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Maternal and Perinatal Outcomes of Pregnant Women with and Without COVID-19 Infection

COVID-19 Enfeksiyonu Olan ve Olmayan Gebelerin Maternal ve Perinatal Sonuçları

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Abstract

Introduction: We aimed to evaluate the maternal and obstetric outcomes of pregnant women with and without COVID-19 infection in any period of their pregnancy.

Materials and Methods: Maternal and neonatal results of all pregnant women who gave birth in Karaman Training and Research Hospital Gynecology and Obstetrics clinic for 1.5 years from the beginning of the COVID-19 pandemic were collected from the hospital data recording system. Pregnant women with or without COVID-19 infection were divided into groups and their results were compared.

Results: A total of 2989 pregnant women gave birth, of which 2918 (97.6%) tested negative for COVID-19, and 71 (2.49%) tested positive. The rate of low birth weight newborn (2500g and below) was 13.1% in COVID-19 negative pregnant, while it was 42.2% in COVID-19 positive pregnant (59.3% in the 3rd trimester). The rate of preterm births (37 weeks and below) was 13.3% in COVID-19 negative pregnant, while it was 22.5% in COVID-19 positive pregnant. The need for neonatal intensive care, Intrauterine ex rate and cesarean delivery rates were higher in COVID-19 positive pregnant women, and they were highest in the third trimester. While the rate of cesarean section due to fetal distress is 27.1% in COVID-19 negative pregnant women, 34.6% in COVID-19 positive pregnant women and the highest cesarean delivery rate due to fetal distress was in third trimester pregnant.

Conclusion: Although the COVID-19 pandemic seems to be over, COVID-19-like symptoms in pregnant women still make obstetricians nervous. Despite the increase in vaccination status, there are still unvaccinated pregnant women. Due to severe neonatal and maternal adverse outcomes, especially in the third trimester, the presence of COVID-19 should be considered.

Keywords: COVID-19; pregnancy; premature birth; cesarean. Section

Özet

Amaç: Çalışmamızda gebeliğinin herhangi bir döneminde COVID-19 geçiren gebelerle geçirmeyen gebelerin maternal ve obstetrik sonuçlarını değerlendirmeyi amaçladık.

Gereç ve Yöntem: Çalışmamıza COVID-19 pandemisinin başından itibaren 18 ay süreyle Karaman Eğitim ve Araştırma Hastanesi Kadın Hastalıkları ve Doğum kliniğinde normal vajinal yolla veya sezaryen ile doğum yapan tüm gebelerin verileri ve yenidoğan sonuçları hastane veri kayıt sisteminden toplanmıştır. Herhangi bir dönemde COVID-19 enfeksiyonu geçiren ve geçirmeyen gebeler gruplara ayrılarak sonuçları karşılaştırılmıştır.

Bulgular: Toplam 2989 doğum yapan gebenin 2918 (%97.6)'i COVID-19 negatif, 71 (%2.49)'i COVID-19 pozitifti. 2500gr ve altında düşük doğum ağırlıklı bebek oranı, COVID-19 negatif gebelerde %13.1 iken; COVID-19 pozitif gebelerde %42.2, 2. trimester COVID-19 pozitif gebelerde %45.2, 3. trimester COVID-19 pozitif gebelerde %59.3 olup istatistiksel açıdan anlamlı olarak daha yüksekti. 37 hafta ve altı erken doğum yapan gebe oranı COVID-19 negatif gebelerde %13.3 iken; COVID-19 pozitif gebelerde %22.5, 1. trimester COVID-19 pozitif gebelerde %30.8, 2. trimester COVID-19 pozitif gebelerde %16.1, 3. trimester COVID-19 pozitif gebelerde %25.9 olup daha yüksekti. Yenidoğan yoğun bakım ihtiyacı, intrauterin ex oranı ve sezaryen doğum oranları COVID-19 pozitif gebelerde daha yüksek olup, 3. trimester COVID-19 pozitif gebelerde en yüksekti. Fetal distrese bağlı sezaryen doğum oranı COVID-19 negatif gebelerde %27.1 iken COVID-19 pozitif gebelerde %34.6 ve en yüksek fetal distrese bağlı sezaryen doğum oranı 3. trimester gebelerdedir.

