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Original Research

Pediatric Patients with COVID-19: A Retrospective Single-Center Experience

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Abstract

Objectives: The pandemic of coronavirus disease 2019 (COVID-19) is still effective all over the world. Compared to adults, data on pediatric patients are limited. In this study, we aimed to retrospectively examine the demographic, clinical, and laboratory characteristics of pediatric patients who were followed up with the diagnosis of COVID-19 in the first 3 months of the pandemic in our hospital.

Methods: A total of 190 patients, aged 1 month–18 years, who were followed up with a definite/probable diagnosis of COVID-19, who were treated in the Pediatric Infection Clinic, were included in the study. The demographic features, clinical characteristics, and laboratory findings of the patients were retrospectively analyzed from their electronic medical records.

Results: Eighty (42.1%) of the patients were laboratory confirmed (Polymerase chain reaction positive in nasopharyngeal swab). Mean age was 72 (2–216 months) and 102 (53.7%) patients were female. Family contact history was present in 115 (60.5%) patients. The patients were classified as asymptomatic (5.8%), mild (73.2%), moderate (18.4%), and severe/critical (2.6%) according to the severity of the disease. The most common symptoms were cough (71.1%) and fever (51.1%). Hydroxychloroquine alone or in combination was the most commonly used agent.

Conclusion: In our study, in which we examined the pediatric COVID-19 patients, most of the patients had a mild clinical course, but there were applications with different clinical pictures such as acute appendicitis. Therefore, COVID-19 infection, which is still very unknown, will continue to surprise us with both changing treatment protocols and clinical presentations such as multisystem inflammatory syndrome in children.

Keywords: Children, COVID-19, hydroxychloroquine, multisystem inflammatory syndrome in children, Turkey

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A new member of the enveloped RNA coronavirus was identified in a group of patients with pneumonia of unknown cause in December 2019 in Wuhan, China. It was confirmed that the first patients were connected with the

seafood market in Wuhan and that the virus is transmitted from person to person. On January 7, 2020, the World Health Organization (WHO) defined this virus, spreading rapidly globally, as "severe acute respiratory syndrome

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coronavirus 2" (SARS-CoV-2). The disease caused by this virus was named 2019 coronavirus disease (COVID-19).^[1] The WHO declared COVID-19 as a pandemic on March 11, 2020, and the first adult case from our country was reported on the same date. The first child case was reported from China on January 20, 2020.^[2]

As of February 22, 2021, SARS-CoV-2 has affected more than 200 countries globally, causing the infection of up to 111 million people (confirmed cases) and the death of approximately 2.5 million people. In our country, 2,665,194 confirmed cases and 28,285 deaths were reported.^[3]

In COVID-19 infection, respiratory droplets and close contact are the main modes of transmission of infection, aerosol transmission may occur when exposed to high aerosol concentrations for a long time in a closed environment.^[4] The incubation period is on average 5–7 days (2–14 days). Contagiousness begins 1–3 days before symptoms appear, and contagion continues throughout the disease.^[5]

Children of all ages appear susceptible to SARS-CoV-2 infection. Studies show that clinical findings in pediatric patients are generally less severe than adults, and transmission is generally through family contact.^[6] The possibility of a severe course of the disease is higher in children with underlying diseases (congenital heart disease, chronic lung disease, immune deficiency, metabolic disease, etc.).^[4] Fever, dry cough, and fatigue are the main symptoms, gastrointestinal symptoms such as vomiting and diarrhea can also be seen, and anosmia seen in 3% of patients with COVID-19 is also among the symptoms.^[7]

In April, cases resembling incomplete Kawasaki disease (KD) or toxic shock syndrome associated with COVID-19 disease began to be reported from the UK for the first time in pediatric patients, after which similar cases continued to be reported from various countries. In mid-May, this new form of application for COVID-19 was named multisystem inflammatory syndrome in children (MIS-C), possibly associated with COVID-19.^[8]

In treatment, there are no well-proven antiviral treatment options, but there are a couple of randomized controlled trials investigating agents such as hydroxychloroquine, lopinavir-ritonavir, favipiravir, and remdesivir. Other studies focus on immunomodulatory therapies, including tocilizumab and anakinra.^[9]

In this study, we aimed to examine the demographic characteristics, clinical features, laboratory findings, follow-up and results of treatment of pediatric patients diagnosed with COVID-19 in the first 3 months of the pandemic in our country.

