# Clinical Features and Laboratory Findings of COVID-19 in Children: A Tertiary Center Experience

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# **INTRODUCTION**

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the causative agent of coronavirus disease 2019 (COVID-19), which belongs to the Coronaviridea family. It initially emerged from Wuhan, Hubei province, China, in December 2019. On March 11, 2020, there were more than 118,000 cases in 114 different countries, and the World Health Organization declared the situation as a pandemic.<sup>[1]</sup> In adult patient groups, fever, cough, and fatigue are the most common symptoms; however, severe cases leading to death with acute respiratory distress syndrome have been described.<sup>[2-4]</sup> The clinical findings of COVID-19 are similar in children and adults, but severe COVID-19 is rare in children. COVID-19 appears to be milder in children and the most commonly reported symptoms are fever and cough.<sup>[5,6]</sup>

# ABSTRACT

**Objective:** Despite increasing data on Coronavirus Disease 2019 (COVID-19) in adults, the data in pediatric patients are still limited. The aim of our study is to evaluate the clinical features and laboratory findings of our confirmed pediatric COVID-19 cases.

**Methods:** This retrospective descriptive study was conducted in one of the largest COVID-19 treatment centers in İstanbul, Turkey. Four hundred and fifty-six cases confirmed using reverse transcriptase-polymerase chain reaction (RT-PCR) were included in the study. One hundred inpatients and 356 outpatients were treated. Patients were classified according to the disease severity as asymptomatic, mild, moderate and severe.

**Results:** The number of asymptomatic, mild, moderate or severe cases were 199 (43.6%), 194 (42.5%), 33 (7.2%) and 30 (6.6%) respectively. Most of the hospitalized patients younger than 5 years old had the mild disease (67.7%), whereas most of the patients over 15 years of age had severe disease (54.2%). Lymphopenia and high ferritin levels at admission were more common in severe cases (p<0.05). Also, multiple regression analysis revealed that high ferritin and D-dimer levels were found to prolong hospital stay (p=0.000;  $R^2$ =0.404).

**Conclusion:** Age, lymphocyte count, ferritin and D-dimer levels can be used to estimate the disease severity for COVID-19 infection in children.

The lack of data on pediatric patients led us to evaluate the epidemiological and clinical features of patients with COVID-19 disease in this study.

# MATERIALS AND METHODS

This retrospective descriptive study was conducted between March and May 2020 in a 1000- bed tertiary education and research hospital, one of the hospitals designated for the treatment of COVID-19 patients in Istanbul, Turkey.

During the study period, nasopharyngeal swabs were obtained from 1157 pediatric patients (all younger than 18 years of age), 927 of whom were outpatients and 230 of whom were hospitalized with suspected COVID-19 disease. Suspected cases were defined as children with fever, cough, other acute respiratory disease signs and symptoms, gastrointestinal symptoms like diarrhea, vomiting and history of exposure. Of these, 456 patients were diagnosed with COVID-19 infection using the reverse transcriptase-polymerase chain reaction (RT-PCR) test and included in the study (Fig. 1).

A Nasopharyngeal swab was taken from one nostril of patients according to the National Health Ministry guideline. <sup>[7]</sup> The collected swabs were transferred to the national reference laboratory of the Turkish Public Health Agency until 16 April 2020 and then to the virology laboratory of our hospital. Laboratory confirmation of COVID-19 was performed using RT-PCR.

The patient data were collected from the hospital archive, retrospectively. Age, sex, the potential source of infection, travel history, exposure history, clinical characteristics, laboratory values and radiological findings were evaluated. The patients were allocated to groups according to the disease severity.

### The classification of disease severity

The severity of the disease was classified according to clinical features, laboratory testing, and chest radiograph as asymptomatic, mild, moderate and severe.<sup>[8,9]</sup>

Asymptomatic infection: Patients with normal chest imaging findings but no clinical symptoms or signs with a positive RT-PCR test result.

