Original Article

Comparison of Clinical and Laboratory Features and Treatment Options of 237 Symptomatic and Asymptomatic Children Infected with SARS-CoV-2 in the Early Phase of the COVID-19 Pandemic in Turkey

Ahmet Soysal[1]*, Erdem Gönüllü[1], Hüseyin Arslan[2], Büşra Sultan Kibar[3], Serdar Pop[4], Gözde Nur Yurttaş[5], Hacer Demirbacak[3], Füsun Ünal[2], Sedat Öktem[2], Serkan Atıcı[6], Arife Derda Yücel Şen[3], Nalan Karabayır[2], Metin Karaböcüoğlu[1], and PEDCOVID19 study group**

[1]*Memorial Ataşehir Hospital, Division of Pediatric Infectious Diseases, İstanbul;*
[2]*Medipol University, Department of Pediatrics, İstanbul;* [3]*Yalova State Hospital, Yalova;*
[4]*Erbaa State Hospital, Tokat;* [5]*Tokat State Hospital, Tokat; and*
[6]*Okan University Hospital, Division of Pediatric Infectious Diseases, İstanbul, Turkey*

SUMMARY: Little is known about the therapeutic use of hydroxychloroquine in pediatric patients with coronavirus disease 2019 (COVID-19). Here, we retrospectively retrieved data of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) PCR-positive pediatric patients from 20 hospitals in 8 Turkish cities. We obtained epidemiological, clinical, and laboratory features of the patients, as well as the drugs used for treating COVID-19. A total of 237 nasopharyngeal swab SARS-CoV-2 PCR-positive children were included in the study from March 26, 2020 to June 20, 2020. The mean age of asymptomatic children (118 ± 62 months) was higher than that of symptomatic children (89 ± 69 months). Symptomatic children had significantly lower mean lymphocyte counts and higher mean CRP, D-dimer, procalcitonin, and LDH levels than asymptomatic children in the univariate analysis. Among 156 children, 78 (50%), 15, 44, and 21 were treated with a hydroxychloroquine-containing regimen, hydroxychloroquine + azithromycin + oseltamivir, hydroxychloroquine + azithromycin, and hydroxychloroquine alone, respectively. Among 156 patients who received medical treatment, 90 (58%) underwent pre- and/or post-treatment electrocardiogram (ECG). However, none of them had ECG abnormalities or required hydroxychloroquine discontinuation due to adverse drug reactions.

INTRODUCTION

Following an outbreak of pneumonia of unknown cause in Wuhan, Hubei, China in December 2019 (1), sequencing analysis of lower respiratory tract samples identified a virus named 2019 novel coronavirus (2019-nCoV). The disease was later named coronavirus disease 2019 (COVID-19) by the World Health Organization (WHO) (2), and the virus responsible for COVID-19 was subsequently renamed novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (3). On March 11, 2020, the WHO declared COVID-19 a global pandemic, which is ongoing. As of July 22, 2020, more than 14,500,000 confirmed cases of COVID-19 and 607,781 deaths have been reported globally (2). In Turkey, the first confirmed COVID-19 case was reported by the Turkish Ministry of Health on March 11, 2020; by July 22, 2020, 221,500 confirmed cases and 5,526 deaths were reported in Turkey, despite strict control measures declared by the Turkish government (4). SARS-CoV-2 is more likely to infect the adult population, and the older population and those with chronic comorbidities are at a higher risk of morbidity and mortality. In contrast, studies have shown that children are less likely to be infected with SARS-CoV-2 than adults and often have a milder course of illness and a lower case fatality rate. Children account for an estimated 1%–5% of patients diagnosed with COVID-19 (5,6). However, more recently, reports from the UK, France, Italy, and the USA have made new observations regarding the pathogenesis of the virus in children (7). A relatively small number of children from the above countries were reported to have a Kawasaki syndrome-like condition, which has been named pediatric multisystem inflammatory syndrome temporarily linked to COVID-19 (7–9). Currently, there are no specific therapeutic agents or preventive vaccines available for COVID-19 (10,11). In this
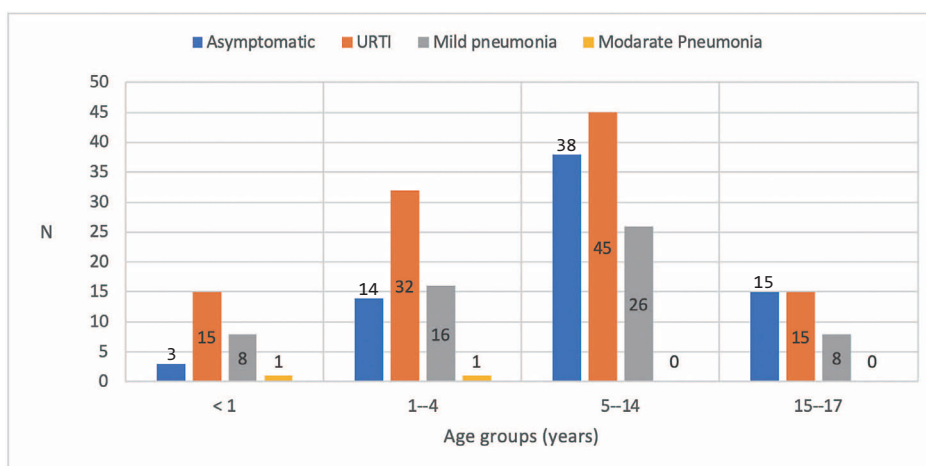
Fig. 1. (Color online) Distribution of clinical types of pediatric COVID-19 infections with respect to age groups.

