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RESEARCH

COVID-19 in hospitalized infants aged under 3 months: multi-center experiences across Turkey

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Abstract

To investigate coronavirus disease 2019 (COVID-19) in infants aged 0 to 3 months because there is currently a significant gap in the literature on the subject. A cross-sectional study was conducted with the involvement of 19 medical centers across Turkey and 570 infants. The majority of the patients were male (58.2%), and the three most common symptoms were fever (78.2%), cough (44.6%), and feeding intolerance (39.9%). The results showed that a small percentage of infants had positive blood (0.9%) or urine cultures (10.2%). Most infants presented with fever (78.2%). Children without underlying conditions (UCs) had mostly a complicated respiratory course and a normal chest radiography. Significant more positive urine culture rates were observed in infants with fever. A higher incidence of respiratory support requirements and abnormal chest findings were seen in infants with chronic conditions. These infants also had a longer hospital stay than those without chronic conditions.

Conclusions: Our study discloses the clinical observations and accompanying bacterial infections found in infants aged under 3 months with COVID-19. These findings can shed light on COVID-19 in infancy for physicians because there is limited clinical evidence available.

What is Known:

- *COVID-19 in infants and older children has been seen more mildly than in adults.*
- *The most common symptoms of COVID-19 in infants are fever and cough, as in older children and adults. COVID-19 should be one of the differential diagnoses in infants with fever.*

What is New:

- *Although most infants under three months had fever, the clinical course was uneventful and respiratory complications were rarely observed in healthy children.*
- *Infants with underlying conditions had more frequent respiratory support and abnormal chest radiography and stayed longer in the hospital.*

Keywords Breastfeeding · Children · Clinical presentation · COVID-19 · Infants · Neonates

Abbreviations

CDC	Centers for Disease Control and Prevention
COVID-19	Coronavirus disease 2019
CSF	Cerebrospinal fluid
IQR	Interquartile range
MIS-C	Multisystem inflammatory syndrome in children
PCR	Polymerase chain reaction
RSV	Respiratory syncytial virus
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
WHO	World Health Organization

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Introduction

Numerous studies on the coronavirus disease 2019 (COVID-19) pandemic have been published since its initial emergence. The majority of these investigations focused on the adult population. After a certain amount of time, children began to feature in the literature [1–3]. Until this point, neonates and infants have remained in a gray area where physicians have had difficulty finding information supported by research. Only a few studies with small sample sizes have focused on the newborn and infant periods [4–6]. No study on COVID-19 with a heterogeneous and large patient population has been identified that focuses on the infant period, particularly the period under 3 months. There is a need for a study on this 0–3-month period that examines the disease's progression, the clinical characteristics that should be considered when deciding on hospitalization, and the specific clinical conditions that may develop during follow-up, and comprehensive examination analyses.

When examining an infant with a fever, it is essential to distinguish clinical features that indicate critical invasive bacterial infections or viral respiratory tract infections, including COVID-19. Infants aged under 3 months are susceptible to invasive bacterial infections due to their immature immune systems and inadequate vaccination. Remarkably, infants younger than 3 months with fever should be evaluated as inpatients. The main objective of this study was to reveal how COVID-19, which causes admission with different clinical presentations other than fever, presented, especially in infants aged under 3 months, and identify accompanying infections. In this context, we wanted to conduct a multi-center study to evaluate inpatient infants with COVID-19, the ratio of fever presentation, and ultimately determine the characteristics of COVID-19 in infants aged under 3 months.

