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Clinical Characteristics and Outcomes of Infants Born to Mothers with COVID-19 Infection and Those with COVID-19 Infection: A Cross-sectional Study

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ABSTRACT

Objective: The aim of this study is to evaluate the risk factors, clinical findings, treatment methods and short-term outcomes of infants born to mothers with COVID-19 infection and infants with COVID-19 infection.

Materials and Methods: Data of infants born to mothers with COVID-19 infection and infants with COVID-19 infection treated in our Newborn Intensive Care Unit between 1 March 2020 and 1 April 2021 were retrospectively reviewed.

Results: A total of 60 newborns were included in the study. Of these, 46 were born to mothers with COVID-19 infection, the gestational week was 36.8±3.3 weeks, 28 were girls. All newborns born to mothers with COVID-19 tested negative for reverse transcriptase-polymerase chain reaction (RT-PCR). The premature birth rate was 30%, the low birth weight rate was 19.4%, maternal mortality was 8.7% and neonatal mortality was 2.2%. 14 of the infants included in the study had community-acquired COVID-19 infection, the gestational age was 38.9±0.9 weeks, 6 of them were girls. The most frequent clinical findings were fever and runny nasal discharge. Most neonates in both groups were formula-fed (65.2% vs. 64.3%, respectively).

Conclusion: We found that pregnant women with COVID-19 infection had a higher maternal mortality rate, preterm birth, and caesarean section. Families should be informed and encouraged about breast milk and breastfeeding during the COVID-19 pandemic.

Keywords: COVID-19, SARS-CoV-2, newborn, pregnancy

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INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), continues to threaten the whole world since December 2019 (1). Although the infected individuals are usually adults, pregnant women and babies can also be infected (1). Although the incidence is low in the childhood age group, the mortality rate is higher in the under 1-year-old group than in adults and other childhood age groups (2).

There is no definite information yet on the vertical transmission of COVID-19 infection from mother to baby (3, 4). Concerns remain about the impact of infection in newborns. In our country, there is not enough data on the babies born to mothers infected with COVID-19 during pregnancy and babies infected with COVID-19 during the newborn period (2, 5). The lack of data diversity hinders the development of effective treatment and follow-up guidelines for the disease. The pandemic dynamic requires not only adequate response to infection but also reinforcement and coordination of data collection and reporting efforts. The more cases reported the more data is available about this new virus. For this reason, our aim in this study is to evaluate the risk factors, clinical findings, treatment methods, and short-term outcomes of infants born to mothers with COVID-19 infection during pregnancy, and infants infected with COVID-19 in the newborn period, which were followed in our clinic during the pandemic in the light of literature information.

MATERIALS and METHODS

The data of infants born to mothers with COVID-19 infection and infants with COVID-19 infection treated in our Newborn Intensive Care Unit between 1 March 2020 and 1 April 2021 were retrospectively analyzed. The study design was descriptive and analytical with a cross-sectional design. Infants born to mothers who had COVID-19 infection during pregnancy and infants who had COVID-19 infection during the neonatal period were included in the study.

The inclusion criteria for the study were as follows;

1. Infants born to mothers with COVID-19 infection during pregnancy
2. Infants with confirmed COVID-19 infection admitted to the outpatient clinic or emergency department at the postnatal days 1–28.