study, we compared symptomatic and asymptomatic SARS-CoV-2-infected children with respect to clinical and epidemiological features and share our treatment experience with hydroxychloroquine (HCQ) and azithromycin in Turkish children.

MATERIALS AND METHODS

Study population: We performed a retrospective observational cohort study at 20 hospitals in 8 cities in Turkey. We included pediatric patients (0–17 years old) with laboratory-confirmed SARS-CoV-2 infection. The diagnosis was based on the guidelines established by the Turkish Ministry of Health COVID-19 Scientific Committee (12,13). SARS-CoV-2 infection was confirmed by reverse transcription (RT)-PCR of samples obtained from upper nasopharyngeal (NP) and/ or oropharyngeal (OP) swabs using the Bio-Speedy® SARS-CoV-2 Double Gene RT-qPCR kit (Bioeksen Istanbul Technical University Ari Teknokent Company, Istanbul, Turkey). This kit achieves rapid diagnosis via one-step RT and real-time PCR (qPCR) (RT qPCR) targeting the SARS-CoV-2 (2019-nCoV)-specific RNA-dependent RNA polymerase (RdRp) gene fragment. The RdRp gene-targeted Wuhan-RdRp oligonucleotide set gives a positive result only with the identification of SARS-CoV-2 (2019-nCoV) (12). To determine the route of transmission, we further evaluated the data of each child by investigating their travel history and close contact with COVID-19-confirmed or -suspected patients within the previous 14 days. The clinical types of COVID-19 on admission were re-determined by 2 independent authors according to published guidelines by the Society of Pediatrics Chinese Medical Association (6,14). The treatment protocols for children were determined according to the Turkish Ministry of Health COVID-19 guidelines (13). The latest revision of the guidelines was published on June 3, 2020, and only HCQ was recommended as an initial drug of choice; the dosage of HCQ was recommended as 6.5 mg/kg (maximum 400 mg/dose) orally twice as a loading dose, followed by 3.25 mg/kg/dose (maximum 200 mg/dose) twice per day for 4 days. If the clinical condition progressed, lopinavir/ritonavir or favipiravir (age >15 years) (1,600 mg twice per day as a loading

dose, and 600 mg twice per day for 4 days orally) were recommended as an alternative drug of choice (13).

This study was approved by the Turkish Ministry of Health COVID-19 Scientific Research Commission and the Istanbul Memorial Şişli Hospital Ethics Committee.

