ORİJİNAL MAKALE / ORIGINAL ARTICLE

Sağlık Bilimlerinde Değer / Sağlık Bil Değer
Value in Health Sciences / Value Health Sci
ISSN: 2792-0542 sabd@duzce.edu.tr 2024; 14(1): 60-65
doi: https://dx.doi.org/10.33631/sabd.1342933

Mild Clinical Presentation of COVID-19 in Childhood FMF Patients Treated with Colchicine

Önder KILIÇASLAN[1], Adem KARBUZ[1], Didem KIZMAZ ISANÇLI[1], Gülay ÇAMLICA[2],Mehmet Ali SUNGUR[3], Hasan DURSUN[4]

ABSTRACT

Aim: Clinical trials continue for several medical protocols for COVID-19. Colchicine is an anti-inflammatory agent that is highly used medicament for autoimmune disorders, including Familial Mediterranean Fever (FMF). Based on immunity disrupting the pathogenesis of SARS-CoV-2, we aimed to describe the clinical course of SARS-CoV-2 infection in patients with childhood-onset FMF on colchicine treatment.

Material and Methods: We prepared a survey investigating contact histories, and clinical presentation of childhood-onset FMF patients treated with colchicine and questioned their parents via phone calls or during outpatient visits. In addition, medical record history, treatment, and medication history were obtained from the hospital database.

Results: A total of 171 patients, 99 (57.9%) male and 72 (42.1%) female, diagnosed with FMF and who have been under colchicine treatment for at least one month were included in the study. Among patients, 56 (32.7%) have contact with a confirmed COVID-19 case; 43 (25.1%) have suspected family member contact and 13 (7.6%) have non-family contact. Only 15 (8.8%) FMF patients treated with colchicine were PCR diagnosed with COVID-19 disease; all had mild symptoms, none required antiviral treatment, and none were hospitalized. The dose and duration of colchicine use did not significantly differ between the patients with confirmed COVID or not (p=0.112, and p=0.344, respectively).

Conclusion: We concluded that pediatric patients with FMF receiving colchicine treatment may not be at increased risk for being infected with SARS-CoV-2 or the severe symptoms of COVID-19.

Keywords: Children; colchicine; COVID-19; familial mediterranean fever; treatment.

Kolşisin ile Tedavi Edilen Çocukluk Çağı FMF Hastalarında COVID-19'un Hafif Klinik Seyri

ÖZ

Amaç: Etkin COVID-19 tedavisi için çeşitli tıbbi protokoller oluşturmak adına klinik çalışmalar devam etmektedir. Kolşisin, Ailevi Akdeniz Ateşi (AAA) de dahil olmak üzere otoimmün hastalıklar için yüksek oranda kullanılan bir anti-enflamatuar ajandır. SARS-CoV-2'nin bağışıklığı bozan patogenezine dayanarak, amacımız kolşisin tedavisi gören çocukluk çağı başlangıçlı AAA hastalarında SARS-CoV-2 enfeksiyonunun klinik seyrini tanımlamaktır.

Gereç ve Yöntemler: Kolşisin ile tedavi edilen çocukluk çağı başlangıçlı AAA hastalarının temas öykülerini ve klinik tablolarını araştıran bir anket hazırlandı ve ebeveynlerini telefon görüşmeleri veya poliklinik ziyaretleri sırasında sorgulandı. Ayrıca hastane veri tabanından tıbbi kayıt geçmişi, tedavi ve ilaç geçmişi elde edildi.

Bulgular: AAA tanısı konmuş ve en az bir aydır kolşisin tedavisi altında olan, 99 (%57,9) erkek ve 72 (%42,1) kadın olmak üzere toplam 171 hasta bu çalışmaya dahil edilmiştir. Hastaların 43'ünün (%25,1) şüpheli aile üyesi teması ve 13'ünün (%7,6) aile dışı teması olmak üzere 56'sının (%32,7) doğrulanmış bir COVID-19 vakası ile teması vardı. Kolşisin ile tedavi edilen AAA hastalarının sadece 15'ine (%8,8) PCR ile COVID-19 hastalığı tanısı konmuştur; hepsinde hafif semptomlar görülmüş, hiçbiri antiviral tedavi gerektirmemiş ve hiçbiri hastaneye yatırılmamıştır. Kolşisin kullanım dozu ve süresi, COVID tanısı olan ve olmayan hastalar arasında anlamlı farklılık göstermedi (sırasıyla p=0,112 ve p=0,344).

