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Original Article

The First Effect of COVID-19 Pandemic on Starting Biological Disease Modifying Anti-Rheumatic Drugs: Outcomes from the TReasure Real-Life Database

Nilüfer Alpay Kanıtez[1], Sedat Kiraz[2], Ediz Dalkılıç[3], Gezmiş Kimyon[4], Rıdvan Mercan[5], Ömer Karadağ[2], Cemal Bes[6], Levent Kılıç[2], Servet Akar[7], Aşkın Ateş[8], Hakan Emmungil[9], İhsan Ertenli[2], Yavuz Pehlivan[3], Belkıs Nihan Coşkun[3], Burcu Yağız[3], Duygu Ersözlü[10], Emel Gönüllü[11], Muhammet Çınar[12], Timuçin Kaşifoğlu[13], Süleyman Serdar Koca[14], Uğur Karasu[15], Orhan Küçükşahin[16], Umut Kalyoncu[2]

ORCID iDs of the authors:
N.A.K. 0000-0003-1185-5816;
S.K. 0000-0003-2802-6061;
E.D. 0000-0001-8645-2670;
G.K. 0000-0003-3775-639X;
R.M. 0000-0003-1537-2192;
Ö.K. 0000-0002-3443-3117;
C.B. 0000-0002-1730-2991;
L.K. 0000-0002-3102-5847;
S.A. 0000-0002-3734-1242;
A.A. 0000-0003-1966-3333;
H.E. 0000-0001-5184-4404;
İ.E. 0000-0002-3904-0769;
Y.P. 0000-0002-1201-8836;
B.N.C. 0000-0003-0298-4157;
B.Y. 0000-0003-4288-7255;
D.E. 0000-0001-6172-7762;
E.G. 0000-0002-6990-4206;
M.Ç. 0000-0002-6150-3539;
T.K. 0000-0002-9941-5884;
S.S.K. 0000-0003-4995-430X;
U.K. 0000-0003-0090-0247;
O.K. 0000-0002-4109-0642;
U.K. 0000-0001-7129-2109.

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[1] Division of Rheumatology, Department of Internal Medicine, Koç University School of Medicine, İstanbul, Turkey
[2] Division of Rheumatology, Department of Internal Medicine, Hacettepe University School of Medicine, Ankara, Turkey
[3] Division of Rheumatology, Department of Internal Medicine, Uludağ University School of Medicine, Bursa, Turkey
[4] Division of Rheumatology, Department of Internal Medicine, Mustafa Kemal University School of Medicine, Hatay, Turkey
[5] Division of Rheumatology, Department of Internal Medicine, Namık Kemal University School of Medicine, Tekirdağ, Turkey
[6] Division of Rheumatology, Department of Internal Medicine, Health Sciences University, Dr. Sadi Konuk Training and Research Hospital, İstanbul, Turkey
[7] Division of Rheumatology, Department of Internal Medicine, Katip Çelebi University School of Medicine, İzmir, Turkey
[8] Division of Rheumatology, Department of Internal Medicine, Ankara University School of Medicine, Ankara, Turkey
[9] Division of Rheumatology, Department of Internal Medicine, Trakya University School of Medicine, Edirne, Turkey
[10] Division of Rheumatology, Department of Internal Medicine, Health Sciences University, Adana City Training and Research Hospital, Adana, Turkey
[11] Division of Rheumatology, Department of Internal Medicine, Sakarya University School of Medicine, Sakarya, Turkey
[12] Division of Rheumatology, Department of Internal Medicine,

Abstract

Objective: The coronavirus disease 2019 pandemic has been resulting in increased hospital occupancy rates. Rheumatic patients cannot still reach to hospitals, or they hesitate about going to a hospital even they are able to reach. We aimed to show the effect of the first wave of coronavirus disease 2019 pandemic on the treatment of biological disease-modifying anti-rheumatic drugs in patients with rheumatoid arthritis or spondyloarthritis.

