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Coronavirus Pandemic

COVID-19 disease characteristics in different pediatric age groups

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Abstract

Introduction: Little is known about the COVID-19 disease characteristics and differences between different pediatric age groups. This study aimed to investigate the disease characteristics according to age groups.

Methodology: We conducted a retrospective, single-center study of pediatric COVID-19 in a tertiary care hospital in Turkey. The patients were divided into three groups: 15 days-24 months old (Group 1), 25-144 months old (Group 2), and 145-210 months old (Group 3) according to age.

Results: A total of 139 pediatric patients with COVID-19 were examined. Twenty-nine patients (20.9%) were in Group 1, 52 (37.4%) were in Group 2, 58 (41.7%) were in Group 3. Thirty-nine patients (28.1%) were hospitalized. The most common symptoms were cough (55.4%) and fever (51.8%). The median chest X-ray (CXR) score of hospitalized patients was 1 (min 0-max 7), and the median CXR score of outpatients was 1 (min 0-max 6). Fever was significantly more frequent in Group 1, and chest pain was more frequent in Group 3. Group 1 had significantly higher WBC, lymphocyte, thrombocyte counts, AST, LDH, D-dimer, and Troponin T levels but lower hemoglobin, total protein, and albumin levels. The treatment included antibiotics, oseltamivir, hydroxychloroquine, and supportive therapy. Only one patient (0.7%) received non-invasive mechanical ventilatory support.

Conclusions: As we know the clinical course of COVID-19 in children is less severe than in adults. We also found significant differences in both clinical and laboratory findings between different pediatric age groups which supports the theory that disease pathogenesis is highly variable according to age.

Key words: Children; COVID-19; pediatric age groups; Turkey.

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Introduction

In mid-December 2019, a series of cases with symptoms resembling viral pneumonia emerged in Wuhan, China, and this has rapidly spread to many countries in the world [1,2]. The virus responsible for the clinical presentation was isolated from a patient's respiratory tract and confirmed as a new type of coronavirus namely "Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2)". The World Health Organization (WHO) named this disease the Coronavirus Disease-2019 (COVID-19) and classified it as a global pandemic on March 11, 2020 [3]. The clinical features are similar to other acute respiratory viral infections and usually include fever, cough,

shortness of breath, breathing difficulties, and fatigue. On January 20, the first pediatric case with COVID-19 was reported in Shenzhen [4].

In Turkey, the first COVID-19 case was diagnosed on March 10, 2020. Since the beginning of the epidemic, the highest number of cases was reported in Istanbul, the city where the population density in the country is the highest. COVID-19 management guidelines were published by the Public Health Agency of Turkey, since the early days of the epidemic. During the first 3 months of the COVID-19 outbreak in Turkey, these guidelines were updated almost every few days [5]. However, due to the lack of guidelines on the management of pediatric cases, The Department of Pediatrics in our hospital, published our own COVID-19 pediatric management algorithm, using adult case management algorithms and publications on a small number of pediatric COVID-19 cases. Thus, we have ensured that patient management has been standard since the beginning of the epidemic.

Table 1. The demographic and clinical characteristics of the patients with COVID-19.

Variables	Min-Max	Mean ± SD (median)
Age (months)	0.5-210	115.06 ± 71.42
Duration of hospitalization (days)	0-14	1.54 ± 3.15 (0)
Duration of fever (days) (n = 72)	1-10	2.06 ± 1.39 (2)
Duration of cough (days) (n = 77)	1-9	1.44 ± 1.77 (1)
Age groups	**n**	**%**
0.5-24 months	29	20.9
25-144 months	52	37.4
145-210 months	58	41.7
Gender		
Female	59	42.4
Male	80	57.6
Household close contact		
No	27	19.4
Yes	112	80.6
Other close contact		
No	116	83.5
Yes	23	16.5
Hospital unit		
Outpatient	100	71.9
Inpatient	39	28.1
Fever		
No	67	48.2
Yes	72	51.8
Cough		
No	62	44.6
Yes	77	55.4
Runny nose		
No	131	94.2
Yes	8	5.8
Sore throat		
No	128	92.1
Yes	11	7.9
Myalgia		
No	133	95.7
Yes	6	4.3
Abdominal pain		
No	137	98.6
Yes	2	1.4
Diarrhea		
No	124	89.2
Yes	15	10.8
Chest pain		
No	125	89.9
Yes	14	10.1

Although there are a few case series investigating COVID-19 in children, the disease seems to have a milder clinical course in children and is even classified as asymptomatic [6,7]. There is little information about the epidemiological and clinical patterns and laboratory findings of COVID-19 in children, especially for different pediatric age groups. We aimed to investigate the epidemiological, clinical, laboratory, and radiological characteristics, treatment, and outcomes in different pediatric age groups with COVID-19 and compared the clinical and laboratory features between these groups.

