Article

Impact of SARS-COV-2 Infection on Maternal, Obstetric and Neonatal Outcomes in a Cohort of Vaccinated Women: A Pilot Study

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María Cruz-Calvente, PhD, MsC[1], Blanca Rueda-Medina, PhD[2,3], Rocío Gil-Gutiérrez, PhD, RN[2,3,4], Irene Medina-Martínez, PhD, RN[2], José L. Gómez-Urquiza, PhD[5], and María Correa-Rodríguez, PhD[2,3]

Abstract

We aimed to investigate the impact of COVID-19 infection on maternal characteristics and obstetric and neonatal outcomes in a cohort of women in labor previously vaccinated who tested positive for SARS-CoV-2 infection, compared to aged-matched healthy controls. A retrospective case-control study was conducted among 66 women in labor. Clinical data were obtained from medical records. The attendance rates at childbirth and parenting classes, as well as the implementation of a birth plan, were significantly lower in the COVID-19 infection group (6.1% vs. 48.5%, <0.001; 6.1% vs. 33.3%, p = .005, respectively). Women with COVID-19 had a higher prevalence of prolonged postpartum hospital stay (33.3% vs. 9.1%, p = .016), and significantly higher prevalence of spontaneous preterm birth (27.3% vs. 1.09%, p = .006). Breastfeeding within the first 24 hr was also lower in women with COVID-19 (72.7% vs. 97.0%, p = .006). Maternal characteristics and neonatal outcomes are influenced by COVID-19 infection in vaccinated women. Complications include spontaneous preterm birth, prolonged postpartum hospital stay, and lack of breastfeeding within the first 24 hr. Childbirth education, parenting classes and implementing a birth plan may be associated with a decreased risk of COVID-19 infection.

Keywords

birth plan, breast feeding, COVID-19, neonatal nursing, obstetric nursing, prenatal education, SARS-CoV-2

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARSCoV-2) is an RNA virus that causes coronavirus disease 2019 (COVID-19) (Hu et al., 2021). After the virus emerged in January 2020, substantial data are now available characterizing how infection may affect pregnancy outcomes (Jamieson & Rasmussen, 2022). A systematic review study showed that the COVID-19 disease spectrum was mild in 95.6% pregnant women, severe in 3.6%, and critical in 0.8% (Juan et al., 2020). Pregnancy has been proposed as a risk factor for severe illness due to the relative state of immunosuppression and physiological cardiopulmonary changes (diaphragm elevation, increased consumption of oxygen, and respiratory tract mucosal edema) (Oakes et al., 2021).

Protocols for isolation and social distancing in pregnant women were the same as those for the general population (Knight et al., 2020). During the pandemic, certain practices such as delayed cord clamping, mother/infant skin-to-skin contact and breastfeeding have been modified (Mejía Jiménez et al., 2021; Vouga et al., 2021). However, the World Health Organization and several scientific societies, including the Centers for Disease Control and Prevention (CDC, 2023), the American College of Obstetricians and Gynecologists (ACOG), the Spanish Society of Obstetrics and Gynecology (SEGO), and the Spanish Neonatology Society (SENEO), recommend these practices in SARS-CoV-2-positive mothers because the benefits outweigh the risks. Additionally, some centers have suppressed or minimized antenatal and parenting

[1]Maternity Unit, Hospital Universitario San Cecilio, Granada, Spain
[2]Department of Nursing, Faculty of Health Sciences, University of Granada, Granada, Spain
[3]Instituto de Investigación Biosanitaria (ibs.GRANADA), Granada, Spain
[4]Sport and Health University Research Institute (iMUDS), University of Granada, Granada, Spain
[5]Department of Nursing, Ceuta Faculty of Health Sciences, University of Granada, Ceuta, Spain

Corresponding Author:
Blanca Rueda-Medina, Department of Nursing, Faculty of Health Sciences, University of Granada, Avenida de la Ilustración, 60, Granada 18016, Spain.
Email: blarume@ugr.es

education and the implementation of birth plans during pregnancy in the context of COVID-19 pandemic (Hui et al., 2021).

