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ORIGINAL ARTICLE

A multicenter study on epidemiological and clinical characteristics of 125 newborns born to women infected with COVID-19 by Turkish Neonatal Society

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Abstract

Limited data are available on pregnant women with COVID-19 and their neonates. We aimed to evaluate the epidemiological and clinical characteristics of newborns born to women infected with COVID-19. A multicenter cohort study was conducted among newborns born to mothers with COVID-19 in 34 neonatal intensive care units (NICUs) in Turkey. Pregnant women ($n = 125$) who had a positive RT-PCR test and their newborns were enrolled. Cesarean section, prematurity, and low-birthweight infant rates were 71.2%, 26.4%, and 12.8%, respectively. Eight of 125 mothers (6.4%) were admitted to an intensive care unit for mechanical ventilation, among whom six died (4.8%). Majority of the newborns (86.4%) were followed in isolation rooms in the NICU. Four of 120 newborns (3.3%) had a positive RT-PCR test result. Although samples taken on the first day were negative, one neonate became positive on the second day and the other two on the fifth day. Sample from deep tracheal aspirate was positive on the first day in an intubated case.

Conclusion: COVID-19 in pregnant women has important impacts on perinatal and neonatal outcomes. Maternal mortality, higher rates of preterm birth and cesarean section, suspected risk of vertical transmission, and low rate of breastfeeding show that family support should be a part of the care in the NICU.

Trial registration: ClinicalTrials.gov identifier: NCT04401540

The Neo-Covid Study Group Collaborators list have been uploaded in the appendix for publication in PubMed

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What is Known:

- *The common property of previous reports was the conclusions on maternal outcomes, rather than neonatal outcomes.*
- *Published data showed similar outcomes between COVID-19 pregnant women and others.*

What is New:

- *Higher maternal mortality, higher rates of preterm birth and cesarean section, suspected risk of vertical transmission especially in a case with deep tracheal aspiration during the intubation, and the possible role of maternal disease severity on the outcomes are remarkable findings of this study.*
- *In contrast to recommendation for breastfeeding, parents' preference to formula and expressed breast milk due to anxiety and lack of information shows that family support should be a part of the care in the NICU.*

Keywords SARS-CoV-2 · COVID-19 · Pregnancy · Newborn

Introduction

The new type of coronavirus (severe acute respiratory syndrome coronavirus-2, SARS-CoV-2) infection called coronavirus disease 2019 (COVID-19) has caused a huge pandemic starting from Wuhan to worldwide [1, 2]. Although the first case in the world was seen in China in December 2019, COVID-19 was detected in Turkey on March 9, 2020, much later than in many countries [3]. The elderly population and those with underlying diseases are more susceptible to the virus, but the disease can be seen in the childhood and neonatal periods, too. Children are reported to have fewer symptoms, less severe disease, and a lower case–death rate [4–8]. A multinational, multicenter cohort study including 40 newborns with PCR-confirmed SARS-CoV-2 infection reported that COVID-19 was generally a mild disease in children, including infants. However, a small proportion developed severe disease requiring intensive care unit admission and prolonged ventilation, although fatal outcome was overall rare. In multivariable analysis, the factor that remained associated with intensive care unit admission was being younger than 1 month [8].

The information on the vertical transition from mother to fetus is still insufficient. Limited case series on the effect of COVID-19 pregnant women and their infants is available in the literature [9–11]. SARS-CoV-2 infection during pregnancy is known to cause maternal complications including premature rupture of membranes, preeclampsia, gestational diabetes, hypertension, and neonatal complications such as respiratory distress, pneumonia, early and late onset infection, low birthweight, rash, disseminated intravascular coagulation, asphyxia, and perinatal death [11–18].

We aimed to evaluate epidemiological and clinical characteristics of 125 newborns born to women infected with COVID-19 in this study. To the best of our knowledge, the present study is the most comprehensive one, which evaluated neonates born to women with proven SARS-CoV-2 infection.

Materials and methods

A multicenter cohort study was conducted among newborns born to mothers with a reverse transcriptase–polymerase chain reaction (RT-PCR)–proven SARS-CoV-2 infection in 34 neonatal intensive care units (NICUs) in Turkey. The management of newborn with or at risk of COVID-19 was in accordance with the proposal provided by the Turkish Neonatal Society (TNS) [2, 19]. The study was approved by the Online Studies Scientific Steering Committee of the TNS, by the Rize University School of Medicine local ethics committee, and by the Ministry of Health. Written informed consent was obtained from the parents or guardians of the newborns. The trial was registered to ClinicalTrials.gov under identifier NCT04401540.