*Mild:* Patients with the symptoms of acute upper respiratory tract infection, including fever, fatigue, myalgia, cough, sore throat, runny nose, sneezing and/or digestive symptoms such as nausea, vomiting, abdominal pain, and diarrhea. Pulmonary auscultation and the chest imaging results were normal.

Patients with symptoms of acute upper respiratory tract infection such as fever, fatigue, myalgia, cough, sore throat, runny nose, sneezing and/or digestive symptoms such as nausea, vomiting, abdominal pain and diarrhea. Lung aus-

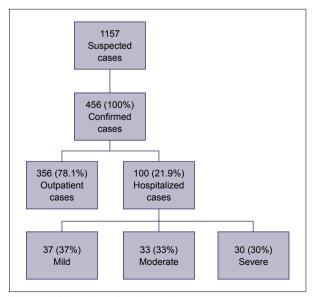


Figure 1. Flow-chart of patient cohort.

cultation and lung imaging results were normal.

*Moderate:* Patients with pneumonia, persistent fever and cough (mostly dry cough, followed by productive cough); some had wheezing or crackles, but no respiratory distress. In some cases, chest computed tomography (CT) showed parenchymal lesions.

Severe: The criteria for the severe disease were persistent fever (>38.5°C) with at least one of the following: tachypnea (defined as <2 months old  $\geq$ 60 breaths/min; 2–11 months old  $\geq$ 50 breaths/min, 1–5 years old  $\geq$ 40 breaths/min and 5 years old  $\geq$ 30 breaths/min), oxygen saturation less than 92%, apnea, nasal flaring, lethargy, grunting, cyanosis, chest retractions, feeding difficulty, dehydration or shock.

#### Statistical analysis

Normally distributed quantitative variables were expressed as mean±standard deviation (SD), whereas nonnormally distributed quantitative variables were expressed as median with interquartile ranges (IQR). The Chi-square test was used for comparing categorical variables. The one-way analysis of variance (ANOVA) test was used for comparing normally distributed quantitative data, and Mann-Whitney U and Kruskal-Wallis tests were used for comparing non-normally distributed quantitative variables. Multiple regression analysis was performed to assess confounding factors. All analyses were conducted using SPSS 20 software (IBM SPSS Statistics, New York) and p<0.05 indicated a statistically significant difference.

# RESULTS

There were 456 patients (39.4% of total patients tested) diagnosed with COVID-19 infection and included in the analyses. The epidemiological and clinical features of these children are shown in Table 1. One hundred (21.9%) of these children were hospitalized, whereas 356 (78.1%) were treated as outpatients. The median age of the patients was 11 (IQR: 4.62–15 years). The number of asymptomatic, mild, moderate, or severe cases were 199 (43.6%), 194 (42.5%), 33 (7.2%) and 30 (6.6%), respectively. This is also shown in Table 2 according to patients' ages. 92.5% of patients had contact information about confirmed cases. None of the patients had a recent travel history to another country.

The clinical features of hospitalized children are further detailed in Table 3. These patients were subcategorized as mild, moderate and severe. Patients younger than 6 years of age had mild disease mostly (67.7%), while patients aged 5–15 years had similar rates of mild, moderate and severe disease (33.3%), and patients over 15 years of age had mostly severe disease (54.2%) (Fig. 2). We did not have a critically ill patient. Boys and girls were equally affected in all groups.

The most common symptoms among the patients were cough and fever. However, the cough was more frequent

in patients with severe disease (p<0.05). Severe cases had longer hospital stays compared to mild and moderate cases (p<0.05).