Sonuç: COVID-19 pandemisi bitmiş gibi görünse de gebelerde görülen COVID-19 benzeri semptomlar hala kadın doğum uzmanlarını tedirgin etmektedir. Aşılama durumu artmasına rağmen hala aşı karşıtları ve aşısız gebeler mevcuttur. Nitekim aşılama aşısız gebelerle COVID-19 pozitif gebelikler tespit edilmiştir. Özellikle üçüncü trimesterde ciddi olarak artan neonatal ve maternal olumsuz sonuçlar nedeniyle, son dönem gebeliklerde semptomlar varsa COVID-19 varlığı düşünülmeli ve rutin COVID-19 yaklaşımına dikkatle devam edilmesi önerilir.

Anahtar Kelimeler: COVID-19; gebelik; erken doğum; sezaryen doğum.

Introduction

Since its initial identification in late 2019, COVID-19, caused by the SARS-CoV-2 virus, has rapidly disseminated across the globe, leading to

significant changes in healthcare paradigms. Evidentiary support from various sources, including registries of pregnant women and both

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single- and multi-center cohorts, has highlighted the distinctive vulnerability of pregnant individuals to the effects of this novel virus (1). Studies have consistently demonstrated that pregnant women affected with COVID-19 are at an elevated risk when compared to nonpregnant women of reproductive age, in terms of their susceptibility to severe morbidity, mortality, and the need for intensive care unit (ICU) support (2,3). The process of delivery itself emerges as a potential intervention that can improve maternal conditions, especially in cases of severe COVID-19 (1,4). Therefore, there has been a noticeable increase in preterm births and neonatal unit admissions for infants born to mothers with confirmed infections (1,5-7). The prevalence of perinatal complications remains uncertain due to the lack of adequate data for assessing the impact of COVID-19 infection on pregnant women and pregnancy outcomes. An international registry study revealed higher rates of adverse maternal and neonatal outcomes among pregnant women with COVID-19, while a Swedish national data analysis linked COVID-19 infection to elevated rates of preterm birth and negative neonatal outcomes (5,8). More than 95% of infants born to mothers diagnosed with COVID-19 are asymptomatic at birth. Mild infection symptoms (not requiring respiratory support) have been observed in some newborns of mothers. In most of these cases, respiratory droplets from the mother to the newborn have been considered as the route of transmission. According to the analysis of data obtained from 12 countries, pregnant individuals with COVID-19 infection have reported early neonatal mortality rates attributed to all causes at 0.2-0.3%; this rate is similar to pre-COVID-19 data (7). Few studies have compared the maternal and neonatal outcomes between COVID-19 positive and negative pregnant women. An international cohort study highlighted notable increases in severe maternal morbidity and mortality with increasing cases of neonatal complications (5). In this study, we aimed to compare the maternal and neonatal outcomes of COVID-19 positive and negative pregnant women who gave birth in the first wave of the COVID-19 pandemic. Additionally, for the first time in the literature, we tried to demonstrate the early and late pregnancy effects of COVID-19 infection by classifying COVID-19 positive pregnant women according to their trimesters.

Materials and Methods

The data of pregnant women who gave birth between March 2020 - May 2021 through normal vaginal delivery or cesarean section at the Gynecology and Obstetrics Clinic of Karaman Training and Research Hospital and newborn results were collected from the hospital's data recording system for a duration of 1.5 years starting from the onset of the COVID-19 pandemic. Pregnant women with additional diseases such as diabetes and hypertension were excluded from the study. Pregnant women who tested positive for COVID-19 were categorized according to the trimester in which they were infected. A total of 2989 deliveries were compared. The COVID-19 positive diagnosis was confirmed in our hospital's laboratory through a positive result from the COVID-19 test. Maternal age, nationality, parity, birth weight, birth week, neonatal outcomes, and delivery method were recorded. Maternal age was grouped as under 19 years old, between 19-35 years old and over 35 years old. Parity and previous cesarean section were recorded. Immigrant pregnant women and Turkish pregnant women were recorded. Birth weight <2500g infants were considered low birth weight infants. Preterm birth was defined as pregnant women who delivered prior to reaching 37 weeks of gestation. Pregnant women were grouped according to normal vaginal delivery and cesarean section. Cesarean section indications were recorded. Infants requiring neonatal intensive care, stillborn infants, live-born infants, and postpartum complications were all documented.

