

Preferences of inflammatory arthritis patients for biological disease-modifying antirheumatic drugs in the first 100 days of covid-19 pandemic

ABSTRACT

Objective: To evaluate treatment adherence and predictors of drug discontinuation among patients with inflammatory arthritis receiving bDMARDs within the first 100 days after the announcement of COVID-19 pandemic.

Method: A total of 1871 patients recorded in TReasure registry for whom advanced therapy was prescribed for rheumatoid arthritis (RA) or spondyloarthritis (SpA) within the 3 months (6-9 months for rituximab) before the declaration of COVID-19 pandemic were evaluated and 1394 (74.5%) responded the survey performed by phone call. Patients' data regarding demographic, clinical characteristics and disease activity before the pandemic were recorded. The patients were inquired for the diagnosis of COVID-19, the rate of continuation on bDMARDs, the reasons for treatment discontinuation, if any, and the current general disease activity (visual analog scale, [VAS]).

Results: A total of 1,394 patients (493 RA [47.3% on anti-TNF] patients and 901 SpA [90.0% on anti-TNF] patients) were included. Overall, 2.8% of the patients had symptoms suggesting COVID-19, and 2 (0.15%) patients had polymerase chain reaction (PCR) confirmed COVID-19. Overall, 18.1% of all patients (13.8% of the RA and 20.5% of the SpA; $p=0.003$) discontinued their bDMARDs. In the SpA group, the patients who discontinued bDMARDs were younger (40 [21-73] vs. 44 years [20-79]; $p=0.005$) and had higher general disease activity; however, no difference was relevant for RA patients.

Conclusion: Although the COVID-19 was quite uncommon in the first 100 days of the pandemic, nearly one-fifth of the patients discontinued bDMARDs within this period. Long-term effects of the pandemic should be monitored.

Keywords: COVID-19, biologic DMARDs, rheumatoid arthritis, spondyloarthritis

INTRODUCTION

In the recent pandemic, the Coronavirus Disease 2019 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Fever, dry cough, sore throat, muscle and joint pain are general disease manifestations and a severe clinical picture requiring hospital admission is encountered in 15-20% of the patients [1,2]. According to the data collected from various countries, COVID-19 fatality rate is about 1-10% [3]. Patients with inflammatory arthritis such as rheumatoid arthritis (RA) and spondyloarthritis (SpA) regularly and continuously receive synthetic or biological disease-modifying antirheumatic drugs (DMARDs) as the main component of their treatment. On the other hand, temporary discontinuation of particularly biological DMARDs (bDMARDs) in the presence of infection is an accepted recommendation [4]. Currently, the world is re-experiencing a pandemic after a period of nearly 100 years. After March 11, 2020 when the World Health Organization (WHO) announced the pandemic, American, European and local societies of rheumatology have claimed general recommendations about drug usage [5,4,6]. The Turkish Society for Rheumatology released COVID-19 recommendations on March 27, 2020 and left the decision on the use of synthetic/biological DMARDs during the pandemic mainly to the primary physician that follows the patient [6]. On the other hand, the behavioral pattern of patients with inflammatory arthritis using biological/synthetic DMARDs during the COVID-19 pandemic is not known in Turkey or in the rest of the world.

Accordingly, the present study aimed to evaluate treatment adherence of patients with inflammatory arthritis receiving bDMARDs within the first 100 days after the announcement of COVID-19 pandemic.

METHODS

Patient Selection

The TReasure registry is a web-based, prospective, observational cohort including RA and spondyloarthritis (SpA) patients from 17 centres in different regions of Turkey and was established in December 2017. Details of the establishment of Treasure registry was previously reported[7]. As of March 2020, there were a total of 7,471 patients with inflammatory arthritis (2,560 RA patients and 4,911 SpA patients) receiving bDMARDs in this registry. The bDMARDs were as follows (arranged in alphabetical order): abatacept, adalimumab, certolizumab, etanercept, golimumab, infliximab, rituximab, secukinumab, and tocilizumab.

