




Research Article

Postpartum Maternal and Neonatal Outcomes of SARS-CoV-2 Infection During Pregnancy

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Abstract

Background: The coronavirus pandemic was associated with increased maternal and neonatal morbidity and mortality. The inflammatory mediators related to SARS-CoV-2 infection may be associated with low perinatal outcomes. It is essential to understand the clinical presentation and complications of the SARS-CoV-2 virus in order to provide the best postpartum care. **Objective:** To assess postpartum maternal and neonatal outcomes in COVID-infected mothers. **Methods:** A case-control study was done in the labor ward of Azadi Teaching Hospital in Kirkuk City, Iraq, from May 1st, 2020, until May 1st, 2021. The study included 380 pregnant women who attended for delivery, 150 women with proven SARS-CoV-2 infection, and 230 women in the control group without COVID infection. **Results:** Emergency CS and postpartum hemorrhage (PPH) were significantly higher in cases when compared to the control group ($p=0.001$ and $p=0.005$, respectively), and pulmonary embolism (PE) occurred in 4 cases in comparison to 0 among the control group ($p=0.01$). Low APGAR score at 5 minutes, low birth weight, respiratory distress syndrome (RDS), and early neonatal death showed a significant association with cases in comparison to controls ($p<0.05$). **Conclusion:** There were increased adverse maternal and neonatal outcomes in the postpartum period as a result of COVID-19 in Iraqi pregnant women.

Keywords: COVID-19; Pregnant women; Maternal complications; Neonatal outcomes.

نتائج ما بعد الولادة للأمهات والموليد لعدوى SARS-CoV-2 أثناء الحمل

الخلاصة

الخلفية: ارتبط وباء الفيروس التاجي بزيادة معدلات المراضة والوفيات بين الأمهات والأطفال حديثي الولادة. وقد تكون التفاعلات الالتهابية الناتجة عن SARS-CoV-2 هي السبب في انخفاض نتائج الفترة المحيطة بالولادة. من الضروري فهم العرض السريري ومضاعفات فيروس SARS-CoV-2 من أجل توفير أفضل رعاية بعد الولادة. **الهدف:** تقييم نتائج الأمهات والموليد بعد الولادة لدى الأمهات المصابات بكوفيد-19. **الطريقة:** تم إجراء دراسة الحالات والشواهد في جناح الولادة في مستشفى آزادي التعليمي في مدينة كركوك، العراق، من 1 مايو 2020 حتى 1 مايو 2021. شملت الدراسة 380 امرأة حامل حضرن للولادة، منهن 150 امرأة مصابة بعدوى SARS-CoV-2 مؤكدة، و 230 امرأة في المجموعة الضابطة دون عدوى. **النتائج:** كان إجراء العملية القيصرية الطارئة ونزيف ما بعد الولادة أعلى بشكل ملحوظ في الحالات عند مقارنتها بالمجموعة الضابطة، وتم تسجيل الانسداد الرئوي في 4 حالات مقارنة ب 0 بين المجموعة الضابطة. أظهرت درجة APGAR المنخفضة في 5 دقائق، وانخفاض الوزن عند الولادة، ومتلازمة الضائقة التنفسية، ووفيات الأطفال حديثي الولادة المبكرة ارتباطاً كبيراً بالحالات مقارنة بالمجموعة الضابطة. **الاستنتاج:** كانت هناك زيادة في النتائج السلبية للأمهات والأطفال حديثي الولادة في فترة ما بعد الولادة نتيجة ل COVID-19 لدى النساء الحوامل العراقيات.

