Original Investigation / *Özgün Araştırma*

DOI: 10.5578/ced.20240202 • *J Pediatr Inf 2024;18(2):e74-e81*

COVID-19 Effect in Pediatric Rheumatology Patients

Pediyatrik Romatoloji Hastalarında COVID-19 Etkisi

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Cite this article as: Limon T, Kaya Aksoy G, Akman S, Koyun M, Öngüt G, Mutlu D, et al. COVID-19 effect in pediatric rheumatology patients. J Pediatr Inf 2024;18(2):e74-e81.

Abstract

Objective: This study aimed to determine the seroprevalence of SARS-CoV-2 in pediatric patients with rheumatic disease during the COVID-19 pandemic and to evaluate the effects of medication used for rheumatic disease on seroprevalence.

Material and Methods: Between September 2020 and September 2021, 170 patients aged 2-18 years with a diagnosis of rheumatological disease and with a follow-up period of higher than six months were included in the study. Anti-SARS-CoV-2 antibodies against the S1 domain of the SARS-CoV-2 spike protein were investigated with a micro ELISA kit.

Results: Of the 170 patients, 92 (54.1%) were females, and the mean age was 12.16 ± 4.18 years. *MEFV* mutation was investigated in 131 of the patients. Of the patients, 14.7% were on steroids and 16.5% were on biologic agents. Anti-SARS-CoV-2 IgG antibody was positive in 40 (23.5%) of the patients. IgG seropositivity of the patients with and without *MEFV* mutation were similar (p= 0.991). IgG was positive in 25% of the patients with biologic agents and in 23.2% of those who did not (p= 0.505). Thirty-eight (22.4%) of the patients had close contact with an individual diagnosed with COVID-19. Thirty two (18.9%) patients underwent PCR testing for SARS-CoV-2. Of these 32 patients, 28.1% were positive for IgG. During the pandemic period, 19 (11.2%) had a new symptom/sign of their disease. The rate of patients with a new symptom/sign was higher in the seropositive group than in the seronegative group (20.0% vs. 8.5%, p= 0.046).

Conclusion: We found that SARS-CoV-2 seroprevalence was 23.5% in children with a diagnosis of rheumatic disease. The distribution of the primary disease and medical therapies used were similar between seropositive and seronegative patients. We found that patients with a new symptom/sign of their disease was higher in the seropositive group than in the seronegative group.

Keywords: Pediatrics, COVID-19, pediatric rheumatology

Öz

Giriş: Bu çalışmanın amacı, COVID-19 pandemisi sırasında romatizmal hastalığı olan pediyatrik hastalarda SARS-CoV-2 seroprevalansını belirlemek, romatizmal hastalık için kullanılan ilaçların seroprevalans üzerine etkilerini değerlendirmektir.

Gereç ve Yöntemler: Eylül 2020-Eylül 2021 tarihleri arasında 2-18 yaş arası romatolojik hastalık tanılı ve takip süresi altı aydan fazla olan 170 hasta çalışmaya dahil edildi. SARS-CoV-2 spike proteininin S1 alanına karşı anti-SARS-CoV-2 antikorları, bir mikro ELISA kiti ile araştırıldı.

Bulgular: Yüz yetmiş hastanın 92 (%54.1)'si kadındı ve yaş ortalaması 12.16 ± 4.18 idi. *MEFV* mutasyonu hastaların 131'inde araştırıldı. Hastaların %14.7'si steroid, %16.5'i biyolojik ajan kullanmaktaydı. Anti-SARS-CoV-2 IgG antikoru hastaların 40 (%23.5)'ında pozitifti. *MEFV* mutasyonu olan ve olmayan hastaların IgG seropozitifliği benzerdi (p= 0.991). Biyolojik ajan kullanan hastaların %25'inde, kullanmayanların ise %23.2'sinde IgG pozitifti (p= 0.505). Hastaların 38 (%22.4)'inde COVID-19 tanılı bir kişi ile yakın temas öyküsü bulunmaktaydı. Otuz iki (%18.9) hastaya SARS-CoV-2 için PCR testi uygulandı. Bu 32 hastanın %28.1'inde IgG pozitifti. Pandemi döneminde 19 (%11.2)'unda hastalıklarının yeni bir semptomu/belirtisi vardı. Seropozitif grupta yeni semptom/belirtisi olan hasta oranı seronegatif gruptan daha yüksekti (%20.0'ye karşı %8.5, p= 0.046).