The present study included patients who were prescribed bDMARDs and for whom disease activity were recorded within the 3-month period before the declaration date of pandemic (March 2020) in the TReasure registry. This period was determined to be 6-9 months before the declaration date of pandemic for rituximab therapy. In the TReasure registry, the target population consisted of 1,871 patients, of whom 1,394 (74.5%) completed the standard telephone questionnaire, 39 (2.1%) refused to participate in the study, and the remaining could not be reached. The patients who participated and those who did not participate in the study did not differ in terms of demographic and clinical characteristics (data not shown).

Demographic and Clinical Characteristics of the Patients

The demographic and clinical data collected from the patients were defined previously [7]. In brief, the following data were recorded for both RA and SpA patients: age, sex, disease duration, comorbidities (the Charlson comorbidity index), erythrocyte sedimentation rate (ESR) (mm/h), C-reactive protein (CRP) level (mg/L), number of swollen (66 joints) and tender (68 joints) joints, Visual Analog Scale (VAS)-pain score, patients global assessment-VAS, and VAS-fatigue score, and the names of the currently used synthetic DMARDs or bDMARDs. Additionally, in RA patients, positivity for rheumatoid factor (RF) and anti-cyclic citrullinated

peptide (anti-CCP) was determined and the scores of the Disease Activity Score-28 (DAS-28), the Crohn's Disease Activity Index (CDAI), the Simple Disease Activity Index (SDAI), and the Health Assessment Questionnaire (HAQ) were calculated to assess disease activity. In 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) based on CRP (ASDAS-CRP) were used for the assessment of disease activity. The diagnoses in SpA patients were classified as ankylosing spondylitis (according to the modified New York criteria), non-radiographic SpA (according to the axial SpA criteria), peripheral SpA (according to the peripheral SpA criteria), psoriatic arthritis (according to the CASPAR criteria), and enteropathic arthritis (based on the presence of inflammatory bowel disease [IBD] and arthritis/sacroiliitis) [8-11]. In SpA patients, the positivity of HLA-B27 and the presence of psoriasis, IBD, uveitis, dactylitis, and enthesitis (according to the Leeds enthesitis index [LEI]) were also recorded.

Questionnaire Inquiring the Pandemic Period

A standard questionnaire was applied to the patients via phone call. The phone calls were carried out in June 2020. Accordingly, the following information questioned for the time period between March 10, 2020 and the day of telephone call: presence of any signs of coronavirus infection; whether or not being diagnosed with COVID-19; if diagnosed with COVID-19, the place (hospital, home) where the patient was followed-up; whether or not being quarantined due to COVID-19 infection; whether or not having biological or synthetic DMARDs on hand; whether or not the medications were administered during this time; if not administered, the reason(s); whether or not being contacted with his/her physician; and the current disease activity. For the assessment of the current general health status and disease activity; the patients were asked about their general health status (patient global assessment) and rate it from 0 (excellent) to 10 (very bad) and about current disease activity, the patients

were asked to rate their disease activity as ‘‘completely under control’’, ‘‘mild’’, ‘‘moderate’’, ‘‘active’’, and ‘‘highly active’’.

Assessments in the Study

In the present study, comparisons for the patients who discontinued their bDMARDs were performed for the following parameters: age (also categorized in decades), sex, mean disease duration (categorized as 1, 5 and 10 years), seropositivity, sequence of use of bDMARDs (bDMARD-naïve, second-line, third-line), and usage of anti-TNF versus non-anti-TNF bDMARDs. The disease activity scores within the 3 months before the declaration of the pandemic was also recorded; these included mean DAS-28 score, CDAI, and SDAI scores (patients were dichotomized as those with and without low disease activity according to the DAS-28, SDAI, and CDAI scores), mean HAQ score (patients were dichotomized according to the scores of 0.5 and 1), mean BASDAI, BASFI and ASDAS-CRP scores (patients were grouped according to ASDAS-CRP score), CRP level (<5 mg/L and >5 mg/L), patients global assessments-VAS score (grouping with 10-unit intervals), general health status (completely under control, mild, moderate, severe, highly severe), and presence of suspected COVID-19. Patient global assessment -VAS scores before the pandemic was compared with those during the pandemic. Accordingly, an increase by >2 units in the score was defined as worsened disease activity and a decrease by <2 units in the score was defined as improved disease activity. Remission was defined as a general health status-VAS score of ≤ 2 , whereas active disease was defined as a VAS score of ≥ 4 .