Methods

The electronic medical records of the patients who were followed up with a definite/probable diagnosis of COVID-19 who received outpatient/inpatient treatment in the Pediatric Clinic between March 17, 2020, and June 20, 2020, were retrospectively reviewed. 190 patients diagnosed with COVID-19 were included in the study. The study was approved by the Sisli Hamidiye Etfal Training and Research Hospital Ethics Committee (Ethics Committee No: 2743).

COVID-19 diagnosis, treatment, and management of patients was made according to the Turkish Republic Ministry of Health COVID-19 Child patient management guide (Coronavirus Scientific Advisory Board in Turkey) and the criteria were updated according to the changes made over time by the scientific committee.^[10] Children between 1 month and 18 years old were included in the study. The patients whose clinical and exposure history was compatible with COVID-19 according to the criteria set by the National Ministry of Health Coronavirus advisory board were considered as suspected COVID-19 patients. In the nasopharyngeal swab samples of these patients, those with positive COVID-19 reverse transcription polymerase chain reaction (RT-PCR) test and/or suspicious cases with serum-specific antibodies against 2019-nCoV were defined as confirmed/definite cases. Both suspected and confirmed cases were included in the study.

The demographic characteristics, clinical features, signs and symptoms, contact history, presence of chronic diseases of the patients were questioned. Laboratory results, chest radiographs, and thorax computed tomography (CT) examinations were recorded. Treatment practices, supportive treatments, and intensive care needs were obtained from the records.

The severity of the disease was classified as follows according to clinical features, laboratory examination and radiological imaging results defined by Dong et al.^[6] (a) asymptomatic infection: test positivity only without any clinical or imaging findings; (b) mild infection: Symptoms of acute upper respiratory tract infection such as mild fever, fatigue, myalgia, cough, sore throat, running nose and sneezing, and normal lung auscultation findings; (c) moderate infection: Presence of pneumonia with respiratory symptoms such as fever, cough, wheezing, or subclinical lung lesions in thoracic tomography without clinical signs and symptoms (no respiratory distress and hypoxemia); (d) severe infection: Early respiratory symptoms such as fever and cough accompanied by gastrointestinal symptoms such as diarrhea, presence of respiratory distress, and central cyanosis; and (e) critical disease: Patients who progressed to acute respiratory distress syndrome or respiratory failure

and who developed shock, encephalopathy, myocardial damage, heart failure, coagulation disorder, acute renal failure, and organ dysfunction.^[6]

COVID-19 Antibody Test

The presence of immunoglobulin (IgM and IgG antibodies against SARS-CoV-2 was investigated with the lateral flow immunochromatographic based card test Weimi Diagnostic Kit (Weimi Bio-tech Co., Ltd., Guangzhou, China).

SARS-CoV-2 PCR Test

For the detection of COVID-19 agent SARS-CoV-2, one-step reverse transcription (RT) targeting RNA-dependent RNA polymerase gene fragment and bio-speedy COVID-19 RT-quantitative PCR (qPCR) detection kit version 2 (Bioeksan Ar-Ge Teknolojileri Ltd., Istanbul, Turkey) for real-time PCR (qPCR) were used.

Screening

In accordance with the guidelines set by the National Ministry of Health Coronavirus advisory board, chest radiography or thorax CT was performed according to the clinical findings of the patients.^[10] Lung CT reviews were performed with the number of lesions, distribution, ground glass opacity (GGO), consolidated GGO, reticulation from intralobular/interlobular septal thickening, consolidation, air bronchogram, cavitation, lymphadenopathy, and pleural effusion. While GGO was defined as a hazy increase in density in the lung by preserving vessel margins, consolidation was defined as opacification that conceals vessel margins.^[11]

Treatment was prescribed to the patients according to the recommendation of The Ministry of Health of Turkish Republic treatment protocol.