Table 1. Demographic characteristics of newborns

Demographic characteristics	Infants born to mothers with COVID-19 (n=46)	Infants with COVID-19 (n=14)	p
Gestational age, weeks[a]	36.8±3.3	38.9±0.9	**0.008**
	38 (26–41)	39 (37–40)	
Birthweight, g[a]	3052.0±848.5	3411.8±379.5	**0.030**
	3065 (970–4640)	3300 (2990–4060)	
Home population[a]	3.7±1.1	2.3±0.5	<**0.001**
	3 (2–6)	2 (2–3)	
Apgar at 1 min[a]	7.4±1.9	8.6±0.5	<**0.001**
	8 (0–9)	9 (8–9)	
Apgar at 5 min[a]	8.7±1.3	9.9±0.4	<**0.001**
	9 (2–10)	10 (9–10)	
Healthcare worker parent[b]	1 (2.2%)	1 (7.1%)	0.415
Positive RT-PCR results[b]	0 (0%)	100 (100%)	–
Low birthweight[b] (<2500 g)	9 (19.6%)	0 (0%)	–
Gender (female/male)[b]	28/18	6/8	0.234
Mode of delivery[b] (cesarean)	39 (84.8%)	9 (69.2%)	0.128
Resuscitation[b]	5 (10.9%)	0 (0%)	0.329
Asphyxia[b]	2 (4.3%)	0 (0%)	1.000
Type of feeding[b]			1.000
Expressed breast milk	16 (34.8%)	5 (35.7%)	
Formula	30 (65.2%)	9 (64.3%)	
Place of living[b]			0.173
Urban	20 (43.5%)	9 (64.3%)	
Rural	26 (56.5%)	5 (35.7%)	

a: Values are given as mean±SD, median and IQR (25–75%); SD: Standard deviation; b: Values are given as n (%); The Shapiro–Wilk test, Chi-square test, Student's t-test and Mann-Whitney U test were used

The exclusion criteria for the study were as follows;

1. Those older than 28 days postnatal age
2. Those with no suspicion of COVID-19 infection
3. Those hospitalized from the outpatient clinic or emergency department with the suspicion of COVID-19 infection, but whose real-time reverse transcription-polymerase chain reaction (RT-PCR) test was negative

At least one nasopharyngeal swab sample was taken from all infants included in the study, and an RT-PCR test (New Coronavirus PCR Fluorescent Diagnostic Kit) was performed. The diagnosis of COVID-19 was made by documenting the positivity for the RT-PCR test in at least one nasopharyngeal sample. Asymptomatic cases were discharged after at least two negative test results. Infants who were hospitalized for COVID-19 infection were retested at one-week intervals. These infants were discharged after their symptoms resolved and with at least two negative test results 24 hours apart. Demographic characteristics, clinical findings, laboratory data, treatment methods, length of stay, and short-term outcomes of the infants were recorded in the data form. The infants included in the study were divided into 2 groups; infants born to mothers who had COVID-19 infection during pregnancy and infants who had COVID-19 infection during the neonatal period. The data of the patients were compared.

Permissions for the study were obtained from the Ministry of Health Public Health Platform and the Kanuni Training and Research Hospital Ethics Committee (Approval no: 2021/83).

Statistical analyses were performed using IBM SPSS (Statistical Package for Social Sciences) statistical software, version 24 (IBM Corp, Armonk, NY, USA). Descriptive statistics were expressed in numbers and percentages. The Chi-Square test and Fisher's exact test were used to examine the relationships between categorical variables. The Student's t-test was used to compare normally distributed groups; the Mann Whitney U test was used to compare non-normally distributed groups. The results were evaluated within the 95% confidence interval, and a p-value of <0.05 was considered significant.

RESULTS

A total of 81 infants underwent RT-PCR testing during the study period. The RT-PCR test results were positive in 17.3% of 81 infants. Of the infants included in the study, 46 were born to mothers with COVID-19 infection, and all tested negative for RT-PCR.

Table 2. Clinical features of newborns

Clinical features	Infants born to mothers with COVID-19 (n=46)		Infants with COVID-19 (n=14)		p
	n	%	n	%	
Symptomatic cases	24	60	14	100	
Tachypnea	27	58.7	1	7.1	**0.001**
Retractions	16	34.8	0	0	0.427
Moaning	9	19.6	1	7.1	**0.013**
Cyanosis	7	15.2	0	0	0.184
Cough	0	0	2	14.3	0.051
Nasal discharge	0	0	5	35.7	<**0.001**
Poor feeding	11	23.9	2	14.3	0.713
Vomiting	1	2.2	1	7.1	0.415
Fever	0	0	8	57.1	<**0.001**
Diarrhea	0	0	2	14.3	0.051
Jaundice	0	0	2	14.3	0.051
Cutis marmoratus	0	0	1	7.1	0.233
Exanthema	2	4.3	0	0	1.000

The Chi-square test was used

Fourteen infants were hospitalized from the outpatient clinic or the emergency department, and all had positive RT-PCR test results. The remaining 21 infants were those admitted to the emergency department or outpatient clinic with the suspected COVID-19 infection but had negative RT-PCR test results; hence, these infants were excluded from the study. Consequently, a total of 60 infants were included in our study; 46 were infants of mothers with COVID-19 infection, and 14 had confirmed COVID-19 infection. The demographic characteristics of the infants included in the study are shown in Table 1.