Materials and methods

Study design and population

This study employed a cross-sectional design and included infants aged 0 to 3 months (0–90 days) who were diagnosed as having COVID-19. Inclusion criteria were infants aged between 0 and 90 days with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) positivity and hospitalized. Infants without symptoms, who were hospitalized due to surgical procedures or other interventions and tested positive for SARS-CoV-2, constituted the exclusion criteria. Twenty-one centers including Tepecik Training and Research Hospital, Dokuz Eylül University Faculty of Medicine, Behçet Uz Child Disease and Pediatric Surgery Training and Research Hospital, Buca Seyfi Demirsoy Training and Research Hospital, Izmir Katip Çelebi University Faculty of Medicine from the city of İzmir; Gazi University Faculty of Medicine, Gülhane Training and Research Hospital, Ankara University Faculty of Medicine from the city of Ankara; Ümraniye Training and Research Hospital, Marmara University Faculty of Medicine, Istinye University Faculty of Medicine, Yeditepe University Faculty of Medicine, Koç University Faculty of Medicine, Başakşehir Çam ve Sakura City Hospital, Cerrahpaşa University Faculty of Medicine, Bezmialem Foundation University Faculty of Medicine, Şişli Hamidiye Etfal Training and Research Hospital from the city of İstanbul; Kayseri City Hospital from the city of Kayseri; Adana City Hospital from the city of Adana; Manisa City Hospital from the city of Manisa; and Mersin University Faculty of Medicine from the city of Mersin participated in the study.

Definitions

A diagnosis of COVID-19 was made using polymerase chain reaction (PCR) on nasopharyngeal samples. Chronic conditions included prematurity with or without chronic lung disease, symmetrical small for gestational age, congenital heart diseases, neurologic and metabolic diseases, spina bifida and hydrocephaly, nephrologic diseases, chronic allergic conditions and primary immune deficiencies, gastrointestinal diseases, and congenital infections. Multisystem inflammatory syndrome in children (MIS-C) was diagnosed according to the criteria determined by the Centers for Disease Control and Prevention (CDC). Accordingly, infants who were SARS-CoV-2-positive with a fever of $\geq$ 38.0 °C for $\geq$ 24 h, had severe illness requiring hospitalization, $\geq$ 2 organ system involvement, laboratory evidence of inflammation, and no alternative diagnosis were accepted as having MIS-C [7].

Data collection

Patients were selected from neonatal intensive care units and pediatric wards between September 1st, 2021, and August 31st, 2022. Patients' age (days), sex, the clinical presentation including fever, cough, runny nose, vomiting, diarrhea, rapid breathing, decreased breastfeeding or feeding intolerance, rash, seizure, irritability, somnolence, as well as underlying conditions (UCs), breastfeeding status, respiratory support requirements, complications related to COVID-19, imaging findings, and serum laboratory analyses were recorded. Cultures of normally sterile body fluids [e.g., blood, urine, and cerebrospinal fluid (CSF)] and co-infections with other respiratory viruses were collected. Some positive cultures were determined as contaminants due to the absence of clinical and

laboratory proof of invasive bacterial disease in a patient, along with the growth of pathogens that were skin and environmental flora members. The patients' records were obtained through the online database programs of hospitals.

Statistical analyses

The SPSS Statistics for Windows package program ver. 25 (IBM Corporation, 2017; Armonk, NY) was used for data analysis. The descriptive distribution and prevalence criteria (mean ± SD, minimum–maximum, median) of all variables determined by measurement were reviewed and presented according to the normality test. The number and percentage (%) distributions of the variables defined as categorical and ordinal were evaluated according to the categories. The statistical methods for comparing the research groups were determined based on the results of homogeneity (Levene's test) and normality (Kolmogorov–Smirnov test). According to the test results, parametric test assumptions were not met for the variables; therefore, the Mann–Whitney *U* test was used to compare the independent groups. We analyzed categorical data using Fisher's exact test and the chi-square test. Statistical significance was accepted as $p < 0.05$.