Sonuç: Kolşisin tedavisi alan AAA'lı pediatrik hastaların SARS-CoV-2 ile enfekte olması veya bu hastalarda COVID-19'un şiddetli semptomlarının görülebilmesi açısından yüksek riskte olmadığını düşünebiliriz.

Anahtar Kelimeler: Ailevi akdeniz ateşi; COVID-19; çocuklar; kolşisin; tedavi.

1 Prof. Dr. Cemil Tascioglu City Hospital, Department of Pediatric Infection, Istanbul, Turkiye
2 Prof. Dr. Cemil Tascioglu City Hospital, Department of Pediatrics, Istanbul, Türkiye
3 Duzce University Medical Faculty, Department of Biostatistics and Medical Informatics, Düzce, Türkiye
4 Prof. Dr. Cemil Tascioglu City Hospital, Department of Pediatric Nephrology, Istanbul, Türkiye

Sorumlu Yazar / Corresponding Author: Onder KILICASLAN , e-mail: dronderklcsln@gmail.com
Geliş Tarihi / Received: 14.08.2023, Kabul Tarihi / Accepted: 04.12.2023

INTRODUCTION

It has been almost two years since the world has struggled with the pandemics caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). Approximately 170 million patients have been infected worldwide. Since the number of asymptomatic cases is high, we postulate that the exact number is much higher. The average mortality rate is 2%, while 20-30% of the cases may experience severe symptoms of a life-threatening event (1). Patients with underlying comorbidities and the elderly are at a higher risk, and pediatric cases are mostly asymptomatic or present with mild-moderate symptoms (2).

COVID-19 is characterized by mild symptoms in the majority of children. Children may, however, develop a hyperinflammatory response similar to what has been observed in adults with COVID-19 (3, 4). COVID-19 is a viral disease with a systemic implementation (5). In COVID-19 disease, three phases of clinical development can be distinguished. The "viremic phase" is characterized by fast viral replication, and a direct cytopathic effect is in the matter. The second phase could be named the "pneumonia phase," generally requiring close observation and management. The patient's immune system begins to develop a reaction that, if balanced, leads to the final healing; if exaggerated, it brings to the exacerbation. This third phase, a minority, is characterized by systemic hyperinflammatory syndrome; it is referred to as a cytokine storm due to an over-reaction of the immune system with over-production of pro-inflammatory cytokines and other mediators (6). Principally, it is essential to understand disease pathogenesis to make the best treatment choices. For instance, the direct cytopathic effect of the virus may predispose to the use of anti-viral drugs in the initial phases of the infection, whereas, at the later stages of COVID-19 disease, theoretically, the most appropriate treatment options would be those that affect the immune system (5, 7).

As knowledge grows about SARS-CoV-2 immune pathogenesis, strategies for preventing and controlling an uncontrolled spread of infection and inflammation are being developed (3). Colchicine is an anti-inflammatory agent that inhibits cellular microtubule polymerization and inflammasome formation (8). Thus, this agent treats several rheumatic disorders, including pro-inflammatory cytokine activation and inflammasome activation (9, 10). In addition, the colchicine effect mechanism inhibits interleukin-1, interleukin-1b, and chemokine release; theoretically, colchicine is expected to improve the clinical course in patients with COVID-19 (6, 8).

We have presented here the results of a survey that we conducted to investigate the overall health status, contact history, rates of being infected, and clinical features of pediatric age Familial Mediterranean Fever (FMF) patients during pandemics. Our hospital is a clinical referral center for pediatric nephrology and infectious diseases. We have a considerable number of registered patients followed up for FMF. As anticipated, because of the general conviction that comorbidities seem to be a risk factor for COVID-19 infection, most parents of our patients got anxious if they were more vulnerable to severe COVID-19 compared to the general population. The pandemic has led to many questions and calls about risk factors or the need for alteration in our patients' treatment protocols. We have continued to close follow-ups and enlighten them about the current pandemic risks. As of now, there are few data on the clinical status and frequency of severe complications associated with SARS-CoV-2 infection in children with FMF. With our findings, we hope to contribute to the literature.