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INTRODUCTION

The first coronavirus diagnosed in 2019 was detected in December in Wuhan, Hubei, China. It was designated as acute severe respiratory syndrome (SARS-CoV-2), and the resulting disease was termed Coronavirus Disease 2019. The World Health Organization declared the outbreak a "pandemic" on March 11, 2020 [1]. Several viral infections have been shown to increase the complications rate for newborns and mothers during pregnancy [2–4]. Physiological changes during pregnancy have a significant effect on the coagulation, immune, respiratory, and cardiovascular systems of the fetus and can also have an effect on the progression of COVID-19 [5]. Most non-pregnant patients with SARS CoV-2 infections develop less complicated diseases (81%), while some develop severe diseases associated with the phenomenon of inflammation through cytokines, including IL-6 associated with mechanical ventilation requirements [6]. Initial studies showed a similar effect in pregnant women [7]. The inflammatory mediator related to SARS-CoV-2 infection was associated with low perinatal outcomes [8]. Evidence indicates that pregnant women are more likely to develop complications of COVID-19 than non-pregnant women, including the need for invasive ventilation assistance, intensive care, and death. In addition, it has been shown that COVID-19 during pregnancy is associated with an increased risk of premature birth, preeclampsia, and stillbirth [9]. Given the poor immune status of mothers and the increased risk of respiratory infections in newborns, it is essential to understand the clinical presentation and complications of the SARS-CoV-2 virus in order to provide the best postpartum care [10]. The number of COVID-19 studies in pregnant and puerperal women is increasing exponentially, but due to the nature of these studies (cases and retrospective study analysis), data are limited, and a lot of questions are still obscuring [11]. A CDC study including pregnancy-infection-related symptoms revealed an increase in the mortality risk during pregnancy compared to non-pregnant women with SARS-CoV-2 [12]. Although syncytiotrophoblast is an effective barrier to viral infection, the presence of infections at the placenta level and transmission through the placenta by amniotic fluid aspiration have been noticed [13]. Many clinical studies indicate that the increase in immune responses during pregnancy associated with cytokine storms caused by SARS-CoV-2 virus infection may cause higher levels of consumption coagulopathy [14]. Early studies in pregnant women revealed that COVID-19 significantly raises the risk of stillbirth, miscarriage, preterm labor, intrauterine growth restriction, delivery of neonates with low body weight, and mortality [15]. Some researchers have also confirmed that maternal COVID-19 may alter the supply of oxygen to the fetus, resulting in placental insufficiency, intrauterine growth restriction, distress, and/or the death of the fetus [16]. Recent

epidemiological and clinical studies have revealed different results for the maternal and fetal outcomes of COVID-19 [17]. Researches on the complications of COVID-19 infection during pregnancy are still limited. In contrast, many studies were present and evaluated the rate of complications in COVID-19-infected people. It has been shown that COVID patients with fatty liver have more progressive changes in the chest CT scan [18], and others have evaluated the relationship between vitamin levels and disease severity [19]. The aim of this study is to determine the effect of COVID-19 infection during labor on the maternal complications and neonatal outcomes of COVID-19-infected mothers.

METHODS

The current research is a case-control study that was done in the labor ward of the Gynecology and Obstetrics Department in Azadi Teaching Hospital, Kirkuk, Iraq, from May 1st, 2020, until May 1st, 2021.

Ethical consideration

The study was conducted in accordance with the Helsinki Declaration through the oral informed consent of pregnant women, the agreement of health authorities, and the management of postpartum neonatal complications accordingly. The study has been registered at the University of Kirkuk College of Medicine. Ethical approval was obtained from the Ethical Committee of the University of Kirkuk, College of Medicine (Issue 19).

Study design and patient selection

The study included 380 pregnant women who underwent prenatal care: 150 with SARS-CoV-2 infection and 230 without COVID-19 infection. Twenty to forty-year-old pregnant women with a gestational age of 24 to 42 completed weeks met the inclusion criteria. Maternal age less than 20 years and greater than 40 years, hypertension and preeclampsia, chronic hypertension, pre-gestational and gestational diabetes, post-term pregnancies, gestational age less than 24 weeks, and maternal anemia were exclusion criteria. Using a prepared questionnaire, information about pregnant women was gathered directly. The questionnaire asked about the mode of delivery, the parity, the maternal age, and the gestational age. Obstetricians determined the maternal complications and mode of delivery based on the condition of the pregnant woman in the delivery room. Mothers were observed till the end of puerperium by direct communication through their phone number or by seeing them directly when they admitted to the hospital with complications e.g., postpartum hemorrhage, thromboembolism, sepsis and maternal death. The neonatal outcomes (APGAR score at 5 minutes, birth

weight, neonatal sepsis, stillbirth, respiratory distress syndrome (RDS), neonatal convulsions, and neonatal mortality) were evaluated by the pediatrician and followed up for one week after delivery.

Statistical analysis

Version 23 of the statistical package for the social sciences (SPSS) software was used for data processing and analysis. Continuous data, such as means, standard deviations, and minimum and maximum values, are used in sociodemographic descriptive statistics. The included data is represented as numerical and percentage values. To investigate the association between common and classification variables, independent sample *t*-test was utilized. To determine the association between two variable categories, the Chi-square test was used. The statistical significance level is set at $p < 0.05$.

RESULTS

The number of participants was 380, divided into two groups: pregnant women who get COVID-19 infection during pregnancy (Group A, $n=150$) and pregnant women who do not get COVID-19 infection during pregnancy (Group B, $n=230$). The mean maternal age across cases was 29.1 ± 5.8 years and across controls 29.4 ± 6.1 years, with no significant difference in age between both groups ($p=0.62$). For parity, 66% of cases and 73.5% of controls were para 1–5, with no significant difference in the distribution of parity between both groups ($p=0.3$) (Table 1).