Methodology

Study design, data collection, and definitions

This retrospective, a single-center study examined data of 139 patients with laboratory-confirmed COVID-19 coming from a tertiary care center that serves as a pandemic hospital in Turkey. The medical records of pediatric patients (aged 0–18 years) were obtained from the hospital data network. The following demographic information, clinical features, laboratory results, management, and outcome data were collected retrospectively: age, gender, underlying medical conditions, a history of travel to epidemic areas or exposure to close contact with an infected person, family history of COVID-19, complete blood count, liver and kidney function, inflammatory biomarkers (procalcitonin, C-reactive protein), biologic enzymes (lactate dehydrogenase, creatine kinase, and creatine kinase-MB), D-dimer, coagulation tests, chest X-ray and CT scan imaging, treatment modalities, duration of antibiotic therapy, duration of hospital stay. The diagnosis of COVID-19 was confirmed by reverse-transcriptase polymerase chain reaction (PCR) analysis of oropharyngeal and/or nasopharyngeal swabs. All chest X-rays (CXR) were scored by an experienced radiologist according to the classification system of Borghesi and Maroldi (8). The CXR scoring system includes two steps. First, the lungs were divided into six zones on frontal chest projection (two upper, two middle, and two lower zones). Second, each zone was scored based on the following: 0: No lung abnormalities; 1: Interstitial infiltrates; 2: Interstitial and alveolar infiltrates (interstitial predominance); 3: Interstitial and alveolar infiltrates (alveolar predominance).

Statistical analysis

Data were entered into Microsoft Office Excel 2010 (Microsoft, Redmond, WA, USA). Statistical analyses were performed using SPSS version 22.0 (IBM, SPSS).

Normally distributed data were assessed using the One-way Anova test. The significance of nonparametric data was assessed using the Kruskal Wallis test. The statistical significance of dichotomous outcomes was determined using the Chi-square test and Fisher Freeman Halton test. A value of $p < 0.05$ was considered statistically significant.

Marmara University-The Clinical Research Ethics Committee (No:08.05.2020/521-522) and The Republic of Turkey Ministry of Health approved this study.

Results

Patient characteristics

A total of 139 patients with COVID-19 were examined during the study period. The patient characteristics are summarized in Table 1.

Twenty patients (14.4%) had underlying medical conditions. The most common underlying medical conditions were oncologic malignancies in five patients and cerebral palsy-epilepsy in four patients. Other underlying medical conditions were asthma in three patients, immune deficiency in two patients, type-1 diabetes mellitus, renal agenesis, prematurity, migraine, systemic lupus erythematosus, and familial Mediterranean fever in one patient. None of the patients had a history of exposure to epidemic areas. One hundred and twelve (80.6%) patients had a history of close contact with COVID-19 positive family members in their household in this study. Hydroxychloroquine (HCQ) plus azithromycin was given to 13 patients (9%) according to the guideline recommendations of the Turkish Ministry of Health, Public Health Agency (5). The following antibiotics and antiviral agents were used for treating COVID-19: azithromycin, 75 patients (54%); ampicillin-sulbactam, six patients (4.3%); amoxicillin-clavulanate, 57 patients (41%); meropenem, one patient (0.7%); amoxicillin-clavulanate and oseltamivir combination, 28 patients (20.1%); ampicillin-sulbactam and oseltamivir combination, 14 patients (10.1%); teicoplanin and piperacillin-tazobactam combination, four patients (2.9%); ampicillin and cefotaxime combination, four patients (2.9%); ceftriaxone, three patients (2.2%). No antibiotics and antiviral agents were administered to 22 (15.8%) patients.

Azithromycin was given to 62 patients for the empirical treatment of acute-community acquired pneumonia.