Eight (8%) of the patients had an underlying disease. Three had a renal disease (I chronic kidney disease, I nephrotic

Table 1.         Epidemiological and clinical features of 456 children with confirmed COVID-19				
Age				
Median (IQR)	11 yrs (4.62–15)			
Min-Max	22 days-17.9 yrs			
Age group, n (%)				
<l td="" yr<=""><td>26 (5.7)</td></l>	26 (5.7)			
≥1–<5 yrs	92 (20.2)			
≥5–<15 yrs	220 (48.2)			
≥15 yrs	118 (25.9)			
Gender, n (%)				
Male	235 (48.5)			
Female	221 (51.5)			
Severity of illness, n (%)				
Asymptomatic	199 (43.6)			
Mild	194 (42.5)			
Moderate	33 (7.2)			
Severe	30 (6.6)			
Patient cohort, n (%)				
Outpatient	356 (78.1)			
Inpatient	100 (21.9)			
Exposure history, n (%)				
Family cluster	422 (92.5)			
Symptoms, n (%)				
Cough	124 (27.2)			
Fever	105 (23)			
Headache	26 (5.7)			
Fatigue	22 (4.8)			
Myalgia	16 (3.5)			
Shortness of breath	13 (2.9)			
Sore throat	12 (2.6)			
Vomiting	9 (2)			
Loss of taste	7 (1.5)			
Diarrhea	4 (0.9)			
Respiratory distress	4 (0.9)			
Hemoptysis	2 (0.4)			

COVID-19: Coronavirus Disease 2019; IQR: Interquartile range.

syndrome, I hydronephrosis), 2 had a neurodevelopmental disorder, I had type I diabetes mellitus (DM) and I had mitral insufficiency due to previous acute rheumatoid fever.

Laboratory findings of hospitalized patients are summarized in Table 4. There were significant differences between the groups in terms of lymphocyte counts, hemoglobin, creatinine and ferritin levels. Lymphocyte counts were lower in patients with severe disease compared to other groups (p<0.05), however, there was no significant difference between mild and moderate groups (p=0.40). Hemoglobin levels were higher in patients with severe disease (p=0.004). Patients with moderate and severe disease had higher creatinine levels (p < 0.05), however, there was no difference between the moderate and severe groups (p=0.08). Patients with severe disease had higher ferritin levels compared to the mild group (p=0.004), whereas there was no difference between the other groups. Multiple regression analysis was performed using hospitalization days as dependent variables and age, lymphocyte count, Ddimer and ferritin levels as independent variables. Only Ddimer (p=0.000) and ferritin (p=0.000) levels were found to affect the days of hospitalization (p=0.000;  $R^2=0.404$ ). (Table 5) Patients with severe disease had more positive C-reactive protein (CRP) results (p<0.05); however, when CRP levels were compared in CRP-positive patients, there was no difference among groups.

CT scan demonstrated abnormal findings in all patients with severe disease. Abnormal findings on CT scan in these patients were unilateral ground-glass opacity in 12 patients (40%), bilateral ground-glass opacity in 17 patients (56.7%) and consolidation in one patient (33%). Twenty- three patients (69.9%) with moderate disease had abnormal CT findings. These were fibrotic sequelae in 16 patients, minimal ground-glass opacity in 6 patients, consolidation in 1 patient.

All moderate and mild inpatient cases received azithromycin treatment and the treatment was initiated at the time of hospitalization. However, in severe cases, 17 (56.7%) were given azithromycin and hydroxychloroquine, 9 (30%) were given hydroxychloroquine, 2 (6.7%) were given azithromycin, hydroxychloroquine and favipiravir. Also, 2 patients (6.7%) (2 months old and 2 years old) with the severe disease received azithromycin and lopinavir-ritonavir combination.

