

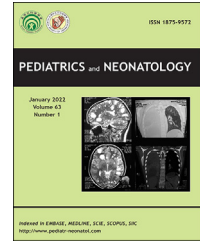


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Original Article

Effects of COVID-19 pandemic period on neonatal mortality and morbidity

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Key Words

COVID-19;
neonatal;
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Background: Corona Virus Disease 2019 (COVID-19) in pregnant women has important impacts on perinatal and neonatal outcomes. However, there are a limited number of studies investigating the effect of the pandemic period on newborns. With this study, we aimed to determine the impact of the 2020 COVID-19 outbreak on prenatal care, obstetric outcomes, neonatal mortality and morbidity.

Methods: The retrospective results of patients hospitalized to the Tertiary Neonatal Intensive Care Unit between 1 March and 30 May 2020, the first peak period of the pandemic in our country, were compared with the data of the same period of the previous year.

Results: A total of 307 cases were included in our study. The mean gestational weeks of the neonates hospitalized in the Neonatal Intensive Care Unit during the COVID-19 period were higher than those in the control group ($p: 0.003$). During the pandemic period, an increase was found in the frequency of pregnant women presenting to obstetric emergency services in emergencies requiring acute intervention ($p: 0.01$). Compared to the control group, there was an increase in the number of infants with small for gestational age (SGA) diagnosis, 5th-minute Apgar score of <7 , and newborns with a diagnosis of hypoxic-ischemic encephalopathy who were treated with hypothermia in the study group ($p < 0.05$). No difference was found in terms of maternal and neonatal mortality ($p > 0.05$).

Conclusions: During the COVID-19 pandemic, it was shown that pregnant women disrupted their regular antenatal care, and more pregnant women were admitted to the obstetric emergency department with emergencies requiring acute intervention. This led to an increase in the number of cases diagnosed with SGA and hypoxic-ischemic encephalopathy in newborns. Our results will be useful for better management of current and future pandemic periods.

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1. Introduction

The first known case of the new type of coronavirus 2019 was detected in Wuhan city of Hubei state, China in December 2019. It was named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), and the resulting disease was named after Corona Virus Disease 2019 (COVID-19). The outbreak was declared a “pandemic” by the World Health Organization on 11 March 2020.¹ The first case was identified in Turkey on 9 March 2020.² To prevent the spread of the virus and its negative consequences in Turkey, very strict measures, including full lockdown against travel and gathering, were implemented from March until June 2020. Despite the strict measures implemented during this period, Covid-19 continued to maintain its effects as a health problem worldwide.

Routine obstetric care is vital, especially in high-risk pregnancies. During the COVID-19 pandemic period, the guidelines recommended by health authorities suggest that antenatal and perinatal care should not be disrupted.³ Traditional prenatal care guidelines were based on WHO 2016 recommendations. These guidelines recommend that a pregnant woman consult healthcare providers at least eight times for positive perinatal and maternal results.⁴ It is recommended that these admissions occur in the first trimester, at the 20th and 26th weeks, and the next five examinations in the third trimester of the pregnancy, at the 30th, 34th, 36th, 38th, and 40th weeks.⁴ Recommended interventions to improve antenatal care quality include nutritional education, examining the mother and fetus, managing common physiological pregnancy symptoms, and birth preparation measures.⁵ Early detection of cases requiring rapid intervention, such as emergency surgical cesarean section and delivery, is critical in terms of maternal and neonatal mortality and morbidity. Nevertheless, during this global pandemic, it has been necessary to re-arrange antenatal visits not only to reduce the risk of infection of a healthy pregnant woman but also to reduce the likelihood of healthcare workers being exposed to asymptomatic infected individuals.⁵ However, this may have disrupted antenatal health services. Also, fear of infection, travel restrictions across the country, and social distancing norms may have deterred pregnant women from receiving health care.

During the COVID-19 pandemic period, the disease led to radical changes in many important conditions of the society and negative psychological consequences.⁶ During the quarantine period, it was reported that non-COVID-19 diseases such as cardiovascular disease remained in the background, due to the concern that hospitals were not safe owing to infection risk.^{7,8} The pandemic period may have disrupted the routine antenatal care of pregnant women as in other specialties.⁹ The pandemic period is also a risky period for pregnant women. Pregnant women are already at increased risk of getting infections due to the physiological changes experienced. It is known that infections experienced during pregnancy have many negative maternal and fetal consequences, such as maternal death, intrauterine fetal death, and preterm birth.¹⁰ Coronavirus infection is, therefore, a serious source of anxiety and

stress for pregnant women.¹¹ However, the impact of the COVID-19 pandemic on routine obstetric care is still unknown. This study aimed to determine the effect of the pandemic on prenatal care, obstetric outcomes, neonatal mortality, and morbidity by comparing the first peak period of the COVID-19 pandemic of 2020 with the data of the same period in 2019.

