

Demographic and Laboratory Findings of Symptomatic and Asymptomatic COVID-19 in Children

Çocuklarda Semptomatik ve Asemptomatik COVID-19'un Demografik ve Klinik Bulguları

Binnaz Çelik* (0000-0001-8852-0067), Murat Doğan** (0000-0003-2954-3845), Doğan Bahadır İnan* (0000-0001-9785-3939), Süleyman Sunkak*** (0000-0002-6191-9403), Esmâ Saatçi**** (0000-0002-6521-2077), Filiz Tubaş* (0000-0002-5405-937X)

*Kayseri City Training and Research Hospital, Clinic of Pediatrics, Kayseri, Türkiye

**Kayseri City Training and Research Hospital, Clinic of Pediatric Emergency Service, Kayseri, Türkiye

***Kayseri City Training and Research Hospital, Clinic of Pediatric Cardiology, Kayseri, Türkiye

****Kayseri City Training and Research Hospital, Clinic of Clinical Microbiology, Kayseri, Türkiye



Abstract

Introduction: Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a newly described pathogen that is usually transmitted by droplets between person to person. Although the clinical spectrum of COVID-19 ranges from asymptomatic disease to the development of severe acute respiratory distress, children are generally milder than adults. It was aimed to compare the clinical and laboratory values of symptomatic and asymptomatic children followed up with a diagnosis of COVID-19 in this study.

Materials and Methods: The records of children with nasopharyngeal swab SARS-CoV-2 Reverse Transcriptase-Polymerase Chain Reaction test positive were analyzed retrospectively. Children with symptoms such as fever, cough, shortness of breath, diarrhea and/or vomiting were accepted as symptomatic, and children with positive SARS-CoV-2 PCR in a nasopharyngeal swab taken only due to contact history and have no symptoms were considered asymptomatic.

Results: A total of 197 patients, 47 (23.8%) symptomatic and 150 (76.2%) asymptomatic, were included in the study. The mean age of the children was 9.1 ± 5.2 years (range, 1 month-17 years). Cough (8.6%) was the most common symptom at admission. When the symptomatic and asymptomatic children were compared in terms of white blood cell (WBC), WBC subgroups, C-reactive protein there was no statistically significant difference. No significant increase was found in the CRP values of symptomatic patients. Ground-glass opacities compatible with COVID-19 was detected in only 10 (30%) of 33 symptomatic patients who underwent thoracic tomography.

Conclusion: COVID-19 is usually mild in children. At the same time, a significant change in laboratory parameters and imaging findings may not be observed in symptomatic and/or asymptomatic children with positive SARS-CoV-2 PCR.

Öz

Giriş: Şiddetli akut solunum sendromu koronavirus-2 (SARS-CoV-2), genellikle kişiden kişiye damlacık yoluyla bulaşan yeni tanımlanan bir patojendir. COVID-19'un klinik spektrumu asemptomatik hastalıktan şiddetli akut solunum sıkıntısı gelişimine kadar değişse de, çocuklar genellikle yetişkinlerden daha hafif klinik gidiş gösterir. Bu çalışmada COVID-19 tanısı ile izlenen semptomatik ve asemptomatik çocukların klinik ve laboratuvar değerlerinin karşılaştırılması amaçlanmıştır.

Keywords

COVID-19, child, laboratory parameters

Anahtar kelimeler

COVID-19, çocuk, laboratuvar parametreler

Received/Geliş Tarihi : 26.04.2021

Accepted/Kabul Tarihi : 21.10.2021

DOI:10.4274/jcp.2021.47640

Address for Correspondence/Yazışma Adresi:

Binnaz Çelik MD, Kayseri City Training and Research Hospital, Clinic of Pediatrics, Kayseri, Türkiye

Phone: +90 505 489 75 54

E-mail: btekatli2003@gmail.com

Gereç ve Yöntem: Nazofaringeal sürüntü materyalinde SARS-CoV-2 Ters Transkriptaz-Polimeraz Zincir Reaksiyon testi pozitif olan çocukların hastane kayıtları geriye dönük olarak incelendi. Ateş, öksürük, nefes darlığı, ishal ve/veya kusma gibi semptomları olanlar semptomatik, herhangi bir semptomu olmayıp yalnızca temas öyküsü nedeniyle alınan sürüntüde SARS-CoV-2 PCR pozitif saptanan çocuklar asemptomatik kabul edildi.