Table 1: Demographic characteristics of participants

Variable	Cases <i>n</i> =150	Control <i>n</i> =230	<i>p</i> -value
Age (year) (mean±SD)	29.1±5.8	29.4±6.1	0.62*
Parity <i>n</i> (%)			
0	35(23.3)	41(17.8)	
1 - 5	99(66)	169(73.5)	0.29**
> 5	16(10.7)	20(8.7)	

*Independent sample *t*-test, **Chi-Square test

The assessment of postpartum maternal outcomes showed that mode of delivery, postpartum hemorrhage, and pulmonary embolism were significantly different between cases and control groups, in which emergency CS was significantly higher in cases compared to control ($p=0.001$), Postpartum hemorrhage (PPH) was also higher among cases when compared to control group ($p=0.005$), and pulmonary embolism (PE) was occurred in 4 cases compared to zero among control group ($p=0.01$), while other factors such as deep venous thrombosis (DVT), puerperal sepsis, and maternal death did not demonstrate a significant difference between groups ($p > 0.05$) (Table 2).

Table 2: Postpartum maternal outcomes

		Case Count (%)	Control Count (%)	<i>p</i> -value
Mode of delivery	Elective CS	12(8.0)	51(22.2)	0.001
	Emergency CS	71(47.3)	70(30.4)	
	VD	67(44.7)	109(47.4)	
Postpartum hemorrhage	No	131(87.3)	219(95.2)	0.005
	Yes	19(12.7)	11(4.8)	
Deep venous thrombosis	No	143(95.3)	223(97.0)	0.41
	Yes	7(4.7)	7(3.0)	
Pulmonary embolism	No	146(97.3)	230(100.0)	0.01
	Yes	4(2.7)	0(0.0)	
Puerperal sepsis	No	144(96.0)	225(97.8)	0.29
	Yes	6(4.0)	5(2.2)	
Maternal death	No	144(96.0)	227(98.7)	0.09
	Yes	6(4.0)	3(1.3)	

For postpartum neonatal outcomes, the analysis showed that the low APGAR score at 5 minutes, low birth weight, respiratory distress syndrome (RDS), and early neonatal death showed a significant association with cases in comparison to the control group ($p < 0.05$) (Table 3).

Table 3: Postpartum neonatal outcomes

		Case Count (%)	Control Count (%)	<i>p</i> -value
Stillbirth	No	141(94.0)	223(97.0)	0.16
	Yes	9(6.0)	7(3.0)	
Low APGAR at 5 min	No	124(82.7)	213(92.6)	0.003
	Yes	26(17.3)	17(7.4)	
Birth weight (kg)	mean±SD	2.6±1.1	3.2±0.6	0.0001
Neonatal sepsis	No	142(94.7)	222(96.5)	0.37
	Yes	8(5.3)	8(3.5)	
RDS	No	113(75.3)	216(93.9)	0.0001
	Yes	37(24.7)	14(6.1)	
Neonatal convulsion	No	139(92.7)	221(96.1)	0.14
	Yes	11(7.3)	9(3.9)	
Early neonatal death	No	122(81.3)	224(97.4)	0.0001
	Yes	28(18.7)	6(2.6)	

For gestational age (GA), there was a significant lower gestational age among pregnant women with COVID-19 infection (37 ± 4.1 weeks) in comparison to the control group (38.5 ± 2.6 weeks) ($p=0.0001$, Independent sample *t*-test) (Figure 1).

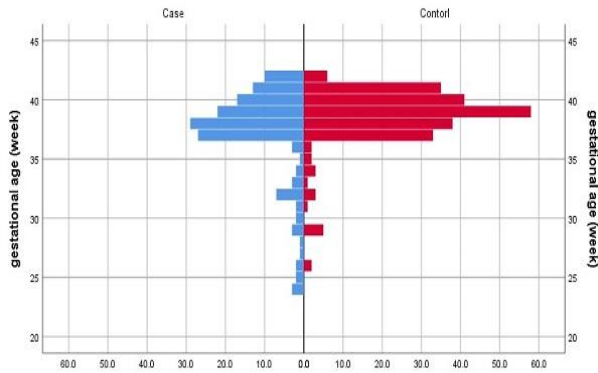


Figure 1: Gestational age population pyramid frequency of participant groups.

Logistic regression analysis was applied using cases as the dependent variable and the variables that showed significant associations in the binary analysis as the independent variables. Four factors were found to be significant independent risk factors. These factors were: mode of delivery (OR = 0.3), postpartum hemorrhage (OR = 0.3), respiratory distress syndrome (OR = 0.3), and early neonatal death (OR = 0.2) (Table 4).