Our study is compliant with the Helsinki Declaration and approved by both local ethical committee (Hacettepe University; Approval number: 2020/08-25 (KA-17058)) and Turkish Ministry of Health (Approval number: 66175679-514.05.01-E.170548).

Patient and Public involvement

Patient and public were not involved in this study.

Statistical Analysis

Data analyses were performed using the Predictive Analytics SoftWare (PASW) 18.0 (SPSS Inc., Chicago, IL, USA) for Windows. The variables were investigated using visual (histogram, probability plots) and analytic methods (Kolmogorov-Smirnov, skewness and kurtosis) to determine whether they are normally distributed or not. The data of descriptive analysis were expressed as, mean standard deviation (SD), the median (minimum-maximum) or percentages for categorical variables. Chi-square test or Fisher's exact test was used for categorical variables. Student-t test was used for comparison of normally distributed variables, Mann-Whitney U test was used for comparison of non-normally distributed variables. The variables identified with univariate analyzes ($p < 0.20$), were further entered the logistic regression analysis to determine independent predictors of drug discontinuation separately for RA and SpA patients.

A p value of < 0.05 was considered statistically significant.

RESULTS

Demographic and Clinical Characteristics of the Patients

The demographic, clinical data and drug preferences in 1,394 patients participated in the study are presented in **Table 1**. In the RA group, RF was positive in 267 (62.7%) patients, anti-CCP was positive in 206 (56.4%) patients, and RF and/or anti-CCP were positive in 368 (74.5%) patients. In the SpA group, there were 664 (73.7%) patients with ankylosing spondylitis, 57 (6.3%) patients with non-radiographic SpA, 101 (11.2%) patients with peripheral SpA, 111 (12.3%) patients with psoriatic arthritis, and 21 (2.3%) patients with enteropathic arthritis. Extra-articular signs of the SpA patients were uveitis in 110 (12.5%) patients, IBD in 40 (4.6%) patients, and psoriasis in 141 (16.1%) patients. The HLA-B27 positivity was determined in 333 (59.1%) of 563 patients. Thirty-seven (4.8%) patients had dactylitis and 120 (19.3%) patients had enthesitis at least one enthesal region according to the LEI. Of the RA patients, 233 (47.3%) were receiving anti-tumor necrosis factor (TNF) agents and 260 (52.7%) were receiving non-anti-TNF bDMARDs. On the other hand, of the SpA patients, 811 (90%) were receiving anti-TNF agents and 90 (10%) were receiving anti-interleukin (IL)-17 treatment.

Detecting COVID-19 in the inflammatory arthritis patients receiving bDMARDs

A total of 1,353 patients were questioned about COVID-19 status. Of all patients, 39 (2.8%) had at least one suspicious sign of COVID-19 and 26 (1.9%) visited a healthcare center for this reason (**Table 2**). Fever (body temperature $\geq 38^{\circ}\text{C}$) was the suspicious sign in 14 (1.0%) patients. The polymerase chain reaction (PCR) test was positive for COVID-19 only in 2 (0.15%) of all patients. Both of these patients were treated at home.

Use of biological DMARDs in the Period of Pandemic

A total of 1,362 patients responded to the question about the continuation on bDMARDs in the period of pandemic. Overall, 247 (18.1%) patients discontinued their bDMARDs. Sixty-

six (13.8%) of the RA patients and 181 (20.5%) of the SpA patients discontinued their bDMARDs ($p=0.003$). The distribution of the patients who discontinued/did not receive their bDMARDs is demonstrated in **Table 3**. Among RA patients, etanercept (5.4%) was the least frequently discontinued bDMARD, whereas tocilizumab (20.5%) was the most frequently discontinued bDMARD. The clinical characteristics and disease activity parameters did not differ between the RA patients who discontinued and who did not discontinue their bDMARDs. In the SpA patient group, those who discontinued their bDMARDs were younger than those who did not (median age, 40 years [range, 21-73 years] vs. median age, 44 years [range, 20-79 years]; $p=0.005$). Moreover, the SpA patients continued their bDMARDs had lower disease activity. The multivariate analysis revealed that an age of <40 years, a poorer general health status, a poorer VAS score, and the suspicion for the presence of COVID-19 were the factors that determine the discontinuation of bDMARD therapy in SpA patients (**Table 4**).