Methods: Patients were divided into three groups as follows: pre-pandemic (Pre-p: starting on biological disease-modifying anti-rheumatic drug therapy for the first time within 6 months before March 11, 2020); post-pandemic A (Post-p A: starting on biological disease-modifying anti-rheumatic drug therapy for the first time within the first 6 months after March 11, 2020); post-pandemic B (Post-p B: starting on biological disease-modifying anti-rheumatic drug therapy for the first time within the second 6 months).

Results: The number of rheumatoid arthritis patients in the Post-p A and B groups decreased by 51% and 48%, respectively, as compared to the Pre-p group similar rates of reduction were also determined in the number of spondyloarthritis patients. The rates of tofacitinib and abatacept use increased in rheumatoid arthritis patients in Post-p period.

Conclusion: The number of rheumatoid arthritis and spondyloarthritis patients starting on biological disease-modifying anti-rheumatic drugs for the first time decreased during the first year of the coronavirus disease 2019 pandemic.

Keywords: Biological disease-modifying anti-rheumatic drug, coronavirus disease 2019, rheumatoid arthritis, spondyloarthritis

Introduction

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has spread across the world since December 2019. This shocking pandemic, which is the first in many aspects, has posed important problems to the health systems of countries. In some countries, hospitals were overloaded by patients with COVID-19 and they even could not provide services to other patients and/or emergency patients. A period of time has emerged, during which access to healthcare services has become anxious, difficult, and sometimes impossible for rheumatic patients, as also for other patients.[1]

During this first wave of the pandemic, treatment algorithms in almost all fields of medicine were reviewed. However, data about the potential risk of anti-rheumatic therapies for COVID-19 were inadequate when initially emergency patients and then other rheumatic patients were able to reach healthcare services during the normalization period that has begun with the decline of the first wave. Although national and international advisory statements have tried to fill this gap as much as possible, it has been inevitable for rheumatologists to make hesitant and changeable decisions in treatment choice.[2] After the first-wave crisis, favorable data on rheumatic diseases and anti-rheumatic treatments including biological disease-modifying anti-rheumatic drug (bDMARD) began to be obtained.[3] The present study aimed to show the

Health Sciences University, Gülhane Training and Research Hospital, Ankara, Turkey
[13] Division of Rheumatology, Department of Internal Medicine, Osmangazi University School of Medicine, Eskişehir, Turkey
[14] Division of Rheumatology, Department of Internal Medicine, Fırat University School of Medicine, Elazığ, Turkey
[15] Division of Rheumatology, Department of Internal Medicine, Pamukkale University School of Medicine, Denizli, Turkey
[16] Division of Rheumatology, Department of Internal Medicine, Yıldırım Beyazıt University, Ankara City Hospital, Ankara, Turkey

Corresponding author:
Nilüfer Alpay Kanıtez
E-mail: nilalpay@gmail.com

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Main Points

- It is estimated that a significant proportion of patients with the chronic rheumatic disease cannot access effective treatment in the COVID-19 pandemic.
- The use of bDMARDs was substantially decreased during the first year of the COVID-19 pandemic. The potential reflection of this situation in the coming years will be to encounter poor clinical outcomes.
- Drug choice among bDMARDs did not change significantly as compared to the before the pandemic.
- For effective treatments, there is a need for patients to be encouraged as well as for obtaining more safety data.

effect of the first wave of COVID-19 pandemic on choosing bDMARDs for the treatment of rheumatoid arthritis (RA) and spondyloarthritis (SpA) in real-life setting.

