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COVID-19-Positive Pregnant Women: Maternal and Newborn Outcomes

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ABSTRACT

Background: Because the maternal immune system is suppressed during pregnancy, pregnant women are a risk group for COVID-19 infection. Thus, this study investigates the pregnancy outcomes of COVID-19-infected women during childbirth.

Methods: A retrospective study was performed at the Department of Obstetrics and Gynecology, University Hospital Mostar, that included a total of 65 COVID-19-positive women who delivered between March 2020 and April 2022. The control group consisted of COVID-19-negative women with no detected SARS-CoV-2 infection during pregnancy or labor (n=65). The data for maternal and newborn outcomes were collected from database and medical records.

Main findings: The pregnancies of COVID-19-positive women were more often completed by cesarean section (35.4%), compared to the control group (26.2%). There were no significant differences in pregnancy complications such as preterm birth, preeclampsia, gestational hypertension, preterm premature rupture of membranes, fetal growth restriction or perinatal asphyxia between the COVID-19-positive mothers and the control group. The percentage of infected newborns was 4.6% in the COVID-19-positive group.

Principal conclusion: The study concludes that COVID-19-positive women experienced more adverse perinatal outcomes compared to the control group, but without statistical significance. Accordingly, the importance of perinatal surveillance of COVID-19-positive pregnancies should be emphasized.

Key words: childbirth, maternal and newborn outcomes, COVID-19 infection.

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (1). The majority of patients with severe clinical presentation are elderly people and those with comorbidities and weakened immune systems as well as pregnant women (2). As the COVID-19 epidemic spread, more pregnant women became infected with SARS-CoV-2, with concerns about its clinical manifestations in pregnancy and the potential risk of obstetric complications (3). The COVID-19 pandemic affects reproductive and perinatal health directly through the infection itself, but also indirectly as a result of changes in health care, social policy or social and economic circumstances (4).

Pregnant women have a higher risk of severe illness caused by influenza viruses and other respiratory infections due to cardiopulmonary adaptive changes, such as increased heart rate and stroke volume and decreased pulmonary residual capacity, that occur during pregnancy and may raise the risk of hypoxemia and contribute to heightened severity. Therefore, there is a concern that COVID-19 in pregnant women may be associated with a higher maternal mortality and morbidity compared to the general population (5). According to Villar et al., pregnant women diagnosed with COVID-19 have a higher risk of developing preeclampsia/eclampsia, as well as hemolysis, elevated liver enzymes and thrombocytopenia (HELLP) syndrome, in addition to gestational hypertension, thrombophilia, premature birth and premature rupture of membranes (6).

Based on the studies conducted so far, higher perinatal morbidity is recorded in pregnancies complicated with COVID-19 infection such as fetal growth retardation (FGR), perinatal asphyxia, a reduced Apgar score, lower birth weight and respiratory disorders (7, 5). Research conducted by Alberca et al. has confirmed that FGR could be a long-term complication in pregnant women recovering from coronavirus infection, therefore the growth of the fetus should be closely monitored (8).

When COVID-19 infection is confirmed in pregnant women, childbirth is also complicated due to the need to implement epidemiological measures to protect health workers and other women in labor from infection.

The aim of the research was to analyze and determine the perinatal outcome in COVID-19-positive mothers. The hypothesis of this paper is that COVID-19-positive mothers and their newborns have an increased risk of adverse perinatal outcomes.

PARTICIPANTS AND METHODS

Participants

The research included COVID-19-positive mothers (n= 65) who gave birth from March 17, 2020, to April 3, 2022, at the Department for Gynecology and Obstetrics, University Hospital Mostar, and their neonates. COVID-19 positivity was confirmed by polymerase chain reaction (PCR) testing.

The control group included mothers with a COVID-19-negative status at the time of delivery and with no detected COVID-19 infection during pregnancy. To select the members of the control group, each respondent from the observed group (COVID-19-positive women) was assigned the first woman who was subsequently entered the birth protocol. The inclusion criterion was COVID-19-positive status for the observed group. The exclusion criteria were multiple pregnancy and unknown COVID-19 status.

