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ORIGINAL RESEARCH ARTICLE

Shared risk factors for COVID-19 and preeclampsia in the first trimester: An observational study

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Abstract

Introduction: The association between preeclampsia and coronavirus disease 2019 (COVID-19) is under study. Previous publications have hypothesized the existence of shared risk factors for both conditions or a deficient trophoblastic invasion as possible explanations for this association. The primary aim of this study was to examine baseline risk factors measured in the first-trimester combined screening for preeclampsia in pregnant women with COVID-19 compared with the general population. A secondary aim of this study was to compare risk factors among patients with mild and severe COVID-19.

Material and Methods: This was an observational retrospective study conducted at Vall d'Hebron Hospital Campus (Catalonia, Spain). Study patients were 231 pregnant women undergoing the first-trimester screening for preeclampsia and positive for severe acute respiratory syndrome coronavirus 2 between February 2020 and September 2021. The reference cohort were 13033 women of the general population from six centers across Catalonia from May 2019 to June 2021. Based on the need for hospitalization, patients were classified in two groups: mild and severe COVID-19. First-trimester screening for preeclampsia included maternal history, mean arterial blood pressure, mean uterine artery pulsatility index (UtAPI), placental growth factor (PlGF), and pregnancy-associated plasma protein-A (PAPP-A).

Results: The proportion of cases at high risk for preeclampsia was significantly higher among the COVID-19 group compared with the general population (19.0% and 13.2%, respectively; $p = 0.012$). When analyzing risk factors for preeclampsia

Abbreviations: MAP, mean arterial blood pressurePAPP-Apregnancy-associated plasma protein-APlGFplacental growth factorUtAPImean uterine artery pulsatility index.

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individually, women with COVID-19 had higher median body mass index (25.2 vs 24.5, $p = 0.041$), higher UtAPI multiple of the median (MoM) (1.08 vs 1.00, $p < 0.001$), higher incidence of chronic hypertension (2.8% vs 0.9%, $p = 0.015$), and there were fewer smokers (5.7% vs 11.6%, $p = 0.007$). The MoMs of PlGF and PAPP-A did not differ significantly between both groups (0.96 vs 0.97, $p = 0.760$ and 1.00 vs 1.01, $p = 0.432$; respectively).

Conclusions: In patients with COVID-19, there was a higher proportion of women at high risk for preeclampsia at the first-trimester screening than in the general population, mainly because of maternal risk factors, rather than placental signs of a deficient trophoblastic invasion.

KEYWORDS
coronavirus disease 2019, first trimester, placental growth factor, preeclampsia, risk factors, screening, severe acute respiratory syndrome coronavirus 2, uterine artery Doppler

1 | INTRODUCTION

The relation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and pregnancy has been under study since the outset of the coronavirus pandemic. Evidence shows that pregnant women with coronavirus disease 2019 (COVID-19) are at an increased risk of severe pregnancy complications, including preeclampsia, admission to the intensive care unit, preterm birth, or maternal mortality.[1]

One of the first studies about COVID-19 and pregnancy, published in February 2020, suggested an increased preeclampsia incidence among pregnant women with COVID-19.[2] This was confirmed in further studies.[3,4] Recently, a large meta-analysis that included 28 studies showed an increased preeclampsia incidence risk, with an odds ratio of 1.62 (95% confidence interval 1.45–1.82).[5]

Different theories have been suggested regarding the association between preeclampsia and COVID-19.[4-8] One of them hypothesizes that preeclampsia and COVID-19 are associated because of sharing risk factors for endothelial damage, such as obesity, hypertension, diabetes, and maternal age. Early uteroplacental insufficiency could be an additional risk factor for endothelial damage, thereby increasing the risk of developing COVID-19, mostly in its severe forms.

The question is whether early uteroplacental insufficiency due to abnormal trophoblastic invasion increases the risk of developing COVID-19 and its severity, or whether the association between both conditions is driven by the fact that COVID-19 and preeclampsia share risk factors for endothelial damage increasing the risk of both conditions.

If abnormal trophoblastic invasion[9] makes patients more vulnerable to COVID-19 (or more likely to develop a severe form of COVID-19), women with COVID-19 would have lower placental growth factor (PlGF) levels, lower pregnancy-associated plasma protein-A (PAPP-A), and increased mean uterine artery pulsatility index (UtAPI) compared with the reference population.

The primary aim of this study was to examine baseline risk factors, as well as biochemical and biophysical markers measured in the first-trimester combined screening for preeclampsia in pregnant women with COVID-19 vs the general population. The secondary aim was to compare these baseline characteristics and markers between women with mild and severe COVID-19.