Methods

TReasure Database and Selection of the Research Groups

Data of the study were retrieved from the TReasure registry, in which data of RA and SpA patients starting on bDMARD therapy were recorded.[4] These patients were evaluated in three groups: (1) post-pandemic group consisted of patients starting on bDMARD therapy for the first time within the first 6 months (Post-p A) and (2) within the second 6 months (Post-p B) after March 11, 2020, when the first case of COVID-19 was confirmed in Turkey and (3) the pre-pandemic group consisted of patients starting on bDMARD therapy for the first time within 6 months (Pre-p) before March 11, 2020. Although tofacitinib is not a bDMARD, patients using this medicine were also included in the study as tofacitinib is a second-line treatment option for RA like bDMARDs, and it has a similar risk profile with bDMARDs.[5]

The ethics committee approval for using the TReasure database was obtained from Hacettepe University (KA-17/058) in May 2017 and from the Republic of Turkey Ministry of Health (93189304 – 14.03.01) in October 2017. Written informed consents of all participants were obtained.

Clinical Characteristics of the Patients

Patients with RA were diagnosed according to the 2010 European League against Rheumatology (EULAR)/American College of Rheumatology (ACR) criteria.[6] The modified New York criteria and 2009 EULAR criteria for axial and peripheral SpA were used in the diagnosis of SpA patients.[7-9]

Data of the patients regarding age, sex, disease duration, disease activity, and functional status before starting bDMARD were recorded. In the RA patients, disease activity was evaluated through the Disease Activity Score 28 using erythrocyte sedimentation rate (DAS28-ESR), the DAS28 using C-reactive protein (DAS28-CRP), the Simplified Disease Activity Index (SDAI), the Clinical Disease Activity Index (CDAI), Health Assessment Questionnaire (HAQ), and Visual Analogue Scale (VAS) for pain, fatigue, patient global, and physician global assessments.[10] In the SpA patients, the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), the Bath Ankylosing Spondylitis Functional Index (BASFI), and the Ankylosing Spondylitis Disease Activity Score (ASDAS) were used to evaluate disease activity and functionality.[11-13]

Statistical Analysis

All statistical analyses were conducted using the PASW Statistics for Windows, Version 18.0 (SPSS Inc., Chicago, Ill, USA). Descriptive statistics were generated; categorical variables were expressed as numbers and percentages, and numerical variables were expressed as median (minimum–maximum). The Chi-square, Fisher's exact, and Mann-Whitney U tests were used to compare variables between the study groups. A *P* value of .05 was considered statistically significant.

Results

The total (RA and SpA) Post-p A comprised 224 patients (132 females), the Post-p B comprised 286 patients (183 females), and the Pre-p comprised 507 patients (329 females). The number of patients in the Post-p A and Post-p B were observed to be decreased by 66% and 44% as compared to the number of patients in the Pre-p, respectively. The distribution of the RA and SpA patients according to the study groups is demonstrated in Figure 1.

Patients with RA

The rates of reduction in the number of RA patients in the Post-p A and B were 51% and 48% as compared to the number of patients in the Pre-p, respectively. Comparison of the Pre-p group with Post-p A group individually revealed no significant differences in terms of age, disease duration, acute phase indicators, and disease activity scores except VAS pain (Table 1). The VAS pain score was significantly higher in the Post-p A group as compared to the Pre-p group ($P = .02$). The ESR, CRP, number of tender joints, DAS28-ESR, DAS28-CRP, and the CDAI scores were found significantly higher in the Post-p B group that those in the Post-p A group ($P = .02$, $P = .026$, $P = .013$, $P = .025$, $P = .035$, and $P = .025$, respectively).

The distribution of bDMARDs in RA patients is shown in Table 2. Compared with the Pre-p group, the rates of choosing abatacept was significantly higher in the Post-p group ($P = .022$). Although the choice of tofacitinib did not reach a significant difference between the Pre-p and Post-p A groups, it was seen that it was statistically significantly more preferred in the Post-p B group ($P = .017$)

Patients with SpA

The number of SpA patients in the Post-p A and Post-B groups decreased by 58% and 41%