Statistical Analysis

The descriptive statistics were presented as frequency and percentages. According to result of Kolmogorov–Smirnov test, the possible association between variables was investigated using Kruskal–Wallis test and continuous variables are given as median and interquartile range. Chi-square test was used for categorical variables. $P < 0.05$ was considered statistically significant. All analyses were performed using the BM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corporation.

Results

A total of 190 (confirmed/probable) COVID-19 patients were included in the study. 80 (42.1%) of the patients were laboratory confirmed. Among all, the confirmation of COVID-19 diagnosis was performed in 69 (36.3%) by RT-PCR from nasopharyngeal swabs and 11 (5.8%) by serum-spe-

cific IgM and G antibodies used detection.

The median age was 72 months (2–216 months), among which 102 (53.7%) were female. There was no significant difference in the number of boys and girls. Asymptomatic and mild cases consisted of 11 (5.8%), 139 (73.2%) patients, respectively. Moderate and severe/critical cases consisted of 35 (18.4%) and 5 (2.6%) patients, respectively. 113 (59.5%) of the patients were followed up in the hospital and 72 (37.9%) were outpatients. The number of severe/critical patients was 5 (2.6%). A history of contact with domestic COVID-19 patients was present in 115 (60.5%) patients.

The median time to onset of symptoms was 48 (1–168) h. The most common complaint was cough (71.1%), followed by fever (51.1%). Other symptoms were respiratory distress (10%), sore throat (7.9%), weakness, fatigue-myalgia (6.3%), and gastrointestinal complaints (5.3%), respectively. Smell disorder developed in one patient. The demographic and clinical characteristics of the patients are summarized in Tables 1 and 2. The patient, who presented with respiratory distress and flank pain, was diagnosed with pneumothorax and had a positive RT-PCR test, was followed up and treated by inserting a chest tube.

One of our patients who presented with different clinical pictures other than the respiratory system presented with clinical findings of acute appendicitis. Appendectomy was performed in our patient because of imaging and clinical compatibility. The other was the patient who was followed up with a diagnosis of incomplete KD. Another patient was the patient who presented with respiratory distress and flank pain, was diagnosed with pneumothorax, had a positive RT-PCR test, and was followed-up and treated by inserting a chest tube.

Another patient, who was followed up with a diagnosis of epilepsy, presented with the complaints of cough and flank pain, and the PCR test was positive. On the 7th day of the patient's hospitalization, a diagnosis of acute deep vein thrombosis was made in Doppler ultrasonography performed due to pain in the left leg. Posteroanterior chest radiography findings of a total of 40 (21%) patients and thoracic tomography findings of 31 patients (16.3%) showed abnormalities.

In complete blood count, the most common parameter was eosinopenia (32.2%), the rate of lymphopenia was 19.5% and leukopenia was 9.5%. The rate of C-reactive protein was found to be elevated with the rate of 44.2%, procalcitonin with the rate of 30.8.7%, D-dimer with the rate of 41.1%, ferritin with the rate of 8.4%, troponin with the rate of 4.9%, brain natriuretic peptide with the rate of 42.6 %, and lactate dehydrogenase with the rate of 13% (Table 3).

