Comparison of Clinic and Demographic Characteristics of Children with Laboratory-Confirmed and Suspected COVID-19 who Admitted to Pediatric Emergency Clinic

Çocuk Acil Kliniğine Başvuran Laboratuvarca Doğrulanmış ve Şüpheli COVID-19 Çocukların Klinik ve Demografik Özelliklerinin Karşılaştırılması

Fatma DURAK[1] , Gulçin BOZLU[1] , Asuman AKAR[2] , Merve HAVAN[3] , Berfin ÖZGÖKÇE ÖZMEN[2] , Necdet KUYUCU[2]

ABSTRACT

Aim: To determine the frequency of COVID-19 infection in children and to compare the parameters of laboratory-confirmed and suspected cases.

Material and Methods: Medical records collected with a prospective design of 1300 pediatric patients who applied to COVID-19 triage of pediatric emergency service. Clinic and demographic characteristics of children with laboratory-confirmed and suspected COVID-19 were compared. Nasopharyngeal swab sample was taken from all pediatric patients in accordance with the possible case definition determined by the national Ministry of Health.

Results: The COVID-19 test was found positive in 94 (7.2%) children. Of those, 34.5% children had a history of contact, and 31.9% of all cases were asymptomatic. The mean age of children who were positive for COVID-19 was higher than those who were negative (p <0.001). COVID-19 positive cases had a higher domestic contact history than those who were negative (79.8% and 31%, respectively, p <0.001). The mean WBC, platelet, neutrophil, RDW, procalcitonin, CRP, LDH and total bilirubin values of COVID-19 positive patients were found as significantly lower than COVID-19 negative patients (p <0.05).

Conclusion: We found that there was a statistically significant difference between COVID-19 positive and negative patients in terms of age and laboratory parameters. We have shown that most patients with positive COVID-19 test are asymptomatic, have a high rate of contact history and require hospitalization.

Keywords: COVID-19, children, emergency, clinical course, laboratory, transmission

ÖZ

Amaç: Çocuklarda COVID-19 enfeksiyonu sıklığını belirlemek ve laboratuvarca doğrulanmış ve şüpheli vakaların parametrelerini karşılaştırmak.

Gereç ve Yöntemler: Çocuk acil servisinin COVID-19 triyajına başvuran 1300 pediatrik hastadan prospektif bir tasarımla toplanan tıbbi kayıtlar alındı. Laboratuvarca doğrulanmış ve COVID-19 şüphesi olan çocukların klinik ve demografik özellikleri karşılaştırıldı. Sağlık Bakanlığı tarafından belirlenen olası vaka tanımına göre tüm pediatrik hastalardan nazofaringeal sürüntü örneği alındı.

Bulgular: 94 (%7,2) çocukta COVID-19 testi pozitif bulundu. Bunların %34,5'inde çocukların temas öyküsü vardı ve tüm vakaların %31,9'u asemptomatiktir. COVID-19 pozitif olan çocukların yaş ortalaması negatif olanlardan daha yüksekti (p <0.001). COVID-19 pozitif vakaların, negatif olanlara göre daha yüksek ev içi temas öyküsü vardı (sırasıyla %79,8 ve %31, p <0,001). COVID 19 pozitif çocuklarda ortalama beyaz kan hücresi, trombosit, nötrofil, kırmızı kan hücresi dağılım genişliği, prokalsitonin, C-reaktif protein, laktat dehidrogenaz ve total bilirubin değerleri istatistiksel olarak anlamlıydı (p <0.05).

Sonuç: Çocuklarda COVID-19 enfeksiyonu oranı nispeten düşüktür ve COVID-19 ile ilişkili bildirilen vaka serileri de pediatrik grupta erişkinlere göre daha azdır. COVID-19'un çocuklarda epidemiyolojik özellikleri ve bulaşma yolları ile ilgili önemli sayıda vaka içeren çalışmalardan biri olduğunu ve bundan sonraki çalışmalara ışık tutacağını düşünüyoruz.