Ethical approval: Our study was designed in accordance with the Declaration of Helsinki. Approval from the Karamanoglu Mehmetbey University Medical Faculty Clinical Research Ethics Committee was acquired through a decision dated April 27, 2022, bearing the reference number 04-07.

Statistical analysis: Descriptive statistics for the continuous variables were presented as Median, Mean, Standard deviation, minimum and maximum values while frequency and percentages for categorical variables. One-way ANOVA was performed for the comparison of group means. Chi-square test was performed to determine the relationship between categorical variables. Statistical significance level was considered as 5% and SPSS (ver: 21) statistical program was used for all statistical computations.

Table 1: Demographic and Clinical Features of Patients n, (%)

		COVID-19 Positive Pregnancy				Total n=2989	p value
		COVID-19 Negative Pregnancy n=2918 (97.6)	1.TR n=13 (0.4)	2.TR n=31 (1.1)	3.TR n=27 (0.9)		
Age (y)	mean±SD	28.07±5.57	29.46±6,3 3	29.97±4,8 5	29.04±6,09	28.10±5.5 7	
	<19	32 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	32 (1.1%)	0.736
	19-35	2559 (87.7%)	10 (76.9%)	26 (83.9%)	23 (85.2%)	2618 (87.6%)	
	>35	327 (11.2%)	3 (23.1%)	5 (16.1%)	4 (14.8%)	339 (11.3%)	
Nationality	Turkish	2759 (94.6%)	13 (100.0%)	30 (96.8%)	27 (100.0%)	2829 (94.6%)	0.459
	Immigrant	159 (5.4%)	0 (0.0%)	1 (3.2%)	0 (0.0%)	160 (5.4%)	
Parity	Nullipar	1023 (35.1%)	6 (46.2%)	6 (19.4%)	14 (51.9%)	1049 (35.1%)	0.494
	1-4	1855 (63.6%)	7 (53.8%)	25 (80.6%)	13 (48.1%)	1900 (63.6%)	
	>4	40 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	40 (1.3%)	
Birth weight (g)	≤2500	381 (13.1%)	0 (0.0%)	14 (45.2%)	16 (59.3%)	411 (13.8%)	0.031
	2500<bw<4 000	2378 (81.5%)	13 (100.0%)	17 (54.8%)	11 (40.7%)	2419 (80.9%)	
	>4000	159 (5.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	159 (5.3%)	
Birth week	<37	387 (13.3%)	4 (30.8%)	5 (16.1%)	7 (25.9%)	403 (13.5%)	0.201
	≥37	2531 (86.7%)	9 (69.2%)	26 (83.9%)	20 (74.1%)	2586 (86.5%)	
Neonatal outcomes	NICU	186 (6.4%)	1 (7.7%)	2 (6.5%)	11 (40.7%)	200 (6.7%)	0.001
	IUEX	18 (0.6%)	0 (0.0%)	0 (0.0%)	2 (7.4%)	20 (0.7%)	
	Postpartum EX	6 (0.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (0.2%)	
	Normal	2708 (92.8%)	12 (92.3%)	29 (93.5%)	14 (51.9%)	2763 (92.4%)	

TR: trimester, SD: Standard deviation, NICU: neonatal intensive care unit, IUEX: intrauterin ex