None of the infants of mothers with COVID-19 infection had a concomitant disease such as preeclampsia, hypertension, chorioamnionitis, premature rupture of membranes, or placental abruption. However, one case had a history of gestational diabetes (1.7%), and one case had obesity (1.7%). The time between RT-PCR test positivity and delivery of mothers who had COVID-19 infection during pregnancy varied between 1–29 days, but it was 5.6 days on average. Of the pregnant women with COVID-19 infection, 84.8% were delivered by caesarean section, and 7 (11.7%) of them were delivered by emergency C-section due to deterioration in non-stress test, and 2 (3.3%) due to impaired flow. Of the infants of mothers infected with COVID-19, 30.4% were premature. While 17 (37%) of these babies were asymptomatic, 29 (63%) had at least one symptom. The most common symptoms were respiratory distress and feeding intolerance (Table 2). Laboratory findings were nonspecific. Neutropenia, lymphopenia, and thrombocytopenia were detected in one case each (Table 3). Of the 46 cases, 16 (34.8%) did

Table 3. Laboratory findings of newborns

Laboratory findings	Infants born to mothers with COVID-19 (n=46)	Infants with COVID-19 (n=14)	p
White blood cells, μ/L (N: 9100–34000)	18447.8±6059.7 (9400–35500)	12420.0±5179.9 (5000–20700)	**0.004**
Neutrophil count, μ/L (N: 2500–5800)	7718.0±3576.7 (2420–20000)	3846.9±2655.1 (1100–10200)	<**0.001**
Lymphocyte count, μ/L (N:1500–3000)	8228.3±4442.9 (800–24300)	6653.8±3921.0 (1600–15600)	0.227
Thrombocyte count, x10^3/ μ/L (N: 150–400)	281739.1±77934.9 (138000–426000)	265153.8±58977.2 (136000–354000)	0.480
Hematocrit, % (N: 35–65)	55.5±7.7 (38–71)	44.8±9.5 (33.1–69.8)	<**0.001**
Hemoglobin, g/dl (N: 11.1–17.4)	18.0±2.5 (11–22.4)	15.0±2.4 (12.3–21.1)	<**0.001**
C-reactive protein, mg/L (N: 0–5)	0.2±0.3 (0.1–1.4)	0.6±0.7 (0.1–2.2)	**0.017**
Alanine aminotransferase U/L (N: 10–40)	13.0±8.1 (6–44)	22.4±9.5 (11–45)	<**0.001**
Aspartate aminotransferase, U/L (N: 22–71)	41.3±19.4 (19–127)	43.6±16.4 (28–81)	0.450
Blood urea nitrogen, mg/dl (N: 3–12)	7.4±4.3 (2–24)	6.1±2.1 (2–9.7)	0.585
Creatinine, mg/dl (N: 0.03–0.50)	0.7±0.1 (0.5–0.9)	0.4±0.07 (0.2–0.5)	<**0.001**
Creatinine kinase, U/L (N: 5–130)	470.7±384.4 (143–2008)	102.7±23.5 (70–134)	<**0.001**
Lactate dehydrogenase	510.5±153.3 (318–1027)	334.3±52.4 (296–394)	0.063
Troponin, ng/ml (N: 0–126)	32.2±38.9 (3.7–141.9)	30.5±24.5 (11.7–80.6)	0.249
Prothrombin time, sec (N: 11–14)	15.3±2.9 (11.8–24.1)	11.6±0.7 (11–12.3)	**0.019**
Partial thromboplastin time, sec, (N: 33.0–47.8)	38.3±172 (18.5–108.4)	31.5±1.5 (30.1–33.4)	0.172
International normalized ratio (INR)	1.3±0.4 (0.2–2.2)	1.0±0.1 (0.9–1.1)	0.084

