HSPI The Open Access Publisher

CJOG CLINICAL JOURNAL OF OBSTETRICS AND GYNECOLOGY
ISSN 2640-2890

Research Article

Is COVID-19 a Risk Factor for Hypertensive Disorders of Pregnancy?

Hannah Childs[1], Cayman Bickerstaff[2]*, Teodora Stoikov[1], Hongyan Xu[3], Katherine Marino[2], Cynthia Li[2], Lina Nguye[2], Bailey Rodgers[2] and Jennifer T Allen[1]

[1]Department of Obstetrics and Gynecology, Augusta University, Augusta, GA, USA
[2]Medical College of Georgia at Augusta University, Augusta, GA, USA
[3]Biostatistics and Data Science, Augusta University, Augusta, GA, USA

Abstract

Objective: This study aims to assess whether COVID-19 infection during pregnancy is a risk factor for hypertensive disorders of pregnancy, including gestational hypertension, preeclampsia, HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome, and eclampsia.

Methods: A retrospective evaluation was conducted on obstetric patients who gave birth between March 2020 and December 2021 at Augusta University Medical Center, an academic urban referral center in Augusta, GA. The patients were categorized into two groups: those who were COVID-19 positive during pregnancy and those who were COVID-19 negative. The primary outcome was the development of a hypertensive disorder of pregnancy. Secondary outcomes included preterm delivery, mode of delivery, maternal death, maternal ICU admission, NICU admission, intrauterine fetal demise/stillbirth, fetal growth restriction, and prolonged hospital stay. The association between COVID-19 status and categorical outcomes was assessed using Chi-squared and Fisher's exact tests. Mean differences between groups were evaluated using Student's two-sample tests. Additionally, a multinomial multiple logistic regression was performed to assess whether COVID-19 is a risk factor for hypertensive disorders of pregnancy when adjusting for potential confounding effects.

Results: Out of the 2760 charts reviewed, 2426 (87.9%) met the inclusion criteria. Of those 2426 patients, 203 were COVID-positive and 2223 were COVID-negative . There were no significant differences in patient sociodemographic information between the COVID-19 positive and negative groups. After adjusting for potential confounding effects, COVID-19 was determined to be a risk factor for combined hypertensive disorders of pregnancy (OR 1.93, 95% CI 1.39-2.66) and preeclampsia specifically (OR 2.01, 95% CI 1.38-2.88). For the observed secondary outcomes, COVID-19 infection during pregnancy was associated with an increased risk of cesarean delivery (p = 0.046), maternal ICU admission (p = 0.008), and prolonged hospital stay (p < 0.001).

Conclusion: The findings of this study suggest that COVID-19 infection during pregnancy is linked to an increased risk of developing preeclampsia. COVID-19 was not a statistically significant risk factor for gestational hypertension when controlling for confounding effects. The study was unable to draw conclusions about more severe hypertensive conditions of pregnancy (HELLP, Eclampsia), likely due to their low prevalence in the study sample. COVID-19 was shown to be a risk factor for cesarean delivery, prolonged hospital stay, and maternal ICU admission in secondary outcome analysis. This research contributes to existing knowledge by examining the association between COVID-19 and hypertensive disorders of pregnancy during a period encompassing multiple strains of the COVID-19 virus.

More Information

***Address for correspondence:**
Cayman Bickerstaff, BS, Medical College of Georgia at Augusta University, 1120 15th Street BA 8412, Augusta, GA 30912, USA,
Email: cbickerstaff@augusta.edu

Submitted: August 28, 2023
Approved: September 09, 2023
Published: September 11, 2023

How to cite this article: Childs H, Bickerstaff C, Stoikov T, Xu H, Marino K, et al. Is COVID-19 a Risk Factor for Hypertensive Disorders of Pregnancy? Clin J Obstet Gynecol. 2023; 6: 120-125.