Patients' medical reports

From 19 centers across Turkey, 570 infants aged under 3 months were included in the study. The median age of the patients was 52.50 (interquartile range [IQR], 35–77; min–max, 1–90) days. There were 238 (41.8%) female infants and 332 (58.2%) male infants. The median length of hospital stay was 5 (IQR, 2–7; min–max, 1–56) days. The three most common symptoms of patients were fever (78.2%), cough (44.6%), and decreased breastfeeding or feeding intolerance (39.9%). The most common five UCs were prematurity with or without chronic lung disease (24%), neurometabolic disease (17%), spina bifida with or without ventriculoperitoneal shunt (15%), congenital heart disease (11%), and primary or secondary immunodeficiency (9%). Clinical conditions secondary to COVID-19 were myocarditis in six infants (five male, one female), multisystem inflammatory syndrome (MIS-C) in five infants, multiorgan failure in two infants, and disseminated intravascular coagulation in two infants. Of the patients, 261 (45.8%) received symptomatic treatment, and 299 (53.3%) were prescribed antibiotics based on clinical suspicion of bacterial infections. Only one (0.2%) infant received oseltamivir. The demographic, clinical, and laboratory characteristics are outlined in Table 1.

When evaluating taken body fluid cultures, four of 439 infants (0.9%) had clinically significant positive blood cultures, and 42 of 409 infants (10.2%) had clinically significant positive urine cultures. The culprit agents of the cultures are shown in Fig. 1. One infant of 30 infants (3.4%) with CSF cultures had clinically significant positivity with S*taphylococcus hominis*.

Multiplex PCR tests were performed on nasopharyngeal swab samples and CSF. Enterovirus and HHV-6 were detected in one of 11 infants (9%) in CSF samples. Thirteen of 42 patients (40.4%) had positive nasopharyngeal swab samples. The most common pathogen was respiratory syncytial virus (RSV) in six patients (46.1%). Two (15.4%) patients had rhinovirus, two (15.4%) patients had influenza A, one (7.6%) patient had bocavirus, one (7.6%) patient had metapneumovirus, and one (7.6%) patient had both rhinovirus and adenovirus positivity.

Results

Comparing infants with and without fever, infants with fever were more frequently monitored in room air than infants without fever ($p < 0.001$). Infants with fever had a higher rate of normal chest radiography and recovery ($p = 0.017$ and $p = 0.010$, respectively). Additionally, clinically significant urine culture positivity rates were higher in infants with fever ($p = 0.018$). Other findings are shown in Table 2.

The clinical features and breastfeeding status of infants were analyzed. The results showed no statistically significant differences in clinical symptoms between breastfed infants and those who were not, except for fever, which was more frequently seen in breastfed infants ($p = 0.004$). In addition, a higher cure rate was found in breastfed babies (99.2% vs. 91.7%, $p = 0.025$) (Table 3).

It was observed that UCs impacted clinical and laboratory characteristics. Cough and vomiting was found to be higher in infants with UCs than infants without UCs ($p = 0.017$, $p = 0.008$, respectively). Infants with chronic conditions had a higher incidence of respiratory support requirements and abnormal chest findings. They also had a longer hospital stay than those without chronic conditions ($p = 0.001$, $p = 0.002$, and $p < 0.001$, respectively). Other results are summarized in Table 3.

Discussion

According to our knowledge, this study has the largest patient population to evaluating infants younger than 3 months diagnosed with COVID-19. There are similar studies in the literature; however, the study populations differed from our research. In a study evaluating infants aged less than 3 months, patients who had fever without source were recruited in the study at first, followed by detecting SARS-CoV-2-positive patients [8]. Similarly, Paret et al. evaluated SARS-CoV-2 among infants aged < 90 days who were admitted for severe bacterial infections [9].