Sonuç: Romatizmal hastalık tanılı çocuklarda SARS-CoV-2 seroprevalansını %23.5 olarak bulunmuştur. Primer hastalığın dağılımı ve kullanılan medikal tedaviler seropozitif ve seronegatif hastalar arasında benzerdi. Hastalığının yeni semptomu/belirtisi olan hastaların seropozitif grupta seronegatif gruba göre daha yüksek olduğu belirlenmiştir.

Anahtar Kelimeler: Pediyatri, COVID-19, pediyatrik romatoloji

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Received: 08.04.2023 **Accepted:** 27.08.2023 **Available Online Date:** 26.06.2024

Introduction

COVID-19 is a respiratory disease caused by the new type of coronavirus that was first detected in Wuhan, China in December 2019 (1,2). A global emergency was declared by the World Health Organization (WHO) on January 30th, 2020, and the epidemic was described as a pandemic on March 11th, 2020. Children constituted the least affected group during the pandemic period (3,4). However, some patient groups at risk have been defined at childhood, similar to adults (5,6). Pediatric patients with a rheumatic disease [Familial Mediterranean Fever (FMF), juvenile idiopathic arthritis (JIA), systemic lupus erythematosis (SLE), etc…] are at increased risk for infectious diseases due to immune dysregulation arising from the disease itself, as well as immunoregulatory or immunosuppressive drugs used. However, there are studies reporting that COVID-19 disease also has a moderate course on children with rheumatic disease (7-9).

In a meta-analysis including 46 studies and examining the frequency of SARS-CoV-2 infection in individuals diagnosed with rheumatic disease, it has been reported that the frequency increased in 15, decreased in four, whereas there was no difference in 27 of the 46 studies (10). The same study has shown that the prevalence of SARS-CoV-2 infection increased 1.53 times (95% CI 1.16-2.01) in those with rheumatic disease than normal population (10). Walters et al. have screened 262 pediatric patients with rheumatic disease for the presence of previous infection with SARS-CoV-2 IgG and found that 35 of 262 patients (13%) were positive for SARS-CoV-2 IgG antibodies (9). In a study reported from our country, only two of 345 pediatric patients with a diagnosis of juvenile idiopathic arthritis have been found to have positive PCR for COVID-19 (11).

In the present study, we aimed to determine the seroprevalence of SARS-CoV-2 in pediatric patients with a diagnosis of rheumatic disease during the COVID-19 pandemic, to evaluate the effects of immunosuppressive drugs and biological agents used for rheumatic disease on seroprevalence, and to investigate the treatment changes applied together with the disruptions at the follow-up phase.

Materials and Methods

Between September 2020 and September 2021, 170 patients aged 2-18 years with a diagnosis of rheumatological disease, followed-up at the Pediatric Rheumatology Unit of Akdeniz University, were included in the study. Patients were selected using the "simple random sampling" method. Inclusion criteria for the study were as follows:

a) Follow-up period after diagnosis >six months,

b) Be compatible with medical treatments for the primary disease,

c) Not have been vaccinated against COVID-19.

Patients who had an additional chronic disease that would suppress the immune system in addition to their rheumatic disease, whose medical records could not be accessed, and who did not agree to sign the informed consent form were excluded from the study. Approval was obtained from the Clinical Research Ethics Committee of Akdeniz University (Date: 21.10.2020, Decision no: 799). All children included in the study and their families were informed, and signed voluntary consent forms were obtained. Our research was supported by Akdeniz University Scientific Research Project Fund (Project No: 5647).

Demographic fetaures of all patients, presence of comorbid diseases (such as obesity, hypertension, diabetes mellitus, chronic kidney disease, immunodeficiency), detailed data on primary rheumatic disease and treatments regimen (induction therapy, *MEFV* gene mutation and disease activity scores), symptoms of COVID-19 disease, and presence of contact with an individual with COVID-19 were recorded. Internationally accepted scoring systems were used for objective evaluation to determine disease activity score (12-15). Laboratory results were acquired retrospectively from the hospital registry system.