Of the patients, 12.6% had a chronic disease and 10% had

Table 1. Demographics features of pediatric patients with COVID-19

Parameters	Total n=190	Asymptomatic n=11	Mild n=139	Moderate n=35	Critical/severe n=5	p
Age, months (median, min-max)	72 (2–216)	93 (14–216)	69 (2–305)	84 (4–237)	42 (7–165)	0.883
Age group, years, n (%)						
<1	21 (11.1)	0 (0)	14 (10.1)	6 (17.1)	1 (20.0)	0.494
1–5	63 (33.2)	3 (27.3)	49 (35.3)	9 (25.7)	2 (40.0)	
6–10	42 (22.1)	5 (45.5)	28 (20.1)	9 (25.7)	0 (0)	
11–15	34 (17.9)	2 (18.2)	26 (18.7)	4 (11.4)	2 (40.0)	
>15	28 (14.7)	1 (9.1)	21 (15.1)	6 (17.1)	0 (0)	
Sex, n (%)						
Male	88 (46.3)	5 (45.5)	60 (43.2)	20 (57.1)	3 (60.0)	0.460
Female	102 (53.7)	6 (54.5)	79 (56.8)	15 (42.9)	2 (40.0)	
Smoking at home, n (%)	93 (48.9)	5 (45.5)	66 (47.5)	19 (64.3)	3 (60.0)	0.197
BCG vaccination, n (%)	168 (88.4)	9 (81.8)	125 (89.9)	29 (82.9)	5 (100)	0.477
Family history/close contact, n (%)	115 (60.5)	10 (90.9)	87 (62.6)	14 (40.0)	4 (80.0)	0.009
Underlying disease, n (%)	24 (12.6)	2 (18.2)	10 (7.2)	7 (20)	2 (40.0)	0.079
Chronic drug use, n (%)	19 (10)	0 (0)	13 (6.7)	7 (20)	2 (40.0)	0.010
Length of stay (days), median (IQR)	7 (5–9.25)	4 (3–5)	6 (4–8)	8.5 (7–11)	12 (8–20.5)	<0.001
Ambulatory, n (%)	72 (37.9)	9 (81.8)	61 (43.9)	2 (5.7)	0 (0)	<0.001
Hospitalized n (%)	113 (59.5)	2 (18.2)	77 (55.4)	30 (85.7)	4 (80.0)	
PICU n (%)	5 (2.6)	0 (0)	1 (0.7)	3 (8.6)	1 (20.0)	

IQR: Interquartile range, BCG: Bacillus Calmette-Guerin, PICU: Pediatric intensive care unit.

Table 2. Clinical features of patients with COVID-19 (n=190)

Time of symptoms (hours), median (IQR ₂₄)	48 (24–72)
Symptoms, n (%)	
Fever	97 (51.1)
Cough	135 (71.1)
Sore throat	15 (7.9)
Gastrointestinal symptoms	10 (5.3)
Dyspnea	19 (10)
Fatigue/myalgia	12 (6.3)
No symptom	11 (5.8)
Severity of infections, n (%)	
Asymptomatic infection	11 (5.8)
Mild	139 (73.2)
Moderate	35 (18.4)
Severe/critical	5 (2.6)
Monitoring place, n (%)	
Outpatients	72 (37.9)
Hospitalized	113 (59.5)
PICU	5 (2.6)
Confirmed cases, n (%)	
PCR positive	69 (36.3)
Antibodies positive	11 (5.8)
RSV positive, n (%)	2 (1.1)
Influenza positive, n (%)	8 (4.2)
Length of hospital stay (days), median (min-max)	7 (2–28)
Outcome	
Recovered	118 (62.1)
Outpatients	72 (37.9)

PICU: Pediatric intensive care unit, IQR: Interquartile range, RSV: Respiratory syncytial virus, PCR: Polymerase chain reaction.

a drug that they used continuously. When the underlying diseases are examined, 10 patients had asthma and 5 patients had neurological problems. Other diseases included nephrological (n=3), oncological (n=2), metabolic (n=1), immunodeficiency (n=1), and heart disease (n=1). About 48.9% of the patients had indoor smoking exposure.

The treatment was arranged in accordance with the recommendations of the national coronavirus diagnosis and treatment guideline, taking into account the clinical and laboratory findings of the patients. The most used agent was hydroxychloroquine. Antibiotic treatment was administered to 74 (38.9%) patients due to the suspicion/confirmation of bacterial superinfection. Lopinavir/ritonavir was used in one patient (Table 4). Hydroxychloroquine treatment was administered to 47 (24.7%) patients and no side effects were observed except nausea which was seen in only 3 (6.4%) of these patients.

Discussion

Our study is a retrospective study involving the pediatric patient group in the first trimester of the COVID-19 epidemic in our country. In studies conducted so far, it has been shown that children are less affected by COVID-19 than adults. In a large case series from China, 2.1% of the cases were reported to be in the 0–19 age group.^[12] It has been reported that 1.7% of the cases reported in the Unit-