Data were shown as mean±SD and (min–max). SD: Standard deviation. The Shapiro–Wilk test; Student's t-test and Mann-Whitney U test were used

Table 4. Neonatal treatment and follow-up of newborns

Treatment and follow-up	Infants born to mothers with COVID-19 (n=46)	Infants with COVID-19 (n=14)	p
Number of patients treated (n, %)	30 (65.2%)	10 (71.4%)	0.756
*Iv antibiotic treatment (n, %)	30 (65.2%)	9 (64.3%)	1.000
Clarithromycin treatment (n, %)	0	5 (35.7%)	<0.001
Azithromycin treatment (n, %)	0	2 (14.3%)	0.051
Oseltamivir treatment (n, %)	0	2 (14.3%)	0.051
Surfactant treatment (n,%)	4 (8.7%)	0	0.564
**DIK (n, %)	1 (2.2%)	0	
Oxygen treatment (n, %)	26 (56.5%)	1 (7.1%)	**0.001**
Time, hour (mean±SD)	45.2±115.0 (0–744)	1.7±6.4 (0–24)	**0.002**
***nCPAP requirement (n, %)	8 (17.4%)	0	0.179
Time, hour (mean±SD)	20.3±74.7 (0–480)		0.076
Mechanical ventilation (n, %)	4 (8.7%)	0	0.564
Time, hour	6.7±24.7(0–144)		0.258
Positive chest radiograph finding	22 (47.8%)	5 (35.7%)	0.887
****Total NICU stay, day	10.2±11.7 (0–75)	13.6±5.7 (7–27)	**0.004**
Neonatal mortality (n, %)	1 (2.2%)	0	
Maternal mortality (n, %)	4 (8.7%)	0	

*: Iv antibiotic treatment: Ampicillin and gentamicin; **: DIC: Disseminated intravascular coagulation; ***: nCPAP: Nazal Continuous Positive Airway Pressure; ****: NICU: Neonatal intensive care unit. Data were shown as mean±SD (min–max) and n (%). The Shapiro–Wilk test; Chi-square test and Mann-Whitney U test were used

not receive treatment, 30 (65.2%) received treatment (Table 4). An anomaly was detected on the chest X-ray of 22 cases (47.8%) (8.7% had ground-glass opacity, 39.1% had signs of infiltration and consolidation). Eight of the cases (17.4%) needed nasal continuous positive airway pressure (CPAP), and 4 (8.7%) needed mechanical ventilator support. Surfactant was administered to 4 cases. The average length of hospital stay of the cases was 10.2±11.1 days. The maternal mortality rate due to COVID-19 infection was 8.7%. The neonatal mortality rate was 2.2%. The cause of death of this case was disseminated intravascular coagulation (DIC) secondary to prematurity and asphyxia (Table 4).

All 14 infants with COVID-19 infection were at term. The mean age at hospital admission was 17.5±7.9 (5–28) days. All infants had a familial contact history. In all cases, the infection was transmitted horizontally. The mothers of these infants had negative PCR tests at the time of birth (routine PCR testing is performed in our hospital before delivery), and the COVID-19 test of 85.7% of these infants was positive after birth. The mean contact time between the PCR test positivity of the mothers and the PCR test positivity of the infants was 2.3 days. The mothers of two infants had negative PCR tests, had a history of transmission from other family members. All infants with COVID-19 infection were clinically symptomatic. Of the cases, 78.6% had mild (signs of upper respiratory tract infection such as fever, nasal discharge, cough), and 21.4% had moderate clinical symptoms (signs of pneumonia and gastrointestinal system findings). The most common clinical findings were fever and nasal discharge. Gastrointestinal system findings were observed (Table 2). Laboratory findings were nonspecific. Neutropenia and thrombocytopenia were detected in one case each (Table 3). None of the cases had lymphopenia (Table 3). In 50% (n=7) of the cases, infiltration or consolidation findings were detected on the chest X-ray. Only one patient needed oxygen. Of the 14 cases, 4 (28.6%) did not receive treatment, 10 (71.4%) received treatment (Table 4). The average length of hospital stay of the cases was 13.6±5.0 days.