DOI: 10.29328/journal.cjog.1001139

Keywords: COVID-19 infection; Pregnancy; Gestational hypertension; Preeclampsia

Introduction

COVID-19 infection during pregnancy is a significant risk factor for maternal morbidity and mortality [1]. Physiological changes in the immune and cardiopulmonary systems during pregnancy increase susceptibility to severe symptoms of respiratory viruses [2]. Available data suggest that symptomatic pregnant patients with COVID-19 are at increased risk of more severe illness and adverse perinatal outcomes such as cesarean section, hypertensive disorders of pregnancy (HDoP), and coagulopathy [3,4]. Current evidence suggests that pregnant patients with comorbidities, such as obesity, diabetes, hypertension, and lung disease, and certain characteristics, such as advanced maternal age and Black and Hispanic race, may be disproportionately affected [1].

Preeclampsia, an HDoP, is responsible for 2% - 8% of pregnancy-related complications , including over 50,000 maternal and 500,000 fetal deaths worldwide [5]. Although the underlying etiology is not well understood, it involves abnormal placentation with subsequent aberrant spiral artery remodeling, placental ischemia, hypoxia, and oxidative stress.

Prompt diagnosis and management are necessary to prevent fetal complications and severe maternal manifestations, including eclampsia, HELLP syndrome, and other end-organ damage [6]. It is important to understand the role COVID-19 plays in pregnant patients given both COVID-19 and HDoP may have devastating multisystem organ effects.

The objective of this retrospective study was to evaluate COVID-19 infection during pregnancy as a potential risk factor for the development of HDoP at a single-site, academic urban referral center for obstetric patients. While emerging data support an association between COVID-19 infection and HDoP, further supporting data are needed to help guide the surveillance and management of patients with COVID-19 in pregnancy. While data, such as the INTERCOVID study, have already established this link [7], very few cover a timespan as large as that of this study.

Methods

This IRB-approved retrospective cohort study was conducted at Augusta University Medical Center in Augusta, GA, a single academic institution, to evaluate the association between COVID-19 infection during pregnancy and hypertensive disorders of pregnancy.

A data request was submitted using the "Diagnosis Related Group Codes" (DRGs) for all deliveries and postpartum care between March 1, 2020 and December 31, 2021. This date range was chosen because it was the timeframe in which universal COVID-19 testing was performed upon admission to all obstetric units at this site, including Labor and Delivery, Antepartum, Obstetrics Emergency Department, and Postpartum.

A total of 2760 patient medical record numbers (MRNs) were initially pulled for analysis within the selected time frame. The sole inclusion criterion for the study was all pregnant patients who delivered at greater than 20 weeks of gestation from March 2020 to December 2021. Patients were excluded if they delivered at less than 20 weeks gestation, had multifetal gestations, did not have a documented COVID test result, or delivered at an outside site. After applying these criteria, 334 patient charts were excluded, and 2426 (87.9%) patients were deemed eligible for inclusion in the analysis.

The chart review included a thorough investigation of several patient variables and outcomes, including demographics. After data collection, patients were grouped into COVID-positive (n = 203) and COVID-negative groups (n = 2223). Diagnosis of COVID-19 infection, which categorized patients as "COVID-positive," was defined by a documented positive PCR test performed in our institution's laboratory from a nasopharyngeal swab, both inpatient and outpatient, at any time point during pregnancy. Given that the study is a retrospective cohort study, the most likely biases to be present in this study are confounding and observer biases. To control for confounding bias, a multivariate analysis was conducted. Given that the data is dependent on adequate documentation by providers to record details such as the presence or absence of COVID-19 symptoms and type of hypertensive disorder, we relied on objective data such as COVID PCR test results, vital signs, and common labs obtained in hypertension workup in the obstetric patients during chart review.

The primary outcome observed in this study was the development of a hypertensive disorder of pregnancy, including gestational hypertension, preeclampsia, HELLP syndrome, and eclampsia. Superimposed preeclampsia in the setting of chronic hypertension was included analytically under preeclampsia. These HDoPs were first analyzed as a single combined group and then individually for their association with COVID-19 infection during pregnancy.

