factors: (i) OBH, (ii) ICU or IMCU stay, (iii) transfusion, (iv) length of stay greater than 5 days, or (v) intraamniotic infection.
[b]Adjusted for delivery mode, BMI, and gestational age.
[c]Adjusted for delivery mode, BMI, and intraamniotic infection.
[d]Adjusted for delivery mode, ICU or IMCU admission, intraamniotic infection, and gestational age.
[e]Adjusted for delivery mode and obstetric hemorrhage.

Maternal outcomes according to COVID-19 status are shown in ►Table 2. Women diagnosed with COVID-19 did not have a significantly higher QBL ($p = 0.64$). After adjusting for delivery mode, BMI and intraamniotic infection, women with COVID-19 had no increased odds of obstetric hemorrhage compared with those without COVID-19 (adjusted odds ratio [aOR]: 0.41, 95% confidence interval [CI]: 0.17–1.04). Furthermore, we observed no difference in the maternal composite outcome in COVID-19 positive patients compared with the women without a COVID-19 diagnosis after adjusting for delivery mode, BMI, and gestational age (aOR: 0.98, 95% CI: 0.50–1.93).

Thirty-eight women (71.7%) with a COVID-19 diagnosis admitted to the hospital during this time were asymptomatic or presymptomatic, seven (13.2%) had mild illness, two (3.8%) had moderate illness, four (7.6%) had severe illness, and two (3.8) had critical illness. Eight (35%) of COVID-19 cesarean deliveries were indicated for worsening COVID-19 related symptoms, six (26%) for nonreassuring fetal heart tracing, five (22%) were scheduled Cesareans, two (9%) for preeclampsia with severe features, and two (9%) for failure to progress. Presentation with moderate or severe COVID-19 symptoms was not associated with increased odds of obstetric hemorrhage (odds ratio [OR]: 2.2, 95% confidence interval [CI]: 0.54–9.01), but was associated with increased odds of delivery by cesarean (OR: 12.3, 95% CI: 1.38–108.74).

Discussion

Deliveries associated with a COVID-19 diagnosis were not found to have an increase in average QBL, risk of obstetric hemorrhage, or risk of maternal morbidity compared with non-COVID deliveries. While not a pre hoc outcome, our cohort did, however, demonstrate an increased proportion of non-White women and a rate of severe preeclampsia twofold higher in the COVID positive cohort compared with the COVID negative cohort.

Few studies have examined hemorrhage risk associated with COVID-19 in pregnancy, and no studies have published any data regarding the average blood loss associated with COVID-19 deliveries. Similar to the findings from our study, one early study from China found no difference in the incidence of postpartum hemorrhage in vaginal deliveries associated with COVID-19 positive compared with COVID-19 negative patients.[5] Another study from China examining a COVID-19 positive cohort delivered via cesarean with no COVID-19 negative comparison group found no difference in risk of postpartum hemorrhage when comparing severity of COVID-19 disease, comparable to the findings from the secondary analysis in our present study.[6]

While some larger studies have examined in detail the medical course of hospitalized COVID-19 positive pregnant patients, few studies have focused on blood-loss and hemorrhage-related outcomes of COVID-19 in pregnancy.[12–15] One case series found coagulopathy-indicating laboratory markers in two pregnant patients; only one of the patients had a delivery associated with postpartum hemorrhage.[4] Furthermore, while reviews and case reports in nonpregnant populations have reported some severe morbidity and even mortality in COVID-19 associated with bleeding or hemorrhage,[1–4] there have been very limited data regarding specific laboratory derangements that may be predictive for or associated with bleeding risk related to COVID-19.[16–18] Further research should continue to investigate the impact of a COVID-19 diagnosis on hematologic physiology, and also its impact specifically in the setting of pregnancy.