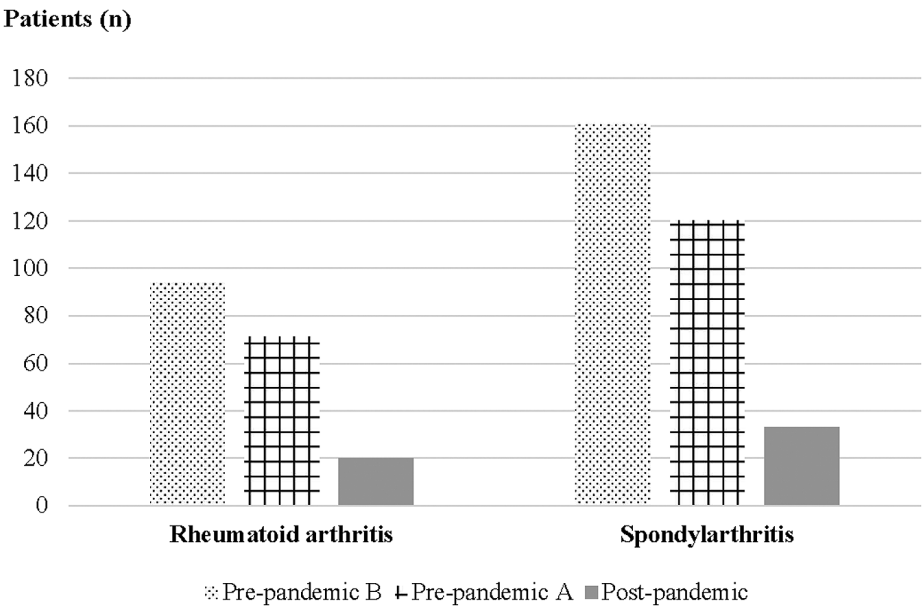

Figure 1. Distribution of the RA and SpA patients according to the time of starting on a bDMARD. RA, rheumatoid arthritis; SpA, spondyloarthritis; bDMARD, biological disease-modifying anti-rheumatic drug.

as compared to the Pre-p group, respectively. There were no statistically significant differences between the Post-p A and Pre-p in terms of acute-phase indicators and ASDAS scores (Table 3). In the Post-p A, the patients were younger, HLA-B27 positivity, the ratio of the male patients and enthesitis were higher as compared to the Pre-p B ($P = .024$, $P = .020$, $P = .013$, and $P = 0.003$, respectively). The BASFI score of the SpA patients in the Post-p B group was significantly higher than those in the Post-p A group ($P = .006$). The other significant difference between the Post-p B and Post-p A groups was obtained in the rate of IBD, which was higher in the Post-p A group ($P = .038$).

The distribution of bDMARD choice was not significantly different between the Pre-p and Post-p groups (Table 4).

Discussion

In Turkey, the first case of COVID-19 was confirmed on March 11, 2020. As of that time, the number of patients has gradually increased and the government has implemented precautions in a gradual manner.[14] On April 11, 2020, when the daily number of cases with highest of 5138 cases, many hospitals across the country failed to provide polyclinic services except for emergency patients. Fortunately, the peak of the pandemic was obtained in a relatively short time and the restrictions have started to be removed as of June 2020. In this study, the 6-month period when the first shock of the pandemic was experienced, the second 6-month period which was stabilized, and the 6-month period before the pandemic were compared. Accordingly, the number of patients starting on bDMARDs decreased by 44-66% during the pandemic periods as compared to the pre-pandemic period. One of the reasons for this decrement was certainly the failure of patients to reach rheumatology polyclinics because of pandemic restrictions, concerns about having COVID-19, and hospitals' occupancy rates. According to the survey carried out by Antony et al.[15] rheumatic

Table 1. Demographic and clinical characteristics of the rheumatoid arthritis patients according to the time of starting on a bDMARD