Methods

Data were obtained from database and medical records, maternal and newborn protocols and the medical histories of mothers and their newborns and retrospectively analyzed for maternal age, parity, gestational age, mode of delivery (vaginal delivery without and with episiotomy, cesarean section, vacuum extraction) and risk factors for COVID-19 infection: body mass index (BMI), type 1 or 2 diabetes mellitus (DM), chronic hypertension,

systemic/autoimmune disease, smoking and medications. Maternal complications and birth outcomes were also investigated: frequency of premature birth, preeclampsia, gestational hypertension, HELLP syndrome, thrombophilia, premature rupture of membranes and transfer of the mother to the COVID-19 ward due to the need for oxygen therapy and mechanical ventilation. Neonatal outcomes that were analyzed included FGR, the Apgar score, perinatal asphyxia, respiratory disorder of the newborn (apnea, respiratory distress syndrome [RDS] or apnea plus RDS), the need for mechanical ventilation, sepsis, fetal death and the newborn's COVID-19 status. The following sociodemographic features of the respondents have been analyzed and presented: place of residence (village, city), employment and partner status (married, single or divorced).

To confirm SARS-CoV-2 infection, swabs of the nasopharynx and oropharynx in the upper respiratory tract were taken. Both swabs were placed together in a liquid medium so that the top parts of the swabs were completely immersed in the liquid. Plastic sticks with synthetic fibers such as nylon were used for swabbing. The pregnant women were mostly positive two or three days before delivery, and the infection interval was within 10 days before delivery.

Statistical analysis

Data were collected in an MS Excel database (version 11, Microsoft Corporation, Redmond, WA, USA), and the SPSS 20.0 statistical program (IBM Corp., Armonk, NY, USA) was used for statistical analysis. The chi-square test, Fisher's exact test and Student's t-test for independent samples were used to test statistical significance. A probability level of $p<0.05$ was taken as statistically significant.

RESULTS

Table 1 shows the sociodemographic characteristics and the presence of comorbidities in the investigated groups.

Table 1. Sociodemographic characteristics and the presence of comorbidities in the group of COVID-19-positive mothers and the control group

	Groups				χ^2	p
	COVID-		COVID+			
	n	%	n	%		
Place of residence					0.293	0.589*
Village	42	64.6	38	58.5		
City	23	35.4	27	41.5		
Employment					1.108	0.293*
No	29	44.6	36	55.4		
Yes	36	55.4	29	44.6		
Comorbidities					3.845	0.427
No	50	76.9	51	78.5		
DM	1	1.5	0	0.0		
Chronic hypertension	0	0.0	1	1.5		
Systemic autoimmune disease	9	13.8	5	7.7		
Medicines	5	7.7	8	12.3		
Smoking					1.612	0.204
No	59	90.8	53	81.5		
Yes	6	9.2	12	18.5		

*Fisher's exact test

Respondents from both groups are mostly from rural areas. SARS-CoV-2-positive women are mostly unemployed and a large percentage consume tobacco products, but there was no statistically significant difference between the variables (Table 1).

Table 2. Clinical characteristics of the COVID-19-positive mothers and controls

	Groups				t	p
	COVID-		COVID+			
	$\bar{X}$	SD	$\bar{X}$	SD		
Age	31.78	4.788	32.02	4.735	0.276	0.783
Parity	2.02	1.02	2.06	1.044	0.255	0.799
BMI	29.18	6.526	28.92	4.577	0.265	0.792

There was no statistically significant difference comparing age, parity and BMI between the

COVID-19-positive mothers and the control group (Table 2).

Table 3. Complications of pregnancy and childbirth in the COVID-19-positive group and the control group

	Groups				χ^2	p
	COVID-		COVID+			
	n	%	n	%		
Mode of delivery					2.466	0.481
Cesarean section	17	26.2	23	35.4		
Vaginal without episiotomy	31	47.7	27	41.5		
Vaginal with episiotomy	17	26.2	14	21.5		
Vacuum extraction	0	0.0	1	1.5		
Premature birth					0	1*
No	58	89.2	57	87.7		
Yes	7	10.8	8	12.3		
Mechanical ventilation					0.508	0.476
No	65	100.0	63	96.9		
Yes	0	0.0	2	3.1		
Preeclampsia					0	1*
No	63	97.0	63	97.0		
Yes	2	3.1	2	3.1		
Gestational hypertension					0.604	0.437
No	60	92.3	63	96.9		
Yes	5	7.7	2	3.1		
Preterm premature rupture of membrane					3.226	0.072*
No	43	66.2	53	81.5		
Yes	22	33.9	12	18.5		
FGR					1.365	0.243
No	65	100.0	62	95.4		
Yes	0	0.0	3	4.6		
Transfer of the mother to the COVID-19 ward					4.127	0.127
No	65	100.0	61	93.8		
Oxygen therapy	0	0.0	2	3.1		
Mechanical ventilation	0	0.0	2	3.1		