Anahtar Kelimeler: COVID-19, çocuklar, acil durum, klinik kursu, laboratuvar, bulaşma

Introduction

Coronavirus disease-2019 (COVID-19), which started in Wuhan city of China in December 2019, is a new infectious disease which caused a pandemic worldwide and can lead to acute severe respiratory disease and death (1). Firstly, a previously unknown virus was detected in the etiology of a group of patients with pneumonia in Wuhan, Chinain December 2019. As a result of the investigations, this virus was defined as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from the beta-coronavirus family, and it was reported to be the cause of coronavirus disease-2019 (COVID-19) (2). The spectrum of disease caused by coronavirus in humans can range from the common cold to severe acute respiratory failure syndrome and even multiple organ failure. It can be asymptomatic in humans and animals, and may cause clinical pictures with various degrees of respiratory, enteric, hepatic, nephrotic, and neurological involvement. Symptoms and severity of the disease are milder in children compared to adults and the case mortality rate is found to be low in children (3).

As far as we know, the first pediatric case was a 10-year-old boy living in Shenzhen, China, diagnosed on January 20, 2020 (4). In a retrospective study in which 366 pediatric patients (≤16 years old) hospitalized due to respiratory tract infections were evaluated, it was reported that COVID-19 started epidemically when it was detected in 6 children (1.6%) (5). It has been observed that children infected with SARS-CoV-2 are often affected asymptomatically (6). Despite its worldwide spread, the epidemiological and clinical patterns of COVID-19 remain largely uncertain, especially among children. The rate of COVID-19 infection in children is relatively low, and the reported case series associated with COVID-19 are also less in pediatric group than in adults (7). In this study, we aimed to determine the frequency of COVID-19 infection in children in the first three months of the pandemic, its effects, epidemiological, clinical and diagnostic features. In addition, the parameters of laboratory-confirmed and suspected pediatric cases were compared.

Material and Methods

This study was conducted after obtaining approvals from the Ministry of Health, Republic of Türkiye and Mersin University Clinical Research Ethics Committee (2020-05-29T14-57-24). This retrospective study included data collected with a prospective design of 1300 pediatric patients aged 0-18 years who applied to COVID-19 Triage Unit of Mersin University Faculty of Medicine Pediatric Emergency Service and Pediatric Coronavirus Outpatient Clinic of Mersin City Training and Research Hospital.   In this study, nasopharyngeal swab sample was taken from all pediatric patients in accordance with the possible case definition determined by the Ministry of Health (8). SARS-CoV-2 was measured by polymerase chain reaction (PCR) in all cases. The Ministry of Health's nasopharyngeal swab collection criteria:

1. Applying to the hospital with at least one of the signs and symptoms of fever, cough, shortness of breath, sore throat, headache, muscle aches, loss of taste and smell or diarrhea during COVID-19 pandemic,

2. This clinical picture cannot be explained by another disease, and
3. Having a close contact history of contacting a patient who is in a high-risk area for the disease or who has been diagnosed with COVID-19 within 14 days before the onset of symptoms.

Complete blood count including white blood cell (WBC), hemoglobin (Hb), mean platelet volume (MPV), red blood cell distribution width (RDW), C reactive protein (CRP), ferritin, creatine kinase (CK), lactate dehydrogenase(LDH), D-dimer, troponin, urea, creatinine, sodium, potassium, chlorine, aspartate transaminase (AST), alanine transaminase (ALT), total and direct bilirubin, total protein, and albumin values were studied among all hospitalized patients and selected outpatients according to their clinic. Posterior-anterior chest X-ray was performed in all patients with fever and respiratory symptoms, and computed tomography (CT) was performed as further examination in all patients with clinical findings suggestive of COVID-19 or significant respiratory distress.

Statistical Analysis

Normality controls of continuous measurements were tested by Shapiro Wilk test. Student t test was used for comparisons of continuous measurements. Mean and standard deviation values were given as descriptive statistics. Pearson chi-square and Likelihood Ratio chi-square tests were used for the differences between categorical variables. Number and percentage values were given as descriptive statistics. Statistical significance was considered as $p < 0.05$.

Results

The COVID-19 test was found positive in 94 (7.2%) of the 1300 cases fulfilling the possible case definition, and the test was serologically negative in the remaining 1206 (92.8%) cases. The mean age of all individuals in the study was calculated as 86.9 ±66.7 months. The demographic characteristics of the patients are summarized in Table 1. Of those, 34.5% patients had a history of contact, and 31.9% of all cases were asymptomatic. 27.2% of the patients were hospitalized and followed up and treated.

