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Evaluation of the novel coronavirus disease in Turkish children: Preliminary outcomes

Kamil Yılmaz[1] | Ayfer Gozupirinççioğlu[2] | Fesih Aktar[2] | Alper Akın[3] | Müsemma Karabel[4] | Ilyas Yolbas[5] | Veysiye Hulya Uzel[6] | Velat Şen[4]

[1]Department of Pediatric Infectious Diseases, Dicle University School of Medicine, Diyarbakir, Turkey

[2]Department of Pediatric Intensive Care, Dicle University School of Medicine, Diyarbakir, Turkey

[3]Department of Pediatric Cardiology, Dicle University School of Medicine, Diyarbakir, Turkey

[4]Department of Pediatric Pulmonology, Dicle University School of Medicine, Diyarbakir, Turkey

[5]Department of Pediatric, Dicle University School of Medicine, Diyarbakir, Turkey

[6]Department of Pediatric Hematology, Dicle University School of Medicine, Diyarbakir, Turkey

Correspondence
Velat Şen, Department of Pediatric Pulmonology, Dicle University School of Medicine, Diyarbakir 21200, Turkey.
Email: drvelatsen@hotmail.com

Abstract

Background: The novel coronavirus disease (Covid-19) can progress with mild to moderate or self-limiting clinical findings in children. The aim of this study was to investigate the disease features of Covid-19 in Turkish children.

Methods: Children diagnosed by the method of real-time reverse transcription-polymerase chain reaction for Covid-19 at the Dicle University Department of Pediatric, between April and June 2020, were evaluated. Hospital records were investigated retrospectively.

Results: One hundred and five patients children with the mean age of 108.64 ± 65.61 months were enrolled in this study. The most common cause of transmission in pediatric patients was in contact with a family member diagnosed with COVID-19 (n = 91, 86.7%). The most common admission complaints were dry cough (n = 17, 16.2%), fever (n = 16, 15.2%), lassitude and fatigue (n = 14, 13.3%) respectively. More than 95% of all children with Covid-19 were asymptomatic, mild, or moderate cases. CRP was identified only independent factor associated with long duration of hospitalization.

Conclusion: The results of this study show the effect of Covid-19 on Turkish children. A clear understanding of the local epidemiology of corona virus infections and identification of risk factors are critical for the successful implementation of the prevention and control program.

KEYWORDS
coronavirus, COVID-19, disease characteristics

1 | INTRODUCTION

Coronaviruses (CoVs) are RNA viruses that are related to human disease.[1] The virus responsible for novel coronavirus disease (COVID-19) is located in the same genus as the severe acute respiratory syndrome coronavirus (SARS-CoV) and the Middle East respiratory syndrome coronavirus (MERS-CoV). The new nomenclature of the virus has been accepted as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[2]

Among the coronaviruses causing disease in humans, HCoV 229E, NL63, OC43, and HKU1 are the most frequently isolated ones. Despite the fact that all coronaviruses can infect subjects of all ages, these subtypes are responsible for endemics of upper respiratory tract infections in adults. However, many other coronavirus subtypes can also cause severe disease in humans.[3–5]

Coronaviruses are capable of undergoing mutations that lead to the emergence of novel CoVs that can be transmitted from animals to humans. SARS-CoV was the first virus that was transmitted from bearcats to humans in 2002, resulting in the death of hundreds of people in 37 countries. After 10 years, in 2012, MERS-CoV was first described in humans and caused 858 fatalities.[6,7]

In December 2019, the novel SARS-CoV-2 was reported in Wuhan, China. After this date, the number of patients increased rapidly, and the disease became prevalent all over the world. A number of studies on the total burden of novel COVID-19 have demonstrated that the disease is generally more dangerous in adults who are at risk of COVID-19 related complications due to chronic underlying diseases such as cardiovascular and cerebrovascular diseases as well as diabetes.[8]