A diagnosis of a hypertensive disorder of pregnancy was made according to the definitions currently accepted by the American College of Obstetrics and Gynecology and StatPearls. During the retrospective chart review, the presence of preeclampsia and other hypertensive disorders of pregnancy were recorded based on the presence of the following criteria. Preeclampsia was defined as new-onset hypertension in pregnancy at greater than 20 weeks gestation through six weeks postpartum with new-onset proteinuria. Gestational hypertension was defined as new-onset hypertension in pregnancy at greater than 20 weeks gestation through six weeks postpartum without new-onset proteinuria. For diagnosis of both disorders, hypertension was defined as a systolic blood pressure of equal to or greater than 140 mmHg or a diastolic blood pressure of equal to or greater than 90 mmHg on two occasions taken at least four hours apart. New-onset proteinuria was defined as urinary excretion of equal to or greater than 300 mg of protein in a 24-hour urine collection sample or a urine protein/creatinine ratio of at least 0.3 mg/dL. When quantitative methods were unavailable, a urine dipstick showing 2+ protein or greater was used for the diagnosis of proteinuria. Other criteria for the diagnosis of preeclampsia in the absence of proteinuria included new-onset thrombocytopenia (platelet count less than 100,000/μL), impaired liver function (serum liver transaminases elevated to at least twice the normal concentration), renal insufficiency (serum creatinine concentration at least two times greater than baseline in the absence of attributable renal diseases or serum creatinine concentration greater than 1.1 mg/dL), pulmonary edema, and visual and cerebral disturbances. These criteria, as well as systolic blood pressure equal to or greater than 160 mmHg and diastolic blood pressure equal to or greater than 110 mmHg on two occasions at least four hours apart, were considered severe features. HELLP syndrome was defined as a triad of symptoms: evidence of hemolysis, elevated serum liver transaminase levels to at least twice the normal concentration, and a platelet count of less than 100,000/μL. Eclampsia was defined as new-onset grand-mal seizures during pregnancy that were not attributable to other causes [5,6].

Patients with underlying chronic hypertension were not excluded from the study because this condition is a major comorbidity at our institution. Exclusion of these patients would limit the sample size and decrease the utility of the study results. The diagnosis of patients with superimposed preeclampsia was based on the development of severe features or new-onset or worsening proteinuria. A subgroup analysis of patients with diagnosed HDoP was performed to assess chronic hypertension as a confounding factor. Further analysis was performed in these patients to evaluate disease severity, defined by the presence of severe features, with respect to COVID-19. The presence or absence of symptoms at the time of COVID-19-positive testing was also reviewed.

Several patient demographics and variables were reviewed in the COVID-positive and COVID-negative groups to evaluate the possible confounding or shared risk factors. Other maternal and fetal outcomes observed in this study included preterm delivery, mode of delivery, maternal death, maternal ICU admission, NICU admission, intrauterine fetal demise (IUFD)/stillbirth, fetal growth restriction (FGR), and prolonged hospital stay (defined as greater than four days). The patient demographics included age, race, and parity. Patient variables included gestational age at delivery, body mass index (BMI), tobacco use, recreational drug use, pregestational or gestational diabetes, chronic hypertension, history of preterm delivery, and history of preeclampsia in prior pregnancies. Vaccination status was not included in this retrospective cohort study because of limited documentation and the fact that the first COVID-19 vaccine was not available in the U.S. until December 2020, approximately halfway through the study. Furthermore, while the presence of symptomatic and asymptomatic COVID-19 infections was originally included in the chart review, this data was not used in the analysis as it was inconsistently recorded in the electronic medical record.

