



Evaluation of Asymptomatic Covid Infection in Children with Pediatric Hemato-Oncologic Disease

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Dear Editor;

The COVID-19 pandemic considerably affects the diagnosis and treatment of pediatric hemato-oncologic patients. For this reason, during the pandemic period, the treatment of patients was mostly tried to be given without hospitalization, dose modifications were made, and they were followed up by phone. COVID-19 infection was excluded by performing a COVID-19 PCR test before receiving treatment and when there is evidence of infection [1, 2]. The present study aimed to examine the incidence of asymptomatic COVID-19 by performing antibody assay in patients who were under follow-up for pediatric hemato-oncologic patients.

This study is a cross-sectional descriptive study. The study included patients aged 2 to 20 years, who were under follow-up for pediatric hemato-oncologic disease between 01.02.2021 and 01.06.2021 in the pediatric

hematology-oncology department of Karadeniz Technical University (KTU) Faculty of Medicine. Age, sex, diagnosis, disease state (receiving treatment, completed treatment) of the patients were recorded. The COVID-19 PCR results, family history of COVID-19, and household size were questioned. Patients were compared according to whether they were anti-SARS-CoV-2 positive or negative. In addition, the cases with anti-SARS-CoV-2 positivity were compared between the groups according to their receiving treatment and completed treatment. Assays with an Anti-SARS-CoV-2 spike antibody level of <0.80 U/ml and ≥ 0.80 U/ml were considered non-reactive and reactive, respectively.

Of 107 study patients, 24 (22.4%) were anti-SARS-CoV-2 positive, and 15 (14.1%) of these cases were male. The mean age of the patients was 8.20 ± 5.28 years. The anti-SARS-CoV-2 total antibodies were detected in 20 of COVID-19 PCR-negative patients (Table 1; Comparison of patients according to the presence of anti-SARS-CoV-2 total antibodies). The anti-SARS-CoV-2 total antibody test was positive in 18 receiving treatment, 6 patients who completed treatment. The most common symptoms presented by PCR-negative COVID-19 patients were cough and fever. We had four PCR-positive COVID-19 patients, all of whom were in the treatment group. One of our patients who was followed up for acute lymphoblastic leukemia (ALL) had a severe COVID-19 infection and was treated as an inpatient. During the last one-year follow-up of our patients who were positive for antibodies, two patients developed acute myeloid leukemia (AML) relapse, three patients died, 13 patients have been on follow-up care, two patients have been continuing their treatment, and four patients have been followed up in another center (Table 2 presents the list of antibody-positive patients).

The COVID-19 pandemic has infected millions of people and caused hundreds of thousands of deaths worldwide. The control of the pandemic could only be achieved after the administration of the developed vaccines. During our study period, vaccination was started for healthcare workers in

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Table 1 Comparison of patients according to the presence of anti-SARS-CoV-2 total antibodies

		anti-SARS CoV-2		
		Negative n = 83(%)	Positive n = 24(%)	p
Age (year)		10.12 ± 4.74	8.21 ± 5.28	0.089
Gender	Female	34 (41%)	9 (37.5%)	0.945
	Male	49 (59%)	15 (62.5%)	
COVID-19 PCR	Negative	83 (100%)	20 (83.3%)	0.002
	Positive	0 (0%)	4 (16.7%)	
Cancer type	Leukemia	49 (59.1%)	14 (58.3%)	
	Lymphoma	17 (20.5%)	3 (12.5%)	
	Solid Tumors	9 (10.8%)	3 (12.5.0%)	
	Brain Tumors	8 (9.6%)	2 (8.3%)	
	Aplastic Anemia	0 (0%)	2 (8.3%)	
Treatment	Receiving Treatment	58 (70%)	18 (75%)	
	Completed Treatment	25 (30%)	6 (25%)	
Intrafamilial COVID-19	No	80 (96.4%)	16(66.7%)	< 0.001
	Yes	3 (3.6%)	8(33.3%)	
Household size	< 5	43 (51.8%)	8(33.3%)	0.173
	> 5	40 (48.2%)	16(66.7%)	

our country, but families were not vaccinated yet [3]. The present study identified leukemia as the type of cancer with the most common positivity for anti-SARS-CoV-2 total antibodies, which was detected in 22% of these patients. In addition, the positivity for anti-SARS-CoV-2 total antibodies was more common in male patients, with a rate of 62.5%. There were 19 patients (17.7%) with no covid symptoms.

