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Original Article

Maternal and Neonatal Outcomes Associated With COVID-19 Infection: A Case-Control Study

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Abstract

Background and aims: Pregnant women are a high-risk group requiring special attention during the COVID-19 pandemic. This study aimed to compare maternal and neonatal outcomes between pregnant women with and without COVID-19.

Methods: A total of 210 hospitalized pregnant women and their newborns were evaluated at Hajar hospital, Shahrekord, Iran, between July 16, 2022, and March 20, 2023. The case group included 70 women with confirmed COVID-19, while the control group consisted of 140 COVID-negative women matched by age and parity. Data on maternal history, pregnancy complications, and neonatal outcomes were extracted and analyzed using t-tests, Chi-square, and Fisher's exact tests in SPSS 22 ($P<0.05$).

Results: Adverse maternal outcomes were significantly more common in the case group, including preeclampsia ($P=0.03$), preterm labor ($P=0.002$), fetal distress ($P=0.01$), reduced fetal movements ($P=0.01$), and cesarean delivery ($P<0.001$). Neonates born to infected mothers had lower birth weight (2881 ± 314 g vs. 3088 ± 384 g, $P<0.001$) and higher rates of respiratory distress (18.6% vs. 2.9%, $P<0.001$), neonatal intensive care unit admission (15.7% vs. 2.9%, $P=0.001$), gastrointestinal issues (8.6% vs. 0%, $P=0.001$), feeding problems (14.3% vs. 4.3%, $P=0.01$), neonatal fever (17.1% vs. 0%, $P<0.001$), and positive polymerase chain reaction (17.1% vs. 0%, $P<0.001$). Eventually, the non-reactive non-stress test was more prevalent in the case group (18.6%, $P<0.001$).

Conclusion: COVID-19 infection during pregnancy was associated with increased maternal and neonatal complications, highlighting the need for enhanced monitoring and care.

Keywords: Pregnancy, Neonatal, Outcomes, Maternal, COVID-19

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Introduction

COVID-19 has emerged as a significant global health threat, causing severe respiratory illness and increased mortality worldwide.[1] Its rapid spread has placed immense pressure on healthcare systems, with morbidity and mortality rates varying across countries depending on epidemiological factors.[2] Among high-risk groups, pregnant women are particularly vulnerable. According to the Centers for Disease Control and Prevention, 6.6% of COVID-19 cases occurred in pregnant individuals.[3] Pregnancy involves physiological and immunological adaptations (e.g., increased oxygen consumption, reduced lung capacity, and immune modulation) that heighten susceptibility to respiratory infections, including COVID-19.[4-6] These changes may increase the risk of severe complications compared to non-pregnant women. Furthermore, the potential for vertical transmission raises concerns regarding fetal and neonatal health, as observed in previous viral epidemics, such as Zika and Ebola.[6]

Although pneumonia is a known contributor to maternal morbidity and mortality during infectious disease outbreaks, data on the specific effects of COVID-19 in pregnancy remain limited.[7] Recent studies suggest that maternal infection may be associated with fetal distress, hypoxia, placental abnormalities, and the need for intensive care.[8] Despite many cases being mild, a substantial proportion of pregnant women with COVID-19 require hospitalization, posing additional strain on healthcare systems.

Given these risks, collecting data on clinical manifestations and pregnancy outcomes in infected versus non-infected women is essential for informing clinical decision-making and managing complications.[9] Accordingly, the present study aims to compare the clinical, paraclinical, and pregnancy outcomes in pregnant women with and without COVID-19 infection.

Materials and Methods

This case-control study was conducted to evaluate maternal and neonatal outcomes between pregnant women diagnosed with COVID-19 and those without COVID-19. The study was conducted at Hajar Hospital, affiliated with Shahrekord University of Medical Sciences, and included all hospitalized pregnant women and their newborns.

The case group comprised all pregnant women diagnosed with COVID-19 during the study period, totaling 70 individuals. The control group included 140 asymptomatic pregnant women or women with negative COVID-19 test results who had been hospitalized during the same period. Both groups were matched in a 2:1 ratio based on age, the number of previous pregnancies, and other predefined criteria to minimize potential confounding factors.