Previous studies have shown that having COVID-19 during pregnancy increases the risk of preterm birth (Andrikopoulou et al., 2020; Karasek et al., 2021; Smith et al., 2022; Villar et al., 2021; Vouga et al., 2021; Weinberger et al., 2022; Yao et al., 2022) and has an increased risk of maternal death and admission to intensive care units (Allotey et al., 2020). However, others report a lack of changes in preterm pregnancies due to COVID-19 (Arnaez et al., 2021; Di Toro et al., 2021), or even shorter labor length and lower incidence of postpartum haemorrhage (Libretti et al., 2023). Therefore, manifesting a contradiction in the published results that requires further investigation. Additionally, the impact of childbirth and parenting classes and implementing a birth plan on the risk of developing COVID-19 disease has not been fully investigated.

Although the maternal and perinatal impact of the COVID-19 pandemic has been examined in numerous publications, the consequences of coronavirus in pregnant women and their infants are unclear, and the published results are inconsistent in most cases (Arnaez et al., 2021; Chmielewska et al., 2021; Kotlar et al., 2021; Oakes et al., 2021). In general, women with COVID-19 are at risk for preterm birth (Karasek et al., 2021; Vouga et al., 2021), cesarean section (Gharacheh et al., 2023; Silva et al., 2023) or fetal distress (Ashraf et al., 2020; Chen et al., 2020). These complications can be attributed to viral infections as well as physiological changes that reduce a pregnant woman's tolerance for hypoxia in late pregnancy (Chen et al., 2020). However, comparing results reported by research is challenging due to fluctuations in the epidemiology of COVID-19 among pregnant populations across study periods and countries (Overton et al., 2022). It should be noted that previous studies have not distinguished between early versus late COVID-19 infection in pregnancy. Furthermore, most previous studies have not considered the vaccination status of women.

In this context, conducting a study characterising the impact of SARS-CoV-2 on obstetric, maternal, and new-born characteristics in a developed country would be a valuable addition to current literature. Thus, we aimed (i) to investigate the impact of COVID-19 infection on maternal and obstetric characteristics in a cohort of women in labor who tested positive for SARS-CoV-2 infection, previously vaccinated against SARS-CoV-2, and age-matched with healthy controls; and (ii) to analyze the impact of maternal COVID-19 infection on neonatal outcomes.

Material and Methods

Design and Participants

A retrospective case-control study was conducted among women in labor attending the Maternity Unit of a public hospital in the Andalusian region of Granada, Spain. We recruited consecutive mothers in labor who tested positive for SARS-CoV-2 infection by respiratory tract reverse transcriptase polymerase chain reaction (RT-PCR) and age-matched healthy controls who tested negative from June 2022 to December 2022. The Biomedical Research Ethics Committee of Granada (CEI/CEIM Granada; 0989-N-22) approved the pilot study.

The inclusion criteria for cases were: (i) pregnant women admitted in labor, (ii) 18 years or older, (iii) COVID-19 positive through laboratory confirmed diagnosis of COVID-19 by RT-PCR, (iv) no previous comorbidities (asthma, chronic hypertension, type 2 diabetes mellitus, autoimmune diseases, and/or type III obesity). Inclusion criteria for controls were the same except for (iii), which was replaced by testing negative for COVID-19 by RT-PCR. Controls were age-matched with cases in a 1:1 ratio.

All participants included in this study have previously received at least two doses of vaccination against SARS-CoV-2. Note that vaccination in pregnant patients has improved after the American College of Obstetricians and Gynecologists (ACOG) and Society for Maternal-Fetal Medicine (SMFM) recommended the vaccine for all pregnant and lactating patients in July 2021. All cases included in this study were asymptomatic or presented mild symptoms. In previous studies, asymptomatic infection or mild symptoms seems to be the most common presentation of COVID-19 among pregnant women admitted for delivery (Breslin et al., 2020). Therefore, focusing on these study cohorts, the total study sample consisted in a total of 66 pregnancy women, including 33 participants per group.

Data Collection

Data were obtained from medical records, including maternal characteristics such as maternal age, number of pregnancies, primigravida status, attendance at childbirth and prenatal education, and birth plan (defined as a written legal document in which pregnant women describe preferences about their care during labor and childbirth (Suárez-Cortés et al., 2015); Obstetric outcomes included start of delivery, type of delivery, epidural labor analgesia, perineal trauma, episiotomy, and prolonged postpartum hospital stay (defined as more than two midnights for vaginal births and more than three midnights for cesarean births) (Handley et al., 2022). Additionally, the following variables were extracted regarding neonatal outcomes: sex, gestational age, spontaneous preterm birth (defined according to the World Health Organisation WHO classification as a birth that occurred before 37 weeks of gestation or fewer than 259 days since first day of the female's last menstrual period (Quinn et al., 2016), birth weight, delayed cord clamping, skin to skin contact in first hour, breastfeeding within the first 24 hr, arterial pH, venous pH, Apgar score at 1 min, Apgar score in 5 min, and respiratory distress. The presence of respiratory distress was documented by healthcare providers in medical record, and its