Key message

Pregnant women with COVID-19 are at a higher risk for preeclampsia mainly because of maternal risk factors rather than placental signs of deficient trophoblastic invasion.

2 | MATERIAL AND METHODS

This was an observational retrospective study conducted at Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain. For the study group, inclusion criteria were women (a) attending our site with confirmed SARS-CoV-2 infection at any point during pregnancy and (b) undergoing the first-trimester combined screening for preeclampsia. The recruitment period for the SARS-CoV-2 group was from February 2020 to September 2021. Our center was a referral hospital for severe COVID-19 pneumonia, especially during pregnancy; therefore, cases were both patients from our area and patients referred from across Catalonia. For the population group, data were obtained from the general population attending first-trimester screening for preeclampsia in six centers across Catalonia (Vall d'Hebron Barcelona Hospital Campus, Hospital Universitari Germans Trias i Pujol, Hospital Universitari de Tarragona Joan XXIII, Hospital Universitari Mútua Terrassa, Consorci Sanitari de Terrassa, and Hospital Universitari de Girona Doctor Josep Trueta) between May 2019 and June 2021.

Infection with SARS-CoV-2 was confirmed either by real-time polymerase chain reaction or an antigen test. Several changes

in screening protocols have occurred during the study period, whereas scientific evidence or assistance care needs were changing. Therefore, our study population included both patients systematically screened at hospital admission and patients screened because of symptomatology or close contact. In the study group, severity of the symptoms was the criterion used for classification: mild forms of COVID-19, including asymptomatic and symptomatic women not requiring hospitalization, and severe forms of COVID-19, including patients requiring hospitalization due to severe pneumonia.

In Catalonia, the first-trimester screening for preeclampsia is routinely performed during the first-trimester scan between 11^{+0} and 13^{+6} weeks of pregnancy. Gestational age is confirmed by fetal crown–rump length measurement during this scan.[10] Demographic characteristics, obstetric history, maternal history, and biophysical and biochemical markers are documented in the clinical records. Biophysical markers, including transabdominal mean UtAPI and mean arterial blood pressure (MAP), are assessed during the first-trimester scan. Biochemical markers, including serum PAPP-A and PlGF, are measured at the routine first-trimester blood test (from 8^{+0} to 13^{+6} weeks of pregnancy). Maternal serum PAPP-A and PlGF levels were determined by the fully automated Elecsys assays for PAPP-A and PlGF on an immunoassay platform (cobas e analyzers; Roche Diagnostics, Rotkreuz, Switzerland). MAP, UtAPI, PAPP-A, and PlGF values were transformed into multiples of the median (MoM) by adjusting by gestational age, body mass index (BMI), ethnicity, and smoking.[11] First-trimester risk for preeclampsia was then calculated.[11] High risk for preeclampsia was defined as a risk for early-onset preeclampsia ≥1/170 as this is the recommended cut-off for the Gaussian algorithm,[11] which is the algorithm used for first-trimester preeclampsia risk assessment in Catalonia. This cut-off value provides a 90.9% detection rate for early-onset preeclampsia at a 12.7% false-positive rate.[12] All examiners were certified by the Fetal Medicine Foundation for preeclampsia risk assessment and Doppler ultrasound assessment.

2.1 | Statistical analyses

Categorical data were reported as frequency and percentage, and comparisons between groups were estimated by chi-squared or Fisher tests, as appropriate. Continuous variables were reported as the median and interquartile range, and Mann–Whitney *U* test was used to assess differences between groups. The statistical significance level was set at *p* values less than 0.05.

The statistical software package R (version 4.0.3) was used for data analysis (R Foundation for Statistical Computing, Vienna, Austria).[13]

2.2 | Ethical approval

This study was approved by the Vall d'Hebron Barcelona Hospital Campus Ethics Committee (PR[AMI]556/2021) on November 5, 2021. A previous study assessing the screening performance of the first-trimester screening for preeclampsia was approved by the same institution (PR[AMI]147/2021), and, therefore, data from the general population was prospectively recorded.

3 | RESULTS

For the study group (or COVID-19 group), 231 women fulfilled the inclusion criteria. In the population group (or reference group), 13 033 women underwent the routine first-trimester screening for preeclampsia.

3.1 | Comparison of the COVID-19 and reference groups

In the COVID-19 group, 44 out of 231 (19.0%) cases were identified to be at a high risk for preeclampsia at the first-trimester screening, and this incidence was significantly higher than the 1719 out of 13 033 (13.2%) found in the general population ($p = 0.012$). When preeclampsia risk factors were examined individually, we found that women with COVID-19 had higher UtAPI and BMI, higher incidence of chronic hypertension, and fewer were smokers. No significant differences were found in MAP, PlGF, PAPP-A, maternal age, black race, or history of preeclampsia or diabetes mellitus between the COVID-19 group and the general population (Table 1).