Patient compliance to mask, distance and social isolation rules during the pandemic period was evaluated with questionnaires. During the pandemic, information about the continuity of regulary follow-up, emergency room visits, difficulties in accessing medicines and postponements of medical treatments were recorded.

For the detection of SARS-CoV-2 antibodies, three mL of peripheral venous blood samples were taken from all patients into a serum tube. The samples were stored at -20°C until runtime. Anti-SARS-CoV-2 antibodies (IgG and IgA) against the S1 domain of the SARS-CoV-2 spike protein were investigated with a micro ELISA kit. The tests were carried out in accordance with the manufacturer's recommendations (Diagnostic Bioprobes Srl, Milan, Italy). Results were evaluated semi-quantitatively by calculating the reaction rate of the patient sample (<0.9 negative; ≥0.9 to <1.1 borderline; ≥1.1 positive).

Statistical Analysis

Descriptive statistics were presented as frequency, percentage, mean ± standard deviation, and median (interquartile range, IQR), where appropriate. The Shapiro Wilk test, histogram, and Q-Q graphics were used for evaluation of normality of distribution. The Fisher's exact test was used to analyze relationships between categorical variables. For the comparison of continuous variables, Student's t-test was used when variables showed normal distribution, whereas the Mann-Whitney U test was used in the contrary case. Statistical analyses were performed using SPSS version 21.0 package program for Windows. P values< 0.05 were accepted to show statistical significance.

Results

Demographic Characteristics of the Patients

Of the 170 patients, 92 (54.1%) were females, and mean age was 12.16 ± 4.18 years. Median age at diagnosis was 7.59 (IQR 4.33-11.30) years, and median follow-up time was 3.24 (IQR 1.87-5.99) years. The frequency of co-morbid diseases was as follows: Obesity 4.7% (n= 8), hypertension 9.4% (n= 16) and chronic kidney disease 5.3% (n= 9).

Distribution of patients according to primary rheumatologic diagnosis was as follows: 72 (42.4%) had FMF, 50 (29.4%) had JIA, 17 (10.0%) had SLE, 12 (7.1%) had Behçet's disease, 9 (5.3%) had vasculitis, 7 (4.1%) had rare autoinflammatory diseases, and scleroderma and dermatomyositis were found in one each (Figure 1). Of the 50 patients with JIA, 22 (12.9%) were oligoarticular, four were polyarticular (2.4%), 14 were systemic (8.2%), 8 were enthesitis-related arthritis (4.7%) and 2 were psoriatic arthritis (1.2%). *MEFV* mutation was investigated in 131 patients; 72 of whom with FMF, 22 with JIA, 12 with Behçet's disease, nine with vasculitis and the rest with other autoinflammatory diseases. Homozygous mutations were found in 16.5% (n= 28), heterozygous mutations in 25.3% (n= 43), and combined heterozygous mutations in 7.1% (n= 12), whereas 48 (28.2%) patients had no *MEFV* mutations. The most common mutations were *M694V* (n= 37), *E148Q* (n= 12) and *V726A* (n= 6).

Seventy-three (42.9%) patients in our study group received induction therapy at the time of diagnosis. Current treatments used in maintenance therapy were as follows: 101 patients (59.4%) received colchicine, 49 (28.8%) disease modifying anti-rheumatism drugs (DMARDs), 25 (14.7%) received steroid, and 28 (16.5%) received biological agents. The most commonly used DMARD was methotrexate (n= 48, 98%), only one patient (2%) used salazoprine. Median steroid dose used was 7.75 mg (minimum 2 mg-maximum 32 mg). The distribution of biological agents was as follows; etanercept six, adalimumab four, tocilizumab two, infliximab three, anakinra four, canakinumab eight, rituximab one.

Features of the COVID-19 Pandemic Period

Although 92.9% of the patients reported that they paid attention to isolation rules during the COVID-19 pandemic period, 40.6% had a travel history, 41.8% used public transportation, 8.8% used a hotel for holiday purposes, and 18.2% attended weddings or similar organizations. Thirty-eight (22.4%) of the patients had close contact with an individual diagnosed with COVID-19. Suspecting the presence of symptoms of COVID-19 infection, 32 (18.9%) patients underwent PCR testing for the detection of SARS-CoV-2; only 4 (2.4%) had positive PCR tests.