Statistical analysis: Data were entered into a Microsoft Office Excel (Microsoft, Redmond, WA, USA) spreadsheet and analyzed using Stata 10.0 Statistics/Data Analysis (StataCorp, College station, TX, USA). We used the Pearson correlation coefficient (r) to measure the correlation between the study age strata and the rate of being asymptomatic. A t-test was performed to determine whether there was a significant difference in the mean values of the compared parameters for each group. Univariate and multivariate regression analyses were performed to determine the independent factors for symptomatic SARS-CoV-2 infection. Statistical significance was set at $P < 0.05$.

RESULTS

Epidemiological and clinical findings: During the study period from March 26, 2020 to June 20, 2020, 237 SARS-CoV-2 PCR-positive pediatric cases were enrolled from 8 cities in Turkey. The cases comprised 124 (52%) boys and 113 (48%) girls, with a male to female ratio of 1.1:1. The median age of the patients was 87 months (mean age, 95 ± 8.6 months; range, 1–217 months). Among 237 children, 27 (11%), 63 (27%), 109 (46%), and 38 (16%) were aged <1 year, 1–4 years, 5–14 years, and 15–17 years, respectively. Most patients were previously healthy, and 5 patients had underlying chronic diseases. One patient had Ewing sarcoma, one had familial Mediterranean fever, one had renal transplantation because of chronic renal disease, one had mental retardation, and one had cerebral palsy.

The route of transmission was close contact with family members in 208 (88%) children, and the route of transmission could not be detected in 29 (12%) children. Among 237 children, 70 (30%) were asymptomatic, 107 (45%) had a clinical diagnosis of upper respiratory tract infection (URTI), 58 (24%) had mild pneumonia, and 2 (1%) had moderate pneumonia. No severe or critically ill cases were observed. Figure 1 shows the clinical diagnoses according to age groups. Asymptomatic cases

Table 1. Summary of pediatric COVID-19 infections characteristics

Characteristic	
Median age (range) months	87 (1–217)
Province *n*	
Istanbul	109
Yalova	72
Tokat	42
Rize	7
Others	7
Girl/boy *n/n*	113/124
Co-morbidity *n*	5
Epidemiological history *n* (%)	
Close contact with confirmed cases	208 (88)
Unknown	29 (12)
Clinical symptoms *n* (%)	
Fever	117 (49)
Cough	93 (39)
Malaise	51 (22)
Sore throat	37 (16)
Myalgia	19 (8)
Nausea/vomiting	17 (7)
Arthralgia	12 (5)
Loss of taste/smell	11 (5)
Diarrhea	10 (4)
Sputum production	7 (3)
Abdominal pain	3 (2)
Dyspnea	3 (2)
Clinical classifications *n* (%)	
Asymptomatic	70 (30)
Upper respiratory tract infection	107 (45)
Mild pneumonia	58 (24)
Moderate pneumonia	2 (1)
Severe or critical	0 (0)
Hospitalization	66 (28)
Intensive care unit admission	3 (1.2)
Radiology *n*	
Chest X ray normal	115
Chest X ray abnormal	48
Thorax CT normal	35
Thorax CT ground glass appearance	24

were observed in 3 (11%), 14 (22%), 38 (35%), and 15 (40%) children aged <1 year, 1–4 years, 5–14 years, and 15–17 years, respectively.

The mean duration of symptoms before the diagnosis was 2.3 days (range: 1–21 days, median: 1 day). Table 1 shows the epidemiological and clinical features of the study population. There were no signs of cardiac, liver, renal failure, or COVID-19-associated pediatric inflammatory syndrome. On admission, 66 (28%) of the 237 pediatric patients with COVID-19 were hospitalized. Among the 70 asymptomatic children, only 2 (3%) were hospitalized for clinical observation, whereas 64 (38%) of the 167 symptomatic children were hospitalized (odds ratio [OR], 21; 95% confidence interval [CI], 5–182; P <0.0001). The hospitalization rate was higher in children with pneumonia (52%) than in those with URTI (31%) (OR, 2.4; 95% CI, 1.1–4.8; P = 0.007). When hospitalization rates were analyzed by age group, 33% of children aged <1 year, 14% aged 1–4 years, 28% aged 5–14 years, and 44% aged 15–17 years were hospitalized. Among the 66 hospitalized patients, 3 were transferred to the intensive care unit (ICU) without intubation. The ICU hospitalization rate was 1.2% among pediatric COVID-19 patients. All patients were cured and discharged from hospitals before being quarantined for a further 14 days.

