

Clinical Characteristics of COVID-19 in Children Compared with Their Families in Turkey: A Tertiary-Care Hospital Experience

Türkiye’de Aileleriyle Kıyasla Çocuklarda COVID-19’un Klinik Özellikleri: Bir Üçüncü Basamak Hastane Deneyimi

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ABSTRACT

Objective: The COVID-19 outbreak that has spread all around the world is still a threat for humankind. Epidemiological, clinical, laboratory, and radiological features of the disease are enlightened day by day. It was aimed to evaluate the characteristics of children and their parents with COVID-19 to aid in diagnosis and treatment.

Material and Methods: A retrospective review of the medical records of pediatric patients and their parents who were confirmed as COVID-19 positive, between April 23, and May 28, 2020, was conducted.

Results: A total of 93 children and 81 adults were evaluated in the present study. Asymptomatic and mild cases accounted for 63.5% of the children and 50% of the parents. Of the children, 3.2% had moderate illness, whereas this was 9.8% for the parents. There was a statistically significant difference in terms of the severity of illness between the children and their parents ($p=0.01$). Although it had a milder clinical course in children, one child died. Increased levels of C-reactive protein (CRP) were observed in 8.6% of the children and 48.1% of the patients, and there was statistically significant difference in terms of CRP levels between the children and their parents ($p=0.001$).

Conclusion: The clinical, laboratory, and radiological features of COVID-19 showed differences in the children and their parents. It should be kept in mind that COVID-19 can be fatal in children, although the course of the disease appears to be milder in children than in their parents.

Key Words: Adults, Children, COVID-19

ÖZ

Amaç: Tüm dünyaya yayılan COVID-19 salgını, insanlık için hala bir tehdittir. Hastalığın epidemiyolojik, klinik, laboratuvar ve radyolojik özellikleri gün geçtikçe gün yüzüne çıkmaktadır. Tanı ve tedaviye yardımcı olmak için COVID-19’lu çocuk ve ebeveynlerinin özelliklerini değerlendirmeyi amaçladık.



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Ethics Committee Approval / Etik Kurul Onayı: This study was conducted in accordance with the Helsinki Declaration Principles. The study was approved by the Ankara Training and Research Hospital, Clinical Research Ethics Committee. (10.07.2020/ E-20/303).

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Gereç ve Yöntemler: 23 Nisan-28 Mayıs 2020 tarihleri arasında COVID-19 olduğu doğrulanan pediatrik ve onların ebeveyni olan yetişkin hastaların tıbbi kayıtlarının retrospektif olarak incelendi.

Bulgular: Bu çalışmada toplam 93 çocuk ve 81 yetişkin değerlendirildi. Asemptomatik ve hafif vakalar çocuklarda %63.5, ebeveynlerde ise %50'di. Çocukların %3.2'si orta şiddette hastalığa sahipken, ebeveynlerin %9.8'inde vardı. Çocuklar ve ebeveynler arasında hastalık şiddeti açısından istatistiksel olarak fark vardı ($p=0.01$). Çocuklarda daha hafif klinik seyretmesine rağmen bir çocuk öldü. Çocukların %8.6'sında ve ebeveynlerin %48.1'inde C-reaktif protein (CRP) düzeylerinde artış görüldü, çocuklar ve ebeveynler arasında CRP açısından istatistiksel olarak anlamlı fark vardı ($p=0.001$).

Sonuç: COVID-19'un klinik, laboratuvar ve radyolojik özellikleri çocuklarda ve yetişkinlerde farklılıklar göstermektedir. COVID-19'un hastalık seyri çocuklarda yetişkinlere göre daha hafif gibi görünse de, COVID-19'un çocuklarda ölümcül olabileceği akıldan tutulmalıdır.

Anahtar Sözcükler: Erişkin, Çocuk, COVID-19

INTRODUCTION

A new underlying cause of pneumonia, called coronavirus disease 2019 (COVID-19) has spread across the world (1). Reports from both the Centers for Disease Control and Prevention (CDC) and China have concluded that a small amount of the infected population was children, at a rate of 1.7 and 8.7%, respectively (2–4). Additionally, the severity of symptoms was different between children and their parents (5). In a study from China, which included 2143 infected children, only one 14-year-old child died and 94.1% of the children were reported to be either asymptomatic or followed a moderate clinical course (6). Wending et al.(5) reported that although there is substantial lung injury among children, the disease was milder, perhaps due to less pronounced inflammatory response. These data suggested that the clinical and radiological features of children differ from those observed in adults, which indicates that disease management and treatment in children may require a different approach from that used in adults.

