Research Article

Pamukkale Medical Journal
doi:https://dx.doi.org/10.31362/patd.1223660

Factors associated with frequency and severity of COVID-19 in patients with axial spondyloarthritis

Aksiyel spondiloartritli hastalarda COVİD-19 sıklığı ve ilişkili faktörler

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Posted date:23.12.2022 Acceptance date:22.03.2023

Abstract

Purpose: The severe course of COVID-19 in individuals with chronic diseases has led to concerns in managing rheumatic diseases during the pandemic; therefore, we aimed to define the factors associated with the frequency and severity of COVID-19 in patients with axial spondyloarthritis (axSpa) in this study.

Materials and methods: Patients with axSpa who were followed up in three tertiary hospitals and used their treatment regularly for at least six months were included. We assessed the relationship between axSpa-associated variables such as disease duration time, radiological severity, treatment and COVID-19 outcomes.

Results: A total of 833 patients with a mean disease duration of 109 months were analyzed; 64.5% of them had ankylosing spondylitis, 35.5% had non-radiographic axSpa, and 59.4% of patients were treated with a biologic agent. The frequency of COVID-19 was 23% (n:192); only five patients (0.5%) had a history of intensive care unit. Advanced age, hypertension (HT), and diabetes mellitus (DM) were found to be significantly more common in those with involvement in high-resolution computed tomography (HRCT) (*p*:0.02, *p*:0.01, and *p*<0.001). In hospitalized individuals, female gender, HT, DM, and disease lasting longer than 10 years were significantly higher (*p*:0.03, *p*:0.011, *p*<0.001, and *p*:0.014). Only DM was found as an independent risk factor for both pulmonary involvement in HRCT (*p*:0.029) and hospitalization (*p*:0.001).

Conclusion: We conducted our study with a homogenous study population and our results suggested that biological agents did not affect poor COVID-19 outcomes; only DM was associated with a more severe COVID-19 course in patients with axSpa.

Key words: COVID-19, axial spondyloarthritis, ankylosing spondylitis, non-radiographic axial spondyloarthritis, diabetes mellitus.

Pekdiker M, Kara M, Koc E, Kimyon G. Factors associated with frequency and severity of COVID-19 in patients with axial spondyloarthritis. Pam Med J 2023;16:404-411.

Öz

Amaç: Kronik hastalığa sahip bireylerde COVİD-19'un ağır seyri romatolojik hastalıkların tedavisinde endişeye yol açmıştır. Bu yüzden çalışmamızda aksiyel spondiloartritli (aSpa) hastalarda COVİD-19 sıklığı ve şiddeti ile ilişkili faktörleri tanımlamayı amaçladık.

Gereç ve yöntem: Üç tersiyer merkezde izlenen ve en az altı aydır tedavilerini düzenli kullanan aSpa'lı hastalar çalışmaya dahil edildi. Hastalık süresi, radyolojik şiddet ve tedavi gibi aSpa ilişkili değişkenler ile COVİD-19 sonuçları arasındaki ilişkiyi değerlendirdik.

Bulgular: Ortalama hastalık süresi 109 ay olan toplam 833 hasta analiz edildi; %64,5'inde ankilozan spondilit ve %35,5'inde non-radyografik aSpa tanısı mevcutken hastaların %59,4'ü biyolojik ajanlarla tedavi edilmekteydi. Çalışma grubumuzda COVİD-19 sıklığı %23 (n:192) olup sadece beş olguda (%0,5) yoğun bakım ünitesi öyküsü vardı. İleri yaş, hipertansiyon (HT) ve diabetes mellitus (DM) yüksek çözünürlüklü bilgisayarlı tomografisinde (YÇBT) tutulum olan hastalarda anlamlı olarak daha fazlaydı (*p*:0,02, *p*:0,01 ve *p*<0,001). Hastaneye yatış gerektiren hastalarda ise ileri yaş, HT, DM ve 10 yıldan uzun hastalık süresi anlamlı olarak daha fazlaydı (*p*:0,03, *p*:0,011, *p*<0,001 ve *p*:0,014). Çok değişkenli regresyon analizinde sadece DM hem YÇBT'de akciğer tutulumu (*p*:0,029) hem de hospitalizasyon (*p*:0,001) için bağımsız bir risk faktörü olarak bulundu.