Laboratory and radiological findings: Among the 237 confirmed SARS-CoV-2 cases, 163 (69%) underwent chest radiography and 59 (25%) underwent thoracic computed tomography (CT). Among 163 children who underwent chest radiography, 48 (29%) had abnormal findings suggesting pneumonia, and among 59 children who underwent thoracic CT, 24 (41%) had pulmonary ground-glass opacities on CT. Among the 70 asymptomatic cases, 46 children underwent chest radiography and 11 children underwent thoracic CT. None of the chest X-rays and thoracic CT results showed evidence of pneumonia.

Fifty-four (77%) of the 70 asymptomatic cases, 77 (72%) of the 107 children with URTI, and 56 (93%) of the 60 children with pneumonia underwent laboratory investigation. In the univariate analysis, we found that the mean lymphocyte counts of symptomatic children ($2.5 \pm 1.7 \times 10^9$ cells/L) were significantly lower than those of asymptomatic children ($3.7 \pm 3.4 \times 10^9$ cells/L) (95% CI, 450–1,964; P = 0.001). The rate of lymphopenia was higher in symptomatic (22%) cases than in asymptomatic (11%) cases, but the difference was not significant (P = 0.06). In contrast, the mean C-reactive protein (CRP) level of symptomatic (12.8 ± 26) children was significantly higher than that of asymptomatic children (3.7 ± 5.6) (95% CI, 1.8–16; P = 0.014). In addition, only 4 children had elevated CRP levels among 38 (11%) asymptomatic children, whereas CRP elevation was observed in 41 (38%) of the 149 symptomatic children (OR, 3.2; 95% CI, 1–13; P = 0.01). The laboratory findings of symptomatic and asymptomatic patients are shown in Table 2. Multivariate regression analysis revealed that none of the aforementioned laboratory parameters nor the age of the subjects was associated with symptomatic SARS-CoV-2 infection (p >0.05). Follow-up PCR was recommended for all patients by NP swabs. Among the 237 pediatric patients diagnosed with COVID-19, 157 (66%) underwent follow-up NP swab PCR. On the 7th day of diagnosis, the first control NP swab PCR was negative in 130 (83%) children and positive in 27 (17%) children. The second control NP swab PCR was performed 12–14 days after diagnosis; 99 children provided second control NP swabs, and 7 of them (7%) remained positive. In 2 children, the NP swab PCR results were still positive 18 and 21 days after the initial diagnosis. Follow-up control NP swab PCR could not be repeated among the remaining 5 positive cases (Table 3). Among the 70 asymptomatic children, the first control NP swab PCR on the 7th day after the initial diagnosis was obtained in 36 (51%) children, 9 (25%) of which were positive. The second control NP swab

Table 2. Demographic and laboratory findings of pediatric COVID-19 infections with respect to clinical types