Herein, the clinical features and management strategies of COVID-19 in children when compared with their families was reported. Few data are available on children who have COVID-19 when compared with adults (5,7). Therefore, it is believed that sharing the available data on families will be beneficial in understanding the epidemiological and clinical features of the disease in both children and their parents.

MATERIAL and METHODS

The retrospective study was performed at a tertiary-care hospital in Ankara, the capital of Turkey, between April 23 and May 28, 2020. The medical records of the pediatric patients enrolled in the study and their parents, including age, sex, signs and symptoms, exposure history, pre-existing co morbidities (i.e. heart disease, chronic lung disease, neurologic diseases), laboratory findings, chest computer tomography (CT) and X-ray results, complications, treatments, and clinical outcomes of patients who were confirmed as COVID-19-positive were evaluated. Total radiological imaging defined x-ray or chest CT. The study was approved by the Ankara Training and Research Hospital, Clinical Research Ethics Committee. (10.07.2020/E-20/303).

Suspected cases of COVID-19 were diagnosed according to national COVID-19 guidelines. Patients suspected of having COVID-19 via positive reverse transcriptase-polymerase chain reaction (RT-PCR) results were accepted as confirmed cases (8). The severity of COVID-19 was categorized based on the clinical characteristics and the results of laboratory examinations and radiologic imaging, and were defined as asymptomatic, mild, moderate, severe, and critical. Asymptomatic included cases with positive diagnoses but without any clinical or radiological findings; mild disease included cases with acute upper respiratory tract infections but without clinical and radiological pneumonia; moderate disease included cases with pneumonia and symptoms of respiratory tract infection; severe disease included cases with progressive respiratory disease, dyspnea, and central cyanosis; and critically ill included cases presented with acute respiratory distress syndrome or respiratory failure, shock, and organ dysfunction, including encephalopathy, myocardial injury, coagulation abnormalities, and acute kidney injury (6, 9).

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows 21.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize the participants' baseline characteristics, including medians and interquartile ranges for continuous variables and frequency distributions for categorical variables. P-values were calculated using the chi square or Fisher exact tests for the categorical variables and the student for Mann-Whitney U tests for the continuous variables according to the normality assumption. $p<0.05$ was accepted as statistically significant.

RESULTS

We obtained and compared the clinical data of pediatric patients ($n=93$) and their parents ($n=81$) who had COVID-19 in our hospital. Detailed data regarding the demographic, clinical characteristics, treatment, and outcomes of the patients are summarized in Table I. The median (minimum-maximum) age of the pediatric patients was 8 (0–17) years and 48.4% were male. The median age (minimum-maximum) of the parents was 36 (31–79) years and 37% were male. Only 8.6% of the pediatric patients had underlying disease, whereas this rate

Table I: Demographic, clinical and laboratory data of patients with COVID-19.

	Children (n=93)	Parents (n=81)	p
Age, years*	8 (0–17)	36 (31–79)	NA
Male†	45 (48.4)	30 (37)	0.08
Underlying disease‡			
None	85 (91.4)	62 (76.5)	NA
Neurologic disease	4 (4.3)	2 (2.4)	
Asthma	1 (1.1)	1 (1.2)	
Hypothyroidism	2 (2.3)	0	
FMF	1 (1.1)	1 (1.2)	
Hypertension	0	6 (7.3)	
Asthma+Hypertension	0	2 (2.4)	
Diabetes+ Hypertension	0	3 (3.7)	
Hepatitis B	0	1 (1.2)	
Symptoms‡			
Fever	34 (36.6)	38 (46.9)	0.16
Cough	37 (39.8)	41 (50.6)	0.15
Dyspnea/tachypnea	5 (5.4)	13 (16)	0.02
Myalgia/fatigue	16 (17.2)	23 (28.4)	0.07
Sore throat	15 (16.1)	14 (17.3)	0.83
Headache	9 (9.7)	13 (16)	0.20
Diarrhea	6 (6.5)	7 (8.6)	0.58
Abdominal pain	7 (7.5)	1 (1.2)	0.06
Vomiting	6 (6.5)	1 (1.2)	0.12
Loss of smell/taste	5 (5.4)	1 (1.2)	0.2
Conjunctivitis	1 (1.1)	0	1
Laboratory findings‡			
Leukocytosis	0	0	NA
Neutropenia	10 (10.8)	2 (2.5)	0.03
Lymphopenia	12 (12.9)	16 (19.8)	0.22
Increased CRP	8 (8.6)	39 (48.1)	0.001
Increased Procalcitonin	0/72 (0)	1/69 (1.2)	NA
Increased LDH	27/74 (36.5)	35/79 (44.3)	0.24
Increased D dimer	7/27 (25.9)	13/78 (16.6)	0.29
Increased troponin	3/53 (5.6)	3/71 (4.2)	1
Total Radiologic imaging‡	92	74	0.01
Normal	59 (63.4)	33 (44.6)	
Anormal	34 (36.6)	41 (55.4)	