Clinical Course of COVID-19 in Seropositive Patients

The first patient was a 17-year-old girl with systemic lupus erythematosus (SLE) who was admitted to the hospital due to disease activation. SARS-CoV-2 was detected on the 28th day of hospitalization, and the patient received nasal oxygen support. Following clinical remission, she was discharged. The second patient, a 13-year-old male with familial mediterranean fever (FMF), tested positive for SARS-CoV-2 after experiencing fatigue following family contact. He continued colchicine therapy and managed the infection at home, achieving clinical cure by the end of the isolation period. The third patient, a nine-year-old male with FMF, remained asymptomatic after a PCR test for control purposes. With completion of the clinical isolation process at home, the patient tested negative for SARS-CoV-2, resulting in full recovery. The final patient,

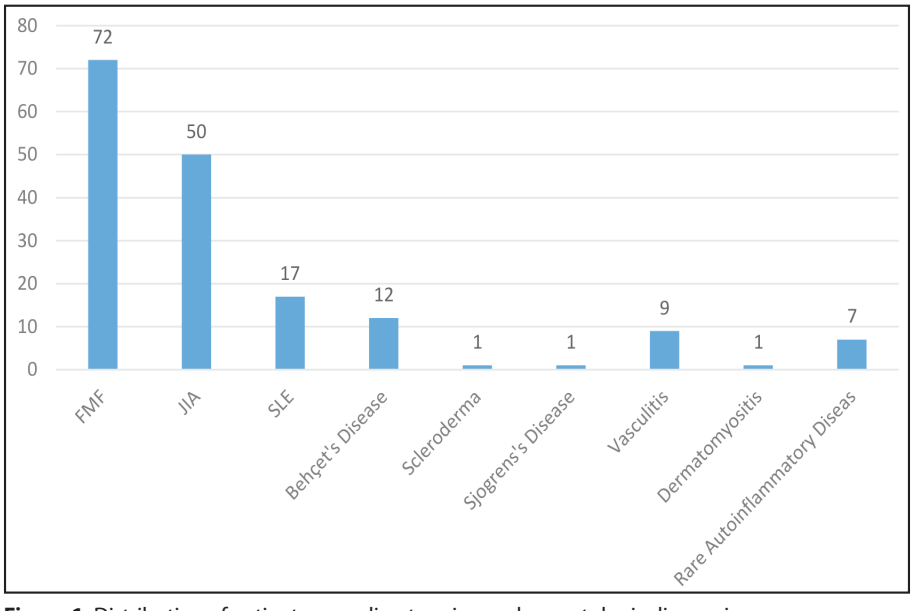

Figure 1. Distribution of patients according to primary rheumatologic diagnosis.

an 18-year-old girl with Takayasu's arteritis on infliximab treatment, presented to the emergency department with cough and headache. Hospitalization was undertaken for follow-up due to the use of biologic agents, but nasal oxygen was not required. The patient was discharged with complete cure after one week. None of the patients developed severe lower respiratory tract infection.

COVID-19 Serology Results and Distribution Among the Groups

Anti-SARS-CoV-2 IgG antibody was positive in 40 (23.5%) of the patients. Sex, mean age, median age at the diagnosis, median follow-up period and primary disease diagnosis distribution were similar between SARS-CoV-2 IgG seropositive and seronegative patients (Table 1). IgG seropositivity rates were similar in different rheumatic diseases. IgG seropositivity rates of the patients with and without *MEFV* mutation were found to be similar (p= 0.991). IgG seropositivity was 32.4% in patients who had *M694V* mutation, 8.3% in patients who had *E148Q* mutation, and 16.4% in patients who had *V726A* mutation; the distribution between the groups was similar (p= 0.218).

The percentage of the patients using colchicine or biologic agents was similar between the seropositive and seronegative groups (p= 0.396 and 0.505, respectively) (Table 1). Although the rate of IgG seropositivity was lower in patients with steroid use, this difference was not significant (32.0% vs. 68.0%, p= 0.202). Current medical treatments of IgG seropositive patients were reviewed; 24 (60%) were using colchicine, 12 (30%) were using DMARD, 9 (22.5%) were using steroids and seven (17.5%) were using biological treatment.