Inclusion Criteria

Pregnant women with a live fetus confirmed by ultrasonography at the time of hospitalization were included in the study.

Exclusion Criteria

Women whose medical records were incomplete, those whose records could not be accessed, or those who contracted COVID-19 during hospitalization were excluded from the investigation.

Study Design and Data Collection

The data were collected from the medical records of all pregnant women admitted to Hajar Hospital between July 16, 2022, and March 20, 2023, based on their hospitalization dates. This hospital has served as the primary center for pregnant women infected with COVID-19 from the onset of the epidemic in Iran (February 19, 2020). The medical records of patients diagnosed with or suspected of having COVID-19 were reviewed.

Collected Variables

The collected and recorded data included maternal demographic information (age, education level, and employment status) and medical and obstetric history (pregnancy history, including gestational age at hospitalization, history of previous pregnancies, recurrent miscarriages, stillbirths, cesarean deliveries, and preterm births). They also included COVID-19 infection status (confirmation of infection and the presence of clinical symptoms) and pregnancy (gestational diabetes, hypertension, preeclampsia, preterm labor, fetal distress, cesarean section, and other maternal complications) and neonatal (birth weight, Apgar score, neonatal respiratory distress, feeding disorders, and neonatal infections) outcomes.

Data Management and Statistical Analysis

The data were extracted from medical records and recorded using a checklist developed by the researchers. They were then summarized using frequencies and percentages for qualitative variables, as well as means ± standard deviations for quantitative variables. Differences between the case and control groups were analyzed using the independent t-test for normally distributed variables. For categorical variables, Fisher's exact test or the chi-square test was employed, as appropriate. Statistical significance was defined as $P < 0.05$ for all tests. Finally, SPSS (version 22) was used for data analysis.

Results

Based on the results (Table 1), the mean age of pregnant women in the case and control groups was 30.76 ± 6.17 years and 31.13 ± 6.01 years, respectively; nonetheless, this difference was not statistically significant ($P = 0.672$). Most participants in both groups were housewives and had non-academic education levels. There were no statistically significant differences between the groups regarding education ($P = 0.404$) and employment status ($P = 0.390$).

The mean gestational age in the case group was 38.47 ± 1.21 weeks, which was significantly lower than that in the control group (39.09 ± 0.93 weeks, $P < 0.001$). Although the proportions of primiparous and multiparous women differed slightly between groups, this difference was not statistically significant ($P = 0.111$). Additionally, no significant differences were found between the groups regarding history of miscarriage ($P = 0.321$), stillbirth ($P = 0.443$), preterm labor ($P = 0.348$), cesarean section ($P = 0.105$), low birth weight infants ($P = 0.441$), infertility ($P = 0.253$), or the use of assisted reproductive methods ($P = 0.316$).

Concerning pre-pregnancy illnesses, both groups were comparable in terms of heart disease, pulmonary disease, thyroid disorders, diabetes, anemia, embolism, and coagulation disorders ($P > 0.05$). However, the prevalence of asthma was significantly higher in the case group (10%) compared to the control group (0.7%) ($P = 0.002$), the details of which are provided in Table 1.

Comparison Between the Case and Control Groups

"Case" referred to pregnant women diagnosed with COVID-19, while "Control" referred to asymptomatic pregnant women who tested negative for COVID-19.

The findings (Table 2) revealed that the most frequently reported symptoms among pregnant women with COVID-19 were muscle pain (74.3%), followed by fever, fatigue, and malaise (each reported by 67.1% of patients). Gastrointestinal symptoms and cough were also relatively common (64.3%), while sore throat was observed in 52.9% of cases. Less frequent symptoms included dyspnea (22.1%) and bleeding from the mouth or nose (10%).