While 64.3% of babies born to mothers with COVID-19 were fed with formula, 65.2% of babies with COVID-19 were fed with formula. Comparison of these two groups revealed that the length of hospital stay was higher in infants with COVID-19 infection (p=0.04). Neonatal and maternal mortality was observed only in infants of mothers with COVID-19 infection.

DISCUSSION

The COVID-19 infection continues to spread rapidly in all age groups around the world. In our study, the SARS-CoV-2 virus was not detected in the RT-PCR test of any infants of mothers with COVID-19 infection. Our study has shown that COVID-19 infection can cause maternal death and high preterm birth rates It was also found that the infection in newborns was generally caused by horizontal transmission and progressed with a mild clinical course.

Current information does not yet elucidate how often pregnant women have COVID-19 infection and its maternal and fetal consequences (4). Most pregnant women with COVID-19 infection are diagnosed in the third trimester of pregnancy (6). In our study, one of the pregnant women was in the second trimester and the others were in the third trimester.

COVID-19 infection in the mother has been associated with spontaneous abortion, preterm delivery, and intrauterine growth (7–9). Smith et al. (10) found that the rate of preterm birth was 63.8%, the rate of low birth weight was 42.8%, and 80% gave birth by caesarean section. In a study evaluating 125 babies from our country, Oncel et al. (1) reported the preterm birth rate as 26.4%, the low birth weight rate as 12.8%, and the caesarean section rate as 71.2%. In our study, the rate of preterm birth was 32.5%, the rate of low birth weight was 15%, and cesarean delivery was 84% in infants born to mothers with COVID-19 infection. Our study determined high rates of premature birth and caesarean delivery due to COVID-19 infection, consistent with the literature. The high rate of premature birth may be associated with fetal distress due to maternal fever and hypoxemia in pregnant women due to COVID-19 infection. The high rate of caesarean delivery in our study may be related to pregnant women's anxiety, as the effect of the delivery method on viral transmission in the early stages of the pandemic is unknown (11).

The prevalence and clinical significance of vertical transmission in COVID-19 infection remain unclear (3, 4). A review by Kotlyar et al. (12) reported that 8 of 397 newborns born to mothers infected with SARS-CoV-2 in China were positive in the nasopharyngeal sample and vertical transmission was 2%. This review also reported that nasopharyngeal samples were positive in 19 of 539 newborns born to mothers with SARS-CoV-2 from outside China, and vertical transmission was 3.5% (12). Oncel et al. (1) also suggested that there may be a relationship between the duration of intrauterine viral exposure and neonatal COVID-19 positivity. Their study demonstrated that the time between maternal symptoms and delivery was longer in SARS-CoV-2 positive newborns than in negative newborns (6 days versus 2) (1). The mean intrauterine viral exposure time of the cases in our study was 5.6 days. In our study, the RT-PCR tests did not detect positive SARS-CoV-2 virus in any of the infants born to mothers with COVID-19 infection. Similar to our study, Yan et al. (13) reported that none of the 86 infants born to mothers with SARS-CoV-2 were positive for SARS-CoV-2 virus in their nasopharyngeal samples. However, a few recent articles have reported that intrauterine placental transmission of SARS-CoV-2 infection may be possible (12, 14, 15). Besides, in some studies, SARS-CoV-2 viral RNA has been detected in cord blood, amniotic fluid, vaginal secretions, and breast milk. (11, 14–18).

A review by Westgren et al. (19) examining 108 pregnant women with COVID-19 infection reported that the disease progression was more severe in pregnant women. Maternal mortality rates due to COVID-19 vary from country to country. In Mexico, Lumbreras-Marquez et al. (20) reported the maternal mortality rate among pregnant women with COVID-19 as 2.3%. In Turkey, the maternal mortality rate was reported as 4.8% (6/125) by Oncel et al. (1). In our study, the maternal mortality rate was 8.7%. The higher rate of maternal mortality in our study compared to the literature suggests that prenatal follow-up of pregnant women is not sufficient, and this may cause a delay in diagnosis and treatment.