SARS-CoV-2 IgA seropositivity was detected in 11.2% (n= 19) of the patients. Demographic characteristics and treatment-related variables were similar between IgA seropositive and seronegative groups (Table 2). The

Table 1. Characteristics of the patients who were seropositive and seronegative for anti-SARS-CoV-2 IgG

Variable	Anti-SARS-CoV-2 IgG Negative Patients (n= 130)	Anti-SARS-CoV-2 IgG Positive Patients (n= 40)	p
Age (Years)	11.96 ± 4.19	12.80 ± 4.14	0.528
Sex (%) Female	 67 (72.8%)	 25 (27.2%)	0.150
Median Age at Diagnosis (Years)	7.56 ± 4.03	8.69 ± 4.75	0.195
Median Follow-up Time after Diagnosis (Years)	4.39 ± 3.27	4.11 ± 3.19	0.891
Diagnosis (%) -FMF and Other Autoinflammatory Disease - Juvenile idiopathic arthritis - SLE ve other autoantibody related diseases - Behçet's disease - Vasculitis	 62 (78.5%) 39 (78.0%) 16 (80.0%) 8 (66.7%) 5 (55.6%)	 17 (21.5%) 11 (22.0%) 4 (20.0%) 4 (33.3%) 4 (44.4%)	0.166
MEFV Mutation Homozygous Heterozygous No mutation	 30 (75.0%) 33 (76.7%) 36 (75.0%)	 10 (25.0%) 10 (23.3%) 12 (25.0%)	0.991
Presence of Colchicine Usage Yes No	 76 (75.2%) 54 (78.2%)	 25 (24.8%) 15 (21.7%)	0.396
Colchicine Dose (mg/day)	1.09 ± 0.44	1.13 ± 0.42	0.842
DMARD Usage Yes No	 37 (75.5%) 93 (76.9%)	 12 (24.5%) 28 (23.1%)	0.499
Steroid Usage Yes No	 17 (68.0%) 113 (77.9%)	 8 (32.0%) 32 (22.1%)	0.202
Median Steroid Dose (mg/day)	10.50 ± 8.91	14.71 ± 11.95	0.333
Biological Agent Usage Yes No	 21 (75.0%) 109 (76.8%)	 7 (25.0%) 33 (23.2%)	0.505
New Symptom/Sign of Primary Disease	11 (8.5%)	8 (20.0%)	0.046
Primary Disease Reactivation	20 (15.0%)	9 (21.2%)	0.450

Table 2. Characteristics of the patients who were seropositive and seronegative for anti-SARS-CoV-2 Ig A

Variable	Anti-SARS-CoV-2 IgA Negative Patients (n=151)	Anti-SARS-CoV-2 IgA Positive Patients (n=19)	p
Age (Years)	12.15 ± 4.16	12.25 ± 4.44	0.883
Sex (%) Female	 81 (88.0%)	 11 (12.0%)	 0.460
Median Age at Diagnosis (Years)	7.83 ± 4.25	7.79 ± 4.08	0.671
Median Follow-up Time after Diagnosis (Years)	4.31 ± 3.22	4.45 ± 3.53	0.459
Diagnosis (%) -FMF and Other Autoinflammatory Disease - Juvenile idiopathic arthritis - SLE ve other autoantibody related diseases - Behçet's disease - Vasculitis	 75 (94.9%) 43 (86.0%) 16 (80.0%) 10 (83.3%) 7 (77.8%)	 4 (5.1%) 7 (14.0%) 4 (20.0%) 2 (16.7%) 2 (22.2%)	0.022
MEFV mutation Homozygous Heterozygous No mutation	 35 (87.5%) 40 (93.0%) 43 (89.6%)	 5 (12.5%) 3 (7.0%) 5 (10.4%)	0.777
Colchicine Usage Yes No	 91 (90.1%) 60 (87.0%)	 10 (9.9%) 9 (13.0%)	0.345
Median Colchicine Dose (mg/day)	1.09 ± 0.43	1.20 ± 0.53	0.216
DMARD Usage Yes No	 42 (85.7%) 109 (90.1%)	 7 (14.3%) 12 (9.9%)	0.284
Steroid Usage Yes No	 21 (84.0%) 130 (89.7%)	 4 (16.0%) 15 (10.3%)	0.297
Median Steroid Dose (mg/day)	11.64 ± 9.33	12.33 ± 15.37	0.200
Biological Agent Usage Yes No	 22 (78.6%) 129 (90.8%)	 6 (21.4%) 13 (9.2%)	0.067

seropositivity rates in the patients followed up with the diagnosis of FMF were lower than the other diagnoses (p= 0.022).