Table 1 Demographic, clinical, and laboratory characteristics of the infants

Demographic characteristics		
Age (days)	52.50 (median[a])	35–77 (IQR)
Sex		
Female	$n=238$	(41.8%)
Male	$n=332$	(58.2%)
Clinical characteristics	***n***	%
Underlying conditions ($n=46$)		
Prematurity ± chronic lung disease	11	24
Neurometabolic disease	8	17
Spina bifida/ ± VP shunt	7	15
Congenital heart disease	5	11
Primary or secondary immunodeficiency	4	9
Hydronephrosis	3	7
Atopic dermatitis	3	7
CMPA	1	2
Cystic fibrosis	1	2
Congenital CMV	1	2
GORD	1	2
Symmetrical SGA	1	2
Manifestation of infants		
Fever	446	78.2
Cough	254	44.6
Decreased breastfeeding or feeding intolerance	227	39.9
Runny nose	202	35.6
Tachypnea	100	17.5
Diarrhea	65	11.4
Vomiting	52	9.1
Rash	20	3.6
Somnolence	14	2.5
Irritability	6	11.4
Seizure	4	0.7
Status of respiratory support ($n=570$)		
Room air	464	81.4
Low flow oxygen therapy	68	11.9
HFNC therapy	31	5.4
CPAP	4	0.7
IMV	3	0.5
Breastfeeding ($n=545$)	521	91.4
Chest radiography ($n=439$)		
Normal	343	78.1
Ground glass opacity	45	10.3
Consolidation	32	7.3
Ground glass opacity and consolidation	19	4.3
Outcome ($n=570$)		
Cured	559	98.1
Died	3	0.5
Referred to PICU	3	0.5
Discharged against medical advice	5	0.9
Laboratory characteristics	**Median[a]**	**IQR**
WBC ($\times 10^3/\mu L$)	7900	5400–11,000
ANC ($\times 10^3/\mu L$)	2800	1600–4800

Table 1 (continued)

Demographic characteristics		
Age (days)	52.50 (median[a])	35–77 (IQR)
ALC ($\times 10^3$/μL)	3200	1800–4900
Platelets ($\times 10^3$/μL)	308,000	218,000–398,000
CRP (mg/L)	2.6	0.8–6.3
Procalcitonin (μg/L)	0.15	0.10–0.28
Ferritin (μg/L)	265.5	112.2–517.5

IQR interquartile range, *VP* ventriculoperitoneal shunt, *CMPA* cow's milk protein allergy, *CMV* cytomegalovirus, *GORD* gastroesophageal reflux disease, *SGA* small for gestational age, *HFNC* high flow oxygen cannula *CPAP* continuous positive airway pressure, *IMV* invasive mechanical ventilation, *PICU* Pediatric Intensive Care Unit, *WBC* white blood cell, *ANC* absolute neutrophil count, *ALC* absolute lymphocyte count, *CRP* C-reactive protein

[a]Median values and IQR were provided because variables were not normally distributed

To explore the characteristics of COVID-19 in infancy, we included all SARS-CoV-2-positive infants between specific dates across Turkey in our study to examine a wide variety of infants with the disease. Even though the World Health Organization (WHO) has declared the end of the COVID-19 pandemic, it is one of the circulating respiratory