Statistical analysis was performed using the software *R 4.2.2* and completed using Chi-squared and Fisher's exact tests to evaluate any association between categorical outcomes and COVID status. Student's two-sample tests were used to evaluate the mean difference between the groups. A multinomial multiple logistic regression (multivariate analysis) was performed to evaluate the effect of COVID-19 on the development of HDoP when including age and other demographic factors as covariates to adjust for potential confounding effects. p - values < 0.05 were considered to be statistically significant.

Results

For the defined study period, 2760 patient charts were reviewed. A total of 334 charts were excluded based on the defined inclusion and exclusion criteria, and the final sample size for data analysis was 2426 patients. Of these, 203 (8.4%) were COVID-positive and 2223 (91.6%) were COVID-negative. The average age in the COVID-positive group was 27.69 and the average age in the COVID-negative group was 27.75 (p = 0.907). Race was listed as "Black," "White," or "Other" in statistical analysis, and the racial differences between groups were nonsignificant (p = 0.13). Differences in BMI were non-significant (p = 0.528), as were the differences in what percentage of the patients in each group were nulliparous (p = 0.256). The average gestational age at delivery was 37.63 in the COVID-positive group and 37.80 in the COVID-negative group (p = 0.429). Other demographic and confounding variables assessed and determined to be non-significant between the groups were preexisting chronic hypertension (p = 1.0), diabetes (gestational or pregestational) (p = 0.409), history of preeclampsia in prior pregnancies (p = 0.808), tobacco use (p = 0.739), and recreational drug use (p = 0.293) (Table 1).

In the COVID-positive group, 78 patients (38.4%) met the criteria for diagnosis of at least one of the four hypertensive disorders of pregnancy (gestational hypertension, preeclampsia, HELLP syndrome, and eclampsia) compared to 514 patients (23.1%) in the COVID-negative group (p =<0.001, OR 2.08, 95% CI 1.37- 2.01) (Table 2).

The hypertensive disorders of pregnancy were then analyzed individually (Table 2). In the COVID-positive group, 25.6% of patients met the criteria for preeclampsia compared to 14.5% in the COVID-negative group (p =<0.001, OR 2.03, 95% CI 1.37-2.28). In the COVID-positive group, 15.8% met the criteria for gestational hypertension compared to 10.6% in the COVID-negative group (p = 0.032, OR 1.59, 95% CI 1.06-2.10). The reason that 25.6% of patients meeting the criteria

Table 1: Patient demographics and variables between the COVID-positive and COVID-negative groups.

	COVID-Positive (n = 202)	COVID-negative (n = 2224)	p - value
Age (mean ± SD)	27.69 ± 6.44	27.75 ± 6.11	0.907
Race (%)			
Black	90 (44.6)	1024 (46.0)	0.13
Other	46 (22.8)	384 (17.3)	
White	66 (32.7)	816 (36.7)	
Body Mass Index (kg/m^2, %)			
Underweight BMI <18.5	0 (0.0)	5 (0.2)	0.528
Normal BMI 18.5-24.9	17 (18.5)	224 (10.1)	
Overweight BMI 25.0-29.9	52 (26.0)	581 (26.1)	
Class 1 Obesity, BMI 30.0-34.9	47 (23.5)	611 (27.5)	
Class 2 Obesity, BMI 35.0-39.9	44 (22.0)	393 (17.7)	
Class 3 Obesity, BMI > 40	40 (20.0)	408 (18.4)	
Nulliparity (%)	83 (41.1)	817 (36.8)	0.256
Gestational age at delivery (mean ± SD)	37.63 ± 2.83	37.80 ± 3.04	0.429
Preexisting chronic HTN (%)	26 (12.9)	284 (12.8)	1
Gestational or pregestational diabetes (%)	29 (14.4)	269 (12.1)	0.409
History of preeclampsia in prior pregnancies (%)	19 (9.4)	192 (8.6)	0.808
Tobacco use* (%)	17 (8.4)	209 (9.4)	0.739
Recreational drug use† (%)	21 (10.4)	178 (8.0)	0.293

*Documented use in current pregnancy; all forms of tobacco
†Recreational drugs included recreational prescription drugs, marijuana, and all other recreational street drugs; documented use in current pregnancy

Table 2: COVID-19 infection as a risk factor for preeclampsia and related hypertensive disorders of pregnancy.