Variable	All patients $n = 237$	Asymptomatic infection $n = 70$	Symptomatic infection			*P-value
			Total symptomatic infection $n = 167$	URTI $n = 107$	Pneumonia $n = 60$	
Female n, (%)	113 (48)	34	79	53	26	
Male n, (%)	124 (52)	36	88	54	34	
Mean age, months (range)	95 ± 8.6 (1–214)	118 ± 62 (3–214)	89 ± 69 (0–214)	86 ± 13 (1–214)	94 ± 18 (0–210)	0.017
Age group (yr)						
Age < 1- n, (%)	27 (11)	3 (4)	24	15	9	
Age 1–4 n, (%)	63 (27)	14 (20)	49	32	17	
Age 5–14 n, (%)	109 (46)	38 (54)	71	45	26	
Age 15–17 n, (%)	38 (16)	15 (21)	23	15	8	
Mean WBC ($\times 10^9$ cells/ L), $n = 187$	7.2 ± 0.5 (2.3–30)	7.0 ± 3.4 (2.3–19.8)	7.3 ± 3.8 (2.3–28.5)	7.0 ± 0.9 (2.3–28.5)	7.8 ± 0.9 (3.7–17.4)	0.68
Mean Lymphocytes ($\times 10^9$ cells/ L), $n = 187$	2.9 ± 0.3 (0.29–19)	3.7 ± 3.4 (1.1–17)	2.5. ± 1.7 (0.29–10.9)	2.5 ± 0.4 (0.29–10.7)	2.6 ± 0.4 (0.68–8.5)	0.001
Lymphopenia [Total test number], n (%)	[187] 35 (19)	[54] 6 (11)	[133] 29 (22)	[77] 19 (25)	[56] 10 (18)	0.06
Mean CRP (mg/L) $n = 183$	10.1 ± 3.3 (0–158)	3.7 ± 5.6 (0.1–26)	12.8 ± 26 (0–158)	9.0 ± 3.5 (0–94)	18.1 ± 9.7 (0–158)	0.014
Increased CRP (≥ 5 mg/L) [Total test number], n (%)	[149] 41 (28)	[38] 4 (11)	[111] 37 (33)	[66] 21 (32)	[45] 16 (36)	0.004
Increased procalcitonin (> 0.5 ng/mL) [Total test number], n (%)	[59] 4 (7)	[18] 0 (0)	[41] 4 (10)	[26] 1 (4)	[16] 3 (19)	<0.05
Increased AST (≥40U/L) [Total test number], n (%)	[151] 15 (10)	[53] 5 (9)	[98] 10 (10)	[56%] 4 (7)	[42] 3 (7)	0.56
Increased ALT (≥40U/L) [Total test number], n (%)	[151] 8 (5)	[53] 1 (2)	[98] 7 (7)	[56] 4 (7)	[42] 3 (7)	0.16
Increased LDH (≥ 280 U/L) [Total test number], n (%)	[74] 25 (34)	[24] 4 (17)	[50] 21 (42)	[34] 14 (41)	[16] 7 (43)	0.02
Mean D-dimer (μg/mL), $n = 72$	0.31 ± 0.08 (0.02–2.5)	0.19 ± 0.13 (0.1–0.6)	0.38 ± 0.43 (0.1–2.5)	0.33 ± 0.4 (0.1–1)	0.44 ± 0.1 (0.1–2.5)	0.045
Increased D-dimer (≥ 0.5 μg/mL) [Total test number], n (%)	[62] 12 (19)	[27] 1 (4)	[35] 11 (31)	[27] 7 (26)	[18] 4 (22)	0.005

WBC, white blood cells; CRP, c-reactive protein; AST, aspartate transferase; ALT, alanine aminotransferase; LDH, lactate dehydrogenease.

*P: asymptomatics vs symptomatics.

PCR was still positive in 3 (8%) children 12–14 days after diagnosis. Among the 121 symptomatic children, 18 (15%) had a positive PCR control NP swab on day 7 and 4 (3%) remained positive by the second control NP swab PCR 12–14 days after diagnosis (Table 3). The clearance rates of SARS-CoV-2 in the first and second control NP swab PCRs were not significantly different between asymptomatic and symptomatic children (P = 0.12 and 0.28, respectively). The clearance rate of SARS-CoV-2 in the first and second control NP swab PCRs was not significantly different between children with URTI and those with pneumonia (P = 0.07 and P = 0.39, respectively) (Table 3).

Treatment features: Initially, 156 (66%) of the 237 pediatric COVID-19 patients were treated with a combination of HCQ, azithromycin, and oseltamivir (Table 4). Among the 70 asymptomatic children, 32 (46%) received the treatment, and among the 167 symptomatic children, 124 (74%) received the treatment. Symptomatic children had a higher treatment usage rate than asymptomatic children (OR, 3.4; 95% CI, 1.8–6.4; P = 0.0001) (Table 4).