The characteristics of laboratory-confirmed and suspected cases are given in Table 2. The mean age of those who were positive for COVID-19 was higher than those who were negative (109.2 ±63.9 months and 85.2 ±66.6 months, respectively, $p < 0.001$). There was no significant difference in gender between COVID-19 positive and negative patients (p = 0.372).71.3% of COVID-19 positive patients were asymptomatic cases with history of contact. Those with a positive diagnosis of COVID-19 had a higher domestic contact history than those who were negative (79.8% and 31%, respectively, $p < 0.001$). 89.4% of COVID-19 positive cases were treated by hospitalization. Treatment was required in only one of those cases by hospitalization in the pediatric intensive care unit. Of the patients with COVID-19 positive, infiltration was detected in 10.6% and 7.4% in chest X-ray and thorax CT respectively. Laboratory findings of the patients are shown in Table 3.

Variables		n	(%)
PCR COVID-19	Positive	94	7.2
	Negative	1206	92.8
Age group	0-60 months (0-5 years)	593	45.6
	61-143 months (6-11 years)	392	30.2
	≥144 months (≥12 years)	315	24.2
Gender	Male	735	56.5
	Female	565	43.5
Clinical classifications	Asymptomatic with contact history	415	31.9
	Acute upper respiratory tract infection	674	51.8
	Acute lower respiratory tract infection	165	12.7
	Acute gastroenteritis	43	3.3
	Respiratory failure	3	0.2
Hospitalization status	Home isolation	946	72.8
	Hospitalization	312	24.0
	Pediatric intensive care unit	42	3.2
Contact history	Yes	449	34.5
	No	851	65.5
Clinical symptoms	Asymptomatic	415	31.9
	Fever	275	21.2
	Cough	126	9.7
	Fever + cough	219	16.8
	Respiratory problem	52	4.0
	Fever + cough + diarrhea	49	3.8
	Fever + sore throat	135	10.4
	Cough + dyspnea	30	2.3
Comorbidity	Yes	44	3.4
	No	1255	96.6
Chest X-ray	Normal	938	72.2
	Infiltration	130	10.0
Thorax computed tomography	Normal	272	20.9
	Infiltration	74	5.7

Table 1: The characteristics of children

Mean values of CRP, troponin, D-dimer and RDW of all patients were above the normal reference range. The mean Hb and total protein values of COVID-19 positive patients were found as significantly higher than COVID-19 negative patients ($p < 0.05$). The mean WBC, platelet, neutrophil, RDW, procalcitonin, CRP, LDH and total bilirubin values of COVID-19 positive patients were found as significantly lower than COVID-19 negative patients ($p < 0.05$).

Discussion

Our study is one of the studies involving a considerable number of cases conducted on the epidemiological characteristics and transmission routes of COVID-19 in children. However, few data are available on epidemiological features and transmission patterns in children with COVID-19 and there are a limited number of cases in the literature. We found 94 (7.2%) laboratory-confirmed cases and 1296 (92.8%) suspected cases. Most of the children included in our study had a mild course and no patient died. In the study including 2135 pediatric patients reported by Dong et al., only a 14-year boy from Hubei province died and the severe or critically ill rate was 5.8% (9). We had only 1 critical patient who was positive for COVID-19 and required follow-up in intensive care, and completely recovered after treatment. Our study also supports the findings published in the literature to date and shows that

the clinical course of COVID-19 in children may be less severe. It has been demonstrated that children have a milder form of COVID-19 compared to adults.[3] Among the reasons, the immune characteristics of the host are important. The host cell surface receptor for SARS-CoV is angiotensin enzyme 2 (ACE2). It is estimated that the maturity and function of ACE2 is lower in children, so children are less susceptible to COVID-19 (10,11). The virus can be transmitted to all ages, including newborns and young children. The youngest COVID-19 case in the literature is a 36-hour newborn (12).

We found that there were no COVID 19 positive neonatal patients among our cases. In a large case series, 728 (34.1%) children were laboratory-confirmed COVID-19 patients with a median age of 7 years (9).