MATERIAL AND METHODS

Study design

We conducted a survey with patients diagnosed with FMF and receiving colchicine therapy. All the patients on follow-up in our pediatric nephrology clinic were called or questioned face-to-face during hospital visits, and the parents of the patients were accepted as a responder. Parents were informed about the research and asked for verbal consent on the phone call. The written permission and signature were obtained via an online survey afterward. The sociodemographic data about the family's general health and demographics were obtained from the parents. In addition, we collected the clinical follow-up data and FMF-related information from the patient's medical records: length of the treatment with colchicine, disease status at the last visit, comorbidity, and concomitant drugs.

Subjects and data collection

All the patients followed up at the Pediatric Nephrology Department in Prof. Dr. Cemil Taşçıoğlu Research Hospital diagnosed with FMF and aged between 2 and 18 years were enrolled in the study.

All patients were reached for 15 days in December 2021 as part of the ongoing study. All the involved patients' diagnoses were genetically confirmed. The patients aged 2-18 were involved. The patients with any additional clinical condition or comorbidity, patients under additional or multiple medical therapies other than colchicine, and those receiving colchicine for less than one month were excluded. In addition, to prevent possible new variant strain contaminations and related clinical variables, we excluded from the study individuals with a history of international travel or contact with someone who had been recently abroad.

The study survey contained questions on present disease flares, colchicine use duration, dose knowledge, symptoms related to COVID-19, any need for confirmation of COVID-19, clinical signs, and severity of the symptoms after confirmation of the infection, attendance to hospital, or need for medical treatment. History and number of contacts with COVID-19 confirmed cases, and presence of family members with confirmed COVID-19 were evaluated.

Ethics Approval

Written informed consent was obtained from parents/legal guards of children included in the study. All the patients included were under 18 years of age. Ethical approval was obtained for the study from the Institutional Ethics Committee of a tertiary-care hospital numbered 416, dated 06.12.2021. The recommendations of the Declaration of Helsinki for biomedical research involving human subjects were followed.

Statistical Analysis

The Kolmogorov-Smirnov test was used to analyze the distribution of continuous variables, and the Mann-Whitney U test was used to compare groups. Categorical variables were analyzed with Pearson chi-square and Fisher-Freeman-Halton tests according to the expected count rule. Descriptive statistics were given as median, interquartile range, minimum, and maximum for numerical variables, and categorical variables were presented as frequency and percentage. Statistical analyses were performed with the IBM SPSS v.22 package program, and the significance level was taken as 0.05.

RESULTS

We launched a phone call-based and face-to-face survey among our 241 registered patients with FMF. During the circulation, 11 participants were excluded due to their older age (>18 years), another 29 because of the presence of another autoimmune disease or comorbidity, 22 were excluded due to multidrug use, and finally, eight were excluded because their colchicine therapy was initiated less than one month earlier. Finally, 171 FMF patients were involved in the study.

The demographic and clinical features of the study patients are presented in Table 1.

Table 1. The demographics and medical history data of the FMF patients on colchicine treatment (n=171)

Gender (male), n (%)	99 (57.9)
Age (years), median (IQR) [min-max]	12 (7) [2-18]
Colchicine use duration (months), median (IQR) [min-max]	58 (48) [1-180]
Dose of Colchicine, n (%)	
0.5 mg/day	53 (31.0)
1 mg/day	89 (52.0)
1.5 mg/day	29 (17.0)
Contact history with a PCR test confirmed COVID-19 case, n (%)	
A family member	43 (25.1)
Non-family member	13 (7.6)
COVID-19 diagnosed patient	15 (8.8)

FMF- familial Mediterranean fever, IQR: interquartile range

As shown in the table, few patients have confirmed diagnosed with COVID-19, and the diagnosed ones had mild symptoms; none required hospitalization or antiviral treatment.