2. Materials and methods

This study is a retrospective cohort study comparing prenatal care, obstetric outcomes, neonatal mortality, and morbidity results of patients admitted to the Tertiary Neonatal Intensive Care Unit between 1 March and 30 May 2020, with those of the same period of 2019. The cases hospitalized in the Tertiary Neonatal Intensive Care Unit of Trabzon Kanuni Training and Research Hospital during the first peak period of COVID-19 (study group) and the cases hospitalized in the same period of 2019 (control group) were included in the study. Demographic, obstetric, and neonatal data were obtained from medical records and the hospital's laboratory database.

In the cases included in the study, maternal pregnancy history (age, gravidity, parity, frequency of prenatal follow-up, premature rupture of membranes, presence of maternal hypertension/diabetes, presence of meconium in amniotic fluid, perinatal mortality results), neonatal data (gestational week, birth weight, gender, mode of delivery, place of birth, Apgar score, reason for hospitalization, duration of hospitalization, treatments applied, mortality results) were retrospectively reviewed and recorded. According to the gestational week, those with a birth weight below the 10th percentile were accepted as small for gestational age (SGA).¹² Hypothermia treatment was considered if patients met all the following criteria: gestational weeks of >36, blood gas pH \leq 7.0, be \leq -16mmol/L, 10th minute Apgar score of <5, and clinical findings of moderate or severe encephalopathy in the first postnatal hour.¹³

2.1. Statistical analyses

Statistical analyses were performed using IBM Statistical Package for the Social Sciences statistics software, version 24 (SPSS, IBM Corp, Armonk, NY, USA). Descriptive statistics were expressed in numbers and percentages. Relations between variables in the categorical structure were examined using the Chi-Square test and Fisher's exact test. Normally distributed groups were compared through Student's t-test, and non-normally distributed groups were compared through Mann Whitney U test. Results were evaluated at a 95% confidence interval, and the p-value of <0.05 was considered significant.

2.2. Ethical approval

The study was approved by the local institutional review board (Approval no: 2021/20). Informed consent was waived due to the retrospective design of the study.

3. Results

While there were 1269 births in our hospital between March and June, in the first peak period of the COVID-19 pandemic in 2020, 1272 births took place in the same period of 2019. In the study period of 2020, 153 patients were hospitalized in the tertiary neonatal intensive care unit while this number was 154 in 2019. A total of 307 cases were included in our study. In the study group of the cases hospitalized in the neonatal intensive care unit, 116 (75.8%) were born in our hospital, 36 (23.5%) in another center, and 1 (0.7%) at home. One hundred fourteen of the control group (74%) were born in our hospital and 40 (26%) in another center. It was found that 23.3% (n: 27/116) of the pregnant women followed up in our hospital in the study group and 2.6% (n: 3/114) in the control group disrupted their routine antenatal follow-ups and had not visited the obstetrics clinic within the previous 30 days ($p < 0.001$). The pregnant women's last application time to the obstetrics clinic before delivery was an average of 25.1 ± 28.4 days in the study group, and for those in the control group it was an average of 6.3 ± 6.8 days ($p < 0.001$). The characteristics of maternal follow-up and obstetric complications of the cases included in the study are presented in Table 1. No intergroup difference was found in terms of maternal age, gravidity, parity, maternal diabetes, hypertension, presence of meconium in amniotic fluid, anhydramnios, and umbilical cord entanglement rates ($p > 0.05$). However, during the pandemic period, an increase in the number of cases taken from the emergency department to emergency cesarean section due to conditions such as uterine rupture, placental abruption, and fetal distress was detected. Maternal mortality was observed in neither the study nor the control group.