Management of COVID-19 in the delivery room and NICU

All deliveries were performed in isolated rooms including all protective equipment in the operating room or delivery room. Delivery decisions were made in conjunction with a neonatologist. Timing and mode of delivery were determined by an obstetrician in terms of obstetric indications. The assigned teams coordinated the hospitalization and maintenance of the newborns born to SARS-CoV-2-infected mothers [19]. In the presence of high-risk factors including maternal fever, premature rupture of membrane, premature birth, low birthweight, or small for gestational age, the newborn was admitted and taken into an isolation room or to an allocated place for the COVID-19 patients in the NICU. Access to the patient's room and patient care were performed depending on the recommendations of the proposal. The decision about breastfeeding was made on a case-by-case basis after consulting with the parents. Mothers were encouraged to breastfeed their infants or express their breast milk to establish and maintain milk supply. While feeding at the breast, all possible precautions were taken to avoid contamination of the virus including careful handwashing and wearing a face mask [19].

Samples of the newborn were taken by a staff who was trained and designated by the NICU and delivered to the relevant laboratory. Staff performing invasive procedures (aspiration, intubation, respiratory sample) used disposable waterproof gowns, N95 masks, goggles/eye protection, and gloves. Hand hygiene was attained before and after gloves.

Nasopharyngeal/pharyngeal swabs were tested after birth and on subsequent 2 days [19]. Samples of nasopharyngeal and pharyngeal swabs were tested for SARS-CoV-2 by using a kit (Bioeksen, Istanbul, Turkey), following the World Health Organization guidelines for RT-PCR. Newborns who had positive RT-PCR from respiratory tract were defined as a COVID-19 case. Newborns with SARS-CoV-2 were classified according to international classification [20]. Nasopharyngeal/pharyngeal swabs and deep tracheal aspirates were collected and tested every 2 days until two consecutive results show negative for COVID-19 with at least a 24-h interval in COVID-19 cases. All patients were monitored for vital signs, and respiratory, cardiovascular, and gastrointestinal symptoms closely. Laboratory and radiological examinations including complete blood count, liver function tests, creatine phosphokinase, lactate dehydrogenase, and chest radiography (if necessary) were investigated. Supportive treatments such as oxygen therapy, fluid–electrolyte treatment, total parenteral nutrition support if necessary, and advanced respiratory support if necessary (non-invasive/invasive with exhalation filter) were used on a need basis. Patients were discharged according to discharge criteria defined in the proposal [19]. All neonates, whether in the NICU or not, were followed up and monitored by the Ministry of Health for at least 14 days.

Data collection

Pregnant women were not routinely screened for COVID-19 before delivery. RT-PCR samples were taken only from symptomatic women and/or history of COVID-19 contact, and only pregnant women with positive RT-PCR results were included in this study. Antenatal, natal, and postnatal risk factors; data regarding demographic, epidemiologic, and clinical features; treatment strategies; and breastfeeding history were recorded by the participating neonatologist on electronic case report forms (eCRF) through the online data registry system (www.trials-network.org). The registry system did not allow the collaborator to proceed and submit the data if no response was received for any question in the eCRF. The study period comprised March 15 to June 15, 2020, and the records from 34 NICUs were pooled together and analyzed at the end of the study. Mendeley Data: https://doi.org/10.17632/4gczscr6fz.3

Statistical analyses

Statistical analyses were conducted using the SPSS statistical software for Windows, V.21.0 (SPSS, Chicago, Illinois, USA). The Shapiro–Wilk test was used to test for the normality of data. Difference between two groups was examined by using the independent samples *t* test for normally distributed variables and the Mann–Whitney *U*-test for non-normally distributed variables. Since there were 4 patients in one of the groups, the significance value was calculated by using the *Exact* method of the Mann–Whitney *U*-test which was used in comparison of the groups. The chi-square test was used for categorical variables. The results are presented as numbers (*n*), frequencies (%), and medians with their interquartile range (IQR, 25–75%). A p value of less than 0.05 was considered significant for the statistical tests.

Role of the funding source

This study was supported by the TNS. TNS funded the online registration system only, and did not have any role in study design, data analysis, and in the preparation of the article. The corresponding author had full access to all eCRFs and takes the final responsibility for the decision to submit for publication. The final version of the manuscript was approved by all authors.