		Suspected (n=1206)		Confirmed (n=94)		p
		n	(%)	n	(%)	
Age group	0-60 months (0-5 years) (n=593)	566	46.9	27	28.7	
	61-143 months (6-11 years) (n=392)	358	29.7	34	36.2	0.002
	≥144 months (≥12 years) (n=315)	282	23.4	33	35.1	
Gender	Male (n=735)	686	56.9	49	52.1	0.372
	Female (n=565)	520	43.1	45	47.9	
Clinical classifications	Asymptomatic with contact history (n=415)	348	28.9	67	71.3	
	Acute upper respiratory tract infection (n=674)	654	54.2	20	21.3	
	Acute lower respiratory tract infection (n=165)	158	13.1	7	7.4	<0.001
	Acute gastroenteritis (n=43)	43	3.6	0	0	
	Respiratory failure (n=3)	3	0.2	0	0	
Hospitalization status	Home isolation (n=946)	936	77.6	10	10.6	
	Hospitalization (n=312)	229	19	83	88.3	<0.001
	Pediatric intensive care unit (n=42)	41	3.4	1	1.1	
Contact history	Yes (n=449)	374	31	75	79.8	<0.001
	No (n=851)	832	69	19	20.2	
Clinical symptoms	Asymptomatic (n=414)	348	28.9	66	70.2	
	Fever (n=275)	268	22.2	7	7.4	
	Cough (n=126)	124	10.3	2	2.1	
	Fever + cough (n=219)	212	17.6	7	7.4	<0.001
	Respiratory problem (n=52)	52	4.3	0	0	
	Fever + cough + diarrhea (n=49)	49	4.1	0	0	
	Fever + sore throat (n=135)	127	10.5	8	8.5	
	Cough + dyspnea (n=30)	26	2.2	4	4.3	
Comorbidity	Yes (n=44)	43	3.6	1	1.1	
	No (n=1255)	1162	96.4	93	98.9	
	Normal (n=938)	859	71.2	79	84	0.319
	Infiltration (n=130)	120	10	10	10.6	
	Normal (n=272)	235	19.5	37	39.4	
	Infiltration (n=74)	67	5.6	7	7.4	

Table 2: The characteristics of laboratory-confirmed and suspected cases

	PCR COVID-19 (-) (n=1206)	PCR COVID-19 (+) (n=94)	p
WBC(x10³/µL)	10.27 ± 5.56	6.47 ± 3.32	<0.001
Hb (g/L)	11.77 ± 2	12.27 ± 1.57	0.013
Platelet (x10³/µL)	320.27 ± 130.03	290.03 ± 95.35	0.015
Lymphocyte (x10³/µL)	3.11 ± 2.46	2.81 ± 1.70	0.174
Neutrophil (x10³/µL)	5.51 ± 4.26	3.28 ± 1.88	<0.001
MPV(fL)	9.76 ± 2.67	9.42 ± 2.10	0.212
RDW (%)	13.98 ± 2.02	13.35 ± 1.28	<0.001
Procalcitonin (ng/mL)	0.61 ± 1.89	0.23 ± 0.61	0.002
CRP (mg/L)	10.78 ± 34.15	2.83 ± 16.41	0.001
CK	172.47 ± 333.24	148.89 ± 147.55	0.547
LDH (U/L)	314.13 ± 125.27	262.60 ± 82.10	<0.001
D-dimer (ng/mL)	1.075 ± 3.287	0.854 ± 2.818	0.594
Troponin	0.544 ± 2.343	0.402 ± 1.184	0.612
BUN (mg/dL)	23.14 ± 10.42	23.50 ± 5.54	0.647
Creatinine (mg/dL)	0.42 ± 1.71	0.40 ± 0.18	0.903
Na (mEq/L)	136.32 ± 9.19	137.18 ± 13.63	0.476
K (mEq/L)	4.216 ± 0.602	4.186 ± 0.392	0.555
Cl (mEq/L)	103 ± 6.12	103.27 ± 3.65	0.838
AST (U/L)	41.52 ± 51.97	31.54 ± 14.32	0,097
ALT (U/L)	24.53 ± 37.74	18.72 ± 9.37	0.183
TBIL (mg/dL)	0.619 ± 0.617	0.307 ± 0.213	0.042
DBIL (mg/dL)	0.131 ± 0.129	0.072 ± 0.051	0.077
Total protein (g/dL)	6.36 ± 0.74	6.65 ± 0.58	0.035
Albumin (g/dL)	4.35 ± 0.44	4.46 ± 0.35	0.179

Table 3: Laboratory findings of the patients

WBC=white blood cell, Hb=hemoglobin, MPV=mean platelet volume, RDW= red blood cell distribution width, CRP=C-reactive protein, CK=creatine kinase, LDH=lactate dehydrogenase, BUN=blood urea nitrogen, Na=sodium, K=potassium, Cl=chlorine, AST=aspartate transaminase, ALT=alanine transaminase, TBIL=total bilirubin, DBIL=direkt bilirubin

Of those, 56.6% were male. Lu et al. reported that 171 (12.3%) children were confirmed to have SARS-CoV-2 infection and the median age of the infected children was 6.7 years and 60.8% of them were male (13). We found that 52.1% of COVID-19 positive children were male and our finding was consistent with the literature.