None of the patients required intensive care admission or had any complications. The need for non-invasive mechanical ventilatory support (high-flow oxygen) occurred only in one patient aged seventeen months. All patients including those with underlying medical conditions were discharged without any complications.

Laboratory and radiological findings

Laboratory findings of patients are summarized in Table 2.

Chest X-ray was performed in 130 patients (93.5%) and CXR scoring results are summarized in Table 3.

The median CXR score of hospitalized patients was 1 (min 0-max 7), and the median CXR score of outpatients was 1 (min 0-max 6). No statistically significant difference was found between the two groups *(p: 0.503)*.

Chest computed tomography (CT) scan performed on 23 patients revealed that 17.3% had bilateral ground-glass opacity and 13% had unilateral ground-glass opacity (Table 3).

Table 2. The laboratory findings of the patients with COVID 19.

	Min-Max	Mean ± SD (median)
Hemoglobin, g/dl (n=136)	5.8-16	12.48 ± 1.74
White blood cells,/mm^3 (n=136) *(median)*	100-18900	7111.03 ± 3088.51 (6500)
Thrombocytes, /mm^3 (n=136)	16000-448000	242786.76 ± 80995.97
Lymphocytes, /mm^3 (n=136) *(median)*	0-13900	2597.06 ± 2093.3 (2100)
Granulocytes, /mm^3 (n=136)	0-11000	3619.85 ± 2217.93
C-reactive protein, mg/dl (n=134) *(median)*	3-133	9.79 ± 17.13 (3.1)
Alanine aminotransferase, IU/L (n=132) *(median)*	3-157	20.23 ± 16.54 (16)
Aspartate aminotransferase, IU/L(n=132) *(median)*	15-227	34.62 ± 25.34 (29)
Lactate dehydrogenase, IU/L(n=133) *(median)*	113-638	234.49 ± 68.33 (226)
INR (n=68) *(medyan)*	0.86-1.6	1.8 ± 0.13 (1.1)
D-dimer, mg/L (n=65) *(median)*	0.12-20	1.18 ± 2.9 (0.4)
Total bilirubin, mg/dl (n=135) *(median)*	0-13.6	0.62 ± 1.38 (0.4)
Indirect bilirubin, mg/dl (n=135) *(median)*	0-12.8	0.47 ± 1.29 (0.3)
Total protein, g/L(n=129)	46-84	70.97 ± 6.45
Albumin, g/L(n=136) *(median)*	28-51	43.93 ± 3.67 (45)
Creatine kinase, U/L (n=56) *(median)*	0-1085	122.97 ± 179.85 (80.5)
Troponin T, ng/L (n=84) *(median)*	3-162	7.63 ± 19.14 (3)
Urea mg/dl (n=134)	2-40	22.43 ± 6.74

Table 3. Radiological findings of the patients with COVID 19.

	n (%)
Chest X-ray (n=130)	
Normal	64 (49.2)
Right paracardiac infiltration	36 (27.7)
Bilateral paracardiac infiltration	12 (9.2)
Peribronchial infiltration	11 (8.5)
Bilateral interstitial infiltration	2 (1.5)
Left paracardiac infiltration	2 (1.5)
Consolidation	1 (0.8)
Atelectasis	1 (0.8)
Right pleural effusion	1 (0.8)
Chest computed tomography (n=23)	
Normal	13 (56.5)
Bilateral ground-glass opacity	4 (17.4)
Consolidation	3 (13)
Right ground-glass opacity	2 (8.7)
Left ground-glass opacity	1 (4.4)

Table 4. Comparison of patient characteristics of three age groups.