Characteristics	Pre-p, n = 184	Post-p A, n = 89	Post-p B, n = 95	*P*, Post-p A/Post-p B	*P*, Post-p A/Pre-p
Female	154 (84)	76 (85)	81 (84)	.913	.265
Age, years	55 (22-84)	52 (19-75)	51 (19-77)	.550	**.036**
Disease duration, months	100 (12-539)	86 (8-612)	82 (3-466)	.922	.258
ESR, mm/h	27.5 (2-114)	25 (2-85)	37 (2-115)	**.020**	.456
CRP, mg/L	11 (0.4-173)	11.5 (0.5-208)	19.8 (0.2-180)	**.026**	.835
VAS patient global	78 (20-100)	80 (0-100)	80 (0-100)	.267	.338
VAS pain	75 (0-100)	80 (0-100)	80 (10-100)	.961	**.020**
VAS fatigue	70 (0-100)	78 (0-100)	80 (0-100)	.150	.762
HAQ	0.9 (0-2.9)	0.8 (0-2.9)	1.0 (0-2.7)	.215	.935
Swelling joints, n	2 (0-24)	2 (0-26)	4 (0-30)	**.013**	.911
Tender joints, n	5 (0-24)	6 (1-28)	6 (0-33)	.740	.203
DAS28-ESR	4.6 (1.5-8.7)	4.7 (1.7-7.9)	5.2 (2.2-8.9)	**.025**	.398
DAS28-CRP	4.1 (0.9-8.9)	4.2 (1.6-7.9)	4.7 (1.4-8.7)	**.035**	.250
CDAI	21 (3-66)	21 (4-70)	25 (6-78.5)	.088	.501
SDAI	34 (6-228)	38 (11-195)	53 (12-221)	**.025**	.352

Data are presented as number (%) and median (minimum–maximum), where appropriate.
Pre-p, pre-pandemic (within 6 months after March 11, 2020); Post-p A, post-pandemic A (within the first 6 months after March 11, 2020); Post-p B, post-pandemic B (within the second 6 months after March 11, 2020); ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; VAS, visual analog scale; HAQ, health assessment questionnaire; DAS28-ESR, disease activity score 28 using erythrocyte sedimentation rate; DAS28-CRP, disease activity score 28 using C-reactive protein; CDAI, clinical disease activity index; SDAI, simplified disease activity index.
bDMARD, biological disease-modifying anti-rheumatic drug.

Table 2. Drug choices in the rheumatoid arthritis patients according to the time of starting on a bDMARD

	Pre-p, n (%)	Post-p A, n (%)	Post-p B, n (%)	*P*, Post-p A vs. Post-p B	*P*, Post-p A vs. Pre-p
Abatacept	1 (0.5)	4 (4.5)	2 (2.1)	.362	**.022**
Adalimumab	45 (24.5)	27 (30.3)	21 (22.1)	.204	.301
Etanercept	15 (8.2)	4 (4.5)	12 (12.6)	.06	.266
Golimumab	2 (1.1)	3 (3.4)	1 (1.1)	.281	.187
Infliximab	2 (1.1)	1 (1.1)	1 (1.1)	.963	.978
Rituximab	28 (15.2)	7 (7.9)	10 (10.5)	.533	.089
Certolizumab	16 (8.7)	10 (11.2)	6 (6.3)	.237	.503
Tofacitinib	48 (26.1)	17 (19.1)	33 (34.7)	**.017**	.204
Tocilizumab	27 (14.7)	16 (18)	9 (9.5)	.092	.482

Pre-p, pre-pandemic (within 6 months before March 11, 2020); Post-p A, post-pandemic A (within the first 6 months after March 11, 2020); Post-p B, post-pandemic B (within the second 6 months after March 11, 2020).
bDMARD, biological disease-modifying anti-rheumatic drug.

Table 3. Demographic and clinical characteristics of the spondyloarthritis patients according to the time of starting on a bDMARD