Results

Clinical and laboratory characteristics of mothers with COVID-19

Eighty-five pregnant women (68%) had at least one symptom of COVID-19, whereas the others had history of close contact with other family members with COVID-19. While most of the mothers lived in the urban areas (*n*: 119, 95.2%), a few lived in the rural areas (*n*: 6, 4.8%). Eight of the mothers (6.4%) were healthcare professionals. Most of the cases gathered in the largest three cities of the country (Istanbul, Ankara, and Izmir).

Cesarean section, prematurity, and low-birthweight infant rates were 71.2%, 26.4%, and 12.8%, respectively. Eight of 125 mothers (6.4%) were admitted to an intensive care unit for mechanical ventilation, among whom six died (4.8%). Clinical and laboratory characteristics of COVID-19 mothers according to their newborns with/without SARS-CoV-2 infection are summarized in Table 1. Time between symptoms and delivery was longer in neonates with a positive RT-PCR test, but this was not statistically significant (median 6 (5–7) days vs. 2 (1–5) days, $p = 0.085$). Median serum levels of C-reactive protein (CRP), plasma levels of prothrombin time (PT), and international normalized ratio (INR) were significantly higher in mothers with SARS-CoV-2-positive newborns in comparison with mothers who did not have SARS-CoV-2-positive newborns (95% confidence interval (CI) 1.001–1.014, $p = 0.004$; 95% CI 1.001–1.309, $p = 0.023$; and 95% CI 14.559–56,659, $p = 0.007$, respectively).

Clinical and laboratory characteristics of the neonates

Four of 120 newborns (3.3%) who had RT-PCR evaluation revealed positive result. Asymptomatic five neonates could not be tested. Nasopharyngeal and pharyngeal swabs were positive in three cases. Although samples of these cases taken

Table 1 Clinical and laboratory characteristics of COVID-19 mothers according to their newborns with/without SARS-CoV-2 infection

Characteristics	Newborns without SARS-CoV-2 ($n = 121$)	Newborns with SARS-CoV-2 ($n = 4$)	p value
Gestational age diagnosed with COVID-19, weeks[a]	37 (35–38)	35 (29–38)	0.306
Time between symptoms and delivery, days[a]	2 (1–5)	6 (5–7)	0.085
Gestational age at delivery, weeks[a]	38 (36–39)	36 (30–38)	0.157
Prematurity (< 37 weeks)[b]	31 (25.6)	2 (50)	0.284
Birthweight, grams[a]	3140 (2775–3415)	2465 (1480–3340)	0.233
Low birthweight (< 2500 g)[b]	14 (11.6)	2 (50)	0.079
Gender (Male)[b]	66 (54.5)	3 (75)	0.392
Mode of delivery (Cesarean)[b]	86 (71.1)	3 (75)	0.674
Apgar at 1 min[a]	8 (7–8)	8 (5–8)	0.177
Apgar at 5 min[a]	9 (9–10)	8 (7–9)	0.039
Mother and newborn separation[b]	110 (90.9)	4 (100)	0.689
Type of feeding[b]			0.273
Breastfeeding with caution	9 (7.4)	-	
Expressed breast milk	45 (37.2)	-	
Formula	67 (55.4)	4 (100)	
Maternal comorbidities[b]	16 (13.2)	-	0.574
Gestational diabetes	7 (5.8)		
Preeclampsia	6 (4.9)		
Hypertension	2 (1.6)		
Placenta previa	1 (0.8)		
Smoking[b]	8 (6.6)	-	0.765
Home population[a]	4 (3–5)	4 (3–5)	0.481
Maternal laboratory tests[a]*			
White blood cell count, /μL	9280 (7000–11,900)	6310 (5155–15,655)	0.362
Neutrophil count, /μL	6790 (4700–9025)	4595 (3705–12,990)	0.419
Lymphocyte count, /μL	1300 (1000–1850)	995 (445–1660)	0.272
Platelets, $\times 10^3/\mu L$	216 (171–260)	207 (148–267)	0.790
C-reactive protein (CRP), mg/L	9.7 (3.5–43)	124 (4.95–310)	0.004
Creatinine, mg/dL	0.56 (0.49–0.64)	0.53 (0.45–0.98)	0.740
Aspartate aminotransferase (AST), U/L	23 (17–38)	21 (9–46)	0.542
Alanine aminotransferase (ALT), U/L	14 (9–25)	14 (11–18)	0.774
Creatine kinase (CK), U/L	85 (44–159)	112 (28–275)	0.944
Lactate dehydrogenase (LDH), U/L	255 (196–344)	428 (275–580)	0.227
Prothrombin time (PT), sec	12.3 (11.2–13.4)	14.1 (13.3–20.9)	0.023
International normalized ratio (INR)	1 (0.93–1.05)	1.34 (1.09–1.74)	0.007
Activated partial thromboplastin time (aPTT), sec	29 (25.5–33.5)	28.7 (18.8–32.2)	0.557
Maternal treatment and follow-up[b]			
Medical treatment for COVID-19**	79 (65.3)	4 (100)	0.190
Mechanical ventilation	7 (5.8)	1 (25)	0.235
Intensive care unit admission	7 (5.8)	1 (25)	0.235
Maternal mortality[b]	5 (4.1)	1 (25)	0.181
Neonatal treatment and follow-up			
Duration of supplemental oxygen, h[a]	24 (8.5–72)	69 (12–400)	0.359
Duration of nasal CPAP, h[a]	24 (8–48)	58 (6–240)	0.496
Duration of mechanical ventilation, h[a]	48 (40–78)	252 (144–360)	0.178
Mechanical ventilation or nasal CPAP[b]	23 (19)	3 (75)	0.028
Length of NICU stay, days[a]	7 (3–11)	26 (15–48.5)	0.033
Neonatal mortality[b]	1 (0.8)	-	0.968