Otherwise COVID-19 also commonly occurs in healthy children, a considerable proportion of whom experience severe disease leading to hospitalization, more frequent outpatient visits, prescription of pharmaceutical medications, and (although rarely) even death.[9] The first-ever pediatric COVID-19 case in the world was reported from Shenzhen, China on January 20, 2020.[10]

Although several studies from Asia and America have reported that the new coronavirus disease may be less serious in children than adults,[11,12] subsequent studies from European countries have shown that the number of pediatric multisystem inflammatory syndrome cases related to COVID-19 has increased over time; since then, case reports of the pediatric patients have been published from different regions of the world.[13–15]

The optimal management of the COVID-19 disease is not clear and no treatment with proven reliability and effectiveness is yet available. Although there are several studies on possible drugs altering the prognosis of pediatric COVID-19, there is no consensus for its treatment.[16–22] The drugs already used for the treatment often cause adverse effects.

To our knowledge, no major study has yet been published on pediatric COVID-19 in Turkish children. Therefore, we aimed to evaluate the clinical, radiological, and laboratory features of the disease in Turkish children and to compare the data about disease characteristics with the data reported from other countries. In addition, this retrospective study also aimed to identify risk factors associated with COVID-19 in Turkish children.

2 | MATERIALS AND METHODS

This study included 105 patients aged 0–18 years, who were diagnosed with COVID-19 at Dicle University Faculty of Medicine, Department of Pediatrics between April 2020 and June 2020. This department is the main tertiary center for the management of pediatric COVID-19 patients in the southeastern region of Turkey. The diagnosis of COVID-19 was made by real-time reverse transcription-polymerase chain reaction (RT-PCR) studied from upper respiratory tract samples obtained via nasopharyngeal swabbing. Individuals who have had close contact with a person who has a confirmed or probable COVID-19 infection without taking protective measures against droplet infection are tested in our hospital. In the first 3 months of the pandemic, very strict rules were implemented in our country. All adult and pediatric patients who were diagnosed with COVID-19 were hospitalized, and after being followed up for the first few days, discharged home. Afterward, they were instructed to stay at home for 14 days and stay away from public areas.

During the diagnostic procedures, BUN, creatinine, alanine aminotransferase (ALT), aspartate aminotransferase (AST), serum electrolytes, coagulation parameters, C-reactive protein (CRP), procalcitonin, troponin I, CK-MB, and D-Dimer were studied in all patients. A posterior-anterior (PA) chest radiogram was taken in every pediatric patient included in the study to determine whether the disease had lung involvement. Chest computed tomography (CT) was performed in cases of pathological findings on the radiogram or in clinically severe and critical cases.

All data presented in the study related to biological tests and X-Ray were obtained on the first day of hospital admission. The patients' demographic data, laboratory data, clinical data, and data on previous treatment approaches were accessed retrospectively from the patients' written medical records and computer-based medical records.

The severity of the disease was classified as asymptomatic, mild, moderate, severe, and critical according to the clinical characteristics, laboratory results, and chest radiography findings.[23]

- Asymptomatic: Cases with a positive RT-PCR test without any clinical or radiological findings.
- Mild: Cases with symptoms of upper respiratory tract infection, such as fever, fatigue, myalgia, cough, sore throat, nasal discharge, but a normal respiratory system examination.
- Moderate: Cases with pneumonia with fever and cough but without dyspnea and hypoxemia, or cases with COVID-19 findings on chest CT scan without symptoms.
- Severe: Cases with fever and cough in the early period who develop dyspnea and central cyanosis within a week (arterial oxygen saturation <92%).
- Critical: Cases who rapidly develop acute respiratory distress or respiratory failure, and who tend to develop shock, encephalopathy, myocardial involvement, coagulation defects, and acute kidney injury.

The patients were divided into three age groups across which the study data were compared. These groups were as follows: Group 1, patients aged 0–1 year (0–12 months); Group 2, patients aged 1–10 years (13–120 months); Group 3, patients aged 10 to 18 years (130–216 months).