NA: Nonapplicable, **FMF:** Familial Mediterranean Fever, **CRP:** C-Reactive Protein, **LDH:** Lactate Dehydrogenase, **CT:** Computer Tomography, *Values were given at median (min-max), †%, ‡Values were given at number (percentage).

was 23.5% in the parents. The most common underlying disease was neurologic diseases in the pediatric patients, while it was hypertension in their parents. Moreover, 5 of the mothers were pregnant.

The most common symptoms were cough and fever in the children, similar to the parents; however, there was a statistically significant difference between the parents and children in terms of the rate of dyspnea/tachypnea, as dyspnea/tachypnea were more common in the parents than in the children (p=0.02, Table I). The rate of the other symptoms, such as fatigue/myalgia, sore throat, diarrhea, headache, vomiting, loss of smell or taste, and conjunctivitis were similar between the parents and the children.

Table II: Severity of illness, treatment, and outcomes of patients with COVID-19.

	Children (n=93)	Parents (n=81)	p
Severity*			0.01
Asempotomatic	22 (23.7)	7 (8.5)	
Mild	37 (39.8)	31 (41.5)	
Moderate	31 (33.3)	35 (47.6)	
Severe/ Critical	3 (3.2)	8 (9.8)	
Antiviral treatment*			0.001
Hq	0	60 (74.0)	
Favipiravir	0	8 (9.8)	
Favipiravir+azithromycin	0	1 (1.2)	
Hq+Favipiravir	3 (3.9)	3 (3.7)	
Hq+azithromycin	0	6 (7.4)	
ICU*	1 (1.1)	0	NA
Outcome*			NA
Recovered	92 (98.9)	100	
Death	1 (1.1)	0	

Hq: Hydroxychloroquine, **ICU:** Intensive care unit, **NA:** Nonapplicable, * Values were given at number (percentage).

Neutropenia was detected in 10.8% of the children and 2.5% of the parents (p=0.03). Lymphopenia was present in 12.9% of the children and 19.8% of the parents. There were no statistically differences in terms of lymphopenia and leukocytosis between the children and the parents.

Increased levels of C-reactive protein (CRP) were seen in 8.6% of the children and 48.1% of the parents, and this difference was statistically significant (p=0.001). The parents with severe clinical condition had high CRP levels. However, there was no statistically significant difference in terms of CRP levels and severity of the parents or the children (Figure 1).

Increased lactate dehydrogenase (LDH) levels were detected in 44.3% of the parents and 36.5% of the children. The D dimer level was increased in 25.9% of the children and 16.6% of the parents. There were no statistically differences in terms of increased LDH, D dimer, and procalcitonin, and troponin levels between the children and the parent groups.

All of the children and 14.8% of the parents were evaluated via chest X-ray. In the children, 23.6% were evaluated with CT, whereas in the parents, 91.3% were evaluated with thorax CT. Total of 55.4% children and 36.6% of parents presented remarkable abnormalities on X-ray or chest CT. There was a statistically significant difference in terms of the radiologic abnormalities between the groups (p=0.01). Asymptomatic and mild cases accounted for 63.5% of the children and 50% of the parents. In the children, 3.2% had severe/critical illness, whereas this rate was 9.8% for the parents. There was a statistically significant difference in terms of the severity of illness between the children and their parents. Clinical severity, treatment, and outcomes are shown in Table II.

Antiviral treatment was used in only 3.9% of the children who had critical disease, whereas 96.2% of the parents received antiviral treatment (p=0.001). A combination of hydroxychloroquine (hq)

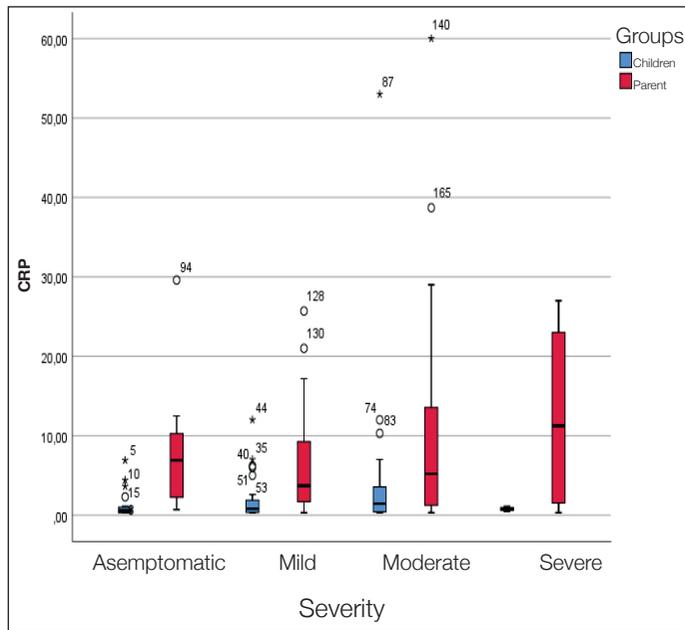


Figure 1: CRP levels and severity of parents and children.