Bulgular: Çalışmaya 150 (%76.2) asemptomatik, 47 (%23.8) semptomatik olmak üzere toplam 197 çocuk dahil edildi. Çocukların ortalama yaşı 9.1 ± 5.2 yaş (1 ay-17 yaş) idi. Başvuruda en sık görülen şikayet öksürüktü (%8.6). Semptomatik ve asemptomatik çocuklar arasında beyaz küre ve alt grupları sayısı açısından anlamlı fark bulunamadı. Semptomatik hastaların C-reaktif protein değerinde de anlamlı yükseklik belirlenmedi. Toraks tomografisi çekilen 33 semptomatik hastanın yalnızca 10'unda (%30) COVID-19 ile uyumlu buzlu cam manzarası saptandı.

Sonuç: COVID-19, çocuklarda genellikle hafif seyirlidir. Aynı zamanda SARS-CoV-2 PCR pozitif saptanan semptomatik ve/veya asemptomatik çocuklarda laboratuvar parametreleri ve görüntüleme bulgularında önemli bir değişiklik görülmez.

Introduction

In December 2019, cases of pneumonia with an unknown cause began to be reported in Wuhan city, China. The virus, which rapidly spread throughout the world, was isolated from the lower respiratory tract of patients and determined to be a new type of coronavirus (2019 novel coronavirus (2019-nCoV), severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)) by genome sequencing (1). The virus is thought to be transmitted by close contact from person to person. Virus transmission from asymptomatic or mildly symptomatic patients usually continues for up to 14 days (2).

The clinical spectrum of COVID-19 ranges from asymptomatic illness to the development of severe acute respiratory distress. Younger children especially less than 1 year are more susceptible to severe or fatal disease than older children; the majority of children who are infected with SARS-CoV-2 experience milder symptoms than for adult, and do not require hospitalization (2,3). It is not clear why children have milder illness. This may be related to well care and protection of children. Angiotensin-converting enzyme II (ACE2) was known as the receptor required for COVID-19 bind to cells. Less developed ACE2 receptor maturity and function in children may also be the reason for mild disease. Since the disease is generally asymptomatic or mild in children, they pose a risk in terms of the disease's spread (4).

In children affected by COVID-19, the white blood cell (WBC) count may be normal or decreased, lymphocyte count also increased or decreased. However, their C-reactive protein (CRP) may be normal or increased. Muscle and liver enzymes may also increase in severe cases (5). In the initial period of the disease, pneumonia is usually found in the

chest radiography. In severe cases, ground-glass opacity and consolidation may be seen. Bilateral lobar consolidation may also be seen in children with severe infection (6).

However, knowledge of the disease in pediatric patients is limited since they usually experience asymptomatic or mild infections. We aimed to compare the epidemiological and laboratory findings of asymptomatic children who were screened for close contact with COVID-19 positive patients and symptomatic patients presenting with symptoms such as cough and/or fever in this study.

Materials and Methods

A total of 197 children were included in this retrospective study who presented to our hospital from March 11 to June 30, 2020. All children were tested with COVID-19 real-time reverse transcriptase-polymerase chain reaction (RT-PCR) tests from the nasopharyngeal specimen and were found to be positive. Nasal or nasopharyngeal swab specimens tested positive for 2019-nCoV nucleic acid using RT-PCR assay. These RT-PCR tests were performed in pediatric pandemic outpatient clinics due to household and social close contact with a confirmed COVID-19 case or with someone presenting with symptoms of COVID-19, such as fever, cough, diarrhea, and/or vomiting.

The patients' epidemiologic, demographic, laboratory, and radiologic imaging results were recorded from electronic medical report. The patients were divided into two groups, symptomatic and asymptomatic, according to the presence or absence of fever, cough, shortness of breath, diarrhea, and/or vomiting. If the patients had no symptoms at the

time of RT-PCR test and the test was performed due to the patient's contact history, they were included in the asymptomatic group. Patients who presented with fever, cough, diarrhea, vomiting, and/or shortness of breath and whose RT-PCR test was positive were included in the symptomatic group. All patients who tested positive using a COVID-19 RT-PCR test performed for any reason were closely followed. Laboratory tests (complete blood count, C-reactive protein) and when necessary, radiological imaging were also performed on the patients.