Patients older than 18 years of age, those who had suspected COVID-19 infection based on clinical, laboratory, and radiological findings but a negative RT-PCR test result were excluded from the study.

All patients and their legal guardians were informed in detail about the study protocol and provided written informed consent. The approval was taken from the Republic of Turkey Ministry of Health and Dicle University Faculty of Medicine local the Ethics Committee.

2.1 | Statistical analysis

Data analyses were performed by using Statistical Package for Social Sciences (SPSS), Version 20.0 for Windows (SPSS Inc.). The variables were investigated using visual (histograms, probability plots) and

analytical methods (Kolmogorov–Smirnov test) whether or not they were normally distributed. Normally distributed variables were shown by means and standard deviations, and non-normally distributed variables were shown by median and range (maximum and minimum). The $\chi 2$ test was used to analyze categorical variables. Correlations between various parameters were studied using Pearson or Spearman correlations. Multiple groups were compared using a one-way analysis of variance (ANOVA) with a posthoc Bonferroni correction and Kruskal–Wallis test for the normally and non-normally distributed variables, respectively. The independent predictors of length of hospital stay were investigated by using stepwise multiple linear regression analysis. p values < .05 were considered statistically significant.

3 | RESULTS

The mean age of the patients was 108.64 ± 65.61 months (1.5 months–18 years). Of the patients, 51.4% (54/105) were male. There were 13 patients in Group 1, 46 patients in Group 2, and 46 patients in Group 3. The most common route of COVID-19 transmission in pediatric patients was a contact with a family member with COVID-19 (n = 91, 86.7%).

Four (3.8%) patients had an accompanying disease at the time of diagnosis. A 17-year-old patient had more than one comorbidity (Diabetes Mellitus + Beta thalassemia major + chronic respiratory disease). A 5.5-month-old patient was followed-up for primary hemophagocytic lymphohistiocytosis before the diagnosis. A patient had Down syndrome and acute lymphoblastic leukemia, and another patient had epilepsy and was on antiepileptic drugs.

The most common admission complaints were dry cough (n = 17, 16.2%), fever (n = 16, 15.2%), lassitude and fatigue (n = 14, 13.3%), and headache (n = 12, 11.4%). The admission complaints of the patients were summarized in Table 1.

Chest CT was performed in 48 patients. Pulmonary ground-glass opacities (n = 11, 10.4%) were the most common chest CT finding. Other common findings were local patchy shadows (n = 5, 4.7%) and bilateral patchy shadows (n = 4, 3.8%), respectively (Figure 1). Pleural effusion was also seen in one of our patients.

A significant number of patients were asymptomatic (n = 59, 56.2%). However, three patients required intensive care. The classification based on clinical severity was summarized in Table 1. The mean length of hospital stay was 4 (range 1–19) days for the patients who required hospitalization. No mortality was observed in any of our patients.

Antibiotics and antiviral agents were used to treat the patients. The most commonly used drugs were the combinations of azithromycin (n = 72, 68.6%), hydroxychloroquine (n = 21, 20%), antibiotics (n = 10, 9.5%), oseltamivir (n = 8, 7.6%), and lopinavir-ritonavir (n = 4, 3.8%). Only three patients required oxygen supplementation. High flow oxygen was administered to a patient who required intensive care.

TABLE 1 Demographic and clinical characteristics of the patients (n:105)

Meanage ± SD (month)	**108.64 ± 65.61**
Median (month)	**108 (1.5–216)**
Age group	*N* (%)
≤1 years	13 (12.4)
1–10 years	46 (43.8)
>10 years	46 (43.8)
Gender (male/female)	54/51
Symptoms	
Dry coughs	17 (16.2)
Fever (above 38°C)	16 (15.2)
Lassitude and fatigue	14 (13.3)
Headache	12 (11.4)
Sore throat	8 (7.6)
Diarrhea	5 (4.8)
Anosmia	4 (3.8)
Vomiting	3 (2.9)
Dyspnea or tachypnea	3 (2.9)
Loss of taste	2 (1.9)
Severity of illness	
Asymptomatic	59 (56.2)
Mild	32 (30.5)
Moderate	11 (10.5)
Severe	3 (2.9)
Critical	0 (0)
Length of hospital stay (in days)	4.0(1–19)
Treatment regimen	
Azithromycin	42 (40)
Hydroxychloroquin	21 (20)
Empirical antibiotic therapy	10 (9.5)
Oseltamivir	8 (7.6)
Lopinavir-Ritonavir	4 (3.8)
Favipiravir	1 (0.9)
Mortality	0 (0)