Characteristics	Pre-p, n = 323	Post-p A, n = 135	Post-p B, n = 191	*P*, Post-p A/Post-p B	*P*, Post-p A/Pre-p
Male	148 (46)	79 (59)	89 (47)	.034	**.013**
Age, year	40 (18-85)	38 (19-73)	38 (17-69)	.520	**.024**
Disease duration, months	88 (9-527)	65 (3-454)	77 (1-552)	.540	**.016**
HLA-B27	80 (41)	46 (56)	65 (52)	.563	**.020**
Uveitis	19 (6)	14 (11)	15 (8)	.451	.110
Dactylitis	17 (6)	10 (8)	9 (5)	.305	.374
Enthesitis	32 (12)	29 (24)	32 (18)	.255	**.003**
IBD	12 (4)	9 (7)	4 (2)	**.038**	.162
Psoriasis	55 (17)	28 (21)	32 (17)	.399	.340
BASDAI	6.2 (0.6-9.6)	6.2 (0-9.8)	6.2 (0.1-9.8)	.855	.160
BASFI	4.6 (0-10)	4.6 (0-10)	5.5 (0.2-10)	**.006**	.287
VAS patient global	80 (8-100)	80 (0-100)	80 (0-100)	.705	.292
VAS pain	80 (0-100)	80 (0-100)	80 (0-100)	.328	.073
VAS fatigue	70 (0-100)	70 (0-100)	75 (0-100)	.152	.167
ESR	22 (2-130)	17 (2-81)	19 (2-83)	.776	.207
CRP	8.3 (0.2-307)	11.6 (0.6-121)	7.2 (0.5-170)	.149	.554
ASDAS-ESR	3.4 (1.1-5.5)	3.4 (1-5.7)	3.2 (1-5.3)	.487	.669
ASDAS-CRP	3.7 (1-9)	3.8 (1.1-5.7)	3.4.(1-5,9)	.251	.929

Data are presented as number (%) and median (minimum–maximum), where appropriate.
Pre-p, pre-pandemic (within 6 months before March 11, 2020); Post-p A, post-pandemic A (within the first 6 months after March 11, 2020); Post-p B, post-pandemic B (within the second 6 months after March 11, 2020).
HLA-B27, human leukocyte antigen-B27; IBD, inflammatory bowel disease; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; VAS, visual analogue scale; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; ASDAS-ESR, Ankylosing Spondylitis Disease Activity Score using erythrocyte sedimentation rate; ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score using C-reactive protein; bDMARD, biological disease-modifying anti-rheumatic drug.

patients considered themselves at risk for COVID-19 due to both their illnesses and the medications they were receiving, and they were worried about going to a hospital. The effect of pandemic on rheumatology practice, in which early and effective treatment provides a substantial advantage, will no doubt be quite unfavorable.

The COVID-19-related fatality rate is high in elderly and in people with comorbid conditions such as hypertension, cardiovascular diseases, diabetes, and cancer.[16] Data obtained from transplant patients have revealed that long-term use of immunosuppressant drugs is another factor increasing the fatality rate.[17] DMARDs are immunosuppressive and immunomodulatory agents and are classified as either conventional DMARDs or biologic DMARDs. However, it has been reported that severe infections, tuberculosis, and herpes zoster infections are more common among RA and SpA patients receiving bDMARDs.[18] On the other hand, it is also known that RA patients with active disease

Table 4. Drug choices in the spondyloarthritis patients according to the time of starting on a bDMARD

	Pre-p, n (%)	Post-p A, n (%)	Post-p B, n (%)	*P*, Post-p A vs. Post-p B	*P*, Post-p A vs. Pre-p
Adalimumab	165 (51.1)	78 (57.8)	117 (61.3)	.528	.191
Etanercept	34 (10.5)	18 (13.3)	22 (11.5)	.623	.388
Golimumab	21 (6.5)	8 (5.9)	9 (4.7)	.627	.818
Infliximab	19 (5.9)	8 (5.9)	5 (2.6)	.133	.986
Secukinumab	33 (10.2)	9 (6.7)	6 (3.1)	.135	.23
Certolizumab	49 (15.2)	13 (9.6)	31 (16.2)	.089	.114

Pre-p, pre-pandemic (within 6 months before March 11, 2020); Post-p A, post-pandemic A (within the first 6 months after March 11, 2020); Post-p B, post-pandemic B (within the second 6 months after March 11, 2020).
bDMARD, biological disease-modifying anti-rheumatic drug.