Results

A comprehensive examination of 2989 pregnancies was conducted for this study. Among these, 2918 (97.6%) exhibited negative results for COVID-19, while 71 (2.49%) were confirmed as COVID-19 positive. The demographic and clinical features of patients are shown in Table 1. The mean age of all pregnant women was 28.1±5.5 years, and no significant differences were observed among the groups. The rate of pregnant women over the age of 35 is 16.9% in COVID-19 positive pregnant women and 11.2% in COVID-19 negative pregnant women, showing a higher

rate in the COVID-19 positive group. The rate of migrant pregnant women who gave birth in our province was 5.4%, and the rate of adolescent pregnant women was 1.1%. While the rate of COVID-19 positivity was 0.6% in immigrant pregnant women, it was 2.4% in Turkish pregnant women. The first pregnancy rate was 35.1%, the 1-4 pregnancy rate was 63.6%, which was statistically insignificant. While the rate of low birth weight newborns of 2500 g and below is 13.1% in COVID-19 negative pregnant women; It is 42.2% in COVID-19 positive pregnant women, 45.2% in 2nd trimester COVID-19 positive pregnant women, and 59.3% in 3rd trimester COVID-19 positive pregnant women, which is statistically significantly

higher ($p < 0.05$). The rate of preterm labor (at 37 weeks and below) was 13.3% in COVID-19 negative pregnant women; It was 22.5% in COVID-19 positive pregnant women. It was 30.8% in the 1st trimester COVID-19 positive pregnant women, 16.1% in the 2nd trimester COVID-19 positive pregnant women, 25.9% in the 3rd trimester COVID-19 positive pregnant women, and it is higher in the 3rd trimester. Considering the neonatal outcomes, the rate of newborns requiring intensive care unit in pregnant women

who have not had COVID-19 infection is 6.4%, while it is 7.7% in pregnant women who have had an infection in the 1st trimester, 6.5% in those with an infection in the 2nd trimester, 40.7% in those with an infection in the 3rd trimester, it was significantly higher ($p < 0.05$). The highest intrauterine ex rate was observed in pregnant women who had an infection during the 3rd trimester, at 7.4%. The mode of delivery for pregnant women and indications for cesarean section (C/S) are summarized in Table 2.

Table 2: Delivery Methods of the Patients n, (%)

		COVID-19 Negative Pregnancy n=2918 (97.6)	1.TR n=13 (0.4)	2.TR n=31 (1.1)	3.TR n=27 (0.9)	Total n=2989	p value	
Delivery Method	NVD	1528 (52.4%)	6 (46.2%)	11 (35.5%)	6 (22.2%)	1551 (51.9%)	0.004	
	C/S	1390 (47.6%)	7 (53.8%)	20 (64.5%)	21 (77.8%)	1438 (48.1%)		
C/S end	Previous C/S	727 (24.9%)	6 (46.2%)	12 (38.7%)	5 (18.5%)	750 (25.1%)	0.448	
	FD	180 (6.2%)	0 (0.0%)	2 (6.5%)	7 (25.9%)	189 (6.3%)		
	CPD	108 (3.7%)	0 (0.0%)	0 (0.0%)	4 (14.8%)	112 (3.7%)		
	Prolonged labor	150 (5.1%)	0 (0.0%)	2 (6.5%)	3 (11.1%)	155 (5.2%)		
	Primer C/S	Malpresentation	97 (3.3%)	1 (7.7%)	3 (9.7%)	1 (3.7%)		102 (3.4%)
	MP	32 (1.1%)	0 (0.0%)	0 (0.0%)	1 (3.7%)	33 (1.1%)		
	Macrosomia	55 (1.9%)	0 (0.0%)	1 (3.2%)	0 (0.0%)	56 (1.9%)		
Other	33 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	33 (1.1%)			
	Abruption placenta	6 (0.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (0.2%)		
	Placenta previa	2 (0.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.1%)		

TR: trimester, **NVD:** normal vaginal delivery, **C/S:** cesarean section, **FD:** fetal distress, **CPD:** cephalopelvic disproportion, **MP:** multiple pregnancy

Out of a total of 2989 pregnancies, 1551 (51.9%) had vaginal deliveries, and 1438 (48.1%) had C/S deliveries. The C/S rates were 47.6% in COVID-19 negative pregnancies, 67.6% in all COVID-19 positive pregnancies, 53.8% in pregnancies with a history of infection in the 1st trimester, 64.5% in COVID-positive pregnancies in the 2nd trimester, and 77.8% in the 3rd trimester, which is significantly higher statistically ($p < 0.05$). The primary C/S rates were 47.7% in COVID-19 negative pregnancies and 54.1% in COVID-19 positive pregnancies. The C/S rates due to fetal distress were 27.1% in COVID-19 negative pregnancies and 34.6% in COVID-19 positive

pregnancies, with the highest rate of C/S due to fetal distress occurring in the 3rd trimester.