Regarding treatment, the vast majority of patients (97.1%) received antibiotics, 74.3% required oxygen therapy, and 60% were administered antiviral medications. Chest X-rays and CT scans were performed in a limited number of cases (10% and 7.1%, respectively). A small

Table 1. Demographic and Obstetric Characteristics of the Case and Control Groups

Variable	Case Group (n = 70)	Control Group (n = 140)	*P* Value
Age (y)	30.76 ± 6.17	31.13 ± 6.01	0.672
Education			
Non-academic	36 (51.4%)	68 (48.6%)	0.404
Academic	34 (48.6%)	72 (51.4%)	
Employment status			
Housewife	55 (78.6%)	106 (75.7%)	0.390
Employed	15 (21.4%)	34 (24.3%)	
Gestational age (wk)	38.47 ± 1.21	39.09 ± 0.93	< 0.001
Primiparous	40 (57.1%)	66 (47.1%)	0.111
Multiparous	30 (42.9%)	74 (52.9%)	
History of miscarriage	7 (10.0%)	10 (7.1%)	0.321
History of stillbirth	0 (0.0%)	2 (1.4%)	0.443
History of preterm labor	4 (5.7%)	5 (3.6%)	0.348
History of cesarean section	8 (11.4%)	27 (19.3%)	0.105
History of low-birth-weight infant	4 (5.7%)	6 (4.3%)	0.441
History of infertility	3 (4.3%)	11 (7.9%)	0.253
Use of assisted reproductive methods	3 (4.3%)	10 (7.1%)	0.316
Pre-pregnancy illness			
Heart disease	3 (4.3%)	6 (4.3%)	0.652
Pulmonary disease	13 (18.6%)	16 (11.4%)	0.116
Hypothyroidism	16 (22.9%)	21 (15.0%)	0.113
Hyperthyroidism	2 (2.9%)	4 (2.9%)	0.682
Diabetes	5 (7.1%)	6 (4.3%)	0.285
Asthma	7 (10.0%)	1 (0.7%)	0.002
Anemia	8 (11.4%)	18 (12.9%)	0.478
Embolism	3 (4.3%)	4 (2.9%)	0.429
Coagulation disorders	1 (1.4%)	4 (2.9%)	0.459

proportion of patients required critical interventions, including mechanical ventilation (1.4%), resuscitation (5.7%), and intubation (1.4%), the related data of which are presented in Table 2.

Based on the results (Table 3), no statistically significant differences were found between the case and control groups in terms of gestational diabetes, hypertension, or stillbirth ($P > 0.05$). However, pregnant women infected with COVID-19 experienced a significantly higher incidence of preeclampsia (10% vs. 2.9%, $P = 0.035$), preterm labor (21.4% vs. 6.4%, $P = 0.002$), fetal distress (17.1% vs. 6.4%, $P = 0.016$), maternal perception of reduced fetal movements (15.7% vs. 5.7%, $P = 0.019$), and cesarean delivery (18.6% vs. 5%, $P < 0.001$).

Postpartum complications were also more prevalent among women in the case group. Specifically, the rates of postpartum fever (12.9% vs. 0.7%, $P < 0.001$), postpartum hemorrhage (7.1% vs. 1.4%, $P = 0.043$), gastrointestinal issues (7.1% vs. 0.7%, $P = 0.016$), and seizures (5.7% vs. 0%, $P = 0.012$) were significantly higher in the case group. In contrast, there were no significant differences between the groups regarding postpartum thrombosis or respiratory distress that began after delivery ($P > 0.05$, Table 3).

Table 2. Clinical Characteristics of Pregnant Women With COVID-19 (Case Group: 70 Participants)

	Symptom	No. (%)
Clinical manifestations	Fever	47 (67.1)
	Cough	45 (64.3)
	Dyspnea	16 (22.1)
	Sore throat	37 (52.9)
	Fatigue	47 (67.1)
	Malaise	47 (67.1)
	Muscle pain	52 (74.3)
	Gastrointestinal symptoms	45 (64.3)
	Bleeding from the mouth or nose	7 (10)
Therapeutic measures	CT scan results	5 (7.1)
	CXR results	7 (10)
	Oxygen therapy	52 (74.3)
	Antibiotic	68 (97.1)
	Antiviral drugs	42 (60)
	Need for intubation	1 (1.4)
	Need for resuscitation	4 (5.7)
	Need for mechanical ventilation	1 (1.4)

Note. CT: Computed tomography; CXR: Chest X-ray.

Table 4 presents the number and percentage of women in each group who experienced at least one prenatal complication (e.g., preeclampsia, preterm labor, fetal distress, and the like). The frequency was significantly higher in the COVID-19 group than in the control group ($P = 0.001$, Fisher's exact test, Table 4).