	Number of Patients COVID-negative *(%)*	Number of Patients COVID-positive *(%)*	*p* - value (Unadjusted)	Unadjusted OR (95% CI)	Multivariate Analysis *p* - value	Adjusted OR (95% CI)
Diagnosis of a hypertensive disorder of pregnancy	514 (23.1%)	78(38.4%)	< 0.001	2.08 (1.53- 2.80)	< 0.001	1.93 (1.39-2.66)
Diagnosis of preeclampsia	232 (14.5%)	52(25.6%)	< 0.001	2.03 (1.44-2.82)	< 0.001	2.01 (1.38-2.88)
Diagnosis of gestational hypertension	235 (10.6%)	32(15.8%)	0.032	1.59 (1.05-2.34)	0.123	
Diagnosis of HELLP	7(0.31%)	2(0.99%)	0.17	3.31 (0.45-14.25)		
Diagnosis of eclampsia	12 (0.54%)	1 (0.49%)	1	1.03 (0.04-5.31)		
Diagnosis of severe features	217 (42.2%)	31 (39.7%)	0.77			
Diagnosis of chronic hypertension	110 (21.4%)	14 (17.9%)	0.58			

Table 3: COVID-19 infection as a risk factor for other obstetric outcomes.

	Number of COVID-negative *(%)*	Number of COVID-positive *(%)*	*p* - value	Unadjusted OR (95% CI)
Preterm Delivery	388 (17.5%)	44 (21.7%)	0.16	
Cesarean Delivery	648 (29.1%)	73 (36.1%)	0.046	1.38 (1.01-1.86)
Maternal Death	1 (0.04%)	0 (0%)	1	N/A
Maternal ICU admission	22 (0.99%)	7 (3.47%)	0.008	3.64 (1.41-8.29)
Neonatal ICU admission	453 (20.4%)	49 (24.3%)	0.23	1.25 (0.89-1.74)
Intrauterine Fetal demise	30 (1.35%)	3 (1.49%)	0.75	1.16 (0.27-3.31)
Fetal growth restriction	233 (10.5%)	26 (12.9%)	0.35	1.27 (0.80-1.92)
Prolonged hospital stay	210 (9.4%)	38 (18.8%)	< 0.001	2.23 (1.50-3.23)

for preeclampsia and 15.8% of patients meeting the criteria for gestational hypertension is greater than the 38.4% of patients positive for any hypertensive disorder of pregnancy is that some patients developed gestational hypertension, and then preeclampsia sequentially during gestation. The rates of HELLP syndrome (n = 9) and eclampsia (n = 13) were not significantly different between the two groups.

A multinomial multiple logistic regression was performed to evaluate the effect of COVID-19 on the risk of the three groups of interest (combined hypertensive disorders, preeclampsia, and gestational hypertension). After including age and other demographics in the multivariate analysis as covariates to adjust for potential confounding effects, there was a statistically significant association between COVID-19 and combined hypertensive disorders of pregnancy (p =< 0.001, OR 1.93, 95% CI 1.39-2.66). Similarly, there was a statistically significant association between COVID-19 and preeclampsia (p =< 0.001, OR 2.01, 95% CI 1.38-2.88). Furthermore, there was no longer a statistically significant association between COVID-19 and the development of gestational hypertension (p = 0.123) when this multivariate analysis was performed (Table 2).

In the combined group of patients who met the criteria for one of the disorders, no difference was observed in the development of severe features between the COVID-positive and COVID-negative groups (Table 2). There was also no significant difference in the percentage of patients with underlying chronic hypertension between the COVID-positive and negative groups (Table 2). Among the patients who tested positive for COVID-19 during pregnancy and met the criteria for a hypertensive disorder of pregnancy, 26 were considered symptomatic at the time of testing, and 41 were considered asymptomatic.