The clinical and laboratory findings of the patients were summarized in Table 2.

A comparison between Groups 1, 2, and 3 revealed that the rate of contact history was significantly lower in Group 1 than the other two groups (p < .001). The ratio of male gender was significantly higher in Group 2 (p = .032) than the other two groups. Sore throat and cough were significantly more frequent in Group 3 than the other two groups (p = .004, p = .008, respectively; Table 3).

The distribution of the clinical parameters according to disease severity was shown in Table 4. A comparison of clinical symptoms by gender revealed no statistically significant difference. A comparison of the laboratory parameters by gender revealed that the procalcitonin level was significantly higher in girls (0.227 ± 0.943) compared to boys (0.014 ± 0.05; p = .031).

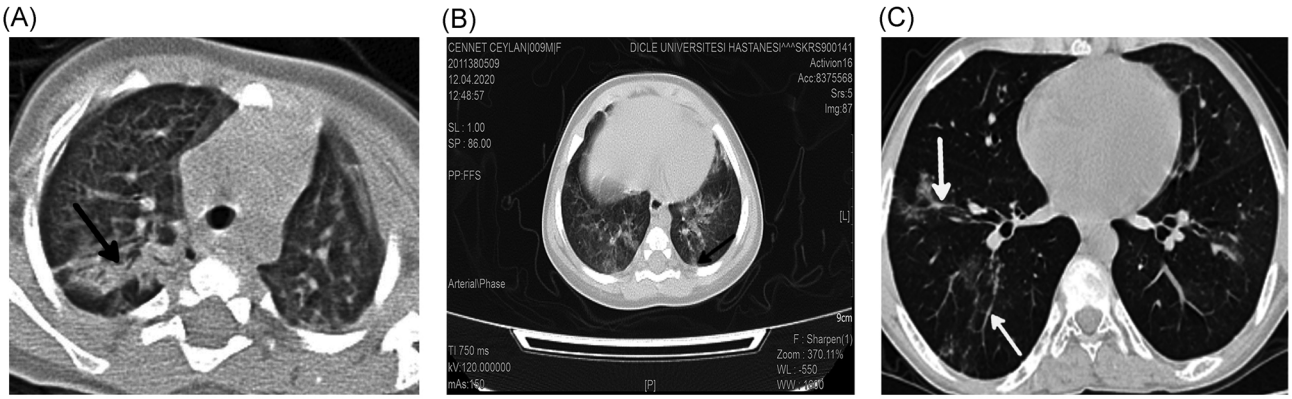

FIGURE 1 (A) Bilateral ground glass and consolidation areas (black arrow) in a 7- month old girl with fever and cough,; (B) The CT image of a 9- month old girl with a history of fever, cough and close contact with a family member, revealing peripheral ground-glass areas (black arrow) in both lungs; (C) Computed tomography (CT) of a A 17-year-old girl with dyspnea and cough revealing ground glass and peribronchial consolidation areas (White arrow)

The WBC and D-dimer levels, lymphocyte, and platelet counts were significantly higher in Group 2 compared to the other two groups (p = 007, p = .05, p < .001, p < .001, respectively). The creatinine levels were lower in Group 1 than the other two groups (p < .001). Creatinine values are known to vary by muscle mass, so this finding was considered uninterpretable. The blood urea levels were lower in Group 1 than Group 3 (p = .048). The laboratory parameters that have shown significant differences across the study groups are summarized in Table 5.