		Age groups			
Variable		**15 days-24 months (Group 1) Mean ± SD (median)**	**25-144 months (Group 2) Mean ± SD (median)**	**145-210 months (Group 3) Mean ± SD (median)**	
Duration of hospitalization		2.59 ± 4.21 (0)	0.65 ± 1.64 (0)	1.81 ± 3.4 (0)	[1]0.105
Duration of fever		1.95 ± 0.85 (2)	2.03 ± 1.3 (2)	2.17 ± 1.85 (2)	[1]0.947
Duration of cough		1.34 ± 1.72 (0)	1.37 ± 2.04 (0)	1.55 ± 1.54 (2)	[1]0.269
		n (%)	n (%)	n (%)	
Gender	Female	14 (48.3%)	18 (34.6%)	27 (46.6%)	[2]0.348
	Male	15 (51.7%)	34 (65.4%)	31 (53.4%)	
Household close contact	No	9 (31%)	12 (23.1%)	6 (10.3%)	[2]0.055
	Yes	20 (69%)	40 (76.9%)	52 (89.7%)	
Other close contact	No	23 (79.3%)	41 (78.8%)	52 (89.7%)	[2]0.250
	Yes	6 (20.7%)	11 (21.2%)	6 (10.3%)	
Hospital unit	Outpatient	18 (62.1%)	42 (80.8%)	40 (69%)	[2]0.160
	Inpatient	11 (37.9%)	10 (19.2%)	18 (31%)	
Fever	No	10 (34.5%)	22 (42.3%)	35 (60.3%)	**[2]0.042***
	Yes	19 (65.5%)	30 (57.7%)	23 (39.7%)	
Cough	No	15 (51.7%)	27 (51.9%)	20 (34.5%)	[2]0.127
	Yes	14 (48.3%)	25 (48.1%)	38 (65.5%)	
Runny nose	No	26 (89.7%)	49 (94.2%)	56 (96.6%)	[3]0.458
	Yes	3 (10.3%)	3 (5.8%)	2 (3.4%)	
Sore throat	No	27 (93.1%)	47 (90.4%)	54 (93.1%)	[3]0.919
	Yes	2 (6.9%)	5 (9.6%)	4 (6.9%)	
Myalgia	No	29 (100%)	50 (96.2%)	54 (93.1%)	[3]0.431
	Yes	0 (0%)	2 (3.8%)	4 (6.9%)	
Abdominal pain	No	29 (100%)	51 (98.1%)	57 (98.3%)	[3]1.000
	Yes	0 (%0)	1 (1.9%)	1 (1.7%)	
Diarrhe	No	23 (79.3%)	48 (92.3%)	53 (91.4%)	[2]0.153
	Yes	6 (20.7%)	4 (7.7%)	5 (8.6%)	
Chest pain	No	28 (96.6%)	50 (96.2%)	47 (81%)	**[2]0.013***
	Yes	1 (3.4%)	2 (3.8%)	11 (19%)	
Chest X-ray	Normal	14 (48.3%)	19 (39.6%)	31 (58.5%)	[2]0.358
	Right paracardiac infiltration	11 (37.9%)	16 (33.3%)	9 (17%)	
	Bilateral interstitial infiltration	1 (3.4%)	1 (2.1%)	0 (0%)	
	Peribronchial infiltration	0 (0%)	5 (10.4%)	6 (11.3%)	
	Bilateral paracardiac infiltration	2 (6.9%)	6 (12.5%)	4 (7.5%)	
	Consolidation	0 (0%)	0 (0%)	1 (1.9%)	
	Left paracardiac infiltration	1 (3.4%)	0 (0%)	1 (1.9%)	
	Atelectasis	0 (0%)	1 (2.1%)	0 (0%)	
	Right pleural effusion	0 (0%)	0 (0%)	1 (1.9%)	
Chest CT	Normal	2 (66,.7%)	1 (50%)	10 (55.6%)	[2]0.956
	Bilateral ground-glass opacity	1 (33.3%)	1 (50%)	2 (11.1%)	
	Right ground-glass opacity	0 (0%)	0 (0%)	2 (11.1%)	
	Left ground-glass opacity	0 (0%)	0 (0%)	1 (5.6%)	
	Consolidation	0 (0%)	0 (0%)	3 (16.7%)	
HCQ use	No	28 (96.6%)	50 (96.2%)	48 (82.8%)	**[3]0.030***
	Yes	1 (3,4%)	2 (3.8%)	10 (17.2%)	
Azithromycin use	No	21 (72.4%)	24 (46.2%)	19 (32.8%)	**[2]0.002***
	Yes	8 (27.6%)	28 (53.8%)	39 (67.2%)	
Other drugs	No	3 (10.3%)	13 (25%)	6 (10.3%)	**[2]0.016***
	Ampicillin-sulbactam	1 (3.4%)	2 (3.8%)	3 (5.2%)	
	Amoxicillin clavulanate+oseltamivir	6 (20.7%)	13 (25%)	9 (15.5%)	
	Ampicillin-sulbactam+ oseltamivir	2 (6.9%)	3 (5.8%)	9 (15.5%)	
	Teicoplanin+ piperacillin-tazobactam	0 (0%)	2 (3.8%)	2 (3.4%)	
	Meropenem	1 (3.4%)	0 (0%)	0 (0%)	
	Amoxicillin clavulanate	11 (37.9%)	18 (34.6%)	28 (48.3%)	
	Ceftriaxone	1 (3.4%)	1 (1.9%)	1 (1.7%)	
	Ampicillin+ cefotaxime	4 (13.8%)	0 (0%)	0 (0%)	