+ favipiravir in children and hq in the parents were the most common antiviral treatments. Patients were admitted to either inpatient wards or the intensive care unit (ICU), according to the course of the disease. Only 1 (1.1%) child was admitted to the ICU, while none of the parents were. All of the parents recovered; however, 1 child died due to myocarditis.

DISCUSSION

To the best of our knowledge, this study was one of the very few studies in the literature that focused on the epidemiological, clinical, and management strategies in families with COVID-19. The findings highlighted the fact that the rate of asymptomatic patients with COVID-19 infection was higher in the children than the adults, whereas the rate of severe/critical patients was higher in the adults than the children, similar to the literature (5, 10). Due to the asymptomatic clinical condition, it is difficult for health care workers to recognize the disease early and control the spread of the virus. Hypotheses related to differences in immunity, microbiota, intensity of exposure to SARS-CoV-2, endothelial damage and clotting function, ACE-2 receptors, and co morbidities for the age-related difference in the severity of COVID-19 are still under consideration (11).

Herein, fever and cough were the two most common clinical manifestations presented by both the children and the adults, similar to the literature, whereas dyspnea/tachypnea was more frequent in the adults than the children (12, 13). Clinicians should pay attention as the differences in the signs and symptoms to diagnosis the disease in children and adults.

Included in this study were 5 pregnant women. It is known that pregnant women are likely to be a high-risk population

for COVID-19 (14). Fortunately none of the pregnant patients herein had severe disease.

Since the pandemic outbreak of COVID-19, investigations including laboratory tests and radiologic findings have played an important role in the early diagnosis and treatment monitoring of COVID-19. However, many of the previous reports on COVID-19 laboratory results were based on data from the general population. Additionally, limited information is available based on age differences (15). The most useful and reliable laboratory markers are CRP, LDH, lymphocyte, and procalcitonin levels (15). The expert consensus statement for children with COVID-19 has stated that most patients display increased CRP and LDH levels, but normal procalcitonin levels (16). In contrast to adult patients, only a small number of children with COVID-19 had increased CRP in the current study. This result suggested that inflammation caused by viral infection, especially in the lungs, is less severe in children than in adults, similar to findings of Wenjun et al. (5). Furthermore, radiologic abnormalities in adults were more common in the children than in the adults in the current study.

Several studies have determined that lymphopenia is rarely observed in infected children. However, in adults, lymphopenia occurs more frequently, especially in severe cases (17). In the findings herein, lymphopenia occurred in the adults more than in the children. This may have been attributed to the fact that severe disease was seen at a higher rate in the adults than in the children.

In a retrospective cohort study of 12.306 pediatric COVID-19 patients in the USA, the hospitalization frequency was 5.3%, with 17.6% requiring critical care services and 4.1% requiring mechanical ventilation (18). Only 1 child died among 2.143 children in one of the largest pediatric series from China, and in another study from the USA/Canada, the pediatric ICU (PICU) mortality rate was 4.2% (6, 19). In the most recent CDC data on May 20th, 2021, a total of 391 deaths were reported among pediatric cases in the USA (20). In the cohort herein, of the 93 patients, 1 (1.0%) was admitted to the PICU and died, whereas all of the adults recovered. This mortality rate in the children appeared to be high when compared with reports from other countries; however, the true death rate in Turkey must be clarified by performing studies with larger populations.

No antiviral treatment was used in most of children in contrast to their parents. A huge knowledge gap exists regarding the treatment of patients, especially in children with COVID-19, due to a lack of clear evidence regarding the safety and efficiency of targeted therapies.

In conclusion, clinicians should consider that not only the clinical features, but also the laboratory data are different for different age groups. The disease course of COVID-19 appears to be milder in children than in adults. However, it should keep in mind it can be fatal in children. Increased data regarding the disease

course in children and the outcomes of therapeutic options will guide us in the accurate management of future cases.

This study has some limitations. Firstly, it has a small sample size and single center data. A larger, cohort study population will be needed. Secondly, we could not perform variant analysis and examine its course according to age.

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