The length of hospital stay was higher in patients who used chloroquine + Azithromycin + Oseltamivir and chloroquine + Azithromycin + oseltamivir + Lopinavir-Ritonavir compared to those who did not receive any specific treatment (p = .012, p < .001, respectively). There were significant positive correlations between length of hospitalization and urea, CK-MB, CRP, ferritin, fibrinogen, body temperature, heart rate; length of hospitalization showed negative correlations with oxygen saturation, hemoglobin level (p < .005). We performed a multiple linear regression analysis with the "enter" method to define the independent predictors of the length of hospital stay. Gender, CRP, ferritin levels, fibrinogen, and oxygen saturation were included in the analysis. CRP was the only independent factor associated with a longer duration of hospitalization (p < .001, Table 6).

4 | DISCUSSION

Although many case series have been reported about COVID-19 in children, the epidemiological and clinical patterns of COVID-19 in pediatric patients remain largely unclear despite its rapid spread worldwide. This report aimed to evaluate the epidemiological characteristics, clinical findings, and treatment outcomes of COVID-19 in pediatric patients in the southeastern region of Turkey.

Children can carry the heaviest burden of viral respiratory diseases. However, corona- virus-related infections also vary widely in severity among children. Studies from China and America have suggested that children with COVID-19 might be less sick than adults and that pediatric cases might not describe various symptoms clearly as adults do.[11,12] Nevertheless, disease characteristics have not been described yet for pediatric patients from Turkey. This study aimed to determine the epidemiological characteristics of pediatric COVID-19 patients from Turkey during the first 3 months (April–June 2020) of the disease.

Our study included pediatric cases confirmed with a positive RT-PCR test. The male/female ratio in COVID-19 varies between studies. In earlier reports from China and the United States of America, boys outnumbered girls.[11,12,16,16,24] An American report provided data on signs and symptoms of COVID-19 in 291 of 2,572 pediatric cases aged <18 years. A retrospective analysis of 115 children from China reported a male/female ratio of 1/0.58. The present study showed a male (51.4%) predominance, similar to what has been described in the Chinese and American populations.[25–27] In earlier studies, patients' age ranged between 1 day and 18 years.[11,12,25] In our study, the mean age of the patients was 108.64 ± 65.61 months, and the age range of them was 45 days–18 years. These results suggest that children of all ages are suspectible to COVID-19.

In a Chinese study, the most common symptoms in children with COVID-19 were fever and dry cough (36%, 19%, respectively).[25] Another previous large-scale study also reported that fever and cough are more frequently observed in pediatric COVID-19 cases (56%, 54%, respectively). In our study, the most common symptoms on admission were cough (16.2%), fever (15.2%), lassitude, and fatigue (13.3%). In an American study, the frequency of sore throat, headache, and diarrhea have been found to be quite lower in pediatric patients.[12] The present study recorded various symptoms including sore throat, headache, diarrhea, loss of taste, anosmia, and vomiting (8%, 20%, 4%, 2%, 3%, and 6%, respectively). These findings are in line with other studies from other countries and suggest that children do not always have signs and symptoms such as fever and cough.

Comorbidities were present in 3.8% of our patients and included diabetes mellitus, beta-thalassemia major, chronic respiratory disease, Down syndrome, acute lymphoblastic leukemia, and epilepsy.[28]