A total of 171 patients' contact history was questioned, 56 (32.7%) patients in total reported contact with a COVID-19-confirmed person; 43 (25.1%) patients reported a household contact and 13 (7.6%) with a none a family member person contact (Table 1). In the remaining 115 (67.3%) patients, no contact history with an infected or contacted person was reported. Out of the total study population, only 15 (8.8%) patients were admitted to the hospital due to COVID-19 suspicion, were tested with real-time PCR, and were then confirmed to be infected with SARS-CoV-2. Rest patients were not tested, nor was any admission history to a different hospital for PCR testing detected.

Within SARS-CoV-2 infected FMF patients: 10 patients had household contact, and 5 had a contact out of the family. Thus, household contact was at a significantly higher risk for contamination ($p<0.001$).

Family member numbers differed; the median number of family members (except the patient) where the FMF patients resided was 4 (range, 2-11) persons.

We evaluated the number and frequency of COVID-19 confirmed case contacts; 32 (18.7%) patients contacted with a single person, 19 (11.1%) with two cases, and 5 (2.9%) patients contacted with three or more COVID-19 confirmed cases. The number of people contacted did not significantly affect the getting-infected status of the patients ($p=0.660$). Table 2 presents the number and frequency of patients who got or did not get infected after SARS-CoV-2 positive patient contacts.

Table 2. Number of patients with recurrent contact with SARS-CoV-2 infected cases

Number of recurrent contacts	Total (n=56)	Infected (n,%)	Not Infected (n,%)	p
≥3	**5**	2 (40.0)	3 (60.0)	0.660#
2	**19**	4 (21.1)	15 (78.9)	
1	**32**	9 (28.1)	23 (71.9)	

#: Fisher-Freeman-Halton test

The clinical symptoms and severity of confirmed patients were elaborated. Also, the relation between dose and duration of colchicine treatment and the symptoms was investigated in detail. Only the ratio of nasal discharge was observed significantly higher in patients who received 0.5 mg/day of colchicine ($p=0.032$); no nasal discharge was reported in the other groups (the Dose 2 and Dose 3 groups). The presence and frequency of other COVID-19 symptoms did not significantly differ among the groups according to colchicine dose. Diarrhea, sore throat, earache, shortness of breath, tachycardia, bradycardia, sneeze, hoarseness, sputum, watery eyes, mucositis, debris, hospitalization, intensive care was not seen in all groups (Table 3).

The dose and duration of colchicine use did not significantly differ between the patients with confirmed COVID or not ($p=0.112$, and $p=0.344$, respectively).

Table 3. Frequency of symptoms observed in SARS-CoV-2 infected FMF patients and comparison according to daily colchicine dose

Symptom/Dose	Dose 1 (0.5 mg/day n=2)	Dose 2 (1mg/day n=8)	Dose 3 (1.5 mg/day n=5)	p#
Cough	0 (0.0%)	1 (12.5%)	0 (0.0%)	1.000
Fever	2 (100%)	5 (62.5%)	2 (40.0%)	0.385
Grunt	1 (50.0%)	1 (12.5%)	1 (20.0%)	0.692
Anorexia	1 (50.0%)	1 (12.5%)	1 (20.0%)	0.692
Weakness	2 (100%)	4 (50.0%)	2 (40.0%)	0.608
Nasal discharge	**2 (100%)**	2 (25.0%)	0 (0.0%)	**0.032**
Nasal congestion	0 (0.0%)	1 (12.5%)	0 (0.0%)	1.000
Myalgia	2 (100%)	2 (25.0%)	1 (20.0%)	0.131
Arthralgia	2 (100%)	3 (37.5%)	1 (20.0%)	0.217
Headache	0 (0.0%)	2 (25.0%)	2 (40.0%)	0.795
Stomach ache	0 (0.0%)	1 (12.5%)	0 (0.0%)	1.000
Loss of taste	0 (0.0%)	2 (25.0%)	1 (20.0%)	1.000
Loss of smell	0 (0.0%)	2 (25.0%)	1 (20.0%)	1.000
Mild course	2 (100%)	8 (100%)	5 (100%)	-

FMF: familial Mediterranean fever, #: Fisher-Freeman-Halton test

DISCUSSION

Registered in our pediatric nephrology outpatient clinic, we enrolled a total of 171 patients aged 2 up to 18 years, followed up with FMF, and treated with colchicine during the COVID-19 pandemic. Within this period, only 15 patients have been diagnosed with COVID-19, and all had mild symptoms, none needed antiviral medical treatment or hospitalization. Although there are reports about pediatric patients with several autoimmune disorders, few reports describe the frequency, demographic and clinical features, contamination status, and treatment outcomes in patients with childhood-onset FMF during pandemics (11-13).