Neonates born to mothers with COVID-19 had significantly lower mean birth weights compared to those in the control group (2880.71 ± 314.3 g vs. 3088.35 ± 384.4 g, $P < 0.001$). The proportion of low birth weight infants (< 2500 g) was also higher among the case group (20% vs. 7.9%, $P = 0.011$, Table 4).

Adverse neonatal outcomes were more frequent in the COVID-19 group. They included higher rates of non-reactive non-stress test results (18.6% vs. 3.6%, $P < 0.001$), respiratory distress (18.6% vs. 2.9%, $P < 0.001$), neonatal intensive care unit (NICU) admission (15.7% vs. 2.9%, $P = 0.001$), gastrointestinal problems (8.6% vs. 0%, $P = 0.001$), feeding disorders (14.3% vs. 4.3%, $P = 0.013$), and neonatal fever (17.1% vs. 0%, $P < 0.001$). Moreover, 11.4% of neonates in the case group tested positive for COVID-19 via quantitative real-time polymerase chain reaction, while no positive results were found in the control group ($P < 0.001$, Table 5).

Although the Apgar scores at 1 and 5 minutes were slightly lower in the case group, these differences were not statistically significant. No neonatal deaths occurred in either group.

Discussion

Our findings revealed that pregnant women with

Table 3. Maternal Outcomes in the Case and Control Groups

Variables		Case Group (n=70) n (%)	Control Group (n=140) n (%)	*P* Value
Prenatal problems	Gestational diabetes	10 (14.3)	15 (10.7)	0.294
	Hypertension	3 (4.3)	3 (2.1)	0.318
	Preeclampsia	7 (10)	4 (2.9)	0.035
	Preterm labor	15 (21.4)	9 (6.4)	0.002
	Fetal distress	12 (17.1)	9 (6.4)	0.016
	Reduced fetal movement	11 (15.7)	8 (5.7)	0.019
	Stillbirth	4 (5.7)	3 (2.1)	0.170
	Cesarean	13 (18.6)	7 (5)	<0.001
Postpartum problems	Fever	9 (12.9)	1 (0.7)	<0.001
	Postpartum hemorrhage	5 (7.1)	2 (1.4)	0.043
	Gastrointestinal problems	5 (7.1)	1 (0.7)	0.016
	Seizure	4 (5.7)	0	0.012
	Thrombosis	1 (1.4)	0	0.333
	Respiratory distress starting in the postpartum period	2 (2.9)	0	0.110

Note. Groups were matched with regard to age.

Table 4. Number and Percentage of Prenatal Complications Among Women by Group

	Case Group (n=70)	Control Group (n=140)	Total
Prenatal complications (at least one)			
Yes	38 (54.3%)	34 (24.3%)	72
No	32 (45.7%)	106 (75.7%)	138
Total	70	140	201

Table 5. Neonatal Outcomes in the Study Groups

Neonatal Outcomes	Case Group (n=70) n (%)	Control Group (n=140) n (%)	*P* Value
Non-reactive NST	13 (18.6)	5 (3.6)	<0.001
Neonate with respect to qRT-PCR	8 (11.4)	0	<0.001
Apgar score at one minute less than 7	5 (7.1)	4 (2.9)	0.140
Apgar score at five minutes less than 7	1 (1.4)	1 (0.7)	0.557
Neonate weight)g(	2880.71 (314.3)	3088.35 (384.4)	<0.001
Low birth weight	14 (20)	11 (7.9)	0.011
Admission to the NICU	11 (15.7)	4 (2.9)	0.001
Respiratory distress	13 (18.6)	4 (2.9)	<0.001
Gastrointestinal problems	6 (8.6)	0	0.001
Nutritional disorder	10 (14.3)	6 (4.3)	0.013
Neonatal fever	12 (17.1)	0	<0.001
Neonatal death	0	0	-

Note: Groups were matched in terms of age. qRT-PCR: Quantitative real-time polymerase chain reaction; NST: Non-stress test; NICU: Neonatal intensive care unit.