TABLE 2 Clinical and laboratory findings

Body temperature, °C	36.91 ± 0.6 (36.3–38.7)
Respiratory rate	25.36 ± 6.59 (22–44)
Heart rate	99.64 ± 19.29 (76–160)
Oxygen saturation	95.64 ± 2.34 (88–99)
WBC (10^3/ul)	7.45 ± 2.02
Neutrophil count (10^3/ul)	3.36 ± 1.18
Lymphocyte count (10^3/ul)	3.25 ± 0.64
Platelet count (10^3/ul)	310.46 ± 103.30
Hemoglobin (g/dl)	13.07 ± 2.05
MPV (fl)	8.14 ± 1.32
RDW	11.89 ± 2.17
CRP (mg/dl), ref.: (0.0–0.5)	0.09 (0.02–16)
Procalcitonin (ng/mL), ref.: (0.0–0.12)	0.001 (0.00–4.8)
ALT (U/L)	16.18 ± 4.26
AST (U/L)	30.60 ± 10.27
Sodium (mmol/L)	136.31 ± 2.70
Potassium (mmol/L)	4.30 ± 0.48
Glucose (mg/dl)	101.05 ± 19.74
Urea (mg/dl)	21.36 ± 5.82
Creatinine (mg/dl)	0.38 ± 0.18
LDH (U/L)	263.95 ± 90.29
CK (U/L)	114.65 ± 38.12
CK-MB (ng/ml), ref.: (0.6–6.3)	2.05 (0.36–15.6)
Troponin (ng/L), ref.: (0–11.6)	1.2 (0.10–76.30)
Ferritin levels (ng/ml), ref.: (10–291)	35.55 (3.10–795)
Fibrinogen (mg/dl)	229.40 ± 62.63
APTT, s	27.16 ± 6.45
PT, s	12.91 ± 2.10
INR, s	1.10 ± 0.10
D-DİMER (mg/dL), ref.: (0.08–0.583)	0.30 (0.08–55.10)

Note: Data presented as mean ± standard deviation or median value (the minimum and maximum values are presented in brackets).

Abbreviations: ALT, alanine aminotransferase; APTT, activated partial thromboplastin time; AST, aspartate aminotransferase; CK, creatine kinase; CRP, C-reactive protein; INR, international normalized ratio; LDH, lactate dehydrogenase; MPV, mean platelet volume; PT, prothrombin time; RDW, red blood cell distribution width; Ref: references; WBC: White blood cell.

TABLE 3 Distribution of clinical parameters by age groups

Parameters	Group 1 (*n* = 13)	Group 2 (*n* = 46)	Group 3 (*n* = 46)	*p*
Family members with COVID-19	7 (53.8%)	45 (97.8%)	39 (84.8%)	<.001
Gender (M/F)	8/5	29/17	17/29	.032
Fever	4 (30.8%)	3 (6.5%)	9 (19.6%)	.055
Dry coughs	2 (15.4%)	2 (4.3%)	13 (28.3%)	.008
Loss of taste	0 (0)	0 (0)	2 (4.3%)	.270
Headeche	0 (0)	6 (13%)	6 (13%)	.384
Diarrhea	0 (0)	1 (2.2)	4 (8.7%)	.235
Sore throat	0 (0)	0(0)	8 (7.6%)	.004
Anosmia	0 (0)	1 (2.2%)	3 (6.5%)	.412
Lassitude and fatigue	0 (0)	6 (13%)	8 (17.4%)	.265
Vomiting	0 (0)	1 (2.2%)	2 (4.3%)	.661

However a study from the USA reported that the most common underlying conditions were chronic lung disease, cardiovascular disease, and immunosuppression.

In a previous report on 2135 pediatric patients with COVID-19, the disease followed asymptomatic, mild, moderate, severe, and critical courses. Regarding severity, 4.4%, 51.0%, and 38.7% cases were diagnosed as asymptomatic, mild, and moderate, respectively (total 94.1% of all cases).[11] In another study, it was found that children with COVID-19 had milder clinical manifestations, with nearly half of pediatric patients have been asymptomatic.[25] In our study, 56.2% of the cases were asymptomatic; 30.5% were mild; 10.5% were moderate, and 2.9% were severe; none of our patients was in a critical condition. The percentage of patients requiring ICU admission was 2.9%.