determination was made based on any one of the following parameters: measurement of respiratory rate (normal 40–60); observation for increased work of breathing such as inspiratory sternal, intercostal, and subcostal recession/in-drawing, tracheal tug; assessment for airway noises such as expiratory grunting or inspiratory stridor; assessment for nasal flaring or head bobbing; assessment of color for cyanosis (Sweet et al., 2017). Note that during the COVID-19 pandemic, early breastfeeding and skin-to-skin contact in the delivery room (defined as occurring within the first hour after birth) were promoted in the hospital where the study took place. Additionally, all mothers with COVID-19 at hospital discharge received validated breastfeeding written recommendations (iHan, 2020).

Statistical Analyses

SPSS® Statistics version 26.0 (IBM SPSS Statistics, Chicago, IL, USA) was utilized for all analyses. Continuous variables were presented as mean and standard deviation (SD), and categorical variables as frequencies and percentages. To assess the normality of variable distributions, the Kolmogorov–Smirnov test was employed. Maternal characteristics, obstetric outcomes, and pregnancy outcomes for mother and newborn were recorded and compared between women with COVID-19 and controls using the chi-square test or Fisher's exact test for categorical variables, and the Student's *t* test or Mann–Whitney *U* test for continuous variables. *p*-values less than 0.05 were considered statistically significant.

Results

Maternal and obstetric characteristics of the study population and comparisons between women in labor with COVID-19 infection and age-matched healthy controls are presented in Table 1. Significant differences were observed in primigravida, attendance at childbirth and prenatal education, and implementation of a birth plan based on the presence of COVID-19 infection. The prevalence of attendance at prenatal education and the implementation of a birth plan was significantly lower in the COVID-19 infection group (6.1% vs. 48.5%, $p < .001$ and 6.1% vs. 33.3%; $p = .005$, respectively). Notably, the primigravida rate was significantly higher in positive COVID-19 women compared to controls (66.7% vs. 42.4%; $p = .048$).

Furthermore, women with COVID-19 had a higher prevalence of prolonged postpartum hospital stay compared to women without COVID-19 infection (33.3% vs. 9.1%; $p = .016$). Reasons for prolonged postpartum hospital stay included preeclampsia (3.0%), postpartum hemorrhage (6.1%), and infection (12.1%). For the remaining maternal and obstetric variables, no significant differences were found between groups.

Table 2 presents neonatal outcomes of women with COVID-19 infection and controls. Women with COVID-19 infection had a significantly lower gestational age (weeks) compared to controls (38.52 vs. 39.73; $p = .011$). There was also a significant difference in the prevalence of spontaneous preterm birth, with the COVID-19 infection group having a higher prevalence of prematurity compared to controls (27.3% vs. 1.09%; $p = .006$). Regarding spontaneous preterm birth, one woman (1.5%) delivered at 30 weeks of gestation, another woman (1.5%) at 34 weeks of gestation, one woman (1.5%) at 35 weeks of gestation, and seven women (15.2%) at 36 weeks of gestation.

Additionally, the prevalence of breastfeeding within the first 24 hr was significant lower in the COVID-19 infection group (72.7% vs. 97.0%; $p = .006$). For the rest of the remaining newborn outcomes, no significant differences between groups were found (Table 2).

Discussion

This pilot study provides insight into maternal characteristics and obstetric and neonatal outcomes among COVID-positive women in labor previously vaccinated compared to age-matched healthy controls. We identified a higher rate of spontaneous preterm births and a higher prevalence of maternal prolonged postpartum hospital stay in COVID-19 positive women. In addition, breastfeeding within the first 24 hr was significantly lower in women with COVID-19, and attendance to prenatal education, implementation of a birth plan, and primigravida rates were significantly lower in the COVID-19 infection group.