Table 3. Nasopharyngeal swab SARS-CoV-2 PCR follow-up of the study population

| | Total | Asymptomatic | Symptomatic | | | *P-value |
			Total symptomatic	URTI	Pneumonia	
1th control NP Swab PCR	[157]	[36]	[121]	[74]	[47]	0.12
[Total test number] positive test n (%)	27 (17)	9 (25)	18 (14)	10 (14)	8 (17)	
2nd control NP Swab PCR	[99]	[27]	[72]	[51]	[21]	0.28
[Total test number] positive test n (%)	7 (7)	3 (11)	4 (6)	1 (1)	3 (14)	

1th control NP Swab PCR done on 7 th day of diagnosis, 2nd control NP Swab PCR done on 12-14 day of diagnosis.
NP, nasopharyngeal; URTI, upper respiratory tract infection. *P: between asymptomatic vs total symptomatic cases.

Table 4. Treatment choices of pediatric COVID-19 infections with respect to clinical types

| Treatment | Total $n = 237$ | Asymptomatic infection $n = 70$ | Symptomatic | | | *P-value |
			Total symptomatic infection $n = 167$	URTI $n = 107$	Pneumonia $n = 60$	
None	78	38	40	35	5	0.0001
HCQ + A + O	15	1	14	4	10	-
HCQ + A	44	8	36	18	18	-
HCQ	19	5	14	12	2	-
A	57	14	43	27	16	-
A + 0	21	4	17	11	6	-
Antibiotics	3	0	3	0	3	-
Hospitalization	66	2	64	33	31	0.0001
Mortality	0	0	0	0	0	-

HCQ, hydroxychloroquine; A, azithromycin; O, oseltamivir; URTI, upper respiratory tract infection.
*P: asymptomatic vs symptomatics.

Among the 156 children who received the treatment, 78 (50%) received an HCQ-containing regimen. The rate of children receiving an HCQ-containing regimen did not differ significantly between asymptomatic and symptomatic children ($P = 0.5$). Antimicrobial treatment was administered concomitantly in 26 patients receiving treatment. Among 156 patients who received HCQ or azithromycin treatment, 90 (58%) had an electrocardiogram (ECG) to calculate the QTc interval or any findings of arrhythmia, and none of them reported any ECG abnormalities. None of the children discontinued HCQ and/or azithromycin treatment because of adverse drug effects.

DISCUSSION

In this study, we shared our clinical and treatment experiences of pediatric COVID-19 patients in 237 children from Turkey. We found that 30% of the study population were asymptomatic; the asymptomatic rate of SARS-CoV-2-positive cases was the lowest in children aged <1 year (11%), and the rate of asymptomatic cases increased with increasing age strata ($P < 0.05$). The rate of asymptomatic children aged ≥5 years (36%) was significantly higher than that of children aged <5 years (19%) ($P = 0.049$). A latest systematic review of 7,780 SARS-CoV-2-positive children also showed that 19.3% of children were asymptomatic, which is consistent with our findings (15). Recent findings have assumed that 15%–45% of SARS-CoV-2 infections are asymptomatic (16). It is difficult to distinguish asymptomatic individuals from those in the pre-symptomatic phase, and in our study population, none of the asymptomatic children developed clinical disease during their 14 day-quarantine follow-up period. Data from asymptomatic COVID-19 cohorts showed that a small fraction of asymptomatic patients may eventually develop symptoms (17). However, it should be noted that asymptomatic cases can still transmit SARS-CoV-2 to others as they have the same infectivity as symptomatic infections (18).

Another interesting finding of our study is that we obtained chest radiology in 66% of 70 asymptomatic children, none of whom had evidence of abnormalities on chest radiography or thoracic CT. During the early period of the COVID-19 pandemic in Wuhan, China, 12 SARS-CoV-2-positive asymptomatic patients with radiologic features of pneumonia were reported (19). Given that none of our asymptomatic children progressed to a clinically symptomatic stage nor did radiologically evident diseases develop, we may conclude that asymptomatic children may not have clinically or radiologically subclinical pneumonia.