The present data can help to guide obstetricians and maternal fetal medicine specialists in assessing hemorrhage risk of patients upon admission to labor and delivery. Early identification and frequent reassessment of risk factors can

help with preparing interventions (e.g., type and cross, blood products, and uterotonics) and prepare the clinical team for increased surveillance following birth that all may help prevent adverse outcomes.[19] As COVID-19 diagnosis is not presently associated with either a statistically increased QBL or an increased obstetric hemorrhage risk, we would not recommend adjusting hemorrhage risk assessment calculators based on COVID-19 status.

While demographic and comorbidity incidence were not our primary outcomes, we did have some compelling and concerning findings that are similar to findings in existing COVID-19 literature. In our cohort, there was a significantly higher proportion of pregnant women who identified as non-White with a COVID-19 diagnosis when compared with the COVID-19 negative cohort. Specifically, there was a significantly higher proportion of Hispanic women in our COVID-19 positive cohort compared with the COVID-19 negative cohort. This is aligned with many studies both in pregnant and nonpregnant populations that have demonstrated significant racial disparities in incidence and outcomes.[13,20,21] A multitude of factors, including health care access, social determinants of health, and underlying comorbidities may underlie these disparities in COVID-19 spread, incidence, and outcomes in non-White populations. The etiology of these demographic findings should be interrogated seriously with both qualitative and quantitative approaches.[22]

Lastly, we also found that women with a COVID-19 diagnosis were also more likely to be diagnosed with preeclampsia with severe features. The relationship between COVID-19 diagnosis and hypertensive diseases of pregnancy such as preeclampsia has been an area of intense scrutiny as there are many confounding symptoms (e.g., shortness of breath or neurological manifestations such as headache or seizure) and laboratory abnormalities (e.g., thrombocytopenia, anemia, transaminitis) that these two diseases share.[23,24] At institutions where there is not yet universal testing, for women who present with severe features of preeclampsia, COVID-19 must necessarily be high on the differential and women should be tested and appropriately treated for either disease or possibly both. Further research, both clinical and pathology based, is needed to further explore the relationship between these two diseases.

Our study has several strengths. To date, ours is the first study to specifically address blood loss and hemorrhage in an American population of COVID-19 positive and negative parturients. Furthermore, we were able to present QBL, a more precise measure of hemorrhage than traditional estimated blood loss.[25,26] Most of the limited literature in this field have relied large national cohorts to describe obstetric and surgical morbidity in the setting of COVID-19 infection.[12–15] These databases necessarily combine results from institutions with varying protocols for hemorrhage risk screening and management. Additionally, multicohort studies are limited by misclassification biases secondary to significant variance in study setting. As a single institution cohort study, the patients described here were treated with one set of protocols from our institution; thus, our data are subject to less intersubject variance.

We acknowledge our study limitations as a nonrandomized cohort with unequal sample sizes of our comparison groups. While we attempted to control for known differences between the groups, residual confounding may persist. Furthermore, the utilization of a categorical variable of obstetric hemorrhage, defined by our U.S. national guidelines as a relatively arbitrary threshold of 1,000 mL for poor blood-loss outcomes may not be as predictive or clinically significant as other factors, such as laboratory derangements or hemorrhage treatments utilized.[27] National guidelines on obstetric hemorrhage vary significantly and thus influence treatment specific protocols, which may make international multicohort studies and large-scale meta-analyses difficult to interpret.[28] We are hopeful, however, that our data may contribute to the larger understanding of the interaction of COVID-19 infection and obstetric hematologic physiology.

Conclusion

Mothers with COVID-19 diagnosis were not found to have an increased risk in hemorrhagic morbidity or increased risk of overall maternal morbidity. However, as hemorrhage persists as the leading etiology of severe maternal morbidity and mortality in the United States, obstetricians should continue to practice with clinical vigilance in providing care for the COVID-19 infected parturient as we continue to learn more about the perinatal sequelae of this disease.

Note

This study is approved by Boston University Institutional Reference Board (reference number: 1311956).

Conflict of Interest

None declared.

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