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The Clinical Course of Coronavirus Disease 2019 Under 2 Years of Age

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The coronavirus disease 2019 (COVID-19) disease has a milder course in children than in adults.[1] However, patients under the age of 1 year have been reported to be a risk group for severe COVID-19 disease in the early stages of the pandemic. Subsequently, results that contradicted these findings have been reported. The intensive care unit (ICU) admission rate was reported to be higher for 0-1 years of age, and a severe clinical course is frequently seen in infants.[2] A meta-analysis has reported the mean age of patients admitted to the ICU to be higher and the age of 0-28 days to also be a risk factor for ICU admission.[3] We aimed to investigate the course of COVID-19 in infants under 2 years of age because there are few publications on this subject moreover with conflicting results.

We retrospectively reviewed the charts of all infants aged >1 month to ≤24 months diagnosed with COVID-19 infection as confirmed by real-time reverse transcription polymerase chain reaction testing between July 2020 and October 2021 at Ankara City Hospital. During this period, the delta variant was dominant in Turkey. This period coincided with the period of the third wave of the epidemic in Turkey during which there was an increase in cases.

We collected information on the demographics, history of contact with a COVID-19 case, clinical picture, laboratory results, ICU admission, respiratory support needs, and inotrope needs. The patients were categorized according to their ages, into 1-6, 7-12, 13-18, and 19-24 months age groups. We then compared the clinical picture and disease severity between these groups.

A total of 919 infants were diagnosed with COVID-19 during the study period. Our results show that 5.7% of patients required hospital admission. Fever was the only presenting symptom in 209 (22.7%) infants. According to their clinical presentations, the patients were diagnosed with asymptomatic disease, upper respiratory tract infection, acute fever without focus, acute gastroenteritis, pneumonia/bronchiolitis, and maculopapular rash. Twenty (2.2%) patients were diagnosed with pneumonia/or bronchiolitis, 11 (1.2%) required ICU admission, and 15 (1.6%) needed mechanical ventilation or high-flow nasal oxygen (HFNO). Table 1 presents the clinical pictures and treatment modalities by age group. The asymptomatic presentation rate was lower in the 1-6- and 7-12 months age groups than in the 13-18 months age group. The history of contact with a COVID-19 patient was lower in the 1-6 months group. The rate of pneumonia/bronchiolitis, oxygen treatment, ICU admission, and mechanical ventilation or HFNO was highest in the 1-6 months age group. Table 2 presents the laboratory parameters. C-reactive protein (CRP) was lower in the 0-6 months age group than in the 7-12 months and 19-24 months age group. A 2.5-month-old patient with Down syndrome, a history of premature birth, and congenital heart disease, and a 4.5-month-old patient with *Salmonella* spp. sepsis died.

We found that the ICU admission rate (1.2%) was lower than the reported rate of 2.3% for the <18 years age group.[4] In a study involving 485 pediatric patients, hospitalization rates, hospitalization days, supplemental oxygen requirement rate, and the number of days of

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Table 1. Demographics, Clinical Picture, Respiratory Support Needs, and Inotropic Needs of the Patients

	1-6 Months	7-12 Months	13-18 Months	19-24 Months	
	n = 355	n = 245	n = 180	n = 139	*P*
Gender (male)	190 (38.5)	135 (27.4)	93 (18.9)	75 (15.2)	.91
History of contact with COVID-19 case	229 (64.5)	187 (76.3)	145 (80.6)	117 (84.2)	.00
Comorbidity	26 (7.3)	14 (5.7)	4 (2.2)	5 (3.6)	.06
Asymptomatic	77 (21.8)	45 (18.4)	56 (31.1)	31 (22.3)	.01
Upper respiratory tract infection	140 (39.7)	104 (42.2)	56 (31.1)	65 (46.8)	.02
Acute fever without focus	84 (23.5)	60 (24.5)	40 (22.2)	25 (18)	.5
Acute gastroenteritis	40 (11)	28 (11.4)	27 (15)	14 (10.1)	.49
Pneumonia/bronchiolitis	13 (3.7)	4 (1.6)	0 (0)	3 (2.2)	.04
Rash	1 (0.3)	4 (1.6)	1 (0.6)	1 (0.7)	
Oxygen treatment	18 (5.1)	5 (2)	1 (0.6)	3 (2.2)	
Intensive care unit admission	8 (2.3)	1 (0.4)	0 (0)	2 (1.4)	
Mechanic ventilation or HFNO	8 (1.1)	4 (0.4)	1 (0.6)	2 (0.7)	
Inotropic agent support	3 (0.8)		1 (0.5)	1 (0.7)	