Statistical Analysis

The epidemiological and clinical data were obtained from the COVID-19 positive pediatric patients, and were transferred to the electronic environment. All analyzes were conducted with SPSS 24.0 statistics program. Descriptive values of the data were given as frequency (number and percent), mean and standard deviation (SD). The Shapiro-Wilk test was used to determine whether the data had a normal distribution. Normally distributed data were compared with the t test. Mann-Whitney U test was used for of data that were not normally distributed, and Chi-square test was used for analysis of categorical variables. P-value below 0.05 was considered statistically significant.

Results

Between March 11 and June 30, 2020, a total of 197 COVID-19 positive children (98 girls [49.7%] and 99 boys [50.3%]) were admitted to our hospital's pandemic outpatient clinics. The mean age of the children was 9.1 ± 5.2 years (range, 1 month-17 years). While all of the children had a history of contact, 182 (92.3%) had household contact and 15 (7.6%) had a history of contact from the social environment.

While 150 (76.1%) patients were asymptomatic, 47 (23.8%) were symptomatic (Table 1). The most common symptoms were cough in 17 patients (8.6%) and fever in 13 patients (6.6%) at admission. Six patients (3%) have both fever and cough complaints. Seven patients (3.6%) have gastroenteritis, and four (2%) have myalgia. Only two patients had underlying diseases, including prematurity-chronic lung disease and spinal muscular atrophy (SMA)-chronic lung disease. These two patients were followed and treated in the pediatric intensive care unit.

Table 1. Demographic characteristics of the COVID-19 children

	Symptomatic cases	Asymptomatic cases	Total
Sex			
Girls n (%)	18 (38.3)	69 (46)	98 (49.7)
Boys n (%)	29 (61.7)	81 (54)	99 (50.3)
Age years			
<1 years n (%)	3 (6.4)	2 (1.3)	5 (2.5)
1-5 years n (%)	9 (19.1)	45 (30)	54 (27.4)
6-10 years n (%)	12 (25.5)	42 (28)	54 (27.4)
>10 years n (%)	23 (48.9)	61 (40.7)	84 (42.6)

The number of cases in children over 10 years old was higher than in the other age groups. But this difference was not statistically significant ($p > 0.05$). The mean age of patients with any symptoms such as fever, cough, and diarrhea was 10.2 ± 5.2 years, while the mean age of asymptomatic patients was 8.2 ± 5.1 years ($p > 0.05$).

The mean values of the patients' WBC count and its subgroups are shown in Table 2 according to age group.

While the mean WBC was $6.98 \pm 2.63 \times 10^9 / \text{mm}^3$ in 150 asymptomatic patients, it was $7.07 \pm 3.61 \times 10^9 / \text{mm}^3$ in 47 patients with symptoms. The mean PMNL was $3.57 \pm 2.71 \times 10^9 / \text{mm}^3$ in symptomatic patients and $3.00 \pm 1.66 \times 10^9 / \text{mm}^3$ in asymptomatic patients.

The mean lymphocyte count in the symptomatic group was $2.47 \pm 1.42 \times 10^9 / \text{mm}^3$ and $3.19 \pm 2.05 \times 10^9 / \text{mm}^3$ in the asymptomatic group. No statistically significant difference was found in the mean WBC count and its subgroups between symptomatic and asymptomatic COVID-19 cases ($p > 0.05$).

The C-reactive protein (CRP) value was < 10 mg/L in 170 cases (86.2%). In 19 cases (9.6%), the CRP-value was between 10 and 30 mg/L, and 8 cases (4%) had a CRP-value > 30 mg/L. All patients with a CRP-value > 10 mg/L were symptomatic patients. Although symptomatic, the CRP-value of 20 patients was < 10 mg/L. CRP-value of all asymptomatic patients was < 10 mg/L.