The third interesting finding of this study is that the PCR results obtained from NP swabs with respect to the SARS-CoV-2 clearance rate of symptomatic and asymptomatic children was not significantly different on the 7th and 12–14th days of diagnosis. Previous studies have reported that the median period of asymptomatic patients from viral nucleic acid positive to negative was

9.5 days, while the longest was up to 21 days among the 24 asymptomatic cases (20). In our study population, in 92% of the asymptomatic cases, the NP swab PCR result changed from positive to negative in the 12–14-day period, and the PCR result was positive beyond 14 days only in 3 asymptomatic children. The median period from diagnosis to a negative nucleic acid test result was previously reported as 7.7 days (2–20 days) with normal or atypical chest CT infections and 12.5 (8–22) days with typical CT findings (21). In our study population, only 4 symptomatic children had persistent NP swab PCR positivity longer than 14 days, and the persistence of NP swab SARS-CoV-2 positivity for >14 days did not differ significantly between symptomatic and asymptomatic children ($P = 0.28$).

The symptoms of COVID-19 in children are similar to those in adults, but the frequency of symptoms varies (22). COVID-19 appears milder in children than in adults, including the severity of symptoms. Similar to previous reports (15), the clinical findings of our study population were mild and non-severe; for instance, 45% of patients had mild infection findings resembling URTI, only 25% of patients had clinical or radiological findings of pneumonia, and none of the patients developed severe COVID-19. Unfortunately, unlike in children, the clinical presentation and progression of COVID-19 can be more severe and hazardous in adults (23). However, in our study population, only 3 children received PICU care, and none of the children died from COVID-19. The reason for the mild illness observed in children with COVID-19 has not yet been clearly explained (24).

Another important finding of our study is that symptomatic children had lower mean lymphocyte counts, higher mean CRP and D-dimer levels, higher rates of CRP and procalcitonin positivity, and higher rates of increased D-dimer and lactate dehydrogenase (LDH) levels than asymptomatic children in the univariate analysis. The laboratory findings of COVID-19 in children are variable. The complete blood count was normal in most children; however, low white blood cell (WBC) count, neutropenia or lymphocytopenia, elevated CRP or procalcitonin, creatine kinase, aspartate transferase (AST), and LDH levels have been reported at variable frequencies (25–27). A previous observational study demonstrated that elevated CRP, procalcitonin, interleukin 6, ferritin, and D-dimer levels at admission or during hospitalization were associated with severe disease in children (28). This finding is similar to that observed for the adult population, in that lymphocytopenia (specifically CD4+ and CD8+ T lymphocytes), elevated liver enzymes, LDH, and inflammatory markers (e.g., CRP and ferritin) are associated with increased severity or worse outcomes (29,30). However, laboratory comparisons between asymptomatic and symptomatic children have not been performed in detail. Bai et al. compared 8 asymptomatic children with 17 symptomatic children and found no statistical differences in laboratory results between asymptomatic, mild, and common cases (31). In contrast, Ma et al. compared 11 asymptomatic COVID-19 patients (children and adults) with 36 symptomatic COVID-19 patients (children and adults), including laboratory values, and showed that most

laboratory indicators were not significantly different, but they did observe that lymphopenia was significantly more common in symptomatic patients (32). Du et al. compared 8 symptomatic children with 6 asymptomatic children and found that the mean WBC and lymphocyte counts were significantly lower in symptomatic children (33). Supporting our findings regarding the clinical course of SARS-CoV-2 infection in children, Qui et al. reported that decreased lymphocytes, elevated body temperature, and high procalcitonin, D-dimer, and creatinine kinase MB levels are associated with the severity of COVID-19 in children (34).

An important aspect of our study is the sharing of HCQ usage experiences in children. In this study population, 78 children received an HCQ-containing regimen, including azithromycin and/or oseltamivir. None of the children treated with HCQ discontinued the drug due to adverse side effects. ECG was performed before the initiation of HCQ to calculate the QT_c interval, and follow-up ECG was also performed in the initial days of HCQ treatment. We did not observe any QT_c prolongation or arrhythmia in our HCQ-treated children. There is currently no effective treatment strategy for children and adults. Previous reports have shown that the most commonly used agents for treating COVID-19 in children were interferon, herbs/home remedies, lopinavir/ritonavir, oseltamivir, remdesivir, intravenous immunoglobulin, glucocorticoids, arbidol, ribavirin, tocilizumab, and antimicrobial agents (15). However, there are insufficient data regarding the use of HCQ in children. In our study population, although 75% of cases did not have pneumonia, 66% of patients were treated with a combination of HCQ, azithromycin, and oseltamivir, including some asymptomatic patients. In Turkey, the first case of COVID-19 was reported on March 11, 2020, and the pediatric cases in the first 4 months of the COVID-19 pandemic were analyzed in this study. At that time, the treatment protocol of the Turkish Ministry of Health included HCQ and azithromycin.