Four patients (13.3%) with severe disease required high-

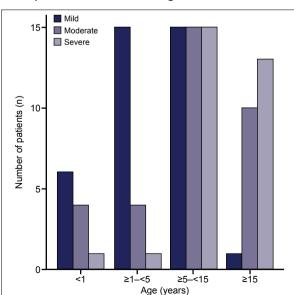
Table 2.	Disease severity	of confirmed	l cases according to age
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	Asymptomatic	Mild	Moderate	Severe	Total
Age group, n (%)					
<l td="" yr<=""><td>12 (6)</td><td>9 (4.6)</td><td>4 (12.1)</td><td>l (3.3)</td><td>26 (5.7)</td></l>	12 (6)	9 (4.6)	4 (12.1)	l (3.3)	26 (5.7)
≥–<5 yrs	40 (20.1)	47 (24.2)	4 (12.1)	l (3.3)	92 (20.2)
≥5–<15 yrs	109 (54.8)	81 (41.8)	15 (45.5)	15 (50)	220 (48.2)
≥15 yrs	38 (19.1)	57 (29.4)	10 (30.3)	13 (43.3)	118 (25.9)
Total	199 (43.6)	194 (42.5)	33 (7.2)	30 (6.6)	456 (100)

	Mild	Moderate	Severe	р
Patient count, n (%)	37 (37)	33 (33)	30 (30)	
Age (yr)‡	4.5 (1.9–11.6)	12.7 (4.6–16.2)	13.8 (11.9–16.1)	0.000*
Age group, n (%)				
<l td="" yr<=""><td>6 (16.2)</td><td>4 (12.1)</td><td>l (3.3)</td><td>0.000*</td></l>	6 (16.2)	4 (12.1)	l (3.3)	0.000*
≥I–<5 yr	15 (40.5)	4 (12.1)	l (3.3)	
≥5–<15 yr	15 (40.5)	15 (45.5)	15 (50)	
≥l5 yr	l (2.7)	10 (30.3)	13 (43.3)	
Gender, n (%)				
Male	19 (51.4)	15 (45.5)	18 (60)	0.511
Female	18 (48.6)	18 (54.5)	12 (40)	
Exposure history, n (%)	36 (97.3)	31 (93.9)	26 (86.7)	0.230
Symptoms, n (%)				
Cough	17 (45.9)	17 (51.5)	25 (83.3)	0.005*
Fever	23 (62.2)	21 (63.6)	22 (73.3)	0.593
Headache	4 (10.8)	3 (9.1)	3 (10.0)	0.972
Fatigue	2 (5.4)	I (3.0)	3 (10.0)	0.499
Myalgia	0 (0.0)	4 (12.1)	2 (6.7)	0.101
Shortness of breath	0 (0.0)	4 (12.1)	4 (13.3)	0.077
Sore throat	0 (0.0)	2 (6.1)	2 (6.7)	0.292
Vomiting	2 (5.4)	2 (6.1)	0 (0.0)	0.406
Diarrhea	l (2.7)	l (3)	0 (0.0)	0.643
Respiratory distress	0 (0.0)	0 (0.0)	5 (16.7)	0.002*
Hemoptysis	0 (0.0)	0 (0.0)	2 (6.7)	0.092
Underlying disease, n (%)	2 (5.4)	3 (9.1)	3 (10)	0.758
Hospital stay (days)‡	5 (3–6)	4 (3–5)	6 (6–7.5)	0.000*
				Mild-Moderate: 0.037*
				Mild-Severe: 0.000*
				Moderate-Severe: 0.000

Table 3. Epidemiologic and clinical features of 100 hospitalized children with COVID-19 in groups of disease severity

COVID-19: Coronavirus Disease 2019; IQR: Interquartile range; \*Statistically significant, p<0.05; #Median (IQR).



flow oxygen therapy. None of the patients in the study developed or died from multi-organ failure.