Disease outcome is closely related to the patients' enhanced immune innate immunity status (1). Generally, children and young people are likely to control infections and suffer fewer severe illnesses, but people receiving immunostimulant treatments are concerned about not being able to. It is reassuring that in a cohort of 200 liver transplant patients on immunosuppressive treatment, only three tested positive for SARS-CoV2, and none developed concomitant disease and a history of contact with a COVID-19 case (11). According to other reports, COVID-19 infection has not been more common or severe among children with primary or secondary immune deficiencies than initially suspected (15,16). All those patients were on colchicine: most asymptomatic, mainly in outpatient therapy, and few were hospitalized. Patients hospitalized with FMF had a greater prevalence of comorbid illnesses and received more IL-1 blockers for treatment. Also, the only lost patient in the study reported by Güven et al. was relatively older, had multiple comorbidities, and was treated with IL-1 inhibitor (17,18).

Most of our patients are under colchicine treatment, only combined with other immune-modulatory drugs. Both in the severe clinical disease (14). Both immune dysregulations of the underlying diseases and immunosuppressive treatment they receive make children with autoimmune or autoinflammatory conditions more vulnerable to infectious diseases (12,15,16). Paradoxically, some studies report the beneficial role of some well-known anti-rheumatic drugs in managing severe COVID-19 (12). The adult series reports show that patients with chronic arthritis treated with modifying anti-rheumatic drugs do not seem to be at increased risk of respiratory or life-threatening complications from SARS-CoV-2 compared with the general population (1,16). The pediatric series reports give resembling details: from the few existing words on pediatric patients; we know that colchicine was not associated with moderate COVID-19 disease in pediatric FMF patients receiving colchicine compared to the control group; most patients present with mild clinical symptoms (11). In their study, Akça et al. evaluated risk factors for COVID-19 infection; getting infected with COVID-19 was associated with

vivo and in vitro studies have confirmed the anti-inflammatory and immunomodulatory effects (10). Colchicine has been used to treat FMF since 1972; it reduces the disease flares and prevents amyloidosis and various severe complications (15). Based on the immune-disruptive mechanism of the SARS-CoV-2 virus, anti-inflammatory target treatment trials, such as the effect of colchicine treatment during SARS-CoV-2 infection, are being investigated (8,19-21).

Consequently, colchicine is one of the off-label medications used in the treatment of COVID-19 currently (13,19). The exciting studies are mainly based on the adult population. Lien et al. have complied with the substantial outcomes in a meta-analyze and report that patients under

colchicine treatment had a significantly lower mortality risk (9). Mikolajewsla et al. review clinical trials on colchicine treatment in COVID-19; they summarize that therapy with oral colchicine reduced the risk of hospitalization compared with placebo (8). Colchicine therapy is associated with a decreased mortality rate in COVID-19 patients and associated with a decrease in hospitalization duration in COVID-19 patients (13, 22). Colchicine may prevent hyperinflammatory states (including cytokine storm); an experimental study showed that colchicine might reduce COVID-19-related lung injury (7). In our study, all the patients under colchicine therapy and infected with the SARS-CoV-2 virus had only a mild clinical course; no one required antiviral medical treatment or hospitalization. Therefore, we propose that the present study may also have a beneficial effect on the prognosis of Coronavirus illness, particularly in the population of FMF patients. It is possible that colchicine may reduce the severity of the disease even if it does not prevent the infection with COVID-19. Colchicine treatment for SARS-CoV-2 infection warrants further study.