*[1]Kruskal Wallis test; [2]Chi-square test; [3]Fisher Freeman Halton test; *p<0.05;* Computed tomography: CT; Hydroxychloroquine: HCQ.

Age group differences

To investigate the differences of disease characteristics between age groups, patients were divided into three groups; patients aged 15 days-24 months (group 1; n:29), 25-144 months (group 2; n:52), and 145-210 months (group 3; n:58). We compared clinical and laboratory features of these three age groups. The rate of fever was 65.5%, 57.7%, and 39.7% in groups 1, 2, and 3, respectively. Fever complaint was significantly more frequent in group 1 *(p:0.042)*. The rate of chest pain was 3.4%, 3.8%, and 19% in groups 1, 2, and 3, respectively. Chest pain complaint was significantly more frequent in group 3 (*p*: 0.013). The rate of hydroxychloroquine use was 3.4%, 3.8%, and 17.2% in groups 1, 2, and 3, respectively. Hydroxychloroquine use was significantly higher in group 3 (*p*: 0.030). The rate of azithromycin use was 27.6%, 53.8%, and 67.2% in groups 1, 2, and 3, respectively. Azithromycin use was significantly lower in group 1 (*p*: 0.002). The rate of amoxicillin-clavulanate use was 37.9%, 34.6%, and 48.3% in groups 1, 2, and 3, respectively. Amoxicillin-clavulanate use was significantly lower in group 2 (*p*: 0.016). No other demographic and clinical characteristics demonstrated significant differences between the three groups (Table 4).

The following laboratory values were significantly higher in Group 1: WBC, lymphocytes, thrombocytes count, aspartate aminotransferase (AST), Lactate dehydrogenase (LDH), D-dimer, and Troponin T levels ($p < 0.05$). Hemoglobin, total protein, and albumin levels were significantly lower in group 1 ($p < 0.05$). Total Bilirubin and indirect bilirubin were significantly higher in group 3 ($p < 0.05$) (Table 5).

Discussion

Earlier data demonstrated that the number of pediatric patients has been lower with milder clinical characteristics, better disease progression, and outcome when compared to adult patients with COVID-19 (9-11). However, the characterization of the disease among pediatric age groups remains unclear. In this study, we have reported that epidemiological, clinical, laboratory, and radiological characteristics, treatment, and outcomes between different pediatric age groups in 139 children with COVID-19. Previous studies have demonstrated that children of all ages can be infected with COVID-19 with a broad median age of infection (range: newborn to 18 years) [12-14]. Similar to previous studies, we detected that the median age was 132 months (range, 15 days to 210 months).

To date, pediatric patients have usually presented with mild clinical symptoms and they had better outcomes compared to adult patients with COVID-19 (15,16). In our hospital, since the beginning of the COVID 19 pandemic, pediatric inpatient cases with COVID 19 are almost one-fourth of adult patients with COVID 19. According to the current literature, the most common clinical symptoms in children have so far been fever, cough, upper respiratory symptoms including nasal congestion and runny nose [4,17,18]. Presentation with gastrointestinal symptoms, such as nausea, vomiting, abdominal pain, and diarrhea have also been reported with less frequency [19,20]. In accordance with the previous reports, the most common clinical

Table 5. Comparison of laboratory findings of three age groups.