[a] Values are given as median and IQR (25–75%)

[b] Values are given as percentage

*Worst laboratory values of mother in diagnosis and follow-up

**Hydroxychloroquine (*n*: 74), azithromycin (*n*: 39), oseltamivir (*n*: 20), favipiravir (*n*: 10), lopinavir–ritonavir combination (*n*: 6), enoxaparin (*n*: 6), and corticosteroid (*n*: 3) were used

CPAP, continuous positive airway pressure; *NICU*, neonatal intensive care unit

on the first day were negative, one neonate became positive on the second day and the other two cases on the fifth day. On the contrary, sample from deep tracheal aspirate was positive on the first day in an intubated case (Table 2). Additional COVID-19 investigations included placenta tissue (*n*: 5), amnion fluid (*n*: 4), deep tracheal aspirate (*n*: 9), serum (*n*: 3), stool (*n*: 2), and breast milk (*n*: 6), which were all negative for SARS-CoV-2 except only one positive deep tracheal aspirate.

The Apgar score at the 5th minute was significantly lower in newborns with SARS-CoV-2 compared with neonates without SARS-CoV-2 (8 (7–9) vs. 9 (9–10), 95% CI 0.263–0.998, $p = 0.039$). Neutrophil count was significantly lower in newborns with SARS-CoV-2 compared with newborns without SARS-CoV-2 (3235 (2235–5500) vs. 8445 (4965–12,385), 95% CI 1.002–1.005, $p = 0.024$). The need for mechanical ventilation or nasal CPAP was higher (75% vs. 19%, 95% CI 1.271–128.5, $p = 0.028$), and the duration of hospitalization was significantly longer in the newborns with SARS-CoV-2 positivity (26 (15–48.5) vs. 7 (3–11) days, 95% CI 1.018–1.148, $p = 0.033$). Imaging findings of four newborns with SARS-CoV-2 are shown in Fig. 1.

Majority of the newborns (*n*: 108, 86.4%) born to COVID-19 mothers were followed in isolation rooms in the NICU for a while, whereas others were monitored with a distance of 2 m away from the mother (*n*: 11, 8.8%) or cared by family members in a separate room (*n*: 6, 4.8%). Most of the neonates were fed by formula (*n*: 71, 56.8%) or expressed breast milk (*n*: 45, 36%), followed by breastfeeding (*n*: 9, 7.2%) with caution. All neonates with COVID-19 (*n*: 4) were fed with formula.

Discussion

We evaluated outcomes of 125 COVID-19 pregnant women and their newborns in this multicenter study. Our data demonstrated that COVID-19 could result in maternal death, might have suspect on risk of vertical transmission, and can cause COVID-19 in newborns after birth. Newborns with COVID-19 can need respiratory support and longer hospital stay in the NICU. The rates of formula and expressed breastfeeding were high among all newborns.