The data on the reasons for drug discontinuation were available in 186 (75.3%) of 247 patients who discontinued their bDMARDs. Of these patients, 60 (32.2%) discontinued the therapy based on recommendation of his/her physician, 84 (45.1%) discontinued on their own demand/fear, 13 (6.9%) discontinued due to suspected COVID-19, 8 (4.3%) discontinued due to the lack of disease activity, and 21 (11.3%) discontinued due to other reasons. No difference was determined between RA and SpA patients in terms of reasons for discontinuation of bDMARDs. In the period of pandemic, 550 patients (213 RA patients and 337 SpA patients) were able to communicate with their physicians. The patients communicated with their physicians through phone calls (314 [57.1%] patients), face-to-face interview (203 [36.9%] patients), message (39 [7.1%] patients), e-mail (19 [3.5%] patients), healthcare staff (assistant, nurse) (13 [2.4%] patients), and relatives (5 [0.9%] patients). In 425 (77.3%) of 550 patients, the physicians recommended their patients to continue bDMARD therapy. In 37 (6.7%) of 550

patients, the physicians recommended their patients to receive bDMARDs on demand and/or to extent drug application intervals.

Disease Activity in the Period of Pandemic

Evaluation of the disease activity in the period of pandemic in all patients revealed that the disease was completely under control in 46.8% of the patients (in 40.8% of the RA patients and in 50.0% of the SpA patients), whereas 19.1% of the patients (21.7% of the RA patients and 17.7% of the SpA patients) had mild disease activity, 24.7% of the patients (27.9% of the RA patients and 23.1% of the SpA patients) had moderate disease activity, 7.0% of the patients (6.8% of the RA patients and 7.1% of the SpA patients) had active disease, and 2.4% of the patients (2.9% of the RA patients and 2.1% of the SpA patients) had very high disease activity ($p=0.016$). The mean general health status-VAS score in all patients in the period of pandemic was 3.1 ± 2.5 ; it was 3.4 ± 2.6 in the RA patients and 2.9 ± 2.5 in the SpA patients ($p<0.001$). The mean general health status-VAS score in all patients in the pre-pandemic period was 3.2 ± 2.5 ; it was 3.6 ± 2.6 in the RA patients and 3 ± 2.4 in the SpA patients ($p<0.001$).

As compared with the period before the pandemic, the ratio of patients with worsened disease activity, those with improved disease activity, those in whom the disease become active (while in remission), those with ongoing remission, those with ongoing active disease, and those showing remission (while having active disease) in the first 100 days of pandemic is demonstrated in **Table 5**. In the RA patients, these variables did not show difference between the patients who discontinued and those who did not discontinue their bDMARDs. In the SpA patients, the ratio of those remained in remission before and during the pandemic was 32.1%. The rate of drug discontinuation was lower in the SpA patients remained in remission (22.0% in those who discontinued bDMARDs and 34.8% in those who did not discontinue bDMARDs; $p=0.002$); other parameters showed no difference between the patients who discontinued and those who did not discontinue bDMARDs.

DISCUSSION

The COVID 19 pandemic, which was announced in March 2020 by the WHO, has directly influenced the daily life in both healthy individuals and individuals with chronic illnesses [12]. Immunosuppressed patients rank first among the patient groups that influenced by the pandemic most. Biological DMARDs, which have introduced into use in the last two decades, have been the group of medications primarily focused on due to their potential of increasing the risk of infection. The American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR), which are among the international expert societies on rheumatology, have recommended identification of the risk groups and continuation of bDMARDs as long as possible within the frame of patient-physician communication [5,4]. However, the period of pandemic has caused severe anxiety and fear in some patients. Uncertainty and fear were more prominent particularly in the early period of pandemic.