Previous studies have shown that pregnancy-related maternal and neonatal complications are increased in women with COVID-19 compared to those without the disease (Villar et al., 2021). SARS-CoV-2 infection may increase preterm births by raising the incidence of preeclampsia and medically indicated preterm births (Khalil et al., 2020), but its effects on spontaneous preterm births are inconclusive. In our study, spontaneous preterm birth was observed in 27.3% of cases versus 1.09% of controls. As reported by Smith et al. (2022), COVID-19 late in pregnancy increased the risk of both medically indicated preterm birth and spontaneous preterm labor compared to no COVID-19. Based on a large population-based study, Karasek et al. (2021) also concluded that COVID-19 diagnosis increased the risk of preterm birth. Similarly, a large study indicated that women with severe COVID-19 infection were at higher risk of preterm labor (Vouga et al., 2021), and a systematic review and meta-analysis support that the COVID-19 pandemic was associated with preterm labor (Yao et al., 2022). The effects of the COVID-19 pandemic on prematurity rates likely reflect the increase in preeclampsia-induced preterm births (Andrikopoulou et al., 2020) and infection-induced spontaneous preterm births (Villar et al., 2021; Weinberger et al., 2022). Nevertheless, reports on the impact of the pandemic on preterm birth remain conflicting, and earlier research has reported a lack of changes in preterm labor during COVID-19

Table 1. Maternal Characteristics and Obstetric Outcomes.

	Total (n = 66)	COVID-19 infection (n = 33)	Age-matched healthy controls (n = 33)	p value
Maternal variables				
Age (years)	32.02 ± 5.31	31.24 ± 5.76	31.79 ± 4.78	0.240
Total number of pregnancies, n (%)	2.02 (1.14)	1.97 (1.21)	2.06 (1.08)	0.749
Primigravida, n (%)	36 (54.5)	22 (66.7)	14 (42.4)	**0.048**
Childbirth and parenting education, n (%)	18 (27.3)	2 (6.1)	16 (48.5)	**<0.001**
Birth plan, n (%)	13 (19.7)	2 (6.1)	11 (33.3)	**0.005**
Obstetric variables				
Start of delivery, n (%)				
Spontaneous	42 (63.6)	18 (54.5)	24 (72.7)	0.265
Induced	20 (30.3)	13 (39.4)	7 (21.2)	
Scheduled caesarean	4 (6.1)	2 (6.1)	2 (6.1)	
Indication for induction, n (%)				
Preterm prelabor rupture of membranes	11 (16.7)	7 (30.4)	4 (17.4)	0.618
Preeclampsia	2 (3.0)	2 (8.7)	-	
Chronic hypertension	3 (4.5)	1 (4.3)	2 (8.7)	
Abruptio placentae	1 (1.5)	1 (4.3)	-	
Fetal intrauterine growth restriction	2 (3.0)	2 (8.7)	-	
Oligohydramnios	2 (3.0)	1 (4.3)	1 (4.3)	
Intrauterine fetal demise	2 (3.0)	1 (4.3)	1 (4.3)	
Type of delivery, n (%)				
Normal labor	53 (80.3)	25 (75.8)	28 (84.8)	0.527
Instrumental	4 (6.1)	3 (9.1)	1 (3.0)	
Caesarean	9 (13.6)	5 (15.2)	4 (12.1)	
Epidural labor analgesia, n (%)	52 (78.8)	27 (81.8)	25 (75.8)	0.547
Perineum, n (%)				
Intact perineum	24 (38.7)	13 (41.9)	11 (35.5)	0.602
Perineal trauma requiring suturing	38 (61.3)	18 (58.1)	20 (64.5)	
Episiotomy, n (%)	7 (10.6)	3 (9.1)	4 (12.1)	0.689
Prolonged postpartum hospital stay, n (%)	14 (21.2)	11 (33.3)	3 (9.1)	**0.016**
Preeclampsia	2 (3.0)	2 (14.3)	-	
Postpartum haemorrhage	4 (6.1)	3 (21.4)	1 (7.1)	
Infection	8 (12.1)	6 (42.9)	2 (14.3)	

Note. Data are expressed as frequencies and percentages and as mean and standard deviation (SD).
Bold values mean p value less than 0.05.

(Arnaez et al., 2021; Di Toro et al., 2021), or even a reduction in preterm birth rates (Delius et al., 2023) or improvement of maternal outcomes such as shorter labor length and a lower incidence of postpartum hemorrhage (Libretti et al., 2023). Conflicting results may be related to the diversity in gestational ages and the contributing etiologic factors for preterm labor in the studied population. It is important to highlight that in our study, only women who were with mild symptoms or asymptomatic were included. Therefore, the results obtained, together with the findings of previous research, suggest that pregnant women with COVID-19 may have an increased risk of spontaneous preterm birth regardless of the severity of the disease.