#### Figure 2. Disease severity according to age in hospitalized patients.

## DISCUSSION

Children of all ages are susceptible to COVID-19, and most children have mild clinical symptoms and have a better prognosis than adults.<sup>[10,11]</sup> However, children with an underlying disease such as chronic lung disease, congenital heart disease, chronic renal disease, or immunodeficiency may show severe symptoms.<sup>[10]</sup> Ludvigsson analyzed 45 studies on COVID 19 and reported that children account for 1%–5% of diagnosed COVID-19 cases.<sup>[11]</sup> According to the available data, COVID-19 is believed to be transmitted through respiratory droplets and close contact.<sup>[12]</sup> Many children with COVID-19 are members of family clusters with COVID-19.<sup>[11,13]</sup>

Various confirmation rates, age, and gender differences have been reported in previously published studies. In the study of Dong et al.,<sup>[9]</sup> 34.1% (728 children) of 2135 suspected children were confirmed and the median age of confirmed cases was 10 years, and there was no difference in terms of gender. Similarly, in Lu et al.'s<sup>[14]</sup> study, 171 (12.3%) of 1391 suspected children were confirmed, with a median age of 6.7 years; however, it was more boys (60.8%) than girls. In our study, 456 (39.4%) of 1157 pedi-

	Mild	Moderate	Severe	р
Hemoglobin (gr/dl) †	12.27±1.42	12.64±1.19	13.32±1.35	0.004*
				Mild-Moderate: 0.004*
				Mild-Severe: 0.004*
				Moderate-Severe: 0.125
Leukocyte (mm³)‡	6500 (4600–8050)	6800 (5000–9250)	5600 (4575–6825)	0.097
Lymphocyte (mm³)‡	2400 (1800–4450)	2000 (1850–2000)	1650 (1200–2375)	0.003*
				Mild-Moderate: 0.403
				Mild-Severe: 0.001*
				Moderate-Severe: 0.011
Platelet (mm <sup>3</sup> ) <sup>‡</sup>	266000	265000	225000	0.117
	(212500–318000)	(196500–303000)	(187500–295250)	
MPV <sup>‡</sup>	7.9 (7.4–8.4)	8.1 (8–8.8)	7.8 (7.5–8.4)	0.117
Creatinine (mg/dl) <sup>‡</sup>	0.32 (0.25-0.42)	0.48 (0.3–0.57)	0.5 (0.39–0.78)	0.000*
	· · ·	, , , , , , , , , , , , , , , , , , ,	· · · ·	Mild-Moderate: 0.011*
				Mild-Severe: 0.001*
				Moderate-Severe: 0.079
ALT (IU/L) <sup>‡</sup>	16.0 (11–23)	12 (10–18)	16.5 (12–31.5)	0.063
AST (IU/L) <sup>‡</sup>	30 (22.5-42.5)	24 (17.5–32.5)	24 (18.5–30)	0.012*
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				Mild-Severe: 0.014*
				Moderate-Severe: 0.831
LDH (IU/L) <sup>‡</sup>	227 (205–284)	207 (75–145)	216 (170–247)	0.134
CK (IU/L) <sup>‡</sup>	100 (75–145)	207 (66-110)	216.5 (57.7–132)	0.227
D-Dimer (µg/L) <sup>‡</sup>	400 (240-400)	360 (295–490	490 (380–632)	0.099
Ferritin (µg/L) <sup>‡</sup>	27.4 (15.1–47.5)	43.4 (26.5-85.6)	57.6 (32.6–93.5)	0.015*
				Mild-Moderate: 0.089
				Mild-Severe: 0.004*
				Moderate-Severe: 0.303
Positive CRP, n (%)	12 (32.4)	9 (27.3)	19 (63.3)	0.007*
				Mild-Moderate: 0.010*
				Mild-Severe: 0.014*
				Moderate-Severe: 0.831
CRP levels of patients with positive CRP	8.32 (3.27–50.9)	8.74 (3.80–41.4)	12.60 (3.52–67)	0.462

 Table 4.
 Laboratory findings of 100 hospitalized children with COVID-19 in groups of disease severity

COVID-19: Coronavirus Disease 2019; IQR: Interquartile range; MPV: Mean platelet volume; ALT: Alanine transaminase; AST: Aspartate transaminase; LDH: Lactate dehydrogenase; CK: Creatinekinase; Positive CRP (C-reactive protein) was defined as levels ≥3.11 mg/dl; "Statistically significant, p<0.05; "Mean±SD; "Median (IQR).