Laboratory findings in pediatric COVID-19 patients are generally similar to those in other coronavirus infections. The number of white cells is often normal or low; neutropenia and /or lymphopenia may accompany COVID-19. Thrombocytopenia may also develop. C reactive protein and procalcitonin levels are normal. In severe cases, liver enzymes and lactate dehydrogenase may increase, and abnormal coagulation and high D-dimer levels have been reported in some cases.[29] In our study, we found abnormal biological markers including elevated lactate dehydrogenase and elevated D-dimer levels in three cases with severe disease. A 6-month-old male patient infected with COVID-19 had high ferritin, D-Dimer, LDH levels, and abnormal coagulation. A 17-year-old girl infected with COVID-19 who had insulin-dependent type one diabetes (HbA1C: 8.6), history of bone marrow transplant due to beta-thalassemia major, and bronchiolitis obliterans had high ferritin, D-Dimer, LDH, C-reactive protein, and procalcitonin values.

Thoracic tomography findings in children are bilateral, multiple, and patchy nodular ground-glass opacities and /or infiltrations in the middle and peripheral zones of the lung or at the subpleural area. In the present study, pulmonary ground-glass opacities (*n* = 11, 10.4%) were the most common finding in chest tomography. Other common findings included local patchy shadows (*n* = 5, 4.7%) and bilateral patchy shadows (*n* = 4, 3.8%). In one of our patients, pleural effusion was seen. These results are consistent with other reports.[16,24,30]

TABLE 4 Distribution of clinical parameters according to disease severity

Parameters	Asymptomatic	Mild	Moderate	Severe	p
Family members with COVID-19	57 (96.6%)	27 (84.4%)	7 (63.6%)	0	<.001
Fever	2 (3.4%)	9 (28.1%)	2 (18.2%)	3 (100%)	<.001
Dry coughs	5 (8.5%)	7 (21.9%)	3 (27.3%)	2(66.7%)	.019
Loss of taste	1 (1.7%)	1 (3.1%)	0	0	.910
Headeche	1 (1.7%)	10 (31.3%)	1 (9.1%)	0	<.001
Diarrhea	2 (3.4%)	2 (6.3%)	0	1(33.3%)	.096
Sore throat	1 (1.7%)	5 (15.6%)	2 (18.2%)	0	.049
Anosmia	1 (1.7%)	3 (9.4%)	0	0	.264
Lassitude and fatigue	3 (5.1%)	10 (31.3%)	1 (9.1%)	0	<.001
Vomiting	1 (1.7%)	1 (3.1%)	0	1 (33.3%)	.014
Tachypnea	0	0	0	3(100%)	<.001
Length of hospita lstay (in days; ±mean age)	2.67 ± 0.63	4.59±1.42[a]	5.45±0.80[a]	16.5±3.53[a,b,c]	<.001

[a]Compared to asymptomatic $p < .001$.
[b]Compared to mild $p < .001$.
[c]Compared to moderate $p < .001$.

The radiological findings are nonspecific and milder than adults.[22,24,30,31] In a French study by Gaboriau et al., there were a total of 192 children with confirmed ($n = 157$) or highly suspected ($n = 35$) SARS-CoV-2 infection. Eighty-five (44.3%) children had a normal chest X-ray. CT was performed in 36 children and showed abnormalities in 26 (72.2%), including consolidations and/or ground-glass opacities.[32]

To date, there are no published controlled clinical trials on specific drug therapies for pediatric COVID-19 infection. As with other age groups, there is insufficient evidence for any drug that can be used in the treatment of COVID-19 in children. Therefore, suggested treatments for COVID-19 in children should be evaluated in accordance with the studies on adults. World Health Organization and the American Center for Disease Control and Prevention do not recommend specific drug treatment of children with COVID-19.[33,34] The management of pediatric patients with COVID-19 is also evaluated by the Scientific Board of Ministry of Health of Turkey at frequent intervals and revisions are made in Turkey.[35,36] Treatment strategies in this study were applied in accordance with the recommendations of