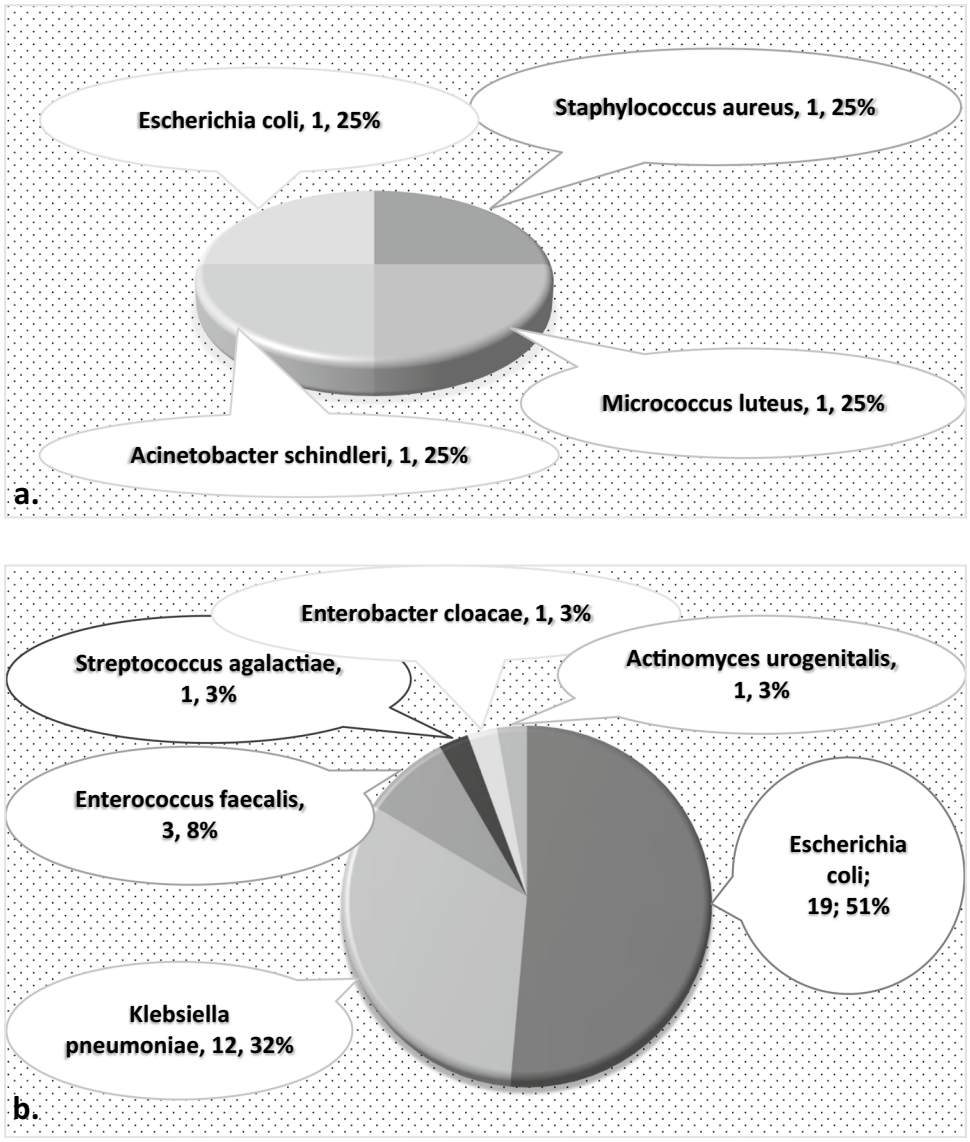

Fig. 1 Culprit agents in blood cultures (**a**) and urine cultures (**b**)

Table 2 Clinical and laboratory differences between infants with and without fever

	Fever		
	Yes	**No**	***p***
Gender			
Male	268 (60.1%)	64 (51.6%)	0.090
Female	178 (39.9%)	60 (48.4%)	
Status of respiratory support (*n*/%)			
Room air	379 (85%)	85 (68.5%)	***0.001****
Low flow oxygen therapy	43 (9.6%)	25 (20.2%)	
HFNC therapy	21 (4.7%)	10 (8.1%)	
CPAP	2 (0.4%)	2 (1.6%)	
IMV	1 (0.2%)	2 (1.6%)	
Chest radiography (*n*/%)			
Normal	284 (80.5%)	59 (68.6%)	***0.017***
Abnormal[a]	69 (19.5%)	27 (31.4%)	
Outcome (*n*/%)			
Cured	440 (99.5%)	119 (96.7%)	***0.010****
Died	2 (0.5%)	1 (0.8%)	
Referred to PICU	0 (0%)	3 (2.4%)	
Growth of blood culture (*n* = 419)			
Yes	4 (1.2%)	0 (0%)	0.588*
No	331 (98.8%)	84 (100%)	
Growth of urine culture (n = 390)			
Yes	37 (11.7%)	2 (2.7%)	***0.018***
No	278 (88.3%)	73 (97.3%)	
Length of hospitalization (days) (median/IQR)[b]	5 (2–7)	5 (2–9)	0.869
Laboratory characteristics (median/IQR)[b]			
WBC ($\times 10^3$/μL)	7500 (5360–10,500)	9350 (6432–11,975)	***0.001***
ANC ($\times 10^3$/μL)	2790 (1600–4500)	3100 (1700–6175)	0.107
ALC ($\times 10^3$/μL)	3100 (1717–4620)	3770 (2270–6100)	***0.002***
Platelets ($\times 10^3$/μL)	297,000 (212,000–381,000)	340,000 (240,000–427,000)	***0.004***
CRP (mg/L)	2.4 (0.85–6.50)	2.7 (0.72–5.52)	0.901
Procalcitonin (μg/L)	0.15 (0.10–0.26)	0.13 (0.08–0.33)	0.165
Ferritin (μg/L)	280 (127–602)	274 (115–470)	0.638