On the other hand, we found a higher prevalence of maternal prolonged postpartum hospital stay in women with COVID-19 compared to controls. This result is especially relevant since all pregnant women with COVID infection included in this study were asymptomatic or presented mild symptoms and had received at least two doses of vaccination against SARS-CoV-2. Early reports indicated that a short postpartum hospitalization length of stay was significantly more common during the COVID-19 pandemic for obstetric patients (Handley et al., 2022). However, the fluctuating epidemiology of COVID-19 in the pregnant population across different periods and countries, along with variations in COVID-19 vaccination rates between countries, make it difficult to compare the results with previous studies.

SARS-CoV-2 can be found infrequently in the breast milk after recent infection, and current evidence supports that breast milk is not a source of transmission of SARS-CoV-2 (Krogstad et al., 2022). Therefore, breastfeeding does not represent a risk factor for transmission of infection to infants,

Table 2. Newborn Characteristics of the Study Population.

	Total	COVID-19 infection	Non-COVID-19 infection	
	(*n* = 66)	(*n* = 33)	(*n* = 33)	*p*-value
Newborn variables				
Sex (male), *n* (%)	40 (60.6)	21 (63.6)	19 (57.6)	0.614
Gestational age (weeks)	39.12 (1.94)	38.52 (2.39)	39.73 (1.09)	**0.011**
Spontaneous preterm birth, *n* (%)	10 (15.2)	9 (27.3)	1 (3.0)	**0.006**
Weight at birth (g)	3279.81 (549.33)	3190.26 (653.43)	3363.94 (422.77)	0.216
Delayed cord clamping, *n* (%)	49 (74.2)	23 (69.7)	26 (78.8)	0.398
Skin to skin contact in 1st hour, *n* (%)	58 (87.9)	27 (81.8)	31 (93.9)	0.131
Breastfeeding within the first 24 h, *n* (%)	56 (84.8)	24 (72.7)	32 (97.0)	**0.006**
Arterial pH	6.93 (1.36)	6.66 (1.92)	7.20 (0.10)	0.161
Venous pH	7.01 (1.39)	6.70 (2.01)	7.29 (0.08)	0.158
Apgar in 1 min	8.02 (2.18)	7.11 (3.02)	8.53 (1.31)	0.073
Apgar in 5 min	9.12 (2.13)	8.17 (3.24)	9.66 (0.78)	0.071
Respiratory distress, *n* (%)	8 (12.1)	4 (12.1)	4 (12.1)	1

Note. Continuous variables were expressed as mean values (standard deviations) and category variables as frequency (percentage).
Bold values mean *p* value less than 0.05.

and breastfeeding mothers with confirmed COVID-19 (regardless of vaccination status) should continue breastfeeding while taking hygiene precautions (CDC, 2023; Sánchez-Luna et al., 2021). Despite this evidence, we identified that the prevalence of breastfeeding within the first 24 hours was significantly lower in women with COVID-19 infection compared to controls. This finding is relevant relevant since all mothers with COVID-19 at hospital discharge received written recommendations for breastfeeding (iHan, 2020). However, we can hypothesize that fear among women, probably due to the poor health professional explanations and the absence of clear, quality, and accessible information on the internet and other media, may have contributed to the decreased rates of breastfeeding within the first 24 hr in COVID-positive women.

Unexpectedly, we also found that the prevalence of primigravida was significantly higher in positive COVID-19 women compared with age-matched healthy controls. A previous study indicated that primigravida was not associated with severe maternal outcomes among positive pregnant women (Vouga et al., 2021) whereas Trovato-Gomez et al. reported that primigravida decreased the risk of severe COVID-19 (Gomez et al., 2022). These inconclusive findings might be due to differences in gestational age and the severity of the diseases, since in the study of Vouga et al., all pregnant women were tested for SARS-CoV-2 infection at any stage of gestation (Vouga et al., 2021). Further studies are needed to evaluate the potential effect of primigravida on COVID-19 infection in pregnant women.