<b>Table 5.</b> Evaluation of the effect of the variables on the day of hospitalization using linear regression analys	Table 5.	Evaluation of the effect	of the variables on the da	y of hospitalization usin	g linear regression analysis
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	Unstandardized Coefficients		Standardized Coefficients		95% Confidence interval for B	
	В	Std. Error	Beta	р	Lower Bound	Upper Bound
Hospital days (Constant)	4.086	0.804		0.000	2.487	5.686
Age	0.028	0.048	0.062	0.558	-0.067	0.124
Lymphocyte count	0.000	0.000	-0.183	0.090	0.000	0.000
D-Dimer	0.002	0.000	0.390	0.000	0.001	0.002
Ferritin	0.010	0.002	0.448	0.000	0.006	0.014

atric cases were diagnosed with COVID-19. The median age was 11 years and the cases were equally distributed

between boys and girls. The different confirmation rates may be attributed to the different definitions of suspected

cases. However, the difference in gender and median age should be evaluated in larger series.

In a study conducted in Italy, exposure to a family cluster was calculated as 45% and exposure to a source outside the family as 55%. The high outer source exposure rate was thought to be related to the late lockdown in the country.<sup>[15]</sup> In a study from China, children were in the family cluster in 90.1% of the cases.<sup>[14]</sup> In our study, 422 (92.5%) children were in a family cluster. Exposure to the family cluster rate was high. Regulations of early school closures and early lockdown of children resulted in higher exposure rates to the family cluster. It is difficult to ensure social distancing and the use of masks within at home.

Although severe COVID-19 cases were reported in children, most of the cases were asymptomatic or mild.<sup>[14,16,17]</sup> It is still unclear why COVID 19 is less severe in children compared to adults. There are some hypotheses for this. These; the different immune responses in children, a stronger immune system stimulated by more frequent viral infections, and decreased angiotensin-converting enzyme 2 (ACE-2) levels to which COVID-19 binds.<sup>[11,18]</sup> In the study of Dong et al.,<sup>[9]</sup> the confirmed pediatric cases were asymptomatic or mild in 56%, moderate in 40.9%, severe in 2.5% and critical in 0.4% of the cases. As in other studies, the majority (86.1%) of our pediatric cases were asymptomatic or mild. Moderate and severe cases were 7.2% and 6.6%, respectively.

Age can be an important but contradictory risk factor for severe disease. In the study of Dong et al.,<sup>[9]</sup> 8.2% of children younger than I-year-old had severe or critical disease, whereas 5.1% of children over 15 years had severe disease. Whereas, in our study, 3.8% of all confirmed cases younger than I-year-old were severe and 11.1% of cases over 15 years were severe.

Of the 171 pediatric cases admitted to Wuhan Children's Hospital, 65% had pneumonia. Three children with underlying diseases (hydronephrosis, leukemia and intussusception) were admitted to the intensive care unit.<sup>[14]</sup> Some studies show that underlying medical illnesses are risk factors for severe disease. Of the 48 children admitted to the pediatric intensive care unit, 83% were found to have underlying medical illnesses and the most common were neurodevelopmental disorders, immunosuppression, malignancy and obesity.<sup>[19]</sup> Shekerdemian et al.<sup>[19]</sup> reported that 23% of 345 confirmed pediatric COVID-19 cases had an underlying disease. These diseases were chronic lung disease (moderate and severe asthma included), cardiovascular disease and immunosuppression. Among children admitted to the hospital, 77% had an underlying disease. <sup>[17]</sup> Compared to other studies, our hospitalized patients had fewer underlying diseases (8%). However, in our study, the underlying disease was not found to be a risk factor for severe disease. Underlying diseases seem to be a risk factor for COVID-19 but their relationship with the disease severity should be further evaluated.