IQR interquartile range, *HFNC* high flow oxygen cannula, *CPAP* continuous positive airway pressure, *IMV*, invasive mechanical ventilation, *PICU* Pediatric Intensive Care Unit, *WBC* white blood cell, *ANC* absolute neutrophil count, *ALC* absolute lymphocyte count, *CRP* C-reactive protein

*Fisher's exact test was used

[a]Abnormal chest radiography findings include ground glass opacitiy, consolidation, or both

[b]Median values and IQR were provided because variables were not normally distributed

viruses. SARS-CoV-2 still threatens vulnerable populations such as infants aged under 3 months. Additionally, it can be difficult to distinguish COVID-19 from other serious infectious diseases in infancy, making it a topic that remains worthy of detailed discussion [10].

The mean age of the infants in our study was higher than that of infants aged under 3 months in previous studies. Male sex was predominant, similar to the literature [8, 9, 11]. The three most common symptoms were fever, cough, and feeding intolerance. Since the onset of the pandemic, fever and cough have been the most prevalent symptoms of COVID-19, regardless of age [12, 13]. Even among other COVID-19 variants, fever has consistently been the most prevalent symptom [14]. It is essential to thoroughly evaluate infants with fever due to the probability of invasive bacterial infections in the first 3 months of life. With the emergence of COVID-19, SARS-CoV-2 should be considered a differential diagnosis because fever is a common symptom of the virus. In Dona et al.'s multi-center study that evaluated the severity of COVID-19 in infants aged under 3 months, poor feeding was one of the most common symptoms, similar to our research. Decreased breastfeeding or feeding intolerance might also indicate invasive severe bacterial diseases [11].

Table 3 Comparison of breastfeeding and underlying conditions status with clinical and laboratory characteristics

	Breastfeeding			Underlying conditions		
	Yes	**No**	***p***	**Yes**	**No**	***p***
Status of respiratory support (*n*/%)						
Room air	424 (81.4%)	18 (75%)	0.098*	38 (67.9%)	426 (82.9%)	*0.001**
Low flow oxygen therapy	64 (12.3%)	2 (8.3%)		7 (12.5%)	61 (11.9%)	
HFNC therapy	27 (5.2%)	3 (12.5%)		7 (12.5%)	24 (4.7%)	
CPAP	4 (0.8%)	0 (0%)		2 (3.6%)	2 (0.4%)	
IMV	2 (0.4%)	1 (4.2%)		2 (3.6%)	1 (0.2%)	
Chest radiography (*n*/%)						
Normal	317 (78.9%)	13 (68.4%)	0.265*	29 (60.4%)	314 (80.3%)	*0.002*
Abnormal[a]	85 (21.1%)	6 (31.6%)		19 (39.6%)	77 (19.7%)	
Outcome (*n*/%)						
Cured	515 (99.2%)	22 (91.7%)	*0.025**	55 (98.2%)	504 (99%)	0.467*
Died	2 (0.4%)	1 (4.2%)		1 (1.8%)	2 (0.4%)	
Referred to PICU	2 (0.4%)	1 (4.2%)		0 (0%)	3 (0.6%)	
Length of hospitalization (days) (median/IQR)[b]	5 (2–7)	5 (3–10)	0.244	7 (5–14)	5 (2–7)	*< 0.001*
Laboratory characteristics (median/IQR)[b]						
WBC ($\times 10^3$/μL)	7890 (5420–10,870)	9780 (6750–14,400)	*0.026*	8275 (5555–11,160)	7900 (5447–11,000)	0.926
ANC ($\times 10^3$/μL)	2810 (1605–4740)	3370 (1675–6600)	0.136	2665 (1600–4315)	2840 (1600–4900)	0.344
ALC ($\times 10^3$/μL)	3200 (1800–4720)	3805 (2352–7650)	0.050	3255 (2042–6100)	3200 (1800–4800)	0.404
Platelets ($\times 10^3$/μL)	310,000 (22,100–398,000)	294,500 (176,250–378,500)	0.559	347,000 (182,750–470,750)	304,000 (221,250–391,500)	0.935
CRP (mg/L)	2.50 (0.80–6.10)	2.82 (0.60–15.70)	0.422	2.15 (0.62–7.83)	2.60 (0.85–6)	0.625
Procalcitonin (μg/L)	0.15 (0.10–0.28)	0.19 (0.12–0.54)	0.310	0.18 (0.94–0.50)	0.14 (0.10–0.28)	0.253
Ferritin (μg/L)	158 (28.25–256.75)	174 (28.25–174)	*0.047*	280 (152.5–882.5)	280 (114–518)	0.210