COVID-19 experienced significantly higher rates of several adverse maternal and neonatal outcomes compared to uninfected controls. Specifically, the frequencies of preeclampsia, preterm labor, fetal distress, reduced fetal movement perception, cesarean delivery, low birth weight, and NICU admission were all significantly elevated in the COVID-19 group ($P < 0.05$). In contrast, no significant differences were observed between the groups in terms of gestational diabetes, gestational hypertension, Apgar scores, and stillbirth. These findings highlight the potential impact of COVID-19 on maternal and neonatal health and warrant further discussion in the following sections.

While Azh et al and Askary et al reported rates of preeclampsia within the normal range,[10,11] the prevalence in our COVID-19 group was higher, consistent with the findings of Wei et al.[12] Preterm labor was also more frequent in the case group (21.4%), aligning with global reports linking COVID-19 to increased preterm birth risk.[13-15] Variations in preterm labor rates may be influenced by pandemic-related behavioral or environmental factors, including reduced maternal workload and improved nutrition,[16-18] as well as heightened stress and reduced access to prenatal care.[19-21]

Cesarean delivery was more common in infected women, often due to fetal distress, as noted in studies by Azh et al and Karimi et al.[10,22] The rate in our study (18.6%) was consistent with the results of Knight et al[23] (16%) and Verma et al (24%),[24] but substantially lower than that reported by Villar et al (72.4%) and Esmailpour Estarkhi et al (67%).[25,26] Differences in institutional policies, physician decision-making, and local practices may explain these variations.[27-29] Moreover, the retrospective study conducted by Salarvand et al demonstrated that COVID-19 infection does not result in adverse outcomes for mothers or newborns, apart from a higher rate of cesarean delivery.[30]

Regarding neonatal outcomes, adverse events, such as low birth weight, fetal distress, intensive care unit admission, and feeding issues, were more frequent in the case group. However, Apgar scores and neonatal mortality did not differ significantly, conforming with the findings of Liu et al and Chen et al.[13,31] The 20% low birth weight rate in our study was comparable to the results of previous

studies[26,31,32] and appeared closely linked to preterm birth, as also observed in severe acute respiratory syndrome and severe pneumonia cases.[33,34] Maternal hypoxia and inflammatory responses may contribute to placental insufficiency and fetal hypoxia.[35,36]

NICU admission was reported in 15.7% of neonates, which was lower than the results reported by Esmailpour Estarkhi et al[26] (30%) but higher than those obtained by Chen et al (6%).[37] Most admissions were due to prematurity and respiratory problems. A key strength of this study was its single-center design, which allowed for consistent data collection. However, several limitations should be noted, including the retrospective nature of the study, incomplete medical records, and the lack of stratification of COVID-19 severity (mild, moderate, or severe), which could influence the outcomes. Additionally, the control group was selected from hospitalized women only, which may not represent the general pregnant population and could introduce bias into the results. The findings may not be generalizable to other populations or healthcare settings with different standards of care, demographics, or viral variants. Furthermore, the small sample size may reduce the statistical power of the study.

Conclusion

The findings of this study indicated that COVID-19 infection during pregnancy was associated with an increased incidence of various maternal and neonatal complications, including preeclampsia, preterm delivery, cesarean section, and neonatal respiratory issues. However, it is crucial to acknowledge that these associations were derived solely from frequency comparisons between the case and control groups, and potential confounders were not controlled for in the analysis. Consequently, caution should be exercised when interpreting these findings. The results highlight the necessity for close monitoring and effective management of pregnant women infected with COVID-19. Further research that accounts for confounding variables is essential to better elucidate the causal relationships involved. These findings can assist healthcare providers in developing targeted treatment strategies aimed at mitigating the risks associated with COVID-19 during pregnancy, ultimately improving maternal and neonatal outcomes.

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Authors' Contribution

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Competing Interests

The authors declare that there is no conflict of interests related to this article.

Ethical Approval

Ethical approval for this research was obtained from the Ethics Committee of the School of Nursing and Midwifery at Shahrekord University of Medical Sciences (under the ethical code IR.SKUMS.REC.1401.082). In addition, data collection began after obtaining ethical approval, and an introduction letter along with necessary explanations was provided to relevant authorities to ensure cooperation and informed consent.

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