TABLE 5 Comparison of laboratory findings by age groups

Parameters	0–1 years (n = 11)	1–10 years (n = 17)	> 10 years (n = 22)	p
Oxygen saturation	94 (88–98)	96 (94–98)	96 (89–100)	156
WBC (K/ul)	10.65 (5.53–19.82)	6.76 (2.63–10.12)[a]	6.32 (3.74–9.36)[a]	.007
Lymphocyte count (10^3/ul)	6.29 (2.2–15.08)	2.31 (1.33–4.61)[a]	2.06 (1.12–3.37)[a]	<.001
Platelet count (10^3/ul)	492 (302–638)	284 (175.6–391.6)[a]	258.7 (124.6–320.5)[a]	<.001
CRP (mg/dl)	0,12 (0.04–16)	0.07 (0.02–0.43)	0.009 (0.02–13.46)	.141
Urea (mg/dl)	15 (6.40–59)	19.40 (13.8–37.80)	22.25 (14–31.30)[a]	.048
Creatinine (mg/dl)	0.16 (0.06–0.45)	0.34 (0.22–0.47)[a]	0.52 (0.22–0.93)[a,b]	<.001
D-Dimer (mg/dl)	0.85 (0.16–55.10)	0.27 (0.17–1.38)[a]	0.27 (0.08–1.05)[a]	.005
ALT (U/L)	15.30 (6–30)	14.25 (5.90–63.70)	12.20 (4.60–34)[b]	.028
AST (U/L)	36.40 (21–60.30)	32.35 (17.30–47.60)	23.20 (15.90–37)[a,b]	<.001
Length of hospital stay (in days)	7.5 (4.14)	5 (3–7)	5 (3–19)	.154

[a]$p < .017$ comparison with patient aged between 0–1 years old.
[b]$p < .017$ comparison with patient aged between 1–10 year old.

TABLE 6 Stepwise multiple linear regression analysis for the independent variables of duration of length of hospital stay

Independent variables	Beta coefficient	95% CI	Standardized beta coefficient	*p*
Gender (0 = female, 1 = male)	−0.347	−1.48 to 0.78	−0.055	.535
CRP	0.942	0.474–1.411	0.853	<.001
Ferritin levels	−0.004	−0.010 to −0.001	−0.186	.102
Fibrinogen	−0.003	0.014–0.007	−0.093	.539
Oxygen saturation (SPO_2)	−0.328	−0.725 to 0.069	−0.253	.101

Note: Confidence interval Model: $p < .001$; $R^2 = 0.806$

Abbreviations: CI, confidence interval; CRP, C-reactive protein.

the guidelines issued by the Republic of Turkey Ministry of Health. Probable adverse effects of drugs must be taken into consideration while making decisions for the treatment of pediatric patients. Treatment should be specifically assessed for each pediatric patient, with medication(s) being reserved for patients with probable severe pneumonia as well as for mild cases with risk factors. Drugs used in the treatment of our patients included azithromycin ($n = 42$, 40%), hydroxychloroquine ($n = 21$, 20%), empirical antibiotics ($n = 10$, 9.5%), oseltamivir ($n = 8$, 7.6%), lopinavir-ritonavir ($n = 4$, 3.8%), and Favipiravir ($n = 1$, 0.9%). Only three patients needed supplemental oxygen therapy. High-flow humidified oxygen was administered to a patient who was followed up at the intensive care unit. Long-term studies are needed to find an effective treatment for children.

There were some limitations to our study. First, this study was hospital-based, second, the data may be incomplete and/or erroneous due to the retrospective study design.

5 | CONCLUSION

To our knowledge, this study is the largest cohort of pediatric patients with COVID-19 reported from Turkey. A clear understanding of the local epidemiology of coronavirus infections and identification of risk factors is critical for the successful implementation of a prevention and control program. Longer term prospective studies are needed to provide a clear understanding of the local epidemiology of respiratory tract infections, to identify risk factors, to successfully implement a prevention and control program, and to clarify the role of respiratory pathogens.

CONFLICT OF INTERESTS

The authors report that there are no conflict of interests. The authors alone are responsible for the content and writing of the paper.

ORCID

Kamil Yılmaz https://orcid.org/0000-0001-5137-0501

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