The comparison of the groups in terms of demographic characteristics, morbidity, and mortality results of the newborn cases in our study is shown in Table 2. No difference was found between the groups in terms of gestational week and birth weight ($p > 0.05$). However, more infants with SGA were detected in the study group than the control group ($p: 0.039$). The most common reason for admission to the tertiary neonatal intensive care unit in both groups was problems with the respiratory system (98 cases (64%) in the study group; 112 cases (72%) in the control group, $p: 0.102$). It was found that 14 cases in the study group and 5 cases in the control group had a 5th minute Apgar score of <7 (9.2% vs. 3.2%, $p = 0.032$). While hypothermia treatment was applied to 8 (5.2%) of the cases with a 5th minute Apgar score of <7 in the study group, none of the control group received hypothermia treatment because they did not meet the treatment criteria ($p: 0.003$). No COVID-19 PCR positive cases were detected in the study group during the study period (first peak period of the pandemic). Although the mortality rate was higher in the study group, no statistically significant difference was found between the groups ($p: 0.104$).

4. Discussion

The results of our study show that there was a decrease in the frequency of antenatal follow-up of pregnant women

Table 1 Comparison of the groups in terms of maternal follow-up and complications.

	Studygroup (N:153)	Control group (N: 154)	P Value
Maternal age (years) (mean \pm SD)	30.5 \pm 5.2	30.9 \pm 6.0	0.547
Gravidity (mean \pm SD)	2.7 \pm 1.4	2.6 \pm 1.4	0.683
Parity (mean \pm SD)	2.3 \pm 1.2	2.1 \pm 1.0	0.429
The number of pregnant women visited to the obstetrics clinic within the last 30 days (n,%)	89 (76.7%)	111 (97.4%)	<0.001
The pregnant women's last application time to the obstetrics clinic before delivery (days)	25.1 \pm 28.4	6.3 \pm 6.8	<0.001
Premature rupture of membranes (n,%)	5 (3.3%)	2 (1.3%)	0.448
Maternal hypertension (n,%)	20 (13.1%)	19 (12.3)	0.847
Maternal diabetes (n,%)	10 (6.5%)	9 (5.8%)	0.801
Anhydramnios (n,%)	1 (0.7%)	0 (0%)	0.498
Entanglement of the umbilical cord (n,%)	3 (2%)	—	0.123
Uterine rupture (n,%)	1 (0.7%)	—	0.498
Placental abruption (n,%)	2 (1.3%)	—	0.248
Presence of meconium in amniotic fluid (n,%)	7 (4.6%)	3 (1.9%)	0.198
Intrauterine fetal death (n,%)	0 (0%)	0 (0%)	—
Urgent events in the emergency department ^a (n,%)	13 (8.5%)	3 (1.9%)	0.010

^a Presentation in the second stage of labor, Cesarean section from the emergency room (uterine rupture, placental abruption, fetal distress etc.)

during the first peak of the COVID-19 pandemic period, and, as a result, compared to the same period data of the previous year, that there was an increase in the frequency of

Table 2 Comparison of the groups in terms of demographic characteristics, morbidity and mortality results of neonatal cases.

	Study group (N:153)	Control group (N: 154)	P Value
Gestational age (weeks) (mean \pm SD)	36.7 \pm 3.8	35.9 \pm 3.2	0.003
Premature delivery <28 gestational weeks (n,%)	6 (3.9%)	5 (3.2%)	0.750
Premature delivery <34 gestational weeks (n,%)	27 (17.6%)	27 (17.5%)	0.979
Premature delivery <37 gestational weeks (n,%)	53 (34.6%)	77 (50%)	0.006
Postdate delivery >40 gestational weeks (n,%)	17 (11.1%)	2 (1.3%)	<0.001
Birth weight (g) (mean \pm SD)	2787 \pm 879.1	2788.5 \pm 856.32	0.989
Gender (n,%)			0.865
Female	78 (51%)	80 (51.9%)	
Male	75 (49%)	74 (48.1%)	
Mode of delivery (n,%)			0.309
Spontaneous vaginal delivery (n,%)	35 (22.9%)	28 (18.2%)	
Cesarean delivery (n,%)	118 (77.1%)	126 (81.8%)	
Postnatal age (day) (mean \pm SD)	2.1 \pm 4.5	2.6 \pm 5.3	0.943
Duration of hospitalization (day) (mean \pm SD)	14.0 \pm 13.7	15.0 \pm 19.5	0.590
Small for gestational age (n,%)	12 (7.8%)	4 (2.6%)	0.039
5.minutes Apgar score <7 (n,%)	14 (9.2%)	5 (3.2%)	0.032
Postnatal 1st hour ph < 7.1 (n,%)	9 (5.9%)	4 (2.6%)	0.153
Respiratory distress requiring surfactan (n,%)	30 (19.6%)	40 (26%)	0.184
Total mechanical ventilator time (day) (mean \pm SD)	1.8 \pm 4.1	1.4 \pm 1.8	0.882
Total non-invasive ventilation time (day) (mean \pm SD)	1.5 \pm 2.3	2.1 \pm 3.6	0.219
Additional oxygen time (day) (mean \pm SD)	1.9 \pm 3.4	3.5 \pm 7.5	0.09
PDA requiring medical treatment (n,%)	5 (3.3%)	4 (2.6%)	0.750
Necrotizing enterocolitis \geq stage II, (n,%)	7 (4.6%)	2 (1.3%)	0.103
Pneumothorax (n,%)	1 (0.7%)	2 (1.3%)	1,00
Hypothermia treatment (n,%)	8 (5.2%)	0 (0%)	0.003
Exchange therapy (n,%)	1 (0.7%)	0 (0%)	0.498
Mortality rate (n,%)	7 (4.6%)	2 (1.3%)	0.104