*Fisher's exact test

Table 3 shows the complications of pregnancy and childbirth among the investigated groups. Cesarean delivery was more frequent in the COVID-19-positive group compared to the control group, but without statistical significance. While preeclampsia was equally common in both groups, gestational hypertension occurred more often in the control group, but not to a statistically significant level. The percentage of preterm births among COVID-19-positive mothers was similar to the control group. Preterm premature rupture of membranes occurs more often in COVID-19-negative mothers. Fetal growth restriction (FGR) was more frequent in COVID-19-positive group. In addition, perinatal asphyxia was also more common in newborns of COVID-19-positive mothers. The percentage of respiratory disorders and mechanical ventilation of newborns was equal in both groups.

Table 4 shows differences in the neonatal outcomes between the COVID-19-positive and control groups. Three newborns from the COVID-19-positive group were also COVID-19-positive. There were no differences in the Apgar score, perinatal asphyxia, mechanical ventilation, neonatal death, newborn weight or respiratory disorders in the investigated groups.

DISCUSSION

Our study investigated the perinatal outcomes of COVID-19-positive pregnant women, shedding light on both maternal and newborn outcomes.

According to the available literature, SARS-CoV-2-positive mothers tend to be mostly asymptomatic or experience mild forms of the disease (9). The results from our research are in line with this data. The majority of SARS-CoV-2-positive mothers exhibited mild symptoms or were asymptomatic. Interestingly, two cases required mechanical ventilation post-cesarean section, consistent with broader research indicating that symptomatic cases among pregnant women typically manifest mild to moderate cold/flu-like symptoms, while in

pregnant women with a severe form of infection, the most common symptoms were dyspnea and fever (10).

Table 4. Differences in neonatal outcomes between COVID-19-positive group and controls

	Groups				χ^2	p
	COVID-		COVID+			
	n	%	n	%		
Apgar score					0	1
0-3	2	3.1	2	3.1		
4-7	2	3.1	2	3.1		
8-10	61	93.8	61	93.8		
Perinatal asphyxia					0.397	0.529
No	61	93.8	58	89.2		
Yes	4	6.2	7	10.8		
Respiratory disorders of the newborn					0	1*
No	60	92.3	60	92.3		
Yes	5	7.7	5	7.7		
Mechanical ventilation of newborns					0	1*
No	63	96.9	63	96.9		
Yes	2	3.1	2	3.1		
Neonatal death					***	***
No	65	100.0	65	100.0		
Yes	0	0.0	0	0.0		
COVID-19 status of the newborn					1.365	0.243
Negative	65	100.0	62	95.4		
Positive	0	0.0	3	4.6		
Birth weight					0.862	0.835
< 1000 g	0	0.0	0	0.0		
1001-1500 g	1	1.5	2	3.1		
1501-2500 g	4	6.2	5	7.7		
2501-3500 g	36	55.4	38	58.5		
3501-4000 g	24	36.9	20	30.8		

*Fisher's exact test

Contrary to expectations, COVID-19-negative mothers presented slightly more comorbidities including type 1 and type 2 diabetes mellitus and systemic autoimmune disease. Chronic hypertension and drug therapy were more common in COVID-19-positive subjects, though without statistical significance. In both groups, the most common comorbidities were autoimmune systemic diseases, mainly Hashimoto's thyroiditis. According to research by Ng et al., it was determined that hypertension, obesity and diabetes are the most common comorbidities in patients with COVID-19, which is inconsistent with this study. The average body mass index (BMI) was higher in the group of COVID-19-negative mothers, and diabetes mellitus was a more common comorbidity in the COVID-19-negative mothers (12). The explanation for this result could be the relatively small sample size, as well as the absence of significant comorbid conditions, so that a small number of pregnant women developed a more severe or critical form of the COVID-19 disease.