Of the secondary outcomes observed, there was a statistically significant association between COVID-19 infection in pregnancy and the following variables: cesarean delivery (p = 0.046, OR 1.38, 95% CI 1.02-1.51), maternal ICU admission (p = 0.008, OR 3.64, 95% CI 1.52-8.10), and prolonged hospital stay (p = <0.001, OR 2.23, 95% CI 1.46-2.73). No relationship was observed between COVID-19 infection during pregnancy and preterm delivery, maternal death, NICU admission, IUFD, or FGR (Table 3).

Discussion

This retrospective cohort study at an urban academic center revealed a significant association between COVID-19 infection in pregnancy and the development of combined HDoP (p = < 0.001, OR 1.93, 95% CI 1.39-2.66) and preeclampsia (p = < 0.001, OR 2.01, 95% CI 1.38-2.88) when using demographic covariates to adjust for potential confounding effects. Univariate analysis suggested that COVID-19 infection may increase the risk of developing gestational hypertension, however, there was no association between the two conditions following multivariate analysis. Additionally, there was no association between COVID-19 and severe forms of HDoP (HELLP, Eclampsia) likely due to the low prevalence of these conditions in the study sample (n = 9 and 13, respectively).

A subgroup analysis of patients diagnosed with one of the HDoPs was performed with regard to chronic hypertension. In this subgroup, the percentage of patients with underlying chronic hypertension was similar between the COVID-positive and-negative groups, reducing the likelihood that chronic hypertension was a confounding variable in our study (Table 2). This suggests that while patients with underlying chronic hypertension are at an increased risk of developing superimposed preeclampsia, the risk of developing HDoP is not compounded by COVID-19 infection.

For secondary outcomes, no relationship was observed between COVID-19 infection during pregnancy and preterm delivery, which is inconsistent with current prospective data in the literature [7]. Maternal ICU admission, prolonged hospital stays, and cesarean delivery, however, were all significantly associated with COVID-19 infection, in congruence with existing evidence [8].

Data regarding maternal and fetal outcomes in the setting of COVID-19 during pregnancy remain limited. The results of this study appear to be consistent with initial published data suggesting that COVID-19 during pregnancy is a risk factor for preeclampsia, independent of risk factors and preexisting conditions [8-10]. Our results are also congruent with the current literature that gestational hypertension is weakly associated with COVID-19, given that gestational hypertension and COVID-19 had a significant association before multivariate analysis ($p = 0.032$).

There is a possible physiological explanation that supports the finding that COVID-19 is a risk factor for preeclampsia. COVID-19 affects microcirculation by causing endothelial damage and microthrombosis [11,12]. The root cause of preeclampsia is abnormal placentation, which causes spiral artery remodeling, resulting in ischemia, hypoxia, and oxidative stress involving endothelial dysfunction [6]. Given these similar vascular physiologies, COVID-19 and preeclampsia may share a common angiopathic process that leads to preeclampsia and combined HDoP after COVID-19 infection [11,12].

Understanding the association between COVID-19 infection and hypertensive disorders of pregnancy may help guide obstetric management, specifically concerning monitoring for the development of preeclampsia and determining appropriate antenatal fetal surveillance in infected mothers. As preeclampsia remains a significant cause of morbidity and mortality in pregnancy, it is important to understand the effect of common viral pathogens on the development of HDoP so that patients can be managed adequately.

The INTERCOVID Multinational Cohort Study [7] evaluated the association of COVID-19 with the development of Preeclampsia and other secondary objectives similar to the current study. This multinational cohort study found a statistically significant link between COVID-19 and Preeclampsia but only evaluated patients from March 2020 – October 2020, which limits the generalization of data across viral strains. In this single, urban center study, this link is evaluated from March 2020 – December 2021, which allows for broader generalization based on the different variants of COVID-19. The first incidence of the COVID-19 Delta Strain in the United States was in March of 2021 [13]. Therefore, despite the lack of COVID-19 genotyping performed, this study offers reason to believe that COVID-19 is likely a significant risk factor for Preeclampsia across multiple strains of the virus.