COVID-19 is a highly infectious disease, and generally, stringent isolation measures have been widely approved since the early pandemic (23). Despite the isolation measurements, the transmission routes for pediatric patients are via contact with a known adult case, particularly with close contact with family members (23). Less exposure to the virus or air population due to lockdowns is one of the theoretical ideas regarding the mild course of childhood COVID-19 (23). Compared to many other countries, we have a big family custom, and family may be pretty crowded. We evaluated the number of household members our patients reside in concerning the close contacts that may increase household infection risk. In our study, the household number did not significantly affect the infected case rate; again, a small number of patients got infected despite crowded living conditions. In our study, most patients get infected from household contact. Many variables could affect the contagion status after contact. Unfortunately, we do not have real-time PCR scanning data for the entire patient group, nor do we have data for comparing transmission rates with a control group. However, we suggest that it is worth investigating if colchicine use has a protective contribution against SARS-CoV-2 contamination.

When we planned this survey study, we tried to filter out all other possible risk factors of the patients in order to identify the possible pure FMF pediatric patients who are on colchicine therapy. No other drug therapy no comorbidity was presented. Patients with a history of traveling abroad were eliminated. Although this is just a clinical observational and survey study, we tried to purify our results. Our results cannot be conclude generalized to society; However, our observations demonstrate that patients with FMF under colchicine treatment did not experience a severe complaint, and therefore this cannot be equated to an increased risk. The importance of the present study and further investigations is that close monitoring of the COVID-19 loop would help identify severe course risk factors to reduce the frequency and contagious state of the disease.

CONCLUSIONS

Many agents have been tested in the treatment of COVID-19. As some of them were being used in the treatment of different primary diseases of the patients, the effect of those agents on COVID-19 were evaluated observationally. In a study conducted with a similar logic to our study, it was emphasized that only 11% of patients with antiphospholipid syndrome using hydroxychloroquine required hospitalization, and none of the patients using antiaggregant/anticoagulants such as acetylsalicylic acid, warfarin or low molecular weight heparin required hospitalization (24). We also investigated the effect of colchicine on COVID-19 in FMF patients and, we may claim that colchicine could have a protective effect for COVID-19 and also may prevent severe complications. Colchicine deserves a further prospective clinical study to clarify its prophylactic, protective, and therapeutic benefits. A collaborative approach is required to safely assess the individual risk of vulnerable patient groups. The best evidence base can only be obtained by collecting prospective data, but until we have reliable data, close clinical monitoring should be prioritized.

Authors's Contributions: Idea/Concept: Ö.K.; Design: Ö.K., A.K., D.K.İ., G.Ç.; Data Collection and/or Processing: Ö.K., D.K.İ.; Analysis and/or Interpretation: Ö.K., A.K., M.A.S.; Literature Review: Ö.K., A.K., D.K.İ., G.Ç., H.D.; Writing the Article: Ö.K., A.K., D.K.İ., G.Ç., M.A.S., H.D.; Critical Review: Ö.K., A.K., D.K.İ., G.Ç., M.A.S., H.D.

REFERENCES

1. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020; 395(10223): 507-13.
2. Akpinar G, Demir MC, Sultanoglu H, Sonmez FT, Karaman K, Keskin BH, et al. The Demographic analysis of the probable COVID-19 cases in terms of RT-PCR results and age. Clin Lab 2021; 67(4).
3. Henderson LA, Canna SW, Friedman KG, Gorelik M, Lapidus SK, Bassiri H, et al. American College of rheumatology clinical guidance for multisystem inflammatory syndrome in children associated with SARS–CoV-2 and Hyperinflammation in pediatric COVID-19: version 2. Arthritis Rheumatol 2021; 73(4): e13-e29.
4. Kharouf F, Ishay Y, Kenig A, Bitan M, Ben-Chetrit E. Incidence and course of COVID-19 hospitalizations among patients with familial Mediterranean fever. Rheumatology (Oxford) 2021; 60(SI): SI85-SI9.
5. Gustine JN, Jones D. Immunopathology of Hyperinflammation in COVID-19. Am J Pathol 2021; 191(1): 4-17.
6. Bartoli A, Gabrielli F, Alicandro T, Nascimbeni F, Andreone P. COVID-19 treatment options: a difficult journey between failed attempts and experimental drugs. Intern Emerg Med 2021; 16(2): 281-308.
7. Grailer JJ, Canning BA, Kalbitz M, Haggadone MD, Dhond RM, Andjelkovic AV, et al. Critical role for the NLRP3 inflammasome during acute lung injury. J Immunol 2014; 192(12): 5974-83.