COVID-19-positive parturients in our investigation were more likely to consume tobacco products, mirroring previous research linking smoking during pregnancy to complications such as premature birth, reduced birth weight and perinatal asphyxia. Smoking during pregnancy increases the rate of complications, such as miscarriage, premature birth, fetal growth restriction and congenital anomalies (11). In an epidemiological study by Haddad et al., a higher prevalence of consumption of tobacco products among patients infected with coronavirus was described. In addition, research shows that people with respiratory diseases caused by smoking have a higher risk of developing severe symptoms of COVID-19. Pathophysiologically, this can be explained by a decrease in the immune response of the mucous membrane and the proliferation of the basal stem cells of the airways (13).

The mode of delivery was mostly vaginal birth in both groups, with cesarean sections being more common in the COVID-19-positive group but not statistically significant. This aligns with recommendations emphasizing that the method of delivery should be individualized, considering the severity of the disease and obstetric indications. Cesarean delivery is associated with increased morbidity in the period immediately after delivery due to increased risks of thromboembolic diseases, infections and blood loss (14). The mode of delivery should continue to be individualized

and based on routine obstetric indications. In general, the management of labor has not changed during the COVID-19 pandemic or in pregnant women with confirmed infection (15). The result of our study is in correlation with these recommendations.

Complications, such as intrauterine growth restriction (IUGR), mechanical ventilation, perinatal asphyxia and respiratory disorders, were more prevalent in the COVID-19-positive group, which is consistent with previous research (3, 19). Intensive surveillance of IUGR in SARS-CoV-2-infected women was recommended, highlighting the need for close monitoring during pregnancy (19). Gestational hypertension and preeclampsia were more common in the control group. This is not in line with previous studies, and is probably due to the small sample size (17, 18).

The Apgar scores of newborns did not differ between the COVID-19-positive and -negative groups. This contrasts with some previous studies, indicating the complexity of the relationship between maternal COVID-19 status and neonatal outcomes (23).

Most of the newborns had an average birth weight (2501-3500 g), but more newborns of COVID-19-positive mothers had a lower birth weight, which is consistent with research conducted by Parums et al. (20).

There were no neonatal deaths in this investigation because the women in labor were infected with COVID-19 within approximately 10 days of delivery. The study identified three newborns from the COVID-19-positive group who tested positive for SARS-CoV-2, indicating the possibility of vertical transmission. However, further work is needed to fully understand the extent of the risk. Research by Mazur-Bialy et al. shows that the incidence of negative outcomes increases proportionally with the severity of the symptoms of COVID-19 (10).

A key limitation of our study is the relatively small sample size, potentially limiting the generalizability of results. A larger cohort would enhance the significance of observed differences. Additionally, tracking the long-term effects on newborns of COVID-19-positive mothers would provide valuable insights into the lasting impacts of maternal infection during pregnancy.

CONCLUSION

The results of our research showed that COVID-19-positive pregnant women and their newborns have an increased risk of adverse perinatal outcome such as premature birth, IUGR and transfer of the mother to the COVID-19 ward. This aligns with the existing literature and highlights critical considerations for clinicians managing the pregnancies of COVID-19-positive mothers. Newborns born to COVID-19-positive mothers exhibited lower birth weights and a higher incidence of perinatal asphyxia compared to those born to COVID-19-negative mothers. These outcomes, while not statistically significant in our study, emphasize the importance of vigilance and tailored care for pregnant individuals infected with the virus.

The absence of statistical significance in our overall results is attributed to the small sample size. A larger sample would likely enhance the statistical power and elucidate the true impact of COVID-19 on perinatal outcomes.

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CONFLICT OF INTEREST
None to declare.

AUTHORS' CONTRIBUTIONS

IG: contribution to study conception and design, acquisition of data, literature review, writing the paper; VT: supervision, contribution to study conception and design, literature review, critical revision of the paper, assistance in writing the paper; MOV: contribution to study conception and design, literature review, critical revision of the paper, assistance in writing the paper; DMG: assistance in writing the paper.

ETHICAL BACKGROUND

Institutional review board statement: The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee.

Informed consent statement: Informed consent was obtained from all subjects involved in the study.

Data availability statement: We deny any restrictions on the availability of data, materials and associated protocols. Derived data supporting the findings of this study are available from the corresponding author on request.

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