are more vulnerable to infections.[19] The fact that tocilizumab, a bDMARD, decreases COVID-19-related-hospital stay duration and COVID-19-related-mortality rates make this subject more complex.[20] There has been no evidence yet that bDMARDs prolong hospital stay or enhance the fatality rate of COVID-19. On the contrary, there are registry studies suggesting that patients receiving bDMARDs are similarly affected by COVID-19 with the general population.[21,22] Since the comorbid conditions are more likely, rheumatologists might have hesitated while starting bDMARDs in RA patients. The fact that the SpA patients starting on bDMARDs during the pandemic were younger might be related to the rheumatologists' concerns about comorbidities; younger patients are expected to have a low comorbidity rate. Among SpA patients, the patients who started bDMARDs are younger in the post-pandemic period. Although more active patients seemed to be preferred in the second 6 months, the trend was not so in the first 6 months. The VAS-pain score was significantly higher in SpA patients starting on a bDMARD during the pandemic. This may be related to the motivating effect of high perception of pain on admitting a hospital.

In the present study, the pandemic may still have had an effect in this regard in favoring tofacitinib more. Indeed, the relatively short half-life of tofacitinib is an advantage in infectious diseases. On the other hand, in spa patients, the choice of bDMARD seems similar to the pre-pandemic period.

The most important limitation of our study, in which patients from different centers were included, is that pandemic conditions did not emerge as a standard in every center. In the first wave, restrictions were taken centrally by the government and covered all centers, but the characteristics of the centers and the regional incidence of COVID-19 may have affected the behavior of patients and physicians.

In conclusion, the number of patients starting on a bDMARD was substantially decreased during the first year of COVID-19 pandemic. Rheumatologists seem to hesitate starting bDMARDs, particularly in RA patients. Nevertheless, their attitudes toward drug choice did not change significantly as compared to the past. Absence of remarkable change in the disease activity of the patients starting on a bDMARD suggested that the more important reason for the decreasing number of patients during pandemic was the patients' concerns about going to a hospital. In the upcoming period, when the pandemic is under control and the healthcare services are able to reach more patients by the new normalization, the number of patients starting on bDMARDs may still be lower than the previous period. In order to ensure that RA and SpA patients can access effective treatments in time, there is a need for patients to be encouraged as well as for obtaining more safety data.

Ethics Committee Approval: The ethics committee approval for using the TReasure database was obtained from Hacettepe University (KA-17/058) in May 2017 and from the Republic of Turkey Ministry of Health (93189304 – 14.03.01) in October 2017.

Informed Consent: Written informed consents of all participants were obtained.

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References

1. Rosenbaum L. The untold toll - the pandemic's effects on patients without COVID-19. *N Engl J Med*. 2020;382(24):2368-2371. [CrossRef]
2. Wahezi DM, Lo MS, Rubinstein TB, et al. American College of Rheumatology guidance for the management of pediatric rheumatic disease during the COVID-19 pandemic: version 1. *Arthritis Rheumatol*. 2020;72(11):1809-1819. [CrossRef]
3. Ouédraogo DD, Tiendrébéogo WJS, Kaboré F, Ntsiba H. COVID-19, chronic inflammatory rheumatic disease and anti-rheumatic treatments. *Clin Rheumatol*. 2020;39(7):2069-2075. [CrossRef]
4. Kalyoncu U, Taşcılar EK, Ertenli Aİ, et al. Methodology of a new inflammatory arthritis registry: TReasure. *Turk J Med Sci*. 2018;48(4):856-861. [CrossRef]
5. Lee YH, Song GG. Relative efficacy and safety of tofacitinib, baricitinib, upadacitinib, and filgotinib in comparison to adalimumab in patients with active rheumatoid arthritis. *Z Rheumatol*. 2020;79(8):785-796. [CrossRef]
6. Aletaha D, Neogi T, Silman AJ, et al. 2010 rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Arthritis Rheum*. 2010;62(9):2569-2581. [CrossRef]
7. van der Linden SVD, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis: a proposal for modification of the New York criteria. *Arthritis Rheum*. 1984;27(4):361-368. [CrossRef]
8. Rudwaleit M, Van Der Heijde D, Landewé R, et al. The development of assessment of spondyloarthritis international society classification criteria for axial spondyloarthritis (Part II): validation and final selection. *Ann Rheum Dis*. 2009;68(6):777-783. [CrossRef]
9. Rudwaleit MV, van der Heijde D, Landewé R, et al. The assessment of spondyloarthritis international Society classification criteria for peripheral spondyloarthritis and for spondyloarthritis in general. *Ann Rheum Dis*. 2011;70(1):25-31. [CrossRef]
10. Slama IB, Allali F, Lakhdar T, et al. Reliability and validity of CDAI and SDAI indices in comparison to DAS-28 index in Moroccan patients with