In conclusion, most of the children acquired SARS-CoV-2 from their close contacts, the asymptomatic rate of SARS-CoV-2 infection in children was higher, and children with SARS-CoV-2 infection had mild illnesses with good outcomes. The clearance rate of SARS-CoV-2 was not significantly different between asymptomatic and symptomatic children. In this study, which analyzed the early period of the pandemic, HCQ and azithromycin were used at high rates and no side effects of HCQ such as ECG abnormalities were detected.

Appendix The members of the PEDCOVID19 Study Group are as follows: Miraç Ergen (Medical Park Bahçelievler Hospital, Department of Pediatrics, İstanbul, Turkey), Eda Ayberkin (Memorial Ataşehir Hospital, Department of Pediatrics, İstanbul, Turkey), Bekir Muhsin Arpaözü (Çakmak Erdem Hospital, Department of Pediatrics, İstanbul, Turkey), Seda Öz (Memorial Ataşehir Hospital, Department of Pediatrics, İstanbul, Turkey), Turan Tunç (Memorial Ataşehir Hospital, Department of Pediatrics, İstanbul, Turkey), Cengiz Kızıltepe (Ersoy Hospital, Department of Pediatrics, Kurtköy, İstanbul, Turkey), Ayşe Yurtsever (Kağıthane State Hospital, Department of Pediatrics, İstanbul, Turkey), Ece Nur Özeke (Afyon State Hospital,

Department of Pediatrics, Afyon, Turkey), Sevil Bilir Göksugür (Hisar Intercontinental Hospital, Department of Pediatrics, İstanbul, Turkey), Ercan Tutak (Memorial Şişli Hospital, Department of Pediatrics, İstanbul, Turkey), Elif Erdem Özcan (Memorial Şişli Hospital, Department of Pediatrics, İstanbul, Turkey), Can Polat (Memorial Şişli Hospital, Department of Pediatrics, İstanbul, Turkey), Mesut Engin (Düzce University Faculty of Medicine, Department of Pediatrics, Düzce, Turkey), Şenay Acar (Ozel 2000 Medical Center, Department of Pediatrics, İstanbul, Turkey), Zeynep İlkşen Hocoğlu (Rize Teaching and Research Hospital, Department of Pediatrics, Rize, Turkey), Gökhan Aydemir (Memorial Ataşehir Hospital, Department of Pediatrics, İstanbul, Turkey), Nesrin Özkan (Memorial Ataşehir Hospital, Department of Pediatrics, İstanbul, Turkey), Dicle Çelik (Memorial Şişli Hospital, Department of Pediatrics, İstanbul, Turkey), Kadir Şahin (Çakmak Erdem Hospital, Department of Pediatrics, İstanbul, Turkey), Ömer Celep (Çakmak Erdem Hospital, Department of Pediatrics, İstanbul, Turkey), Emre Bilgiç (Bingöl State Hospital, Department of Pediatrics, Bingöl, Turkey), Orhan Gürcan Adıgüzel (Medicana International Hospital, Department of Pediatrics, İstanbul,Turkey), Yasin Yıldız (Rize Teaching and Research Hospital, Department of Pediatrics, Rize, Turkey), Mehmet Kenan Kanburoğlu (Rize Teaching and Research Hospital, Department of Pediatrics, Rize, Turkey), Tuğba Çalapoğlu (Rize Teaching and Research Hospital, Department of Pediatrics, Rize, Turkey), Turgay Aydın (Rize Teaching and Research Hospital, Department of Pediatrics, Rize, Turkey).

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