The proportions of severe and critical disease at the time of diagnosis were reported as 10.7%, 7.3%, 4.2%, 4.1%, and 3% for age groups <1, 1-5, 6-10, 11-15 and >15 years, respectively (9). In that study, the prevalence of severe disease was higher in very young children, particularly infants. The mean age of all individuals was 86.9 ±66.7 months in our study, and the mean age of those who were positive for COVID-19 was higher. We found statistically significant difference between COVID-19 positive and negative patients in terms of age.

The disease is mainly transmitted by droplets (7). It can also be transmitted through contact with objects contaminated with respiratory droplets containing the coronavirus, such as toys, door handles. Due to its human-to-human transmission feature, the source in COVID-19 is symptomatic or asymptomatic COVID-19 positive people. Since viruses can be detected in respiratory tract secretions of asymptomatic people, these people can also be contagious. Domestic contact is responsible for most of the contamination in children (14). We showed that 79.8% of COVID-19 positive children had a history of domestic contact and we found a statistically significant difference between the contact history of the negative and positive groups. Similar to the literature, parents or first-degree relatives living in the same house were found to play a role in the transmission of COVID-19 positive children (4). Common symptoms of the

infection are respiratory symptoms, fever, cough, and dyspnea. Headache, sore throat, runny nose, muscle and joint pain, extreme weakness, emerging loss of sense of smell and taste, and gastrointestinal symptoms such as diarrhea, nausea, vomiting and abdominal pain can also be seen. Infected children can also be asymptomatic. However, we found that 71.3% of COVID-19 positive children were asymptomatic cases with history of contact.

In severe cases, pneumonia, severe acute respiratory infection, kidney failure, and even death may occur (14). Most severe cases in children are related to those with significant comorbidities such as heart disease and immunosuppression. Dong et al. reported that more than 90% of the affected children had asymptomatic or mild to moderate disease (9). Of those, 12.9% of the cases were seropositive asymptomatic patients. The findings seen in the rest of patients were reported atypical symptoms seen in respiratory diseases such as fever, cough, sore throat, sneezing, muscle pain and fatigue, wheezing. Gastrointestinal symptoms along with fever may be the only form of clinical presentation in children (15).

In another study in which children with 171 suspects and 14 confirmed diseases followed in Wuhan Children's Hospital were evaluated, the most common symptoms were cough (48.5%), pharyngeal erythema (46.2%), fever ≥37.5°C (41.5%), diarrhea (8.8%), fatigue (7.6%), runny nose (7.6%) and vomiting (6.4%) (13). Four of 171 children (2.3%) had oxygen saturation lower than 92%. We found that the most common presenting symptom in all suspected cases was fever and the second most common symptom was cough. In addition, 4% of all cases had respiratory problems. Five (5.31%) of these patients had respiratory distress and only one patient needed intensive care. In our series, 3.4% (n=44) of all patients had a history of underlying chronic disease. All three patients with a diagnosis of chronic renal failure, spinal muscular atrophy and cerebral palsy were COVID-19 positive.

To date, a limited number of studies have shown that inflammatory markers are slightly elevated in children with COVID-19 (16,17). It has been shown the results from 12 articles on 66 children and found normal WBC (69.6%). However, IL-6 and procalcitonin levels were increased only in cases of unfavorable progression. Henry et al. reported that consistent pattern of laboratory derangements has yet to be observed in children with confirmed COVID-19 (17). We found that the levels of Hb and total protein were significantly higher in COVID-19 positive children and the levels of WBC, platelet, neutrophil, RDW, procalcitonin, CRP, LDH and total bilirubin were significantly lower in COVID-19 negative children.

In the series of Lu et al., ground-glass opacity was observed on chest radiography in one third of 171 pediatric patients diagnosed with COVID-19 (13). Local shading was found in 18.7% of the cases and bilateral irregular shading in 12.3% of the cases. They reported that 64.9% of COVID-19 positive patients were diagnosed with clinical pneumonia. There were no symptoms of infection or radiological signs of pneumonia in 15.8% of children. In our study, 82.2% of the patients had chest X-ray, and we observed that 10% of them had radiologically opacity and unilateral or bilateral patch-like infiltrations. We determined that 84% of the children

diagnosed with COVID-19 had normal chest X-ray and 10.6% had infiltration. CT was performed as a further examination in all patients who had clinical findings suggestive of COVID-19 or applied with significant respiratory distress, and consolidations (26.6%). Of those, 5.7% had infiltrations. Thorax CT was normal in 39.4% of those who were positive for COVID-19, and infiltration was observed in 7.4%.