The present study investigated the therapeutic approaches in the first 100 days after the declaration of pandemic in inflammatory arthritis patients known to receive bDMARD therapy. It was observed that the rate of confirmed COVID-19 cases (0.15%) was extremely rare in the first 100 days and that nearly 3% of the patients needed to be evaluated for suspected COVID-19. The first 100 days of pandemic in Turkey was the period when a strict lockdown was implemented particularly for the people over the age of 65 years and under the age of 18 years. In that period, people having chronic illnesses in particular were on administrative leave and many patients self-quarantined themselves. It is likely that such a lower rate of COVID-19 determined among the patients with inflammatory rheumatic diseases is associated with the above-mentioned strict lockdown. After that period, people began to return to their normal life; therefore, how many of the patients evaluated in the present study will develop COVID-19 infection during their follow-up is an investigation that needs to be performed in the future.

Recent studies supported that patients who take biological and conventional DMARDs have less morbidity in case of COVID-19 [2]. Also, in another study from Turkey consisting of 167 patients with inflammatory rheumatic disease, biologic and conventional DMARDs did not seem to cause worse outcome[13]. However, overall 18% of all inflammatory arthritis patients discontinued bDMARDs in the first 100 days of the pandemic. It was observed that drug discontinuation was more common particularly in the SpA patients than in the RA patients. Etanercept was the least frequently discontinued bDMARD in the RA patients. It was understood that etanercept is being used for almost longer than 20 years and thus considered a relatively reliable therapeutic option for both patients and physicians. The main reason for drug discontinuation was the patient's fear of bDMARD therapy; on the other hand, drug discontinuation was recommended by the physicians in one-third of the patients. In Italy, a survey was conducted between February 2020 and April 2020 in 955 rheumatic patients [14]. In that patient group receiving advanced treatment, modification of biological therapy was performed in nearly 6% of the patients, which is quite lower as compared with the finding found in the present survey study. Accordingly, different cultural factors can be considered determinative. In the present study, among the patients who were able to communicate with their physicians, about 7% were recommended that they could receive treatment on demand or could extend drug application intervals. Receiving bDMARD therapy on demand or extending drug application intervals is a method implemented by clinicians for a long time in daily practice with efficacy and safety proven in the controlled studies. During the pandemic, the physicians preferred this method in some of their patients. On the other hand, there is a patient group trying to reach their physicians but could not achieve. It was understood that a change occurred in the physician-patient communication during the period of pandemic. Specific to the rheumatology, patients' methods of reaching their physicians should be dwelled on and further studies are needed on this subject.

Any factor that might explain bDMARD discontinuation in the RA patients could not be determined. On the other hand, it was observed that the SpA patients with the disease under control were more likely to continue their drugs. This finding is likely to indicate that the SpA patients with the disease under control were more adherent to their medications and they avoided recurrent exacerbations. Fluctuations in disease activity were observed in the first 100 days of pandemic as assessed according to the pre-pandemic period. The rate of being remained in remission during the pandemic for the patients in remission before the pandemic was 21% in the RA group and 32% in the SpA group. It was understood that the patients with high disease activity in the pre-pandemic period experienced more difficulty in the early period of the pandemic.

The present survey study was conducted through the use of a phone interview questionnaire. We could reach three-fourth of the patients; the rates of drug discontinuation and COVID-19 might be higher among those that could not be reached; thus, the results need to be evaluated within the scope of this limitation. The fact that the information regarding steroid use was not inquired could be considered as another limitation.

In conclusion, nearly one-fifth of the RA and SpA patients recorded in the TReasure registry and known to receive bDMARD therapy in the pre-pandemic period discontinued their drugs in the first 100 days of the pandemic. The frequency of COVID-19 was found to be low in the first 100 days of the pandemic, which corresponds to a time period when a strict lockdown was implemented in Turkey. Further investigations need to be performed to find out what will happen when people return to their normal active life. Although patients' fear of treatment appeared to be the main factor, the treatment discontinued or interrupted also due to physicians' recommendation. These treatment modifications in the early period of COVID-19 pandemic may appear as a worsened disease activity in time. Treatment approaches need to be monitored closely in the following period.

Contributorship

All authors contributed equally for conceiving and designing the analysis, collecting the data.

UK and EB performed the analysis and wrote the paper, all authors revised and edited the final version of manuscript.