COVID-19, coronavirus disease 2019; HFNO, high-flow nasal oxygen.

Table 2. Results of Laboratory Examination of the Patients

	1-6 Months		7-12 Months		13-18 Months		19-24 Months		
	Min–Max	Median	Min–Max	Median	Min–Max	Median	Min–Max	Median	*P*
CRP (mg/dL)	0.5-221	1	0-111	3	0.5-199	3	0.5-63	3	<.00
WBC (10^6/L)	1268-30,300	7765	1043-17,600	8200	2170-22,320	8430	3410-23,420	8560	.04
ALC (10^6/L)	160-4210	4080	1010-11,430	3950	490-9810	3995	605-13,830	3980	.97
PLT (10^6/L)	14,000-980,000	374,000	53,000-604,000	316,000	108,000-1,041,000	309,500	166,000-584,000	299,000	<.00

CRP, C-reactive protein; WBC, white blood cell count; ALC, absolute lymphocytes count; PLT, plateletes count.

oxygen support were found to be similar to older age groups in infants <12 months of age.[5] In a multicenter cohort, infants were reported to have a lower risk of severe or critical illness than older children.[6] Similarly, the results of our study showed that the under-2 age group was not at greater risk for the development of a severe disease course.

There are conflicting results in studies about the severity of COVID-19 under 6 months of age. The 0-3 months age group has been reported to be a risk factor for requiring respiratory support in pediatric patients with severe COVID-19.[7] Patients <6 months of age were found to constitute 75% of those under the 1-year age group severe cases.[8] In another study conducted on infants younger than 3 months of age, it was reported that most cases among young infants were mild to moderate and recovered with supportive care.[9] Severe disease was found to be significantly less likely in infants aged <6 months in a study including 2293 children hospitalized for COVID-19.[10] In this study, although we found that a severe clinical picture was more frequent in patients under 6 months, a severe clinical course was also rare in this age group.

In a study involving <90 days infants hospitalized for serious bacterial infection evaluation, it was reported that an isolated fever was the most common presenting finding of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (59%), and an isolated fever was more frequent among infants with SARS-CoV-2 compared to those who tested negative.[11] In another study, it was reported that one-third of 30- to 90-day-old infants presenting with acute fever without focus were diagnosed with COVID-19.[12] About a quarter of our study group presented with an isolated fever. There was no difference among the groups in presentation rates for acute fever without focus. The results of our study show that under 2 years of age, it is not uncommon for COVID-19 disease to present as an acute fever without focus. Severe acute respiratory syndrome coronavirus 2 should be investigated in children <2 years of age who present with isolated fever, especially during periods of increased COVID-19 incidence, as in this study. Contact history and asymptomatic course were less common in the 1-6 months age group, suggesting that the non-contact presentation rate could be higher as they are more often symptomatic.

In a meta-analysis, among children under the age of 1-year cases, lymphopenia and high aspartate aminotransferase (AST) were reported in one-third of the patients, and elevated CRP and lactate dehydrogenase (LDH), and high alanine aminotransferase (ALT) was reported in about half.[13] It was reported that CRP was much more likely to be elevated in older children than in infants.[6] In this study, the median values for the laboratory parameters examined were generally within the normal range, although there were several differences between the groups. This indicates that a differential diagnosis of COVID-19 cannot be made based on laboratory parameters.

Our findings of a very low rate of serious illness suggest that infants under the age of 2, even those under 6 months, are not at greater risk for severe COVID-19.

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