Chest X-rays were taken in 173 (90.4%) of all cases due to physician concern, and 165 (95.3%) of them were normal. Ground-glass opacity compatible with COVID-19 was observed in four of the patients, and the X-ray findings of four patients were nonspecific. All patients with X-ray abnormalities were from the

Table 2. Median values of WBC and its subgroups by age in symptomatic and asymptomatic cases

Age groups	<1 years	1-5 years	6-10 years	>10 years
WBC*				
Symptomatic cases	12930/mm ³	5770/mm ³	6485/mm ³	5640/mm ³
Asymptomatic cases	10320/mm ³	7300/mm ³	6770/mm ³	5760/mm ³
Lymphocyte				
Symptomatic cases	4890/mm ³	2340/mm ³	2940/mm ³	1940/mm ³
Asymptomatic cases	6235/mm ³	3810/mm ³	2830/mm ³	2210/mm ³
PMNL**				
Symptomatic cases	6530/mm ³	2720/mm ³	3945/mm ³	3060/mm ³
Asymptomatic cases	3050/mm ³	2180/mm ³	2630/mm ³	3260/mm ³
Eosinophil				
Symptomatic cases	310/mm ³	30/mm ³	55/mm ³	40/mm ³
Asymptomatic cases	180/mm ³	120/mm ³	105/mm ³	50/mm ³

*WBC: White blood cell **PMNL: Polymorphonuclear leukocyte

symptomatic group. Additionally, thoracic tomography was performed in 44 of the symptomatic cases, and ground-glass opacities consistent with COVID-19 were found in 10 of them. Thoracic CT findings were normal in 31 cases, and the findings of 3 cases were non-specific.

Symptomatic patients were admitted to pandemic wards and were closely followed until PCR results became negative. Non-specific antibiotic therapy was initiated in these patients with suspected secondary bacterial infection. In addition, broad-spectrum antibiotic therapy and supportive treatments were added to two patients who were followed up in pediatric intensive care unit. All patients hospitalized in pediatric pandemic wards were discharged with full recovery. The patient with a history of prematurity died on the 5th day of her admission to the pediatric intensive care unit. Another patient with a history of SMA and chronic lung disease recovered from COVID-19.

Discussion

All over the world, the mortality of COVID-19 is much higher in adults than in children. It is still unclear why mortality and morbidity in children are so low compared to adults (6). Consistent with the literature, only one of the 197 cases followed up died, and 150 of all cases were asymptomatic. Although there was no statistically significant difference between the mean age of symptomatic and asymptomatic children, the mean age of symptomatic children was slightly higher. There was no significant change in WBC, neutrophil,

lymphocyte counts, and CRP levels of children with SARS-CoV-2 positivity.

Previously published studies in the pediatric age group, the number of boys was slightly higher than that of girls, but this difference was not statistically significant (4,7,8). No significant sex difference was also found in our cases.

It is known that COVID-19 can affect children of all age groups. In some studies, the median age of cases was determined between 6 and 11 years (4,7,9). More than 1.2 million SARS-CoV-2 positive children under 18 years of age have been identified in the USA. Children between the ages of 14-17 were 38.3% of all cases, while the proportion of children aged 0-4 was 17.4% (10). Most of our cases with SARS-CoV-2 PCR positivity were over 10 years old.

Children with positive COVID-19 RT-PCR tests usually have a history of household and/or social environmental contact. This clearly shows the person-to-person transmission (4,11). All of our patients had a history of contact with a COVID-19 patients.

Clinical symptoms in children are usually mild, the most common symptoms have been reported as cough, fever and runny nose. Fever and cough are generally reported as the most common symptom (8,12,13). While the most common symptom in our cases was cough, the second was fever. Other symptoms, such as myalgia, headache, and nausea were not common in our pediatric cases.

Laboratory findings of children are generally normal range. However, leukopenia and lymphopenia, have been reported in most adult patients (7-9,13,14). The mean WBC, PMNL, and lymphocyte counts

were found in the normal range. No statistically significant difference was found WBC, PMNL and lymphocyte counts between of these symptomatic and asymptomatic patients. However, our two patients who required intensive care had lymphopenia and their inflammatory markers were very high in accordance with the literature.

The CT manifestations of COVID-19 in children are diverse. It also varies according to the clinical condition and severity of the disease (8,9,11). In previous studies, thoracic CT findings in children were generally reported as normal (8). While 31 of our 44 patients with thorax CT, had no findings, 10 patients had ground-glass densities compatible with COVID-19. Therefore, the role of toracic CT use in the diagnosis of COVID-19 in children is not clear yet.