REFERENCES

1. Carrillo-Vega MF, Salinas-Escudero G, Garcia-Pena C, Gutierrez-Robledo LM, Parra-Rodriguez L. Early estimation of the risk factors for hospitalization and mortality by COVID-19 in Mexico. *PLoS One* 2020;15 (9):e0238905. doi:10.1371/journal.pone.0238905
2. Gianfrancesco M, Hyrich KL, Al-Adely S, Carmona L, Danila MI et al. Characteristics associated with hospitalisation for COVID-19 in people with rheumatic disease: data from the COVID-19 Global Rheumatology Alliance physician-reported registry. *Ann Rheum Dis* 2020; 79 (7):859-866. doi:10.1136/annrheumdis-2020-217871
3. Noor FM, Islam MM. Prevalence and Associated Risk Factors of Mortality Among COVID-19 Patients: A Meta-Analysis. *J Community Health* 2020; 45 (6): 1270-1282. doi:10.1007/s10900-020-00920-x
4. Landewe RB, Machado PM, Kroon F, Bijlsma HW, Burmester GR et al. EULAR provisional recommendations for the management of rheumatic and musculoskeletal diseases in the context of SARS-CoV-2. *Ann Rheum Dis* 2020; 79 (7):851-858. doi:10.1136/annrheumdis-2020-217877
5. Mikuls TR, Johnson SR, Fraenkel L, Arasaratnam RJ, Baden LR et al. (2020) American College of Rheumatology Guidance for the Management of Rheumatic Disease in Adult Patients During the COVID-19 Pandemic: Version 2. *Arthritis Rheumatol*. doi:10.1002/art.41437
6. Babaoglu H. Türkiye Romatoloji Derneği Romatoloji Uzmanları için Koronavirüs (Covid-19) salgını sırasında hastalık yönetimi önerileri. *J Turk Soc Rheumatol* 2020; 12 (1):1-2 doi: 10.4274/raed.galenos.2020.99609
7. Kalyoncu U, Tascilar EK, Ertenli AI, Dalkilic HE, Bes C et al. Methodology of a new inflammatory arthritis registry: TReasure. *Turk J Med Sci* 2018; 48 (4):856-861. doi:10.3906/sag-1807-200
8. van der Linden S, 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. doi:10.1002/art.1780270401
9. Rudwaleit M, van der Heijde D, Landewe R, Listing J, Akkoc N 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. doi:10.1136/ard.2009.108233
10. Rudwaleit M, van der Heijde D, Landewe R, Akkoc N, Brandt J 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. doi:10.1136/ard.2010.133645
11. Taylor W, Gladman D, Helliwell P, Marchesoni A, Mease P et al. Classification criteria for psoriatic arthritis: development of new criteria from a large international study. *Arthritis Rheum* 2006; 54 (8):2665-2673. doi:10.1002/art.21972
12. WHO Director-General's opening remarks at the media briefing on COVID-19/ 11 March 2020. <https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020>. Accessed 27/09 2020
13. Sinem Nihal Esatoglu, Koray Tascilar, Hakan Babaoglu et al. COVID-19 Among Patients With Inflammatory Rheumatic Diseases, PREPRINT (Version 1) available at Research Square. Dec 2020. <https://doi.org/10.21203/rs.3.rs-115378/v1>
14. Favalli EG, Monti S, Ingegnoli F, Balduzzi S, Caporali R et al. (2020) Incidence of COVID-19 in Patients With Rheumatic Diseases Treated With Targeted Immunosuppressive Drugs: What Can We Learn From Observational Data? *Arthritis Rheumatol*. 2020; 72 (10): 1600-1606. doi:10.1002/art.41388