8. Mikolajewska A, Fischer AL, Piechotta V, Mueller A, Metzendorf MI, Becker M, et al. Colchicine for the treatment of COVID-19. Cochrane Database Syst Rev 2021; 10: Cd015045.
9. Lien C-H, Lee M-D, Weng S-L, Lin C-H, Liu LY-M, Tai Y-L, et al. Repurposing Colchicine in Treating Patients with COVID-19: A Systematic Review and Meta-Analysis. Life. 2021; 11(8): 864.
10. Gasparyan AY, Ayvazyan L, Yessirkepov M, Kitas GD. Colchicine as an anti-inflammatory and cardioprotective agent. Expert Opin Drug Metab Toxicol 2015; 11(11): 1781-94.
11. Kaya Akca U, Sener S, Balık Z, Gurlevik S, Oygar PD, Atalay E, et al. Clinical course of COVID-19 infection in paediatric familial Mediterranean fever patients. Mod Rheumatol. 2022; 32(2): 467-72.
12. Hedrich CM. COVID-19–Considerations for the paediatric rheumatologist. Clin Immunol 2020;214:108420.
13. Golpour M, Mousavi T, Alimohammadi M, Mosayebian A, Shiran M, Alizadeh Navaei R, et al. The effectiveness of Colchicine as an anti-inflammatory drug in the treatment of coronavirus disease 2019: Meta-analysis. Int J Immunopathol Pharmacol 2021; 35: 20587384211031763.
14. D'Antiga L. Coronaviruses and immunosuppressed patients: the facts during the third epidemic. Liver Transpl 2020; 26(6): 832-4.
15. Haslak F, Yildiz M, Adrovic A, Sahin S, Koker O, Aliyeva A, et al. Management of childhood-onset autoinflammatory diseases during the COVID-19 pandemic. Rheumatol Int 2020; 40(9): 1423-31.
16. Seo MR, Kim J-W, Park E-J, Jung SM, Sung Y-K, Kim H, et al. Recommendations for the management of patients with systemic rheumatic diseases during the coronavirus disease pandemic. Korean J Intern Med 2020; 35(6): 1317-32.
17. Güven SC, Erden A, Karakaş Ö, Armağan B, Usul E, Omma A, et al. COVID-19 outcomes in patients with familial Mediterranean fever: a retrospective cohort study. Rheumatol Int 2021; 41(4): 715-9.
18. Connelly JA, Chong H, Esbenshade AJ, Frame D, Failing C, Secord E, et al. Impact of COVID-19 on pediatric immunocompromised patients. Pediatr Clin North Am 2021; 68(5): 1029-54.
19. Rojas-Villarraga A, Parra-Medina R, Gómez-López A. Colchicine treatment in COVID-19: the remaining unsolved question. Lancet Respir Med 2021; 9(12): 1351-3.
20. Nas K, Eryilmaz N, Geyik MF, Altaş A. COVID-19 in patients with familial Mediterranean fever treated with colchicine: case based review. Rheumatol Int 2021; 41(4): 811-7.
21. RECOVERY Collaborative Group. Colchicine in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. Lancet Respir Med 2021; 9(12): 1419-26.
22. Günendi Z, Yurdakul FG, Bodur H, Cengiz AK, Uçar Ü, Çay HF, et al. The impact of COVID-19 on familial Mediterranean fever: a nationwide study. Rheumatol Int 2021; 41(8): 1447-55.
23. Wilder-Smith A, Freedman DO. Isolation, quarantine, social distancing and community containment: pivotal role for old-style public health measures in the novel coronavirus (2019-nCoV) outbreak. J Travel Med 2020; 27(2): taaa020.
24. Erden A, Karakas O, Armagan B, C. Guven, B. Ozdemir, E. Atalar, et al. COVID-19 outcomes in patients with antiphospholipid syndrome: a retrospective cohort study. Bratisl Med J 2022; 123(2): 120-4.