	Age groups			
Variable	**0.5-24 months Mean ± SD (median)**	**25-144 months Mean ± SD (median)**	**145-210 months Mean±SD (median)**	**p**
Hemoglobin, g/dl	11.28 ± 1.75	12.26 ± 1.41	13.29 ± 1.62	[1]**0.000***
White Blood Cells, /mm^3	9510.34 ± 4146.37 (10200)	6840 ± 2600 (6750)	6128.07 ± 2110.5 (5800)	[2]**0.000***
Thrombocytes, /mm^3	288793.1 ± 89142.89	240040 ± 80070.62	221789.47 ± 68413.59	[1]**0.001***
Lymphocytes, /mm^3	4179.31 ± 3384.14 (2600)	2448 ± 1551.33 (2150)	1922.81 ± 975.96 (1700)	[2]**0.003***
Granulocytes, /mm^3	4106.9 ± 2884.18	3528 ± 2250.36	3452.63 ± 1763.43	[1]0.408
C-reactive protein, mg/dl	8.77 ± 13.53 (3.1)	10.24 ± 16.14 (3.1)	9.93 ± 19.65 (3.1)	[2]0.701
Alanine aminotransferase, IU/L	25.86 ± 27.23 (18)	18.45 ± 10.86 (16)	18.82 ± 12.41 (14.5)	[2]0.167
Aspartate aminotransferase, IU/L	51.76 ± 30.79 (43)	31.7 ± 8.68 (31)	28.2 ± 27.92 (24)	[2]**0.000***
Lactate dehydrogenase, IU/L	306.03 ± 84.09 (299)	231.08 ± 48.43 (226.5)	200.36 ± 41.3 (187)	[2]**0.000***
INR	1.07 ± 0.12 (1.1)	1.06 ± 0.1 (1.1)	1.1 ± 0.15 (1.1)	[2]0.814
D-dimer, mg/L	3.18 ± 5.83 (1)	0.52 ± 0.37 (0.4)	0.8 ± 1.44 (0.3)	[2]**0.011***
Total Bilirubin, mg/dl	1.2 ± 2.89 (0.3)	0.37 ± 0.22 (0.3)	0.54 ± 0.34 (0.4)	[2]**0.001***
Indirect Bilirubin, mg/dl	1.03 ± 2.7 (0.2)	0.26 ± 0.18 (0.2)	0.37 ± 0.27 (0.3)	[2]**0.020***
Total Protein, g/L	65.86 ± 7.85	70.43 ± 5.16	74.23 ± 4.62	[1]**0.000***
Albumin, g/L	42.59 ± 4.3 (44)	43.98 ± 2.71 (44)	44.58 ± 3.93 (45)	[2]**0.018***
Creatine kinase, U/L	205.46 ± 304.37 (106)	112.96 ± 172.25 (72)	92.18 ± 69.63 (80.5)	[2]0.325
Troponin T, ng/L	22.55 ± 40.42 (6.4)	3.12 ± 0.62 (3)	4.97±6.3 (3)	[2]**0.000***
Urea mg/dl	20.31 ± 8.54	23 ± 6.38	23.04±5.87	[1]0.160

*[1]One-way Anova test; [2]Kruskal Wallis test; *p<0.05.*

symptoms in our study were fever and cough. No neurological or other systems findings were observed as presenting symptoms in our study sample. By the literature, only 1 patient required non-invasive mechanical support, and all patients in our study could be discharged. These results may be explained by potential factors that protect the children against severe COVID-19. Although these factors have not been fully understood yet, there has been some research on this topic. Possible protective factors and mechanisms could include; early school closings and day-care centers resulting in prevention of viral exposure, high angiotensin-converting enzyme-2 (ACE-2) expression, innate immunity, trained immunity caused by live virus vaccines and frequent upper respiratory viral infections, and absence of high-risk factors such as heart disease, obesity, and smoking [11,21-23]. Further studies are needed to describe the immune-pathogenesis of COVID-19 in children.

Most often, SARS-CoV-2 is transmitted to the children through close contact with their family members who are with or without symptoms [9,15,24]. An observational study analyzing the literature published between December 2019 and March 2020 of the household transmission clusters of COVID-19 reported that 9.7% of pediatric index cases were identified in 31 household transmission clusters (25). Following the literature, most of our patients had a history of close contact with COVID-19 positive family members in their household in this study.

Therefore, it can be concluded that children are not usually index cases for household transmission and that they often transmitted the infection from an adult contact.