Table 3. Laboratory characteristics of children's with COVID-19

Parameters	Total, n=190	Asymptomatic, n=11	Mild, n=139	Moderate, n=35	Severe/critical n=5	p
CRP mg/dl, median (IQR)	3.30 (0.62–11.70)	0.6 (0.3–1.0)	2.5 (0.6–10.7)	10.7 (2.3–22.5)	6.0 (2.8–164.0)	0.026
D-dimer, median (IQR)	387 (231–789.75)	600 (197–890)	335 (214–700)	505 (336–1100)	1190 (595–2960)	0.005
Ferritin (µg/L), median (IQR)	27.95 (16.57–52.85)	22.8 (9.5–39.9)	25.9 (15.8–45.8)	41.0 (19.6–105.0)	209.6 (39.8–432.5)	0.007
Procalcitonin (ng/L) median (IQR)	0.30 (0.18–0.60)	0.27 (0.27–0.27)	0.30 (0.18–0.50)	0.34 (0.16–1.60)	0.31 (0.16–4.25)	0.767
Leukocytosis, n (%)	61 (32.1)	1 (9.1)	44 (31.7)	14 (40.0)	2 (40.0)	0.288
Leukopenia	17 (9.1)	2 (18.2)	10 (7.4)	3 (8.6)	2 (40.0)	0.060
Neutropenia	10 (5.3)	1 (9.1)	8 (5.9)	1 (2.9)	0 (0)	0.779
Lymphopenia	37 (19.5)	3 (27.3)	23 (16.5)	8 (22.9)	3 (60.0)	0.094
PNL/LYM, median (IQR)	1.78 (0.94–3.31)	1.93 (0.58–4.00)	1.58 (0.86–2.73)	2.60 (1.41–5.61)	2.85 (1.38–8.80)	0.004
Eosinopenia	63 (33.7)	2 (18.2)	43 (31.6)	14 (40.0)	4 (80.0)	0.076
Increased CRP	84 (44.2)	1 (9.1)	60 (43.2)	20 (57.1)	3 (60.0)	0.038
Increased LDH	21 (13.0)	0 (0)	10 (8.5)	9 (29.0)	2 (40.0)	0.004
Increased procalcitonin (0.5 ng/L)	28 (30.8)	0 (0)	18 (27.3)	8 (42.1)	2 (40.0)	0.538
Increased D-dimer	78 (41.1)	6 (54.5)	50 (36.0)	18 (51.4)	4 (80.0)	0.072
Increased troponin	3 (4.9)	0 (0)	2 (4.3)	1 (8.3)	0 (0)	0.895
Increased Ferritin	13 (8.4)	0 (0)	6 (5.4)	5 (17.2)	2 (50.0)	0.003
Increased BNP	81 (42.6)	5 (45.5)	61 (43.9)	12 (34.3)	3 (60.0)	0.628
Increased Sedimentation	44 (22.3)	2 (18.2)	30 (21.6)	11 (31.4)	1 (20.0)	0.455

IQR: Interquartile range; CRP, C-reactive protein; LDH, Lactate dehydrogenase; BNP, Brain natriuretic peptide.

Table 4. Treatment protocol of patients with COVID-19

Treatment	n (%)
Hydroxychloroquine+Azithromycin	25 (13.2)
Hydroxychloroquine+Azithromycin+Ampicillin/sulbactam	29 (15.3)
No antibiotics	116 (61.1)
Antibiotic treatments	19 (10)
Lopinavir/Ritonavir+Ampicillin/sulbactam	1 (0.5)

ed States between February 12 and April 2, 2020, were under the age of 18.^[13] It has been reported that the COVID-19 disease in children is mostly transmitted by family contact and there is a history of contact with family members up to 90%.^[14,15] In a study conducted in our country including the pediatric age group, it was shown that almost all patients had contact within the family.^[16] In our study, it was observed that more than half of the patients (60%) had contact within the family.

Many studies show that the course and severity of the disease in pediatric COVID-19 patients have a milder clinical picture compared to adults.^[17] However, pediatric cases from asymptomatic cases to severe pneumonia and death have also been reported. In the studies of Dong et al., in which 2143 pediatric patients were evaluated, it was reported that approximately half of the patients had an asymptomatic and mild course, 38.7% had a moderate, 5.8% followed a severe and critical course, and only one patient

died.^[6] In our case series, which included the first trimester of the epidemic in our hospital, 80% of the patients were asymptomatic/mild cases, five severe/critically ill patients were followed, and we did not have any patients who died. Two of the five patients followed in the Pediatric Intensive Care Unit received oxygen support with a reservoir mask, one patient received high-flow oxygen therapy, and two patients were followed on a mechanical ventilator. There was no patient who needed ECMO and underwent renal replacement therapy.