Four (3.3%) among 120 newborns tested had a positive RT-PCR result. The rates of newborns with SARS-CoV-2 vary in a systematic review and two studies (2.7% (1/37), 9.09% (3/33), and 4.2% (3/72)) [21–23]. In our study, it is unclear if this rate was an evidence of vertical transmission or it was contacted post-delivery due to delayed RT-PCR testing 5 days from birth. Some of the cases in reported studies, despite initial testing at birth was negative, had positive RT-PCR results on repeat testing. In addition, it was found that three newborns, whose mother admitted with COVID-19 infection 23 days before birth, had IgM and IgG against SARS-CoV-2 at birth [24, 25]. Recent articles showed the potential intrauterine placental transmission of SARS-CoV-2 infection [26, 27]. Therefore, vertical transmission could not be excluded with the knowledge up to now. Furthermore, median time between symptoms and delivery was longer in the newborns with SARS-CoV-2 group (6 vs. 2 days) in our study, although it was not statistically significant. It can be speculated that there may be a relationship between the duration of intrauterine viral exposure and neonatal COVID-19 positivity. We think that time between symptoms and delivery should be evaluated in the future studies.

One term neonate with COVID-19 did not have any respiratory failure, whereas the other three (a 38-week term, and 26- and 33-week preterm) required mechanical ventilation or nasal CPAP. It is hard to say whether these requirements were due to either SARS-CoV-2 infection or prematurity. Neonatal respiratory failure can result from a wide range of causes, and SARS-CoV-2 testing in newborns when other causes are reasonably suspected may divert laboratory resources while cannot exclude other neonatal etiologies [28].

According to a systemic review in which nine studies and 92 cases were analyzed, 63.8% had preterm delivery, 42.8% had a low birthweight, 80% were delivered by cesarean section, 76.9% of neonates required NICU admission, and only one indeterminate case of potential vertical transmission was observed [21]. In our study, while preterm infants (26.4%) and low-birthweight (12.8%) rates were lower, cesarean section delivery (71.2%) and NICU admission (86.4%) rates were similar. Smith et al. demonstrated that there was no maternal death and only one patient required intensive care and ventilation in a systemic review [21]. However, in our cohort, eight pregnant women (6.4%) required mechanical ventilation in intensive care units, and six of them died. To date, it has been reported that COVID-19 clinics of pregnant and non-pregnant women are similar in the case series, and the mortality rates are low [9, 21]. Mortality rates vary according to countries and severity of COVID-19 case series. Lumbreras-Marquez et al.

Table 2 Demographic and clinical characteristics of newborns with SARS-CoV-2

	Case 1	Case 2	Case 3	Case 4
Gender	Male	Male	Female	Male
Gestational age, weeks	26	33	38	38
Birthweight, grams	1010	1950	2980	3700
Mode of delivery	Cesarean	Vaginal	Cesarean	Cesarean
Apgar at 1 and 5 min	2 and 6	7 and 8	8 and 9	8 and 9
Resuscitation requirement	Yes	No	No	No
Neonatal symptoms	Tachypnea, feeding intolerance	Tachypnea, fever, cough	None	Tachypnea
Respiratory support	Nasal CPAP, MV	Nasal CPAP, MV	-	Nasal CPAP
Laboratory tests				
White blood cell count, /μL	3580	23,500	4400	7960
Neutrophil count, /μL	1500	7500	3500	2970
Lymphocyte count, /μL	1820	13,700	400	3790
Platelets, $\times 10^3/\mu L$	86	244	276	388
C-reactive protein (CRP), mg/L	0.60	0.80	2.1	0.2
Procalcitonin, ng/mL	0.45	0.60	-	-
Creatinine, mg/dL	0.84	0.80	0.82	0.50
Aspartate aminotransferase (AST), U/L	56	15	30	25
Alanine aminotransferase (ALT), U/L	7	6	9	10
Creatine kinase (CK), U/L	102	-	-	744
Lactate dehydrogenase (LDH), U/L	601	539	356	-
Prothrombin time (PT), sec	19	12.2	-	-
International normalized ratio (INR)	1.6	1.02	-	-
Activated partial thromboplastin time (aPTT), sec	44	29.2	-	-
D-dimer, mg/L FEU	5.63	2.05	-	-
COVID-19-specific treatment	No	Yes*	No	No
Breastfeeding	No	No	No	No
Admitted for isolation	Yes	Yes	Yes	Yes
Duration of NICU, days	69	28	6	24
Discharged	Yes	Yes	Yes	Yes
Maternal death	Yes	No	No	No
SARS-CoV-2 RNA (RT-PCR)				
Nasopharyngeal swabs on 1 day	-	Negative	Negative	Negative
Nasopharyngeal swabs on 2–5 day	-	Positive	Positive	Positive
Other	DTA positive	-	-	-
Time of RT-PCR positivity, days	1	5	5	2
Negative RT-PCR result, days	7	11	7	6
According to international classification [20]	Confirmed	Probable	Probable	Probable