Table 1. Demographic and clinical characteristics of the patients

	Patients with RA n=493	Patients with SpA n=901
Female sex, n(%)	400 (81.1)	398 (44.2)
Age, years, median(range)	55 (18-86)	43 (20-79)
Disease duration, months, median(range)	131 (2-509)	111 (2-672)
ESR, mm/h, median(range)	16 (1-120)	12 (1-103)
CRP, mg/L, median(range)	3.96 (0.1-98.9)	3.84 (0.1-91.1)
Global assessment of health–VAS score, median(range)	30 (0-100)	25 (0-100)
Pain-VAS score, median(range)	30 (0-100)	20 (0-100)
Fatigue-VAS score, median(range)	30 (0-100)	20 (0-100)
HAQ score, median(range)	0.38 (0-90)	-
Number of swollen joints, mean±SD	0.58±2.21	0.1±0.71
Number of tender joints, mean±SD	1.31±3.41	0.29±1.6
DAS-28-ESR score, median(range)	2.55 (0.56-8.16)	-
CDAI score, mean±SD	7.97±8.92	-
SDAI score, mean±SD	17.83±20.08	-
BASDAI score, n(%)	-	1.55 (0-9.5)
BASFI score, n(%)	-	1.2 (0-9.7)
Hypertension, n(%)	143 (29.7)	137 (15.4)
Obesity, n(%)	166 (35.3)	220 (24.4)
Diabetes mellitus, n(%)	48 (9.9)	57 (6.4)
Hyperlipidemia, n(%)	71 (15.1)	98 (11.2)

Coronary artery disease, n(%)	20 (4.3)	17 (1.9)
COPD, n(%)	11 (2.4)	3 (0.3)
Asthma, n(%)	26 (5.6)	28 (3.3)
Malignancy, n(%)	5 (1)	8 (0.9)
Presence of at least 1 comorbidity, n(%)	186 (38.2)	462 (51.6)
Presence of ≥ 2 comorbidities, n(%)	121 (24.8)	229 (25.6)
Presence of ≥ 3 comorbidities, n(%)	167 (34.3)	160 (17.9)
ASDAS-CRP, median(range)	-	1.84 (0-5.2)
Abatacept, n(%)	32 (6.5)	-
Adalimumab, n(%)	89 (18.1)	270 (30)
Certolizumab, n(%)	38 (7.7)	146 (16.2)
Etanercept, n(%)	75 (15.2)	182 (20.2)
Golimumab, n(%)	18 (3.7)	90 (10)
Infliximab, n(%)	13 (2.6)	123 (13.7)
Rituximab, n(%)	40 (8.1)	-
Secukinumab, n(%)	-	90 (10)
Tofacitinib, n(%)	77 (15.6)	-
Tocilizumab, n(%)	111 (22.5)	-
Hydroxychloroquine, n(%)	164 (33.3)	13 (1.4)
Leflunomide, n(%)	117 (23.7)	17 (1.9)
Methotrexate, n(%)	135 (27.4)	57 (6.3)
Sulfasalazine, n(%)	23 (4.7)	71 (7.9)

RA, rheumatoid arthritis; SpA, spondyloarthritis; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein, VAS, Visual Analog Scale; HAQ, Health Assessment Questionnaire; DAS-28, the Disease Activity Score-28; CDAI, the Crohn's Disease Activity Index; SDAI, the Simple Disease Activity Index; BASDAI, the Bath Ankylosing Spondylitis Disease Activity Index; BASFI, the Bath Ankylosing Spondylitis Functional Index; COPD, chronic obstructive pulmonary disease; ASDAS, Ankylosing Spondylitis Disease Activity Score; SD, Standard Deviation.

Table 2. Results of the questions about COVID-19 status in the study patients during the period of pandemic

	All patients	RA	SpA
	n=1353	n=487	n=866
Presence of any suspected sign of COVID-19	39 (2.8)	6 (1.2)	33 (3.7)
Admission to a healthcare center for suspected COVID-19	26 (1.9)	5 (1.0)	22 (2.5)
Having PCR testing for COVID-19	21 (1.6)	5 (1.0)	16 (1.8)
Quarantine recommendation for suspected COVID-19	10 (0.73)	0 (0)	10 (1.15)
PCR positivity for COVID-19	2 (0.15)	0 (0)	2 (0.23)
Family history of COVID-19 positivity	9 (0.66)	3 (0.6)	6 (0.7)

Data are presented as number (percentage, %).

COVID-19, Coronavirus Disease 2019; PCR, polymerase chain reaction.