Limitations

The limitation of our study is retrospective design. On the other hand, due to COVID-19, all data are important, because they are recorded in a prospective design in accordance with the pandemic criteria of health policies. The strength of our study is that we analyzed the data of an acceptably large number of pediatric cases with COVID-19 from the series published in the literature.

Conclusion

In conclusion, the pandemic is progressing rapidly, and its ultimate extent and future implications are still uncertain. There are a limited number of studies on the characteristics of COVID-19 in the pediatric population. We showed that statistically significant difference between COVID-19 positive and negative patients in terms of age and most of COVID-19 positive patients were asymptomatic cases with history of contact. In order to better understand the course of COVID-19 in children, more detailed studies, especially showing clinical results and including larger series, are needed. We believe that this is one of the studies involving a significant number of cases on the epidemiological characteristics and transmission routes of COVID-19 in children and will shed light on future studies.

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References

1. Zhu NA, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med. 2020; 382(8): 727–733.

2. World Health Organization. Novel coronavirus (2019-nCoV). Situation report-22 [Internet]. Geneva (Switzerland): World Health Organization; 2020 [cited 2020 Mar 12]. Available from: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200211-sitrep-22-ncov.

3. Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. Acta Paediatr. 2020 Apr 14: doi: 10.1111/apa.15270.

4. Chan JF, Yuan S, Kok KH, To KKW, Chu H, Yang J, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet. 2020;395(10223): 514-523.

5. Liu W, Zhang Q, Chen J, Xiang R, Song H, Shu S, et al. Detection of COVID-19 in children in early January 2020 in Wuhan, China. N Engl J Med. 2020;382(14):1370-1371.

6. Choi SH, Kim HW, Kang JM, Kim DH, Cho EY. Epidemiology and clinical features of coronavirus disease 2019 in children. Clin Exp Pediatr. 2020;63(4):125-132.

7. Zimmermann P, Curtis N. Coronavirus infections in children including COVID-19: an overview of the epidemiology, clinical features, diagnosis, treatment and prevention options in children. Pediatr Infect Dis J. 2020;39(5):355-368.

8. Republic of Turkey Ministry COVID-19 Information Page. https://covid19.saglik.gov.tr/TR-66301/covid-19-rehberi.html.

9. 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(6):e20200702.

10. Lee PI, Hu YL, Chen PY, Huang YC, Hsueh PR. Are children less susceptible to COVID-19? J Microbiol Immunol Infect. 2020;53(3):371-372.

11. Mania A, Mazur-Melewska K, Lubarski K, Kuczma-Napierała J, Mazurek J, Jończyk-Potoczna K, et al. Wide spectrum of clinical picture of COVID-19 in children - from mild to severe disease. J Infect Public Health. 2021;14(3):374-379.

12. Wang S, Guo L, Chen L, Liu W, Cao Y, Zhang J, et al. A case report of neonatal COVID-19 infection in China. Clin Infect Dis. 2020 Jul 28;71(15):853-857.

13. Lu X, Zhang L, Du H, Zhang J, Li YY, Qu J, et al. SARS-CoV-2 infection in children. N Engl J Med. 23;382(17):1663-1665.

14. Cao Q, Chen YC, Chen CL, Chiu CH. SARS-CoV-2 infection in children: transmission dynamics and clinical characteristics. J Formos Med Assoc 2020;119:670-673.

15. Martins MM, Prata-Barbosa A, da Cunha AJLA. Update on SARS-CoV-2 infection in children. Paediatr Int Child Health. 2021;41(1):56-64.

16. Bozlu G, Ozgokce Ozmen B, Akca M, Durak F, Kuyucu N. The Role of Immature Granulocytes Percentage to Predict Severe COVID-19 in Children. Kuwait Medical Journal, (In press).

17. Henry BM, de Oliveira MHS, Benoit S, Plebani M, Lippi G. Laboratory abnormalities in children with novel coronavirus disease 2019. Clin Chem Lab Med. 2020;58(7):1135-1138.