IQR interquartile range, *HFNC* high flow oxygen cannula, *CPAP* continuous positive airway pressure, *IMV* invasive mechanical ventilation, *PICU* Pediatric Intensive Care Unit, *WBC* white blood cell, *ANC* absolute neutrophil count, *ALC* absolute lymphocyte count, *CRP* C-reactive protein

*Fisher's exact test was used

[a]Abnormal chest radiography findings include ground glass opacitiy, consolidation, or both

[b]Median values and IQR were provided because variables were not normally distributed

Although rare, myocarditis was the most prevalent complication of COVID-19, with the preponderance of infants affected being male. In Akin et al.'s study, 176 neonates were evaluated, and myocarditis was detected in 10 (5.7%) infants as the most common complication of COVID-19 [15]. MIS-C was diagnosed in five infants in our study according to the CDC's definition before the diagnostic criteria for MIS-C were changed.[7] However, the new criteria now include cardiac involvement as a criterion [16]. Looking back on these patients, these infants may have been experiencing a type of acute SARS-CoV-2 infection linked to hyperinflammation because they did not have cardiac involvement [17].

In the clinical course of COVID-19, bacterial co-infections are uncommon [18]. A new pediatric emergency department study compared children who were SARS-CoV-2-positive aged under 90 days and those without the virus. The authors indicated no substantial difference between invasive bacterial illnesses [19]. However, more than half of hospitalized patients receive antimicrobial therapy, likely due to concerns about invasive bacterial infections in infants. Our study revealed that clinically significant blood culture positivity in neonates was uncommon. Nevertheless, it is essential to note that relatively higher urine culture results are significant because urinary tract infections (UTIs) in infancy can quickly spread to become bloodstream infections. Furthermore, clinically significant urine culture positivity rates were found to be higher in infants with fever in our study. UTIs could have more significantly influenced the clinical course than the SARS-CoV-2 infection.

Regarding viral respiratory infections other than COVID-19, RSV was the leading pathogen detected in multiplex PCR tests. This outcome was anticipated because RSV is known to be the most prevalent pathogen in respiratory syndrome cases

within this age group [20]. Mask-wearing and social distancing precautions prevented the majority of respiratory pathogens from circulating in the community during the pandemic [21]. However, during the period of our investigation, Omicron was the most prevalent of the SARS-CoV-2 variants. As a result of vaccination efforts and the milder course of COVID-19 caused by the Omicron variant, masks were discarded and other viral pathogens reemerged. For that reason, RSV and other viral pathogens were detected among our infants.