This study has several limitations. First, this study was conducted at a single, urban academic medical center, thus limiting its generalizability. Second, patient information was collected via a retrospective chart review, which can be associated with documentation errors concerning the presence or absence of symptoms and observation bias that impact the results. For example, regarding secondary outcomes, the reason for maternal ICU admission was not documented and all ICU admissions were included in the analysis. Similarly, although COVID-19 and preeclampsia were reasons for longer hospital stays at our institution, the reason for prolonged hospital stays was not analyzed in this chart review. Additionally, the interval between COVID-19 infection and the observed outcomes was not reviewed. Since patients were primarily tested on admission, and the presence or absence of symptoms was poorly documented, it is unclear whether gestational age at diagnosis and the presence of symptoms of COVID-19 are correlated with these processes. Furthermore, vaccination status was not included in the study owing to the timing of COVID-19 vaccine development and poor documentation status. Now that the vaccine is widely available to the general public, this is an important future research consideration. The last limitation is that the number of patients diagnosed with preeclampsia via urine dipstick alone was not recorded during the chart review, which could falsely increase the number of true cases of preeclampsia.

Conclusion

In conclusion, the results of this study suggest that COVID-19 infection in pregnancy increases the risk of developing a combined hypertensive disorder of pregnancy, specifically preeclampsia. When controlling for suspected confounding variables, the observed association between COVID-19 and gestational hypertension is no longer significant. Firm conclusions cannot be drawn regarding more severe HDoP, HELLP syndrome ($n = 9$), and eclampsia ($n = 13$), although this is likely secondary to the low prevalence of these complications in this study sample. This study builds upon current evidence by examining patients during a period that encompasses multiple strains of the virus. Further prospective research is needed to elucidate the answers to these questions.

Acknowledgement

Kathryn Batchler BS and Sara Attari BS.

References

1. The Society for Maternal-Fetal Medicine. Management of COVID Positive Pregnant Patients. 2023. https://www.smfm.org/covidclinical
2. Wang CL, Liu YY, Wu CH, Wang CY, Wang CH, Long CY. Impact of COVID-19 on Pregnancy. Int J Med Sci. 2021 Jan 1;18(3):763-767. doi: 10.7150/ijms.49923. PMID: 33437211; PMCID: PMC7797535.
3. The Society for Maternal-Fetal Medicine. What MFMs need to know. https://www.smfm.org/covidclinical

4. Novel coronavirus 2019 (COVID-19). ACOG Practice Advisory. https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2020/03/novel-coronavirus-2019

5. Karrar SA, Hong PL. Preeclampsia. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2023. https://www.ncbi.nlm.nih.gov/books/NBK570611/

6. Gestational Hypertension and Preeclampsia: ACOG Practice Bulletin, Number 222. Obstet Gynecol. 2020 Jun;135(6):e237-e260. doi: 10.1097/AOG.0000000000003891. PMID: 32443079.

7. Villar J, Ariff S, Gunier RB, Thiruvengadam R, Rauch S, Kholin A, Roggero P, Prefumo F, do Vale MS, Cardona-Perez JA, Maiz N, Cetin I, Savasi V, Deruelle P, Easter SR, Sichitiu J, Soto Conti CP, Ernawati E, Mhatre M, Teji JS, Liu B, Capelli C, Oberto M, Salazar L, Gravett MG, Cavoretto PI, Nachinab VB, Galadanci H, Oros D, Ayede AI, Sentilhes L, Bako B, Savorani M, Cena H, García-May PK, Etuk S, Casale R, Abd-Elsalam S, Ikenoue S, Aminu MB, Vecciarelli C, Duro EA, Usman MA, John-Akinola Y, Nieto R, Ferrazi E, Bhutta ZA, Langer A, Kennedy SH, Papageorghiou AT. Maternal and Neonatal Morbidity and Mortality Among Pregnant Women With and Without COVID-19 Infection: The INTERCOVID Multinational Cohort Study. JAMA Pediatr. 2021 Aug 1;175(8):817-826. doi: 10.1001/jamapediatrics.2021.1050. Erratum in: JAMA Pediatr. 2022 Jan 1; 176(1):104. PMID: 33885740; PMCID: PMC8063132.