Table 4: Logistic regression analysis for association of various risk factors with cases

	B	p-value	Odd ratio	95% C.I.	
				Lower	Upper
Mode of delivery	-0.978	0.0001	0.376	0.228	0.620
Postpartum hemorrhage	-0.961	0.030	0.383	0.161	0.909
Pulmonary embolism	-21.43	0.999	---	---	---
low APGAR at 5 min	-0.100	0.805	0.905	0.410	2.000
Respiratory distress syndrome	-1.104	0.016	0.332	0.135	0.812
early neonatal death	-1.231	0.038	0.292	0.091	0.935

DISCUSSION

Emerging pandemics, such as SARS-CoV-2 and pandemics elsewhere in the world, may affect not only infected patients but also their progeny. In this study, the effects of SARS-CoV-2 infection on postpartum and neonatal outcomes were evaluated. We focused primarily on postpartum complications that had a significant impact on the mother. The assessment of postpartum maternal outcomes in this study revealed that emergency caesarean section (CS), postpartum hemorrhage, and pulmonary embolism were significantly more prevalent among mothers who had SARS-CoV-2 during pregnancy. While a study from Iran by Pirjani *et al.* revealed that only CS was a negative maternal outcome [20], a study from China by

Li *et al.* revealed that the majority of mothers have undergone cesarean delivery owing to the COVID-19 infection [21]. Interestingly, the early systematic review of reports of maternal and neonatal complications with COVID-19 revealed an increased risk of CS following infection with COVID-19 during pregnancy. Similarly, subsequent meta-analysis investigations [22,23] have reported the same results. Even though numerous studies have demonstrated an association between COVID-19 infection and an increased risk of CS, particularly emergency CS, we are unable to identify the underlying mechanism. There may be a delay in the presentation of COVID-19-infected mothers to obstetrical units in the event of labor pain, reduced fetal movement, or other emergencies due to fear of quarantine, which was strictly applied to infected mothers at the time of the study, or fear of transmitting infection to others, and any delay will increase the rate of emergency cesarean section. During the pandemic in Portugal, the number of admissions to the emergency department for obstetrics and gynecology decreased, but the severity of cases that attended the emergency unit increased [24]. Significant association between increased risk of CS and severity of COVID-19 infection was found in a study by Samadi *et al.* [25]. In addition to other risk factors, a recent study in the United Kingdom involving more than 700 women found that the risk of pulmonary embolism was substantially higher among pregnant women with COVID-19 infection [26]. This may be due to the proven association between the thrombogenic nature of COVID-19 infection and women who are already considered to be hypercoagulable during pregnancy, or due to other comorbidities that may contribute to an increased risk of pulmonary embolism that is not evaluated here. In terms of neonatal outcomes, the analysis revealed that infants born to mothers with COVID-19 had significantly higher rates of low APGAR score at 5 minutes, low birth weight, RDS, and early neonatal death compared to the control group. This was consistent with the findings of another systematic review [27] that reported intrauterine death, preterm delivery, asphyxia, fetal distress, low birth weight, small or large for gestational age, and neonatal mortality in infected mothers as the neonatal complications. In addition to numerous other studies demonstrating a variety of adverse neonatal outcomes in mothers infected with COVID-19 [28-31]. A study by Simeone *et al.* [32] revealed that COVID-19-infected mothers have a higher incidence of fetal growth restriction than the general population. In addition, the gestational age of mothers infected with COVID-19 was substantially lower than that of the control group. This is consistent with the findings of the other two studies [33,34] that indicated COVID-19 infection increased the risk of preterm labor. The cause may be due to stimulation of uterine contractions by release of prostaglandins in any febrile illness. Since the time of getting the infection has crucial role, it is impossible to

assess the direct impact of COVID-19. Importantly, the preterm birth may be related to pandemic stress, as mentioned previously, and this has been confirmed by two longitudinal studies that found the fear of COVID-19 during pregnancy had a significant impact on a lower gestational age, even when the pregnant women did not contract the virus [35,36]. This supported our hypothesis that stress may play a significant role in adverse maternal and newborn outcomes. Interestingly, a cohort study conducted in Iran revealed that pregnant women infected with COVID-19 had an increased risk of cesarean delivery, preeclampsia, and preterm labor, as well as adverse neonatal outcomes such as newborn prematurity, fetal distress, and low Apgar scores [37]. Due to the exclusion of preeclampsia cases from this study, this identical match may be attributable to the same study designation and groups of analysis, excluding preeclampsia. The inflammatory background associated with COVID-19 infection may contribute directly to adverse effects on mothers and neonates, as well as to preexisting comorbidities that increase the risk of COVID-19 and adverse effects.

Conclusion

There were increased adverse maternal and neonatal outcomes in the postpartum period as a result of COVID-19 in Iraqi pregnant women.

Conflicts of interest

There are no conflicts of interest.

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The authors did not receive any source of fund.

Data sharing statement

All data are available upon reasonable request to the corresponding author.

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