In patients who had close contact with an individual diagnosed with COVID-19, IgA seropositivity was 21.1% and IgG seropositivity was 25.0%. Of the 32 patients who underwent SARS-CoV-2 PCR test, 28.1% were positive for IgG and 14.3% for IgA antibodies. Although, IgG seropositivity was observed in 3 (75.0%) of four patients with PCR positivity, IgA seropositivity was not found. Median time between the date of SARS-CoV-2 PCR examination and the SARS-CoV-2 seroprevalence assessment was 10.3 weeks (minimum 2.4 - maximum 19.8 weeks).

Disease Management of the Children with Rheumatic Disease During the Pandemic Process

During the pandemic period, 148 patients (87.1%) continued their regular follow-up. Only eight patients (4.7%) reported that they had communication problems with their doctor; three patients (1.8%) reported that they had difficulty in obtaining the medication they used. During the pandemic period, 24 (14.1%) patients had a reactivation of their disease, and 19 (11.2%) had a new symptom/sign of their disease. The diagnosis of 11 of 19 patients who developed new symptoms of their disease was JIA. Of these patients, nine had arthritis in a new joint and two had uveitis. There were two patients diagnosed with FMF, one had oral aphthae and the other had an erysipelas-like rash. In two patients with SLE and two with vasculitis who developed new symptoms, maculopapular eruptions with a different morphological structure were detected. Finally, genital aphtha developed in a patient with Behçet's diagnosis and a rash developed in a patient with a diagnosis of TRAPS. Medical treatments of six patients (3.5%) were postponed by the decision of the doctor (four patients in the DMARD group, two patients in the biological agent). The rate of patients with a new symptom/sign of their disease was higher in the seropositive group than seronegative group. (20.0% vs. 8.5%, p= 0.046). On the other hand, the frequency of primary disease activation was 15.0% in the seronegative group and 21.2% in the seropositive group, and the difference was not significant (p= 0.450).

Discussion

We found anti-SARS-CoV-2 IgG antibody seropositivity rate as 23.5% and anti-SARS-CoV-2 IgA antibody seropositivity rate as 11.2% in pediatric patients with a diagnosis of rheumatic disease. In a seroprevalence study comparing 62 patients with JIA and 32 healthy pediatric patients in Poland, anti-SARS-CoV-2 IgG positivity has been found to be 4.8% and anti-SARS-CoV-2 IgA positivity to be 9.7% (16). In the study of Walters et al. involving 262 pediatric rheumatology patients, anti-SARS-CoV-2 IgG has been found to be positive in 13% of the patients (9). In a study in Brazil including 100 adult rheumatology patients, anti-SARS-CoV-2 IgG seroprevalence has been found to be 14% (17).

Diagnostic distribution of our patients' seropositivity for anti-SARS-CoV-2 IgG antibody was examined, and it was observed that the distribution of primary diagnosis was similar between seropositive and seronegative groups. In the literature, there are publications showing that the frequency of COVID-19 is not different among rheumatic disease diagnoses, supporting our study (18-20). In our study, anti-SARS-CoV-2 IgG antibody was positive in 21.5%, 22.0% and 20.0% of patients with FMF, JIA, and SLE, respectively. Günendi et al. have found the prevalence of COVID-19 to be 7% in 822 patients with FMF (21). In a study by Boyarchuk et al. investigating the prevalence of COVID-19 in 51 patients with JIA, SARS-CoV-2 infection has been found to be 19.6% (22). In the report published by the Global Rheumatology Alliance for the first six months of the pandemic, 110 cases of COVID-19 with rheumatological disease were reported; 36% of these cases were rheumatoid arthritis, 17% were psoriatic arthritis, and 17% were SLE (23).

The low incidence and mortality rates of the disease in the Mediterranean basin, where *MEFV* gene mutation is common in the first surveillance reports for COVID-19, gave rise to the hypothesis that *MEFV* gene mutation may play a protective role against COVID-19 (24). In our study, SARS-CoV-2 seropositivity rates showed a similar distribution between the groups with and without *MEFV* mutation. The most common mutation, *M694V*, had a seropositivity of 32.4%, with a seropositivity rate of 8.3% of *E148Q* and 16.4% of *V726A*.