3.2 | Comparison between mild and severe forms of COVID-19

In the COVID-19 group, 160 (69.3%) women developed mild COVID-19 and 71 (30.7%) women developed severe COVID-19. Of the 160 women with mild COVID-19, 25 (15.6%) were at a high risk for preeclampsia in the first-trimester screening. Likewise, of the 71 women with severe COVID-19, 19 (26.8%) were also at a high risk for preeclampsia in the first-trimester screening. Nevertheless, this difference was not statistically significant ($p = 0.071$). In women with severe COVID-19, MAP in the first trimester was higher, as was BMI. No other significant differences were found in other markers or risk factors for preeclampsia between the groups with mild and severe forms of COVID-19 (Table 2).

4 | DISCUSSION

This study shows a higher prevalence of risk factors for preeclampsia during the first trimester in women with COVID-19 as compared with the reference population. In the COVID-19 group the proportion of high BMI and chronic hypertension was higher, whereas the proportion of smokers was lower, which are also risk factors for developing preeclampsia. Regarding biochemical and biophysical

TABLE 1 Comparison of preeclampsia risk factors between the COVID-19 group and the general population

	COVID-19 (*N* = 231)	General population (*N* = 13 033)	*p* value
High risk of preeclampsia	44 (19.0%)	11 719 (13.2%)	0.012
Mean arterial pressure (MoM)	1.09 (1.01–1.18)	1.09 (1.01–1.17)	0.906
Uterine artery PI (MoM)	1.08 (0.88–1.31)	1.00 (0.82–1.20)	<0.001
PlGF (MoM)	0.96 (0.77–1.89)	0.97 (0.77–1.20)	0.760
PAPP-A (MoM)	1.00 (0.69–1.42)	1.01 (0.71–1.47)	0.432
BMI (kg/m^2)	25.2 (22.2–29.4)	24.5 (21.8–28.3)	0.041
Maternal age (y)	31.8 (26.8–36.2)	32.6 (28.2–36.4)	0.065
Black race	7/230 (3.0%)	402 (3.1%)	1
Chronic hypertension	6/218 (2.8%)	104/11698 (0.9%)	0.015
History of preeclampsia	9/218 (4.1%)	261/11917 (2.2%)	0.100
Smoking	13/229 (5.7%)	1494/12847 (11.6%)	0.007
Nulliparous	66/219 (30.1%)	4249/11664 (36.4%)	0.065
Assisted reproduction technique	8/231 (3.5%)	303/13033 (2.3%)	0.361
Diabetes mellitus	2/228 (0.9%)	158/12552 (1.3%)	1.0

Note: Continuous variables are shown as the median and interquartile range (first and third quartiles). Categorical data are shown as absolute frequency and percentage.

Abbreviations: BMI, body mass index; COVID-19, coronavirus disease 2019; MoM, multiples of the median; PAPP-A, pregnancy-associated plasma protein-A; PI, pulsatility index; PlGF, placental growth factor.

TABLE 2 Comparison of preeclampsia risk factors between mild and severe forms of COVID-19

	Mild (*N* = 160)	Severe (*N* = 71)	*p* value
High risk of preeclampsia	25 (15.6%)	19 (26.8%)	0.071
Mean arterial pressure (MoM)	1.08 (1.00–1.16)	1.12 (1.05–1.22)	0.008
Uterine artery PI (MoM)	1.07 (0.85–1.33)	1.09 (0.94–1.26)	0.756
PlGF (MoM)	0.97 (0.77–1.22)	0.96 (0.77–1.11)	0.862
PAPP-A (MoM)	0.97 (0.68–1.39)	1.02 (0.73–1.53)	0.308
BMI (kg/m^2)	23.7 (21.7–27.6)	28.2 (24.6–30.8)	<0.001
Maternal age (y)	31.3 (26.3–36.0)	34.1 (28.0–37.9)	0.069
Black race	5 (3.1%)	2 (2.9%)	1.0
Chronic hypertension	3 (2.0%)	3 (4.6%)	0.366
History of preeclampsia	7 (4.6%)	2 (3.1%)	1.0
Smoking	12 (7.6%)	1 (1.4%)	0.069
Nulliparous	49 (31.8%)	17 (26.2%)	0.426
Assisted reproduction technique	5 (3.1%)	3 (4.2%)	0.704
Diabetes mellitus	1 (0.6%)	1 (1.4%)	0.521

Note: Continuous variables are shown as median and interquartile range (first and third quartiles). Categorical data are shown as absolute frequency and percentage.