Describing optimal treatment modalities for COVID-19 in children is difficult because of the limited data about the management of disease and the absence of controlled clinical trials. Although children with underlying conditions or receiving immunosuppressive treatment are likely to become severe cases, it seems to be uncommon (26). Because there are a few children that require hospitalization and are presented with severe disease, the World Health Organization has not recommended any specific treatment. The majority of research studies have suggested supportive therapy including adequate nutrition and calorie intake, fluid, electrolyte, and oxygen supplementation, and antibiotics for bacterial superinfection or co-infections [6,27]. However, some studies have proposed using antiviral agents including ribavirin, lopinavir and ritonavir, oseltamivir, favipiravir, remdesivir, and HCQ when needed [4,6,28-32]. The use of corticosteroids, anti-cytokine and immunomodulatory treatments, intravenous immunoglobulins, and convalescent plasma in the treatment of COVID-19 is controversial. COVID-19 Management Guideline of Turkish Ministry of Health, Public Health Agency recommends that hydroxychloroquine can be used in patients with severe disease and underlying medical conditions [5]. In our study, most of the patients received antibiotics empirically for bacterial co-infection, and HCQ was given only 13 to patients with underlying medical conditions or who had abnormal CT scan findings.

COVID-19 can affect children of all ages, while young children especially infants are more represented among all age groups [12,19]. There are limited data for infants younger than one year with COVID-19 in the literature [17,32,33]. Systematic disease characteristics of children with COVID-19 in different age groups have not been reported. Therefore, we divided our patients into three groups according to their ages and compared the disease characteristics between these groups.

In our study, almost all patients had mild disease. In a nationwide case series of 2135 pediatric patients with COVID-19 reported that young children were vulnerable to COVID-19 and the rate of severe disease were 10.6%, 7.3%, 4.2%, 4.1%, and 3.0% for the age groups <1, 1 to 5, 6 to 10, 11 to 15, and >16 years, respectively (12). Many studies have shown that cough and fever were the most common clinical manifestations in children with COVID-19 [20,34-37]. Similar to previous studies, we found that the most common clinical symptoms were cough (55.4%) and fever (51.8%). In addition, we detected that fever was significantly more frequent in patients aged 15 days-24 months. In accordance with this result, a retrospective study by Sun *et al.* conducted on infants with COVID-19 reported that fever was one of the most common clinical symptoms with a proportion of 47.22% (33). Chest pain is one of the clinical manifestations attributable to COVID-19, especially in adult patients. In a set of retrospective studies with pediatric and adult patients with COVID-19, the frequency of chest pain was reported as 2.4% by Garazzino *et al.*, 2% by Chen *et al.*, and 21.4% by Su *et al.* [18,37,38]. In our study, the frequency of chest pain was 10.1% and chest pain was significantly more frequent in patients older than 12 years. This association can be explained by two reasons. First; patients older than 12 years are able to describe their chest pain more clearly than younger pediatric patients. Secondly; the increased anxiety of adolescents related to disease may be more common because cardiac biomarkers of these adolescent patients

were in normal values and their electrocardiographic (ECG) examinations were also normal.

Although there are limited data, the laboratory findings of children with COVID-19 are non-specific and can vary based on disease severity. We found that patients aged 15 days-24 months had significantly higher WBC, lymphocytes, thrombocytes counts; lower hemoglobin, total protein, and albumin levels, and along with elevated AST, LDH, D-dimer, and Troponin T levels. Similar to our study, a systematic review and meta-analysis by Henry *et al.* reported that WBC, lymphocytes, thrombocytes count, AST, ALT, and LDH levels were significantly higher; hemoglobin and creatinine levels were significantly lower in infants younger than one year with mild COVID-19 (39). These results may be caused by a higher viral burden in infants who had a higher risk of serious disease [33].

This study has some limitations. The most important limitations were the small sample size and retrospective, single-center design of this study.

Conclusions

This retrospective, single-center study examined 139 patients with COVID-19. No deaths or serious complications were seen even in patients with underlying medical conditions. Most patients had close contact with a COVID-19 infected person in their households. Fever was significantly more frequent in the youngest age group and chest pain was significantly more frequent in the oldest age group. The patients aged 15 days to 24 months had significantly higher WBC, lymphocytes, thrombocytes count, AST, LDH, D-dimer, and Troponin T levels; lower hemoglobin, total protein, and albumin levels. Children are likely to be secondary cases and have mild disease. Determining age group differences in pediatric patients can provide significant contributions to understanding disease pathogenesis. Further prospective designed multicenter studies are needed to contribute the pathophysiology of COVID-19 in children to appropriately manage this novel infection.

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