pregnant women admitting to the emergency department due to emergency delivery requiring acute intervention. Also, it was observed that there was an increase in SGA and hypoxic-ischemic encephalopathy cases in newborns.

Various measures have been implemented in many countries to prevent the spread of the virus and its negative consequences during the pandemic's initial period. After the first COVID-19 case was seen in Turkey, education was suspended in all schools. As the spread and consequences of the pandemic increased within the country, all domestic and international flights were stopped. Scientific, cultural, and artistic meeting activities were postponed. Administrative leave or flexible working methods (remote working, working in turns) were applied to employees working in public institutions and organizations. Later, to prevent the spread of the virus, complete lockdown arrangements were implemented at certain intervals. During the quarantine period, it was recommended by the Ministry of Health to reduce the number of routine checks of pregnant women within the bounds of possibility and to get an examination appointment by making a phone call with the health center and the following physicians before the hospital admissions. During the months of March to June, because of the lack of personnel due to the priority of combating the pandemic, outpatient clinic services were restricted. Face-to-face communication was limited by reducing the number of outpatient clinics. In this case, the patients had difficulty in reaching the doctors they followed regularly.

In the study of Kugelman et al.¹⁴ it was reported that more pregnant women were admitted to the obstetric emergency department with emergencies requiring acute intervention during the COVID-19 period, but there was no increase in maternal and neonatal mortality. Similarly, in our study there was an increase in the number of pregnant women who applied to the obstetrics emergency department as a result of the disruption of regular antenatal follow-up of pregnant women during the COVID-19 pandemic period. It was determined that 8.5% of pregnant women were treated in the emergency department for various reasons (presentation in the second stage of labor, cesarean section from the emergency room, uterine rupture, placental abruption, fetal distress, etc.) during the pandemic period. They were admitted to the obstetric emergency room in a significantly advanced week of pregnancy and often in active labor. One pregnant woman in our study delivered at home during the pandemic period. All of these newborns who were born urgently for various reasons were generally resuscitated at birth and taken to the neonatal intensive care unit. This situation may be due to pregnant women not caring sufficiently about their complaints, such as uterine contractions, in the pandemic period. This shows that women avoided coming to the emergency room unless they expected to be in active labor during the pandemic period. The disruption of regular antenatal care of pregnant women during the COVID-19 pandemic is a reflection of the fact that pregnant women

have concerns about healthcare recommendations during the pandemic period and fears of exposure to potential carriers of COVID-19 in hospitals. This fear may have arisen from media reports that of infection spread to hospitalized patients and health care personnel largely due to the lack of personal protective equipment at the beginning of the pandemic. In addition, it may be related to the fact that the recommendations made by various health authorities across the media in the early stages of the pandemic were insufficiently clear and consistent. Health authorities should provide evidence-based, accurate health information to reduce the psychological impact of the pandemic in terms of stress and anxiety levels of general population. In addition, government officials should strive for the wider use of telemedicine systems across the country. Telemedicine systems provide regular check-ups for pregnant women and chronic patients, who are high-risk groups, and ensure the continuity of health counseling services and avoid delays in hospital admissions. Studies suggesting that prenatal visits should be reduced in order to reduce the risk of infection in healthy pregnant women during the pandemic period have been reported.⁵ However, our results show that reducing antenatal visits causes many negative consequences. Unfortunately, telemedicine systems are not widely used in our country. In our opinion, it is not correct to routinely recommend reducing antenatal visits without considering the development level of the countries concerned. Telemedicine systems need to be used widely throughout the country to reduce the number of prenatal visits.