The WHO emphasizes that all women have the right to a safe and positive childbirth experience, regardless of whether they have a confirmed COVID-19 infection (Coronavirus Disease (COVID-19), s. f.). This includes all prenatal, intrapartum, postpartum maternal and neonatal care services (Zhu et al., 2020). However, due to the potential risk of infection during processes such as a pandemic, pregnant women may face a dilemma regarding seeking professional prenatal services (Wu et al., 2020). Interestingly, in this pilot study, we identified that the prevalence of attendance at childbirth and prenatal education, as well as the implementation of a birth plan during pregnancy, were significantly lower in women in labor with COVID-19 infection. Typically, in the Spanish National Health System, childbirth and parenting education courses commence around the 18th week of gestation and conclude by the 32nd week, usually spanning a total of six sessions. Since only one woman delivered prematurely at 30 weeks of gestation and was unable to complete all the sessions, the data do not suggest that attendance at childbirth classes is affected by spontaneous preterm birth, and consequently, it may not influence COVID-19 infection. The lack of prenatal education, which should include safe practices to avoid infection specific to COVID-19 since the pandemic began (Uludağ et al., 2022), could potentially lead pregnant women to engage in risky practices resulting in COVID-19 infection, as supported by our findings and also previous data that has reported that pregnant women who received adequate health education on COVID-19, including its prevention and transmission, are more compliant with the measures established by authorities (Dogan and Ozdemir, 2021), ultimately leading to a lower risk of contracting the disease. The preliminary results of this pilot study support the need for prenatal education as a tool to decrease the risk of infectious diseases such as COVID-19 and emphasize the importance of supporting pregnant women through the prenatal, perinatal, and postnatal care continuum (Villar et al., 2021).

This pilot study has limitations that should be addressed. Firstly, it was conducted in a well-characterized cohort of pregnant women admitted for delivery who were

asymptomatic or had mild symptoms of the disease, and women with severe symptoms were not included. However, it has been reported that COVID-19 disease spectrum was mild in 95.6% pregnant women, severe in 3.6%, and critical in 0.8% (Juan et al., 2020). Secondly, since we only included European Caucasian patients, these findings cannot be generalized to other ethnicities. Thus, the impact of COVID-19 infection on maternal and neonatal complications in different ethnicities and races require further investigation. Due to the limited sample size, we cannot rule out the possibility that our pilot study may have been underpowered to detect significant changes in some variables, and therefore, larger studies across other geographic areas might be helpful to validate these findings. Any generalization of the results should be done cautiously, as in this study, we included women in labor who were currently positive, while previous studies comprised cohorts of women who were infected by COVID-19 in any trimester of gestation. We cannot dismiss the potential impact of the gestational age at the time of COVID-19 infection on obstetrical and neonatal outcomes, and caution should be exercise with pregnant women infected in early pregnancy. Finally, a potential limitation of this research is the inclusion of certain confounding variables such as socioeconomic status, educational level, the presence of previous COVID-19 infections, and patients with school-age children would be of interest. Unfortunately, this information was not available. Since this is a pilot study, it would be beneficial for future works to consider the inclusion of this information. Despite its limitations, it should be highlighted that this single-center study was conducted under harmonized study and management protocols, including routine systematic screening for COVID-19 infection among women in labor independently of compatible symptoms. Other previous studies only tested symptomatic pregnant women, which could have led to a selection bias for more severe symptomatic COVID-19 cases.

Regarding the implications for research and clinical practice, the information provided in this pilot study will allow more nuanced recommendations to health professionals (obstetricians, pediatricians, midwifes, nurses) and mothers concerning the prevention of COVID-19 infection, which is a key factor influencing adverse outcomes. During any emergency or future health crisis, it is essential to have standardized protocols for the management of pregnancy, labor and postpartum in the face of infectious diseases such as COVID-19. Although health professionals made important efforts to disseminate evidence-based information on pregnant women during the pandemic period, there is a need to prioritize safe, accessible, and equitable maternity care within the strategic response to this pandemic and in future health crises.

Conclusion

In conclusion, maternal characteristics and neonatal outcomes appear to be influenced by COVID-19 infection in women in labor. Complications include spontaneous preterm birth, prolonged postpartum hospital stay for mothers, and lack of breastfeeding within the first 24 hr. Prenatal education and the implementation a birth plan may be associated with a decreased risk of COVID-19 infection. Further studies are needed to assess maternal and neonatal outcomes for cases of earlier exposure.

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Declaration of Conflicting Interests

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Ethics Statement

Ethical Approval

Local ethics committee (Biomedical Ethics Committee of Granada CEI/CEIM GRANADA, reference 0989-N-22) approved the study protocol, which was conducted in agreement with the Declaration of Helsinki.

ORCID iDs

Blanca Rueda-Medina https://orcid.org/0000-0002-0263-7000
Maria Correa-Rodriguez https://orcid.org/0000-0001-9165-4349

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