CPAP, Continuous positive airway pressure; *MV*, Mechanical ventilation; *NICU*, Neonatal intensive care unit, *RT-PCR*, reverse transcriptase–polymerase chain reaction; *DTA*, deep tracheal aspirate

*Oseltamivir and azithromycin

reported a 2.3% case fatality rate among pregnant with COVID-19 in Mexico [29]. Also, in a study from Iran, authors demonstrated that of nine pregnant women with severe COVID-19 disease, seven died, one was critically ill requiring mechanical ventilation, and one recovered after long hospital stay [30]. It has been publicized that pregnant women are not at increased risk of susceptibility, infectivity, and severity of COVID-19 compared with the general population or non-pregnant women perhaps with the good intention of reducing anxiety among this vulnerable population group [31–33]. In contrast, a systematic review of 108 cases of laboratory-confirmed pregnancies with COVID-19 reported the possibility of increased risk of severe disease among pregnant women [34]. An analysis based on an estimate of the total number of

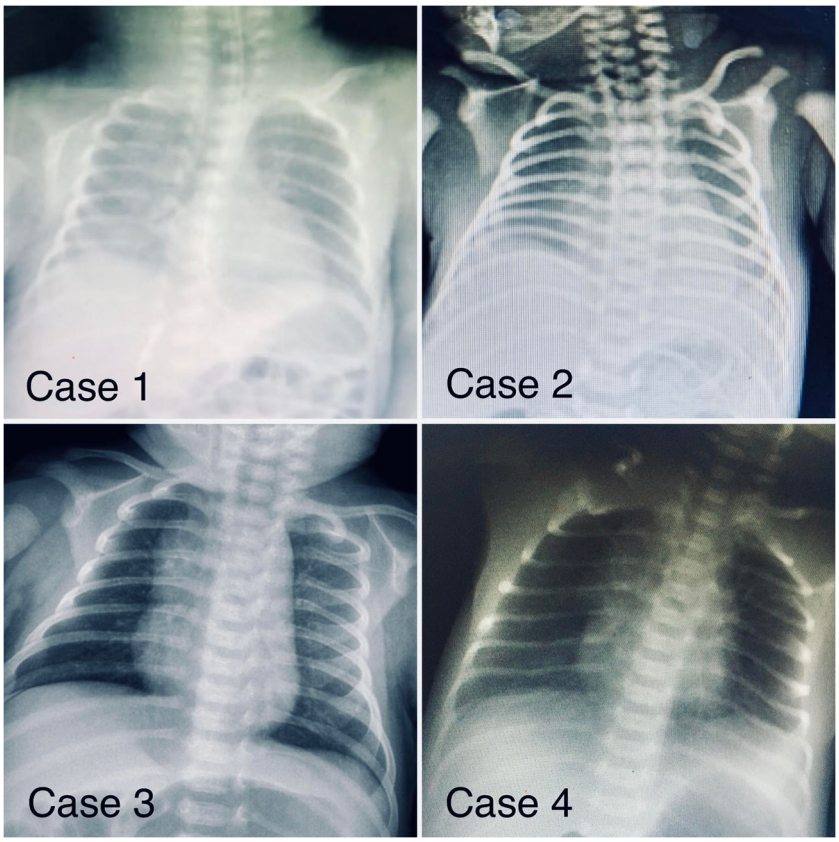

Fig. 1 Imaging findings of four newborns with SARS-CoV-2

pregnant and non-pregnant women in the population of Sweden revealed that the relative risk (RR) for pregnant and early postpartum women (< 1 week) with COVID-19 to receive intensive care was 5.4 and the RR to require invasive mechanical ventilation was 4.0 (95% CI 1.75–9.14) compared with non-pregnant women of similar age [35]. According to the current data of the Ministry of Health, the overall mortality rate in our country has been 2.63% [2]. The cause of high mortality rate in our study may be attributable to underlying conditions in pregnant women, but more information in the literature is needed to interpret it.