Abbreviations: BMI, body mass index; COVID-19, coronavirus disease 2019; PAPP-A, pregnancy-associated plasma protein-A; PI, pulsatility index; PlGF, placental growth factor; MoM, multiples of the median.

markers, no differences were found in PlGF levels. However, in the COVID-19 group there was a small but significant increase in UtAPI (1.08 MoM vs 1.00 MoM).

When we examined the COVID-19 group according to severity (mild or severe), no differences were observed in PlGF and UtAPI. However, women with severe COVID-19 had significantly higher BMI and MAP at the first-trimester screening.

The association between preeclampsia and COVID-19 has been studied since the beginning of the coronavirus pandemic. Some studies have hypothesized that the association between preeclampsia

and COVID-19 may be explained by the fact that both conditions share common systemic risk factors, including obesity, advanced maternal age, diabetes, or hypertension.[4,8] However, the potential association between preeclampsia and COVID-19 due to specific placental risk factors has never been examined.

Giorgione and Thilaganathan suggested that subclinical cardiovascular dysfunction in a general population may induce placental malperfusion and ischemia, so increasing preeclampsia risk.[8] Therefore, subclinical cardiovascular dysfunction due to COVID-19 may lead to acquired uteroplacental malperfusion, potentially causing preeclampsia. Despite placental malperfusion in the third trimester and abnormal placentation in the first trimester being two different entities, they both induce placental ischemia, which increases the risk of developing preeclampsia. For this reason, we agree that maternal systemic risk factors may explain in part the association between COVID-19 and preeclampsia. However, we could not confirm this hypothesis in this study.

Other studies have demonstrated a clear association between diabetes, increased BMI, and the risk of developing COVID-19.[15] Additionally, these studies showed that severe COVID-19 was associated with higher maternal age, higher BMI, hypertension, and diabetes.[16] Our results support these findings.

The findings of this study support the hypothesis that women with COVID-19 are at a higher risk for preeclampsia than the general population; however, it seems that this was due mainly to shared maternal risk factors (BMI and hypertension), as there was no significant difference in PlGF and PAPP-A levels, and the small difference in UtAPI was probably not correlated with abnormal trophoblastic invasion, as first-trimester MoM UtAPI values in our population ranged from 1.12 to 1.67 in women that subsequently developed preeclampsia, whereas MoM UtAPI values were 1.03 in women without preeclampsia.[14] Despite UtAPI MoMs being adjusted for maternal age, ethnicity, and BMI, other maternal conditions could influence their values, which could also explain this difference. Determining whether the association of preeclampsia and COVID-19 was due to shared risk factors or whether it was driven by placental predisposition is crucial to provide appropriate treatment and surveillance. Our data provide evidence that preeclampsia and COVID-19 share systemic risk factors; however, our data suggest that placental insufficiency is unlikely to be involved in the development of COVID-19 or its severity. Aspirin mechanisms of action for preeclampsia prevention involve anti-inflammatory and cardiovascular effects but mostly the improvement of trophoblastic invasion.[9] Given that the INTERCOVID study showed no benefit of aspirin treatment in reducing the risk of preeclampsia in women with COVID-19[9] and that abnormal trophoblastic invasion seems not to be related to the development or severity of COVID-19, aspirin treatment is unlikely to be effective for reducing COVID-19 risk in pregnancies at a high risk for preeclampsia in the first trimester; nevertheless, more research is needed to ascertain the role of aspirin in pregnant women with COVID-19.

The main strength of the present study is that it provides novel evidence that women with COVID-19 are at a higher risk for preeclampsia at the first trimester mainly due to maternal risk factors and that placental insufficiency is unlikely to explain this association. Another strength of this study is the large number of participants. Additionally, the first-trimester screening for preeclampsia was routinely performed; therefore, despite this being a retrospective study, maternal risk factors, MAP, PAPP-A, PlGF, and UtAPI were prospectively recorded for all patients at the time of the routine first-trimester scan.

One of the main limitations of this study is its retrospective nature. Additionally, this study may have a selection bias. On the one hand, cases in the study group with severe disease might be over-represented, as our site was a referral hospital for patients with severe COVID-19 with pneumonia in Catalonia. On the other hand, asymptomatic cases in the study cohort might also be over-represented, because a real-time polymerase chain reaction was incorporated during the pandemic as a routine test for all admitted patients.