Table 3. Distribution of the patients who discontinued their biological disease-modifying anti-rheumatic drugs

	Patients with RA	Patients with SpA
	n/N (%)	n/N (%)
All bDMARDs	66 (14.0)	181 (20.5)
Abatacept	4/31 (12.9)	NA
Adalimumab	15/86 (17.4)	46/264 (17.4)
Etanercept	4/74 (5.4)	38/180 (21.1)
Golimumab	3/18 (16.7)	15/86 (15.6)
Infliximab	2/12 (16.7)	29/118 (24.5)
Certolizumab	3/37 (8.1)	31/146 (21.2)
Rituximab	7/39 (17.9)	NA
Tofacitinib	6/75 (8.0)	NA
Tocilizumab	22/107 (20.5)	NA
Secukinumab	NA	22/89 (24.7)
Hydroxychloroquine	19/157 (12.1)	5/181 (2.8)
Leflunomide	14/113 (12.4)	4/181 (2.2)
Methotrexate	14/134 (10.4)	13/181 (7.2)
Sulfasalazine	2/22 (9.1)	13/181 (7.2)

RA, rheumatoid arthritis; SpA, spondyloarthritis; bDMARDs, biological disease-modifying anti-rheumatic drugs; NA, not applicable.

Table 4. Characteristics of the patients with spondyloarthritis who discontinued their biological disease-modifying antirheumatic drugs

	Patients with SpA who discontinued bDMARDs	Patients with SpA who continued bDMARDs	Univariate p	Odds Ratio 95% CI	Multivariate p	Odds Ratio 95% CI
Age (<40 vs. ≥40)	84 (46.4)	243 (34.6)	0.004	1.64 (1.18-2.28)	0.002	1.76 (1.24-2.51)
General health status						
Completely under control	51 (28.2)	390 (55.8)				Reference
Mild	52 (28.7)	103 (14.7)	<0.001	3.86 (2.48-6.01)	<0.001	3.20 (1.99-5.15)
Moderate	51 (28.2)	153 (21.9)	<0.001	2.55 (1.66-3.92)	0.003	2.03 (1.26-3.27)
Severe	21 (11.6)	41 (5.9)	<0.001	3.92 (2.15-7.15)	0.003	2.65 (1.38-5.10)
Extremely severe	6 (3.3)	12 (1.7)	0.010	3.82 (1.38-10.63)	0.103	2.46 (0.83-7.28)
VAS-PGA, <20 vs. ≥20	38 (21.1)	281 (40.2)	<0.001	2.51 (1.70-3.71)	0.016	1.74 (1.11-2.75)
Suspected COVID-19	12 (6.6)	20 (2.9)	0.019	2.41 (1.16-5.04)	0.136	1.83 (0.83-4.03)

Data are presented as number (percentage, %).

SpA, spondyloarthritis; bDMARDs, biological disease-modifying antirheumatic drugs; CI, confidence interval; VAS-PGA, Visual Analog Scale-Patient Global Assessment; COVID-19, coronavirus disease 2019

Table 5. As assessed according to the pre-pandemic period, changes in disease activity determined by the general health status-Visual Analog Scale scores during the period of pandemic

Status	Definition	Patients with RA	Patients with SpA
		n=428	n=809
Worsened disease activity during the pandemic	>2 units increase in the VAS score after the pandemic as compared with before the pandemic	100 (23.4)	137 (16.9)
Patients with improved disease activity during the pandemic	<2 units decrease in the VAS score after the pandemic as compared with before the pandemic	89 (20.8)	118 (14.6)
While in remission before the pandemic, becoming active during the pandemic	A VAS score of ≤ 2 before pandemic and ≥ 4 after the pandemic,	69 (16.1)	100 (12.4)
Remission both before and during the pandemic	A VAS score of ≤ 2 before the pandemic and ≤ 2 after the pandemic	91 (21.3)	260 (32.1)
Active disease both before and during the pandemic	A VAS score of ≥ 4 before the pandemic and ≥ 4 after the pandemic	121 (28.3)	175 (21.6)
Active disease before pandemic, remission during pandemic	A VAS score of ≥ 4 before the pandemic and ≤ 2 after pandemic	52 (12.1)	86 (10.6)

Data are presented as number (percentage, %). RA, rheumatoid arthritis; SpA, spondyloarthritis; VAS, Visual Analog Scale; bDMARDs, biological disease-modifying anti-rheumatic drugs; NA, not applicable