Oncel et al. (1) evaluated 125 infants born to mothers with COVID-19 infection and reported that 23% of infants needed mechanical ventilation, 19% required nasal CPAP, and one case died. In our study, 63% of infants of mothers with COVID-19 infection were symptomatic, and the most common symptoms were respiratory distress and feeding intolerance. Of our cases, 17.4% needed nasal CPAP, and 8.7% needed a mechanical ventilator. One case died as a result of perinatal asphyxia due to extreme prematurity and severe maternal SARS-CoV-2 infection. The relationship between the symptoms detected in postnatal infants and maternal SARS-CoV-2 infection has not yet been fully understood (1). Fetal outcomes may also be affected by the severity of the maternal infection and/or concurrent obstetric diseases, rather than the possibility of virus transmission to the fetus (21). Since 30% of our cases were premature and the PCR test was negative in all our patients, we think that the severity of the maternal infection and prematurity account for the symptoms developed in our patients.

It has been reported that the incidence of COVID-19 infection in newborns is much lower than in adults and children (1). In our study, the RT-PCR test result was positive in 17.3% of infants and all had a history of droplet transmission from the mother or other family members. All were term, 8 were male, and the mean age at hospital admission was 5–28 days. In the study of Kanburoğlu et al. (5), it was reported that 3 of 37 newborns with COVID-19 infection were premature, 19 were male, and the mean age at diagnosis was 15.6 days. It was reported that the clinical symptoms of COVID-19-infected newborns ranged widely from asymptomatic carrier to critically ill (1). In literature, the most common clinical symptom in neonatal COVID-19 cases is fever (5). In the study by Kanburoğlu et al. (5), the most frequent symptoms in COVID-19-infected newborns were fever, hypoxemia, cough (5). It has been reported that 35% of these cases have a serious course, 40% need oxygen, 15% need nasal CPAP, 3% need mechanical ventilation, and one case with Down syndrome and cardiovascular disease has died (5). It has been reported that gastrointestinal system findings such as feeding intolerance, vomiting and diarrhea are more prominent in some newborns, unlike adults and children (22). It has been reported that neurological symptoms such as irritability, hypertonia, lethargy, and hypotonia can also be seen in newborns with COVID-19 infection (22). In our study, all of our cases with COVID-19 infection were symptomatic, and the most common findings were fever and nasal discharge. Symptoms of 78.6% of our cases were mild. Gastrointestinal system symptoms were evident in two of our cases. Neurological symptoms were not detected in any of our cases. The results of our study show that COVID-19 infection progresses with milder symptoms in newborns than in adults. The milder course of infection in children may be associated with fewer and immature ACE2 receptors (COVID-19 cell receptors) and less proinflammatory cytokine response in children compared to adults (22, 23).

Laboratory findings may be nonspecific in newborns with COVID-19 infection (3). Karabay et al. (22) reported that leukopenia, leukocytosis, and elevation in the levels of d-dimer, liver enzymes, and acute phase reactants may occur in cases with COVID-19. In addition, Kallem et al. (3) reported that newborns with COVID-19 may have lymphopenia, thrombocytopenia, and elevation in various enzyme levels (such as lactate dehydrogenase, alanine aminotransferase, aspartate aminotransferase, and creatine kinase). In our study, neutropenia and thrombocytopenia were detected in one case in each group. In addition, mild elevations in creatine kinase level were detected in both groups, especially in infants of mothers with COVID-19. Other laboratory findings in our study were within normal limits. This result emphasizes the importance of PCR tests in routine diagnosis. Some studies suggested that serological tests may be helpful in diagnosis (24, 25). Detection of positive SARS-CoV-2 IgM antibodies despite negative results of the repeated nasopharyngeal samples was reported in one infant by Dong et al. (24) and in two infants by Zeng et al. (25). Kotylar et al. (12) reported that 3.7% of infants were positive for anti-SARS-CoV-2 IgM antibodies. Since there is no transplacental transfer of IgM, this is finding supports fetal exposure to the SARS-CoV-2 virus in utero (4). However, the sensitivity and specificity of the IgM test were lower than the molecular tests (4).