8. Papageorghiou AT, Deruelle P, Gunier RB, Rauch S, García-May PK, Mhatre M, Usman MA, Abd-Elsalam S, Etuk S, Simmons LE, Napolitano R, Deantoni S, Liu B, Prefumo F, Savasi V, do Vale MS, Baafi E, Zainab G, Nieto R, Maiz N, Aminu MB, Cardona-Perez JA, Craik R, Winsey A, Tavchioska G, Bako B, Oros D, Rego A, Benski AC, Hassan-Hanga F, Savorani M, Giuliani F, Sentilhes L, Risso M, Takahashi K, Vecchiarelli C, Ikenoue S, Thiruvengadam R, Soto Conti CP, Ferrazzi E, Cetin I, Nachinab VB, Ernawati E, Duro EA, Kholin A, Firlit ML, Easter SR, Sichitiu J, Bowale A, Casale R, Cerbo RM, Cavoretto PI, Eskenazi B, Thornton JG, Bhutta ZA, Kennedy SH, Villar J. Preeclampsia and COVID-19: results from the INTERCOVID prospective longitudinal study. Am J Obstet Gynecol. 2021 Sep;225(3):289.e1-289.e17. doi: 10.1016/j.ajog.2021.05.014. Epub 2021 Jun 26. PMID: 34187688; PMCID: PMC8233533.

9. Hill J, Patrick HS, Ananth CV, O'Brien D, Spernal S, Horgan R, Brandt JS, Schwebel M, Miller RC, Straker MJ, Graebe RA, Rosen T. Obstetrical outcomes and follow-up for patients with asymptomatic COVID-19 at delivery: a multicenter prospective cohort study. Am J Obstet Gynecol MFM. 2021 Nov;3(6):100454. doi: 10.1016/j.ajogmf.2021.100454. Epub 2021 Aug 8. PMID: 34375750; PMCID: PMC8349406.

10. Narang K, Enninga EAL, Gunaratne MDSK, Ibirogba ER, Trad ATA, Elrefaei A, Theiler RN, Ruano R, Szymanski LM, Chakraborty R, Garovic VD. SARS-CoV-2 Infection and COVID-19 During Pregnancy: A Multidisciplinary Review. Mayo Clin Proc. 2020 Aug;95(8):1750-1765. doi: 10.1016/j.mayocp.2020.05.011. Epub 2020 May 30. PMID: 32753148; PMCID: PMC7260486.

11. Jayaram A, Buhimschi IA, Aldasoqi H, Hartwig J, Owens T, Elam GL, Buhimschi CS. Who said differentiating preeclampsia from COVID-19 infection was easy? Pregnancy Hypertens. 2021 Dec;26:8-10. doi: 10.1016/j.preghy.2021.07.248. Epub 2021 Jul 24. PMID: 34392167; PMCID: PMC8302825.

12. Østergaard L. SARS CoV-2 related microvascular damage and symptoms during and after COVID-19: Consequences of capillary transit-time changes, tissue hypoxia and inflammation. Physiol Rep. 2021 Feb;9(3):e14726. doi: 10.14814/phy2.14726. PMID: 33523608; PMCID: PMC7849453.

13. Delta Variant. Baptist Health. 2023. https://www.baptisthealth.com/connect-learn/covid19/covid19-resources/covid-19-variants/delta-variant#:~:text=Has%20the%20Delta%20Variant%20Reached,the%20U.S.%20in%20March%202021.