According to WHO, 2.5% of pediatric cases in China showed signs of severe and critical illness (15). This rate was found to be 5-6% in other studies (6,8). It has been reported that the disease has a more severe course under one year old compared to other age groups (8). The rate of severe illness had reported as being lowest in the aged 16 years or older (6). Two of our patients needed intensive care. A patient who died due to severe illness was a 5-month-old baby with a history of prematurity.

Study Limitations

The limitation of our study is that it contains the small number of patients and single-center data. Another limitation is that it has a retrospective character. Future studies are needed with a multicenter and larger number of patients.

Conclusions

COVID-19 affects of all age-groups in children. The common presenting symptom with COVID-19 is nonspecific. The number of children with severe illness is very limited. There is no significant difference in laboratory parameters such as leukocyte and lymphocyte counts. C-reactive protein levels are also normal of children presenting with symptoms when compared with asymptomatic patients.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the local ethics committee (176/03.09.2020).

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. She J, Liu L, Liu W. COVID-19 epidemic: Disease characteristics in children. *J Med Virol* 2020;92:747-54.
2. Carlotti ACP, Carvalho WB, Johnston C, Rodriguez IS, Delgado AF. COVID-19 Diagnostic and Management Protocol for Pediatric Patients. *Clinics* 2020;17;75:e1894.
3. Henry BM, Lippi G, Plebani M. Laboratory abnormalities in children with novel coronavirus disease 2019. *Clin Chem Lab Med* 2020; 25:58:1135-8
4. Fang F, Lu X. Facing the pandemic of 2019 novel coronavirus infections: the pediatric perspectives. *Zhonghua Er Ke Za Zhi* 2020;58(0):E001.
5. Henry BM, Benoit SW, de Oliveira MHS, Hsieh WC, Benoit J, Ballout RA, et al. Laboratory abnormalities in children with mild and severe coronavirus Disease 2019 (COVID-19): A pooled analysis and review. *Clin Biochem* 2020;81:1-8.
6. Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, et al. Epidemiology of COVID-19 Among Children in China. *Pediatrics* 2020;145:e20200702.
7. Lu X, Zhang L, Du H, Zhang J, Li YY, Qu J, et al. SARS-CoV-2 Infection in Children. *N Engl J Med* 2020;382:1663-5.
8. Cui X, Zhao Z, Zhang T, Guo W, Guo W, Zheng J, A systematic review and meta-analysis of children with coronavirus disease 2019 (COVID-19). *J Med Virol* 2021;93:1057-69.
9. Zachariah P, Johnson CL, Halabi KC, Ahn D, Sen AI, Fischer A, et al. Epidemiology, Clinical Features, and Disease Severity in Patients With Coronavirus Disease 2019 (COVID-19) in a Children's Hospital in New York City, New York. *JAMA Pediatr* 2020;174:e202430.
10. Leidman E, Duca LM, Omura JD, Proia K, W. Stephens J, Sauber-Schatz EK, et al. COVID-19 Trends Among Persons Aged 0-24 years-United States, March 1-December 12,2020, *MMWR Morb Mortal Wkly Rep* 2021;70:88-94.
11. The Society of Pediatrics, Chinese Medical Association; The Editorial Board, Chinese Journal of Pediatrics. Recommendation for the diagnosis, prevention and control of the 2019 novel coronavirus infection in children (first interim edition). *Zhonghua Er Ke Za Zhi* 2020;58:169-74.
12. Wu Q, Xing Y, Shi L, Li W, Gao Y, Pan S, et al. Coinfection and Other Clinical Characteristics of COVID-19 in Children. *Pediatrics* 2020;146:e20200961
13. Ke Bai, Wenjun Liu, Chengjun Liu, Yueqiang Fu, Jun Hu, Yanran Qin, et al. Clinical Analysis of 25 COVID-19 Infections in Children. *Pediatr Infect Dis J* 2020;39:e100-e103.
14. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus- Infected Pneumonia in Wuhan, China. *JAMA* 2020;323:1061-9.
15. WHO Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). World Health Organization. Available at [https://www.who.int/publications-detail/report-of-the-who-china-joint-mission-on-coronavirus-disease-2019-\(covid-19\)](https://www.who.int/publications-detail/report-of-the-who-china-joint-mission-on-coronavirus-disease-2019-(covid-19)). Access date; 2020, Feb 28.