Patients with fever in our study were observed more frequently in room air, chest radiography findings were observed to be normal at a higher rate than in patients without fever, and a higher rate of cure was observed in patients with fever. Some studies showed that fever might be a protective factor from diseases' devastating effects by activating the innate immune system, releasing cytokines, and increasing inflammation, which harms inflamed cells and microorganisms [22, 23]. When fever is considered a protective mechanism based on these studies, our findings might be justified accordingly. Otherwise, despite statistical significance, it may not have clinical importance. The same argument may be valid for what was found when comparing breastfeeding status and fever, in which fever and a higher recovery rate were more prevalent among those with a history of breastfeeding. On the other hand, what should be focused on is that infants with fever had higher rates of clinically significant urine culture positivity, reminding us that infants with fever, even with SARS-CoV-2 positivity, should be evaluated in all aspects, including obtaining cultures from normally sterile body fluids. A COVID-19 diagnosis should not restrain physicians from taking blood and urine cultures, especially from infants aged under 3 months.

As is widely acknowledged, SARS-CoV-2 can lead to severe or critical illness in people with pre-existing chronic conditions [24, 25]. In a study conducted in Canada, clinical manifestations and disease severity of infants with SARS-CoV-2 infection were evaluated, and infants with a comorbid condition were found to have higher odds of hospitalization compared to infants with no comorbid conditions [26]. In Hobbs et al.'s study, infants categorized in severe COVID-19 were found to be between 1 and 3 months and have at least one UC [27]. Although we did not classify the severity of the disease in infants, we observed that cough and vomiting were more frequent in those who had UCs. Furthermore, the infants with UCs showed more frequent abnormal chest findings, required more respiratory support, and had longer hospital stays compared to those without UCs. These observations suggest that the clinical course of COVID-19 is seen more severely in infants with underlying conditions. Results are crucial to raise awareness that infants infected with COVID-19 who have UCs should be evaluated more vigilantly.

There are several limitations of this study. The study's primary objective was to identify the clinical characteristics of COVID-19 in infants aged between 0 and 3 months. Only infants who tested positive for SARS-CoV-2 were evaluated to ensure a substantial sample size. Therefore, we could not compare the results of infants with invasive bacterial diseases but without COVID-19. In addition, all infants who tested positive for SARS-CoV-2 were included in the study, regardless of whether they had co-infections with other respiratory viruses detected in nasopharyngeal swab samples. These patients were not excluded with the purpose of analyzing all infants infected with SARS-CoV-2. Not excluding them may have caused bias. However, because multiplex respiratory panel tests are not widely available in many areas of Turkey, excluding infants with documented co-infections would not have prevented bias. Lastly, we did not analyze different COVID-19 variants of concern because they are not studied in most centers. It is worth noting that different variants could potentially result in varying outcomes [14].

As a result, in our study, fever, cough, and decreased breastfeeding or feeding intolerance were the most common symptoms of infants aged under 3 months. The most prevalent complication of COVID-19 was myocarditis. Infants with fever had a higher clinically significant urine culture positivity than infants without fever. Fever was more common in breastfed infants than in non-breastfed infants, and breastfed infants had a higher recovery rate. Infants with UCs were found to have longer hospital stays, more frequent respiratory support requirements, and a higher incidence of abnormal chest findings. In conclusion, practicing pediatricians are still confused about infants aged under 3 months with COVID-19 because of the lack of clinical data, and thus, our study provides preliminary results in the clinical findings and concomitant bacterial infections of these infants.

Authors' contributions All authors have made substantial contributions to all the following: (1) the conception and design of the study, acquisition of data or analysis, and interpretation of data; (2) drafting of the article or critical review of it for important intellectual content; and (3) final approval of the submitted version.

Data availability Not applicable.

Code availability Not applicable.

Declarations

Ethics approval The pediatric infectious disease clinic at Health Science University Izmir Tepecik Training and Research Hospital managed the research, which received ethical approval (decision number: 2022/12–19). Our hospital's ethics committee unit was emailed data from the centers, and ethical approval documents with wet signatures from each participant center were mailed to the unit. All investigative procedures adhered to the principles outlined in the Declaration of Helsinki.

Consent to participate Not applicable.

Consent for publication All the patient data are anonymized, and parents and legal guardians consented to publication of the results of the project.

Competing interests The authors declare no competing interests.

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