rheumatoid arthritis. *BMC Musculoskelet Disord*. 2015;16:268. [CrossRef]
11. Akkoc Y, Karatepe AG, Akar S, Kirazlı Y, Akkoç N. A Turkish version of the Bath Ankylosing Spondylitis Disease Activity Index: reliability and validity. *Rheumatol Int*. 2005;25(4):280-284. [CrossRef]
12. Karatepe AG, Akkoc Y, Akar S, Kirazlı Y, Akkoç N. The Turkish versions of the Bath Ankylosing Spondylitis and Dougados Functional Indices: reliability and validity. *Rheumatol Int*. 2005;25(8):612-618. [CrossRef]
13. Machado P, Landewé R, Lie E, et al. Ankylosing Spondylitis Disease Activity Score (ASDAS): defining cut-off values for disease activity states and improvement scores. *Ann Rheum Dis*. 2011;70(1):47-53. [CrossRef]
14. Demirbilek Y, Pehlivantürk G, Özgüler ZÖ, Alp Meşe EA. COVID-19 outbreak control, example of ministry of health of Turkey. *Turk J Med Sci*. 2020;50(SI-1):489-494. [CrossRef]
15. Antony A, Connelly K, De Silva T, et al. Perspectives of patients with rheumatic diseases in the early phase of COVID-19. *Arthritis Care Res*. 2020;72(9):1189-1195. [CrossRef]
16. Onder G, Rezza G, Brusaferro S. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. *JAMA*. 2020;323(18):1775-1776. [CrossRef]
17. Bhoori S, Rossi RE, Citterio D, Mazzaferro V. COVID-19 in long-term liver transplant patients: preliminary experience from an Italian transplant Centre in Lombardy. *Lancet Gastroenterol Hepatol*. 2020;5(6):532-533. [CrossRef]
18. Ramiro S, Sepriano A, Chatzidionysiou K, et al. Safety of synthetic and biological DMARDs: a systematic literature review informing the 2016 update of the EULAR recommendations for management of rheumatoid arthritis. *Ann Rheum Dis*. 2017;76(6):1101-1136. [CrossRef]
19. Doran MF, Crowson CS, Pond GR, O'Fallon WM, Gabriel SE. Frequency of infection in patients with rheumatoid arthritis compared with controls: a population-based study. *Arthritis Rheum*. 2002;46(9):2287-2293. [CrossRef]
20. Mehta P, McAuley DF, Brown M, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet*. 2020;395(10229):1033-1034. [CrossRef]
21. Sarmiento-Monroy JC, Espinosa G, Londoño MC, et al. A multidisciplinary registry of patients with autoimmune and immune-mediated diseases with symptomatic COVID-19 from a single center. *J Autoimmun*. 2021;117:102580. [CrossRef]
22. Strangfeld A, Schäfer M, Gianfrancesco MA, et al. Factors associated with COVID-19-related death in people with rheumatic diseases: results from the COVID-19 Global Rheumatology Alliance physician-reported registry. *Ann Rheum Dis*. 2021;80(7):930-942. [CrossRef]