Discussion

The COVID-19 pandemic has significantly impacted healthcare systems worldwide, leading to unprecedented challenges for obstetric care and maternal and perinatal outcomes. Pregnant women were considered to be potentially at a higher risk for severe illness from COVID-19 compared to non-pregnant individuals (1). This was based on the fact that pregnant women experience changes in their bodies that could affect their immune and respiratory systems, potentially making them more

susceptible to respiratory infections. We conducted this study because of the lack of data about the effects of COVID-19 on the pregnant women population and weeks of gestation. Only a limited number of studies, involving a small cohort of individuals, have examined the differences in outcomes between pregnant women with and without COVID-19 (5,9,10). Although age was not an important factor, in our study the rate of COVID-19 infection was higher in women over the age of 35. Since advanced age is already considered a risk factor for pregnancy, it can be predicted that there may be a risk in terms of susceptibility to COVID-19 infection. We did not have sufficient data on COVID-19 disease severity or maternal body mass index but body mass index is known as a risk factor for severe infection and neonatal death (4,11). Within our study, it has been established that pregnant women who contract COVID-19 during their third trimester are notably more susceptible to an elevated risk of low birth weight or preterm birth, in comparison to pregnant women unaffected by the virus. Many studies reported increased preterm birth rates in pregnant women with COVID-19 infection, due to the induced labor to improve the maternal condition (1,4,5,12-14). Therefore, increased risk of preterm birth is associated with adverse neonatal outcomes as fetal death, neonatal intensive care unit admission (1,8,13). Aligned with existing literature, our study revealed a noteworthy rise in the rate of neonatal intensive care unit admissions. Specifically, for pregnant women without COVID-19 infection, the increase amounted to 6.4%, while for those with COVID-19 infection during the third trimester, the escalation was substantially higher at 40.7%. Additionally, the intrauterine ex rate was higher in pregnant women with COVID-19 infection in the third trimester in our study. Compared to previous years, we reported higher cesarean rates (48.1%) during the pandemic period. The rate of cesarean delivery was significantly higher in COVID-19 positive pregnant, especially in the third trimester, compared to COVID-19 negative pregnancies. Similarly, recent studies indicated a significant increase in rates of cesarean delivery (1,13,15). Pregnant women with COVID-19 infection were more likely for given birth by emergency cesarean section (1). It is controversial whether this is due to the urgent delivery decision to improve the maternal condition or increased rates of fetal distress. In our study, it was shown that fetal distress rates increased significantly. This has led to an increase in primary cesarean section rates. In our study, cesarean section rates due to

fetal distress are 27.1% in COVID-19 negative pregnant, 34.6% in COVID-19 positive pregnant and the highest fetal distress cesarean section rate is in the third trimester.

Study limitations: The data of the study is limited to the records and information entered into the system. Although our study included sufficient variables for examination, data on the severity of COVID-19 disease and the mother's body mass index were not available. As noted in previous research, maternal obesity is considered a risk factor for both severe COVID-19 and fetal death.

Conclusion

Although the COVID-19 pandemic seems to be over, COVID-like symptoms in pregnant women still make obstetricians obsessed. Although vaccination status has increased, there is still an anti-vaccinated group and unvaccinated group. Indeed, despite vaccination, COVID-19 positive pregnancies have been detected. Due to increased neonatal and maternal negative outcomes especially in the third trimester, if there are symptoms in end-stage pregnancies, the presence of COVID-19 should be considered and routine COVID-19 approach is recommended to continue.

Ethical approval: Approval from the Karamanoglu Mehmetbey University Medical Faculty Clinical Research Ethics Committee was acquired through a decision dated April 27, 2022, bearing the reference number 04-07.

Conflict of interest: The authors confirm that they do not have any conflicts of interest.

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