Fever and cough were the most common symptoms re-

ported in children. In a case series from USA, 56% had fever and 54% had cough.<sup>[17]</sup> In a study done by Lu et al.<sup>[14]</sup> with confirmed pediatric cases with COVID-19, 48.5% had cough and 42% had fever. Other symptoms include malaise, diarrhea and vomiting. 2.3% of cases had oxygen saturation less than 92%. Similar symptom rates were reported from China and Italy in smaller series. Some children had only gastrointestinal symptoms. Other reported symptoms were headache, myalgia, loss of smell and taste. <sup>[15,20,21]</sup> Similarly, the most common symptoms were fever and cough in our study.

Although laboratory changes in adults have been well-documented, these changes are much less known in pediatric cases. In studies with adult COVID-19 patients, lymphopenia was present in 80% of critical cases in one study and 25% of mild cases in another study; therefore, lymphopenia is thought to be associated with the severity of the infection.<sup>[22,23]</sup> Sixty-six pediatric patients have been evaluated in 12 studies in a meta-analysis from China.<sup>[24]</sup> Most of the patients (69.6%) had normal leukocyte count, 15.1% had leukocytosis and 15.2% had leukopenia. However, there were inconsistent results regarding the relationship between the lymphocyte count and disease severity, probably because of the low number of patients. In our study, lymphocyte count was significantly lower in patients with severe disease compared to mild/moderate cases. Therefore, it seems that lymphopenia may also be a risk factor for severe disease in pediatric cases.

Elevated D-dimer and ferritin levels may be observed in pediatric cases with severe disease.<sup>[25]</sup> In a meta-analysis, CRP was also elevated in 13.6% of the cases.<sup>[24]</sup> Furthermore, in the study of Xia et al.,[26] CRP was elevated in 35% of the pediatric cases. In severe cases, ferritin was found to be significantly elevated compared to non-severe cases.<sup>[27]</sup> In a systematic review of 2143 pediatric cases in 8 studies, elevated CRP, lymphopenia and elevated D-dimer was present in 3-35%, 6-38%, and 8-40%, respectively. <sup>[28]</sup> In our study, CRP elevation was found in 63.3% of severe cases, and this rate was found to be significantly higher compared to mild cases. Ferritin levels were also significantly higher in severe cases compared to mild cases. Moreover, multi-regression analyses in our study revealed that elevated D-dimer and ferritin levels affect the hospitalization days. In summary, as in adults, laboratory values of lymphocyte count, D-dimer, ferritin and CRP may help determine the severity of the disease, predict the prognosis and monitor the treatment in pediatric patients.

In moderate cases of pneumonia, there are chest images with multiple small patchy shadows and interstitial changes, especially in the lung periphery. Severe cases can further develop bilateral multiple ground-glass opacity, infiltrating shadows, and pulmonary consolidation. In the study of Lu et al.,<sup>[14]</sup> the most common radiological finding was bilateral ground-glass opacity (32.7%). Other findings were local patchy shadowing in 18.7%, bilateral patchy shadowing in 12.3%.<sup>[14]</sup> In our study, severe cases had 56% bilateral, 40% unilateral ground-glass opacity on CT scans. 18.2% of

moderate cases had minimal ground-glass opacity. Therefore, our radiologic findings were compatible with the previous studies.