In a study evaluating 134 pediatric patients with COVID-19, the most common symptoms were identified as fever and cough, and fatigue, myalgia, runny nose, nasal congestion, sore throat, dizziness, nausea, vomiting, abdominal pain, and diarrhea have emerged as the other clinical findings.^[18] In a study comparing pediatric patients with adult patients, findings indicating the severity of the disease such as fever (36% vs. 86%), cough (19% vs. 62%), and pneumonia (53% vs. 95%) were reported to have a lower prevalence in children.^[14] In our case series, the most common findings were cough and fever.

In children, after COVID-19 disease, which is mostly asymptomatic and has a mild course, a systemic inflammatory response may occur and a symptom resembling a severe form of KD may occur, which is defined as MIS-C in the table. In the case of typically negative PCR and frequently positive antibody test after SARS-CoV-2 infections, a post-infectious

inflammatory process ongoing a few weeks is shown to be characterized by MIS-C.^[19] The first reports of MIS-C came from the United Kingdom in April 2020. In a case series of eight pediatric patients in the United Kingdom with COVID-19 and MIS-C, all individuals presented with dramatic gastrointestinal symptoms including abdominal pain, non-bloody diarrhea, and vomiting.^[20]

The retrospective evaluation of the two cases we followed up in the period when MIS-C was not defined yet were thought to be MIS-C. One of them presented with diarrhea, vomiting, abdominal pain and fever. The PCR test was negative, but the antibody test (IgM, IgG) was positive. Appendectomy was performed when an appendix of 7 mm and 2 cm of invagination in the ileocecal were seen on abdominal USG. Laboratory findings showed lymphopenia, thrombocytopenia, and high ferritin. The patient, who was not compatible with appendicitis in the pathology report, was discharged with full recovery and close follow-up.

Our second patient was a 4-year-old male patient who presented with fever, conjunctivitis and rash lasting more than 5 days. In the follow-up of the patient, who was evaluated as incomplete KD, intravenous immunoglobulin treatment was administered because no clinical response was obtained. The patient, who had no cardiac involvement in the follow-up, was discharged with full recovery.

One of our cases with a different clinical picture other than typical respiratory tract infection was the patient we followed due to pneumothorax. Pneumothorax has been rarely reported in patients with COVID-19. Chen et al. reported that a patient with COVID-19 pneumonia developed pneumothorax at the first presentation.^[21] However, there are also case series that developed pneumothorax at different stages of the disease (from day 2 to day 15).^[22] Our 14-year-old male patient, who presented with respiratory distress, was admitted with symptoms of spontaneous pneumothorax. Thoracic tomography of the patient, who had a thoracic tube, had subpleural GGO in the middle lobe of the right lung. PCR test was negative, COVID specific IgM and IgG antibody tests were positive. He was discharged after 15 days of follow-up and treatment for outpatient follow-up.

In patients with COVID-19, various changes are observed in hematological parameters as in many viral diseases. Eosinophils normally account for only a small percentage of circulating leukocytes (1–3%), but their levels can vary in various diseases and have a potent pro-inflammatory effect.^[23] Zhang et al. reported that more than half the patients admitted with COVID-19 (53%) had eosinopenia (defined as absolute eosinophil counts $<0.02 \times 10^9$ cells/L) on the day of hospital admission.^[24] Similarly, Du et al. reviewed

the medical records of 85 fatal cases of COVID-19 and noted that 81% of the patient had absolute eosinophil counts below the normal range at the time of admission.^[25] The pathophysiology of eosinopenia in COVID-19 has not been fully explained. In our case series, eosinopenia was the most common (32.2%) laboratory finding. Lymphopenia is a common parameter in full blood count in adult patients.^[26] It has been reported that lymphopenia is an early finding for severe and critically ill patients when it develops at an early stage in COVID-19 patients. In very young children, lymphopenia may not occur due to relatively immature immune systems and differences in immune responses compared to adults.^[27,28] Yang et al. reported that 80% of critically ill adult COVID-19 patients had lymphopenia.^[29] Chen et al. reported that only 25% of patients with mild COVID-19 had lymphopenia, suggesting that lymphopenia may be related to the severity of the infection.^[21] At the same time, it has been reported in the literature that blood eosinophil counts show a positive correlation with lymphocyte counts in both severe and non-severe cases.^[24]