Although the World Health Organization, the Academy of Breastfeeding Medicine, and the TNS state that COVID-19 mothers can breastfeed, we found that the rate of formula (56.8%) and expressed breast milk (36%) use was higher than that of exclusive breastfeeding [1, 19]. Information in the literature on breastfeeding data of COVID-19 mothers is still insufficient. According to a systematic review, of the 28 newborns with confirmed COVID-19 infection, seven were breastfed, three formula fed, and one was given expressed breast milk, and in 17 newborns, the method of infant feeding was not reported [36]. All mothers in our study had proven SARS-CoV-2 infection, and majority of the newborns (86.4%) were followed in an isolation room in the NICU. In contrast to recommendations by proposals, isolation of the patients in the NICU, health status of the mothers, and the anxiety of both parents and physicians on the possible contamination to breast milk could have affected the rate of breastfeeding in our cohort. Neonates positive for SARS-CoV-2 must be isolated and clinically monitored, but this does not necessarily require NICU admission. It might be done in a single room, without full NICU capabilities, according to local settings [28]. We believe that the practice in the NICUs deserves further research.

There are several limitations to our study. First, the detection of SARS-CoV-2-specific IgM and IgG antibody may play an important role in the diagnosis of vertical transmission. Unfortunately, we were unable to obtain an antibody test as our time to share data was limited. Second, a small number of samples of placental tissue, amnion fluid, deep tracheal aspirate, serum, stool, and breast milk from the mother–neonate pairs could be investigated for SARS-CoV-2. Unfortunately, newborns with SARS-CoV-2 did not have these investigations. The potential transmissions of SARS-CoV-2 in a newborn born to a mother infected in the last trimester through placenta and by extra-respiratory routes such as breast milk show that suggesting testing for SARS-CoV-2 in placenta, amniotic fluid, and breast milk may be a part of routine evaluation of pregnant women with SARS-CoV-2 infection [17, 26, 27]. However, our study has several strong implications. It is a large multicenter

cohort study throughout Turkey that allowed us to prospectively obtain data via a special network, and RT-PCR results of all pregnant women included in this study were positive, which allowed us to interpret the effects of the disease on transmission, neonatal outcomes, and breastfeeding practice better. We believe that international multicenter initiations such as the EPICENTRE will result in more universal and acceptable data, which will help for the preparedness to the pandemic all throughout the world [37].

Conclusion

COVID-19 in pregnant women has important impacts on perinatal and neonatal outcomes. Maternal mortality, higher rates of preterm birth and cesarean section, suspected risk of vertical transmission, and the possible role of maternal disease severity on the outcomes should be evaluated in future studies. In contrast to recommendation for breastfeeding, parents' preference to formula and expressed breast milk due to anxiety and lack of information shows that a well-defined family support policy should be a part of the care in the NICU in the case of COVID-19.

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Neo-Covid Study Group

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Authors' contributions MYO: conceptualization, writing-original draft, writing-review and editing, read and approved the final manuscript. IMA: conceptualization, acquisition of data, read and approved the final manuscript. MKK: conceptualization, acquisition of data, read and approved the final manuscript. CT: conceptualization, acquisition of data, read and approved the final manuscript. SC: acquisition of data, read and approved the final manuscript. FN: acquisition of data, read and approved the final manuscript. IE: acquisition of data, read and approved the final manuscript. TGO: acquisition of data, read and approved the final manuscript. AM: acquisition of data, read and approved the final manuscript. MC: acquisition of data, read and approved the final manuscript. DO: data analysis, read and approved the final manuscript. OE: writing-original draft, writing-review and editing, read and approved the final manuscript. EK: writing-review, editing, read and approved the final manuscript.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethics approval The study was approved by the Rize University School of Medicine local ethics committee and the Ministry of Health.

Data sharing With the permission of the corresponding authors, we can provide participant data without names and identifiers, but not the study protocol, statistical analysis plan, or informed consent form. Data can be provided after the article is published. Once the data can be made public, the research team will provide an email address for communication. The corresponding authors have the right to decide whether to share the data or not based on the research objectives and plan provided.

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Abbreviations COVID-19, Coronavirus disease 2019; NICU, Neonatal intensive care unit; RT-PCR, Reverse transcriptase–polymerase chain reaction; SARS-CoV-2, Severe acute respiratory syndrome coronavirus-2

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