It was reported that physical and social restrictions applied during the pandemic have negative effects on mental health.¹⁵ In a study conducted with 1210 participants during the COVID-19 pandemic in China, 16.5% of the participants were found to have moderate to severe depression symptoms, while 28.8% had moderate to severe anxiety symptoms. In the same study, it was found that women were affected more negatively by the psychological outcomes of the pandemic than men.¹⁵ Social media news caused anxiety and concerns to increase further. This situation led to a decrease in face-to-face communication of people owing to fear of infection. Diseases other than COVID-19 were left in the background. Especially during the pandemic period, it was reported that there was a decrease in the rate of hospital admissions due to acute coronary syndrome in the United States and Italy, and there was an increase in mortality and morbidity.^{7,16} Similarly, in Italy, it was reported that there was a decrease in the rate of admission to the hospital due to the fear of falling ill in the pediatric patient population with chronic diseases, and an increase in mortality and morbidity due to admission to the hospital in the last stages of disease.¹⁷ Effects of the pandemic on the obstetric population are inevitable. Pregnant women often need doctor visits for a routine check-up and regular follow-up diagnostic tests. Also, the perinatal period is risky in terms of emotional complications, including depression, anxiety, and trauma-related disorders, even under normal conditions.¹¹ Therefore, it is expected that the pregnant population will be more affected by the pandemic.

In our study, no difference was found between the groups in terms of maternal hypertension and maternal diabetes cases during the pandemic period. Similarly, in the study of Mor et al.³ in Israel, it was reported that no difference was found in maternal hypertension and diabetes cases during the pandemic period. On the other hand, Khalil et al.¹⁹ reported a decrease in maternal hypertension and nulliparity rates in the pandemic period in England compared to the previous period.

There are a limited number of studies investigating the effect of the pandemic period on newborns.^{3,9,18,20–22} In our study, while the gestational week of the study group was higher than the control group, no difference was found in terms of birth weight. Similarly, in the study of Kugelman et al.,¹⁴ it was reported that pregnant women during the pandemic period were admitted to the hospital in a more advanced gestational week. In the study of Mor et al.,³ it was reported that there was no difference in terms of gestational week or birth weight. However, we observed an increase in the cases of newborns with SGA in our study. This may be since risk factors such as pre-eclampsia and placental insufficiency associated with the threat of SGA could not be identified sufficiently due to the pregnant women not getting enough standard obstetric care due to the pandemic. A recently reported study showed that most newborns born from COVID-19-infected mothers are asymptomatic, and there is only limited evidence to suggest vertical transmission.¹⁹ However, in studies from Brazil and England, it was reported that there was an increase in the frequency of stillbirths due to chorioamnionitis secondary to infection in pregnant women infected with COVID-19.^{20,21} In the studies of Mor et al.³ and Khalil et al.,¹⁸ an increase was reported in stillbirth frequency during the pandemic period independent of COVID-19 infection. Similarly, Ashish et al.²² reported an increase in stillbirth and neonatal mortality in the pandemic period in Nepal. Meyer et al.⁹ reported that they did not observe any significant difference in terms of birth and neonatal outcomes during the pandemic in Israel. In our study, we did not detect any COVID-19 PCR positive cases during the study period. We also found no increase in the number of intrauterine stillbirths. However, we found an increase in the number of cases who underwent postpartum resuscitation, had a 5-min Apgar score of <7, and were treated with hypothermia due to a diagnosis of hypoxic-ischemic encephalopathy. Although it was not statistically significant during the pandemic period, we found an increase in neonatal intensive care mortality rate compared to data for the same period the previous year.

Our study has some limitations. It is retrospective and a single-center cross-sectional study. We do not have any information about the acceptance rates of the other neonatal intensive care clinics in the region. Possibly due to the pandemic, the decreased acceptance rates in other clinics may have been compensated for by the acceptance rates in our clinic. Also, we do not have sufficient data regarding the antenatal follow-up of patients referred from other medical centers.

In conclusion, the results of this study reveal that during the COVID-19 pandemic, pregnant women disrupted their regular antenatal care; and more pregnant women applied to the obstetric emergency department with emergencies requiring acute intervention. This led to an increase in the number of cases diagnosed with SGA and hypoxic-ischemic encephalopathy in newborns. The results of our study will be useful for better management of the current and future pandemic periods.

Declaration of competing interest

The authors have declared that they have no conflicts of interest relevant to this article.

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