In our patient group, lymphopenia was detected in 19.5% of patients. Although lymphopenia was seen more in the moderate and severe patient group, the difference was not statistically significant. Coagulation disorders are seen as a common complication in adult patients. D-dimer levels increased in 29.3% of adult patients and 12% of children. The mechanisms behind the coagulopathy associated with COVID-19 are not fully elucidated, but it is suspected that the cytokine storm activates a thromboinflammatory pathway that can lead to abnormalities in coagulation. Venous thromboembolism (VTE) is a common complication in hospitalized patients with COVID-19, who are generally elderly and immobile.^[30] It has been reported that in the period when VTE prophylaxis was not given, lower extremity deep vein thrombosis developed in 25% of adult intensive care patients diagnosed with Doppler ultrasound (USG).^[31] In a multi-center study in the USA, the rate of symptomatic VTE (imaging confirmation prompted by signs and symptoms or underlying clinical suspicion) was reported as 7% at 13–<21 years, and 1.3% at 5–<13 years.^[8] One of our patients, who was followed up with the diagnosis of epilepsy, was diagnosed with deep vein thrombosis, which was detected with Doppler USG, which started with leg pain on the seventh day of hospitalization.

There is currently no sufficient scientific evidence for the treatment of COVID-19 infection in children. Therefore, treatment recommendations are made according to adult studies and planned according to the clinical judgment of the child.^[32] The respiratory status, oxygen need, liquid, and electrolyte need of patients with the diagnosis of CO-

VID-19 are determined, and supportive treatment and, if necessary, initiating empirical antibiotherapy in terms of secondary bacterial infections constitute the basis of treatment. We planned our treatment in line with the guidelines suggested by the national scientific board.

Remdesivir is a drug that is found effective in the adult age group, but there is not enough data in the pediatric age group. Emergency use was approved by the FDA for children and adult patients in need of oxygen hospitalized for mechanical ventilation.^[33] Favipiravir is an antiviral approved for influenza in the Asian region with an in vitro antiviral effect. It has been shown to contribute to clinical improvement in adult studies conducted in different countries.^[34] Lopinavir/Ritonavir is the agent of choice for children aged 2 weeks–3 years in need of antiretroviral therapy.^[32] In one of our patient group, lopinavir/ritonavir was administered due to the age in line with the guideline recommendation.

Chloroquine/hydroxychloroquine is among the drugs that can be used in the treatment of both child and adult COVID-19 guidelines, which are constantly updated by the Turkish Public Health Institution. Its benefit has not been clearly demonstrated in the studies, the FDA withdrew on July 15, 2020, its emergency use indication recommendation published on March 28, 2020. Many studies planned to date have been terminated due to their potential side effects. Its use in COVID-19 disease is limited to clinical studies only. The most common side effects are vomiting and diarrhea. Retinopathy and cardiomyopathy have been reported in long-term use.^[35,36] In a study examining pediatric patients admitted to the intensive care unit in North America, hydroxychloroquine alone or combined with drugs such as azithromycin, remdesivir, and tocilizumab was reported as the most commonly used agent.^[37] Chloroquine was used in 47 of our patients in line with the recommendations of the national scientific board, and three patients complained of nausea. No other side effects were encountered during the treatment period.

As a result, children of all ages appear susceptible to SARS-CoV-2 infection. COVID-19 disease often has a mild clinical course in the pediatric age group. Although respiratory system involvement is the main clinical finding of the disease, it may also present with different clinical pictures.

Disclosures

Ethics Committee Approval: The study was approved by the Sisli Hamidiye Etfal Training and Research Hospital Ethics Committee (Ethics Committee No: 2743).

Peer-review: Externally peer-reviewed.

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