In our study, 71.4% of infants with COVID-19 infection and 65.2% of infants born to mothers infected with COVID-19 during pregnancy received treatment, and the treatment was mainly symptomatic in both groups. The most commonly used medical treatment was intravenous antibiotic therapy. Kanburoğlu et al. (5) reported in their study on newborns with COVID-19 infection that 54% of the cases received intravenous antibiotics, 38% received azithromycin, and 32% received oseltamivir as treatment. The review by Li et al. (26) reported a similar symptomatic and supportive treatment given to 40 neonatal COVID-19 cases. It has been reported in the literature that antiviral drugs such as interferon, ribavirin, lopinavir/ritonavir, remdesivir, oseltamivir, and hydroxychloroquine can be given to a few patients with COVID-19 infection (27–29). Accordingly, we gave oseltamivir treatment to 2 patients in our study and did not detect any problems. However, further studies are needed on the necessity and effectiveness of antiviral treatments in newborns.

According to previous studies, most newborns with COVID-19 infection have a good prognosis (23). However, Kanburoğlu et al. (5) reported that myocarditis, DIC, and multiple organ dysfunction (38%, 32%, 54%, respectively) were seen in newborns with COVID-19. Wardell et al. (28) reported that SARS-CoV-2 RNA was positive for 20 days in a newborn's nasopharyngeal sample and needed multiple medical treatments because of fever that recurred 5 times within 4 weeks after discharge. In our study, we did not detect any complications in any of our cases with COVID-19 infection. However, since it is a newly known virus, patients should be followed closely for a long time to reach a definite conclusion about the short and long-term consequences of neonatal COVID-19 infection.

The World Health Organization defines breast milk as the most suitable food for infants (30). There have been great difficulties in feeding newborns in the NICU during the pandemic process (5). Restrictions on NICU visits, especially breastfeeding by infected mothers and transfer of expressed breast milk are sensitive issues. Oncel et al. (1) reported that 56.8% of 125 infants born to mothers with COVID-19 infection were fed with formula. Likewise, Kanburoğlu et al. (5) reported that 26% of 37 infants treated in the NICU due to COVID-19 infection were formula-fed. The World Health Organization declared that standard nutrition guidelines should be followed during the pandemic period, along with all necessary infection control measures (30). However, close contact of babies with their mothers will pose a serious risk for transmission if the conditions preventing transmission are not adequate (3, 4). Besides, one study suggested that the virus may pass into the milk, and hence, breast milk may carry a risk of transmission to the baby (18). ACE-2 receptors are found in many parts of the body, including the oral cavity (e.g., tongue and oral mucosa) and breast tissue and if the mammary epithelial cells express these receptors, the live virus may pass into the milk, and in this case, there may be a risk of transmission to the infant through breast milk (18). In our study, most of the cases in both groups were fed with formula. The reason for this could be that families and healthcare professionals are concerned about the transmission of the virus to the baby through breastfeeding and breast milk, as this issue has not been fully elucidated.

Limitations of the Study

Our study has limitations. First, our study was single-centered and the number of cases was low. Second, the presence of the virus in cord blood, amniotic fluid, placenta, and breast milk could not be investigated due to financial reasons. The detection of IgM and IgG antibodies specific for SARS-CoV-2 may be critical in the diagnosis of vertical transmission. Unfortunately, our study was unable to obtain an antibody test. In the future, testing for SARS COV-2 in the placenta, amniotic fluid and breast milk or detection of SARS-CoV-2-specific IgM and IgG antibodies may be part of the routine evaluation of pregnant women infected with SARS-CoV-2 infection.

CONCLUSION

We found that pregnant women with COVID-19 infection had a higher maternal mortality rate, preterm birth, and caesarean section. Families should be informed and encouraged about breast milk and breastfeeding during the COVID-19 pandemic.

Ethics Committee Approval: Permissions for the study were obtained from the Ministry of Health Public Health Platform and the Kanuni Training and Research Hospital Ethics Committee (date: 23.05.2021, number: 2021/83).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – BSH; Design – BSH, FAA; Data Collection and/or Processing – BSH, FAA; Analysis and/or Interpretation – BSH, FAA; Literature Search – BSH; Writing – BSH; Critical Reviews – BSH, FAA.

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