Currently, there is no approved specific treatment for pediatric COVID-19 cases. Various centers use various agents, but there is not enough data to recommend a routine practice. Therefore, the treatment strategy in pediatric cases is usually determined according to adult data. Furthermore, regarding the efficacy of hydroxychloroquine and chloroquine in the treatment of COVID-19 in pediatric cases, there is not enough evidence. Yet, there are only in vitro studies.<sup>[29]</sup> In a previous study, it was claimed using azithromycin together with hydroxychloroquine rather than hydroxychloroguine alone was more effective. <sup>[30]</sup> Lopinavir-ritonavir combination seems to have no or minimal effect in the treatment of COVID-19. Yet, the lopinavir-ritonavir combination is recommended only for clinical research purposes in COVID-19.[29] In the study of Wang et al.,<sup>[31]</sup> 20 of 34 children with COVID-19 were successfully treated with the lopinavir-ritonavir combination. Clinical studies of favipiravir are still ongoing, but currently, there is no evidence for its use in pediatric cases.<sup>[29]</sup> 4 of our cases with severe disease required high flow oxygen and 2 of these adolescent children received favipiravir in addition to azithromycin and hydroxychloroquine. The other two children, one was 2 months and the other one was 2 years old, received azithromycin and lopinavir-ritonavir. We initiated treatment protocols early, at the time of hospitalization. We think that early initiation of treatment before the development of multiorgan failure seems to be an appropriate approach.

In conclusion, our study shows that pediatric patients with COVID-19 are mostly infected through close contact with infected family members; so we believe that contact and droplet isolation measures are crucial to the containment of spread. Lymphopenia and elevated ferritin levels were more common in severe cases and may be prognostic factors for COVID-19.

#### **Ethics Committee Approval**

This study approved by the Kartal Dr. Lutfi Kirdar Training and Research Hospital Clinical Research Ethics Committee (Date: 29.04.2020, Decision No: 2020/514/176/24).

#### Informed Consent

Retrospective study.

#### Peer-review

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## Authorship Contributions

Concept: C.Ç., A.K., Y.A.; Design: A.K., C.Ç.; Supervision: C.Ç., Y.A., R.D.; Materials: A.K., C.Ç., Y.Ç., Data: A.K., C.Ç., E.S., Y.A.; Analysis: C.Ç., A.K., R.D.; Literature search: C.Ç., A.K., E.S; Writing: C.Ç., A.K., Y.Ç.; Critical revision: C.Ç., A.K.

#### **Conflict of Interest**

None declared.

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# Çocuklarda COVID-19'un Klinik Özellikleri ve Laboratuvar Bulguları: Üçüncü Basamak Merkez Deneyimi

Amaç: Erişkinlerde Coronavirus Hastalığı 2019 (COVID-19) hakkında artan verilere rağmen, pediatrik hastalardaki veriler hala sınırlıdır. Çalışmamızın amacı, doğrulanmış pediatrik COVID-19 olgularımızın klinik özelliklerini ve laboratuvar bulgularını değerlendirmektir.

Gereç ve Yöntem: Bu geriye dönük çalışma, Türkiye'deki en büyük COVID-19 tedavi merkezlerinden birinde yapıldı. Çalışmaya ters transkriptaz polimeraz zincir reaksiyonu (RT-PCR) kullanılarak doğrulanan 456 olgu dahil edildi.Yüz hasta yatarak, 356 hasta ayakta tedavi edildi. Hastalar hastalık şiddetine göre asemptomatik, hafif, orta ve şiddetli olarak sınıflandırıldı.

**Bulgular:** Asemptomatik, hafif, orta ve ağır vaka sayısı sırasıyla 199 (%43.6), 194 (%42.5), 33 (%7.2) ve 30 (%6.6) idi. Hastanede yatan beş yaş altı hastaların çoğu hafif (%67.7) iken, 15 yaş üstü hastaların çoğu ağır hastalığa (%54.2) sahipti. Başvuru anında lenfopeni ve yüksek ferritin düzeyleri ağır olgularda daha yaygındı (p<0.05). Ayrıca çoklu regresyon analizi, yüksek ferritin ve D-dimer düzeylerinin hastanede yatış süresini artırdığını ortaya koydu (p=0.000; R<sup>2</sup>=0.404).

**Sonuç:** Çocuklarda COVID-19 enfeksiyonu için hastalık şiddetini tahmin etmek için yaş, lenfosit sayısı, ferritin ve D-dimer seviyeleri kullanılabilir.

Anahtar Sözcükler: COVID-19 virus; favipiravir; ferritin; lenfopeni; pediatri.