We did not find any difference between the medical treatments used by our patients and the seropositivity rates. Similar to the study conducted by Ihara et al. in pediatric patients with rheumatological disease, no correlation was found between the medical treatments used by the patients and the risk of COVID-19 (25). Walters et al. have studied anti-SARS-CoV-2 IgG in 262 pediatric patients with a diagnosis of rheumatic disease, and no difference has been observed in medical treatments between the seropositive and seronegative groups (9). Despite that, in a retrospective study by Villacis-Nunez et al. on pediatric rheumatology patients, the use of medium/high-dose corticosteroids, mycophenolate, and rituximab has been associated with hospitalization (26). Demir et al. have shown that COVID-19 disease developed in 39 of 436 patients using biological DMARDs (27). The clinical findings of 113 pediatric SARS-CoV-2 infected patients with rheumatic disease were examined, and biological treatment distributions of the patients with and without hospitalization were found to be similar (25). In the study of Favalli et al., anti-SARS-CoV-2 IgG, IgM, and IgA results of 300 adult rheumatology patients were compared on the biological agent-related risk of COVID-19, and it has been shown that seropositivity rates are similarly distributed among the groups using anti-TNF, abatacept, anti-IL6 or JAK inhibitors (28).

We found that patients with positive anti-SARS-CoV-2 IgG had a higher rate of new symptom/sign of their disease than with negative antibodies (p= 0.046). In a study evaluating 62 patients with JIA, it has been observed that the disease activity of patients seropositive for anti-SARS-CoV-2 IgA was significantly higher than that of seronegatives (16). The relation between COVID-19 and primary disease activity has been investigated in adult patients and high disease activity has been found in 72.3% of patients diagnosed with COVID-19 (29). In the 988 JIA cohorts of Hügle et al., 13 patients have shown PCR positive COVID-19 disease; and five of these patients have demonstrated signs of exacerbation of the primary disease after SARS-CoV-2 infection (30). In a study by Naddei et al., disease activations of JIA patients before and after the pandemic have been compared, and it has been found that disease activities were higher in the post-pandemic period than before (16.9% vs 6.3%, p= 0.009). The authors in this study have attributed high disease activity to an increased risk of inflammatory arthritis in children who cannot demonstrate adequate physical activity due to social isolation (31).

There are some limitations of our study. First, it reflects the experience of a single center and includes a limited number of patients. Since all of the patients included in the study did not have PCR sampling results, it can be thought that the data obtained in the immunocompromised patient group do not reflect all patients who encountered the virus. The seropositivity rates of healthy patients in the same age group are not known. Therefore, a comparison of our patient group with the healthy population could not be made. Finally, the presence of comorbid diseases in our study group is limited. Despite all limitations, we thought that it will contribute to the literature because it was designed in the early period of the pandemic, reflects the epidemiological and serological data before vaccination, and reflects the difficulties experienced by the patient group using medical treatment known to suppress the immune system during the pandemic process.

Conclusion

We found that 23.5% of the children with a diagnosis of rheumatic disease was seroprevalent for SARS-CoV-2. The distribution of primary diseases and medical therapies were similar between seropositive and seronegative patients. We found that patients with a new symptom/sign of their disease was higher in the seropositive group than seronegative group. Since our findings belong to a limited population of patients from the first period of the pandemic (pre-vaccination), large-scale and multicenter studies are needed before generalizing these findings to the pediatric population with rheumatic disease.

Ethics Committe Approval: This study was obtained from Akdeniz University Faculty of Medicine Clinical Research Ethics Committee (Decision no: 799, Date: 21.10.2020).

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - GKA, TL; Design - TL, GKA, EÇ; Supervision - MK, SA; Resource - GÖ, DÖ, ÖKÖ; Data Collection and/or Processing - TL, TTK; Analysis and/or Interpretation - TL, GKA; Literature Search - TL, GKA; Writing - TL, GKA; Critical Review- EÇ, MK, SA.

Conflict of Interest: All authors declare that they have no conflicts of interest or funding to disclose.

Financial Disclosure: This study research was supported by Akdeniz University Scientific Research Project Fund (Project No: 5647).

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