A meta-analysis evaluating 33 studies conducted until November 2020 and 226 pediatric cancer patients with COVID-19 found the type of cancer with the highest number of cases to be hematological cancer. The authors reported that patients who were male and receiving intensive therapy were more affected. In addition, 48% of the patients were asymptomatic or with mild symptoms, while 9.6% had a severe infection. The diagnosis of the patients was established by PCR testing in 80.2% and antibody assay in 13% [2].

Changes were observed in the count and morphology of blood cells due to the COVID-19 infection. The most common finding was lymphopenia. In addition, depending on the severity of the COVID-19 infection, other findings in neutrophils included dysplastic anomalies [4]. Dysplastic myelocytes and giant platelets were observed in the peripheral smear of our ALL patient, who had severe COVID-19 infection, and the findings remained unchanged at follow-up. The patient was diagnosed with AML approximately six months later. The coexistence of LBL and AML is also a rare condition, and the presence of antibody positivity in

this patient suggested a previous COVID-19 infection. Viral respiratory infections are the most common type of infection in children. As COVID-19 is highly transmissible, most children and adults will contract this virus during the pandemic. It is not possible to say that SARS-CoV-2 is an oncogenic virus based on available research. However, chronic inflammation and certain viral pathogens can promote oncogenesis. Therefore, we believe that long-term immunological and oncological studies are needed.

We believe that cancer patients who have COVID-19 infection, should be monitored closely for potential effects. There is a need for several randomized controlled studies regarding the effects of this virus on hemato-oncological patients.

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All procedures performed in studies involving human participants

Table 2 Presents the list of antibody-positive patients

Patient no:	Age (years)	Gender	Diagnosis	Treatment	COVID-19 PCR (Pandemi during)	anti-SARS CoV-2 (U/ml)	COVID-19 specific symptoms	Intrafamilial COVID-19 (time)	Hospitalization (Chemotherapy, neutropenic fever)	Patient Current Status
1	4	Male	ALL	Yes	Negative	1.68	No	No	Yes	Remission
2	11	Male	ALL	Yes	Negative	266.3	No	No	No	Another center
3	5	Male	ALL	Yes	Negative	130.9	No	No	Yes	Died
4	9	Female	ALL	Yes	Negative	4.26	No	No	Yes	Remission
5	5	Male	ALL	Yes	Negative	49.85	No	No	No	Receiving treatment
6	6	Female	ALL	Yes	Negative	1.22	No	No	Yes	Receiving treatment
7	11	Female	ALL	Yes	Positive	19	Fever, Cough, Dyspnea, vomiting (3 months ago)	No	Yes	AML relapse, Receiving treatment
8	18	Male	ALL	Yes	Positive	345.2	Cough (3 months ago)	Yes (3 months ago)	No	Remission
9	2	Male	AML	Yes	Negative	1362	Fever, diarrhea (9 months ago) Cough (1 months ago)	Yes (9 months ago)	Yes	Another center
10	2	Male	NHL	Yes	Negative	21.7	Cough, fever (4 months ago)	No	Yes	AML relapse HSCt, Remission
11	18	Female	NHL	Yes	Negative	248.0	No	Yes (5 months ago)	No	Remission
12	2	Male	Neuroblastoma	Yes	Positive	1121	No	No	Yes	Another center
13	2	Female	Wilms Tumor	Yes	Negative	86.15	No	Yes (3 months ago)	Yok	Remission
14	8	Female	Wilms Tumor	Yes	Negative	1.05	No	No	Yes	Died
15	10	Male	Brain Tumors	Yes	Positive	302.3	Cough (6 months ago)	Yes(6 months ago)	No	Remission
16	2	Male	Brain Tumors	Yes	Negative	37.47	No	No	Yes	Remission
17	7	Female	Aplastic Anemia	Yes	Negative	6.28	Fever(6 months ago)	No	Yes	Died
18	4	Female	Aplastic Anemia	Yes	Negative	18.7	No	No	Yes	Another center
19	10	Male	ALL	No	Negative	397.7	No	No	Yes	Remission
20	9	Male	ALL	No	Negative	2500	No	Yes (3 months ago)	No	Remission
21	13	Male	ALL	No	Negative	452.3	No	Yes (3 months ago)	No	Remission
22	13	Male	ALL	No	Negative	669.1	No	Yes (2 months ago)	No	Remission
23	15	Male	ALL	No	Negative	777.5	No	No	No	Remission
24	18	Female	NHL	No	Negative	562.2	No	Yes (3 months ago)	No	Remission

ALL: Acute Lymphoblastic leukemia, AML: Acute Myeloblastic Leukemia, NHL: Non Hodgkin Lymphoma, HSCt: hematopoietic stem cell transplantation

were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Karadeniz Technical University of the Medical School of A (No. 2021/45).

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