Another limitation of the study is that the timing of infection was not analyzed because the moment of COVID-19 infection was not relevant for the aim of this study. Additionally, the general population used as the reference group cannot be considered purely a control group due to the lack of specific information about SARS-CoV-2 infection. For this reason, some asymptomatic and mild COVID-19 cases might be found in the reference group. Nevertheless, this might have reduced the chances of finding differences between groups making our findings even more meaningful.

5 | CONCLUSION

In patients with COVID-19, there was a higher proportion of women at a high risk for preeclampsia at the first-trimester screening than in the general population, mainly due to maternal risk factors, rather than placental signs of a deficient trophoblastic invasion.

Likewise, when comparing according to COVID-19 severity, the proportion of women with a high risk for preeclampsia tended to be greater among those with severe forms of COVID-19 and it was due to maternal risk factors only.

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CONFLICT OF INTEREST

MM, LM, and IGR received lecture fees from Roche Diagnostics. The other authors declare that they have no conflicts of interest.

AUTHOR CONTRIBUTIONS

BS, MM, AS, NM, and EC had full access to all of the data in the study and take full responsibility for the integrity of the data and accuracy of the data analysis. NM, MM, AS, and EC conceived and designed

the study. BS, MM, PGA, EB, IGR, PGM, NFH, ES, NM, and AS contributed to literature research. BS, MM, JG, MAA, RMLM, MR, LM, ELQ, AV, and AM contributed to data collection and confirmation. BS, MM, and NM contributed to data analysis and data interpretation. BS and MM were in charge of writing the manuscript draft. EC and AS made substantial revisions to the manuscript. All authors read and approved the final manuscript.

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REFERENCES

1. Villar J, Ariff S, Gunier RB, et al. Maternal and neonatal morbidity and mortality among pregnant women with and without COVID-19 infection. *JAMA Pediatr*. 2021;175:1-10.
2. 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*. 2020;395:809-815.
3. Di Mascio D, Khalil A, Saccone G, et al. Outcome of coronavirus spectrum infections (SARS, MERS, COVID-19) during pregnancy: a systematic review and meta-analysis. *Am J Obstet Gynecol MFM*. 2020;2:100107.
4. Papageorghiou AT, Deruelle P, Gunier RB, et al. Preeclampsia and COVID-19: results from the INTERCOVID prospective longitudinal study. *Am J Obstet Gynecol*. 2021;225:289.e1-289.e17.
5. Conde-Agudelo A, Romero R. SARS-COV-2 infection during pregnancy and risk of preeclampsia: a systematic review and meta-analysis. *Am J Obstet Gynecol*. 2022;226:68-89.e3.
6. Conde-Agudelo A, Romero R. Mechanisms that may underlie a causal association between SARS-COV-2 infection and preeclampsia. *Am J Obstet Gynecol*. 2022;226:280-281.
7. Khalil A, Samara A, Chowdhury T, O'Brien P. Does COVID-19 cause pre-eclampsia? *Ultrasound Obstet Gynecol*. 2022;59:146-152.
8. Giorgione V, Thilaganathan B. SARS-COV-2 related myocardial injury might explain the predisposition to preeclampsia with maternal SARS-COV-2 infection. *Am J Obstet Gynecol*. 2022;226:279-280.
9. Rolnik DL, Nicolaides KH, Poon LC. Prevention of preeclampsia with aspirin. *Am J Obstet Gynecol*. 2022;226:S1108-S1119.
10. Robinson HP, Fleming JE. A critical evaluation of sonar "crown-rump length" measurements. *Br J Obstet Gynaecol*. 1975;82:702-710.
11. Serra B, Mendoza M, Scazzocchio E, et al. A new model for screening for early-onset preeclampsia. *Am J Obstet Gynecol*. 2020;222:608.e1-608.e18.
12. Mendoza M, Tur H, Garcia-Manau P, et al. Cut-off values for gaussian first-trimester screening for early-onset preeclampsia with maternal history, biochemical markers and uterine artery doppler. *J Gynecol Obstet Hum Reprod*. 2021;50:101827.
13. R: The R Project for Statistical Computing. Accessed November 9, 2021. https://www.r-project.org/
14. Mendoza M, Garcia-Manau P, Arévalo S, et al. Diagnostic accuracy of first-trimester combined screening for early-onset and preterm preeclampsia at 8-10 weeks compared to 11–13 weeks gestation. *Ultrasound Obstet Gynecol*. 2021;57:84-90.
15. Jering KS, Claggett BL, Cunningham JW, et al. Clinical characteristics and outcomes of hospitalized women giving birth with and without COVID-19. *JAMA Intern Med*. 2021;181:714-717.
16. 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*. 2020;370:m3320.

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