Sonuç: Homojen bir hasta grubu ile yaptığımız çalışmamızın sonuçları biyolojik ajanların COVİD-19 ilişkili kötü sonuçlar üzerine etkisini olmadığını göstermiştir; çalışmamızda sadece DM, aSpa'lı hastalarda daha ciddi COVİD-19 sonuçları ile ilişkiliydi.

Anahtar kelimeler: COVID-19, aksiyel spondiloartrit, ankilozan spondilit, radyografik olmayan aksiyel spondiloartrit, şeker hastalığı.

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Pekdiker M, Kara M, Koç E, Kimyon G. Aksiyel spondiloartritli hastalarda COVİD-19 sıklığı ve ilişkili faktörler. Pam Tıp Derg 2023;16:404-411.

Introduction

The COVID-19 pandemic which is caused by SARS-CoV-2 virus affected over 500 million people, and approximately 6.5 million patients died. Advanced age and having comorbidity or cancer are the risk factors for serious COVID-19 disease [1]. Rheumatic diseases are immune-mediated chronic diseases; conventional and biological disease-modifying anti-rheumatic drugs (c/bDMARDs) act on the immune system. Therefore, rheumatologists could be undecided about anti-rheumatic treatment, especially bDMARDS, during the pandemic.

Ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpa) are common diseases in daily rheumatologic practice; sacroiliac joints, vertebral column, peripheral joints, and enthesis are the most targeted sites. Axial spondyloarthritis (axSpa) has a prevalence higher than 1% in selected areas [2, 3]. Biological agents such as tumor necrosis factor inhibitors (anti-TNF) and interleukin inhibitors (ILi) are recommended for the treatment of patients with axSpa who has high disease activity [4]. Five licensed anti-TNF agents have different molecular structures for treating axSpa; their first approvals for AS and nr-axSpa were in 2003 and 2012, respectively [5]. Secukinumab (SEC), which demonstrates long-term efficacy and safety for axSpa, is a fully human monoclonal antibody blocking IL-17A; approved for AS and nr-axSpa in 2016 and 2020, respectively [6].

Both anti-TNF agents and SEC are associated with increased infections (but not serious infections) in patients with axSpa [7] so patients or rheumatologists could avoid biological agents during the COVID-19 pandemic. Do comorbidities, radiological severity or biological agents have a negative impact on COVID-19 in patients with axSpa? Which biologic agent is safer in patients with axSpa during the pandemic? These questions are still unclear.

Over the past two years, most published data on COVID-19 and rheumatic diseases consisted of different rheumatic disease groups, so the results of a homogenous study group with axSpA are rare. In our study, we tried to investigate the answers to the above questions. We hope that our real-life results will provide more confidencely follow-up and treatment protocols in patients with axSpa during the COVID-19 pandemic.

Materials and methods

Patients

We analyzed patients with axSpa who were following up in three central tertiary hospitals, which were localized in three different geographic regions of Turkey. The study started in March 2020, as the first COVID-19 case detection date; the study finished in March 2021, as the first cycle of the COVID-19 vaccination completion date. The patients' electronic files were evaluated retrospectively for demographic, clinical, and treatment data. Inclusion criteria of patients were; aged 18 years or older, diagnosed with AS according to Modified New York Criteria or nr-axSpa according to Assessment of Spondyloarthritis International Society (ASAS) criteria [8, 9], regularly using cDMARD or bDMARD at least six months. Exclusion criteria were; aged 65 years or older, concomitantly immunosuppressive drug therapy (such as >7.5 mg/day prednisolone, azathioprine, mycophenolate mofetil, cyclophosphamide or any chemotherapeutic agent), having an immunosuppressive disease/status such as active cancer (solid or hematologic), transplantation history, HIV infection, chronic pulmonary disease (CPD: chronic obstructive pulmonary disease, COPD or interstitial lung disease, ILD), and liver cirrhosis. Comorbidities such as hypertension (HT), diabetes mellitus (DM), and chronic kidney disease (CKD: defined as glomerular filtration rate <60 [min/1.73m^2 and lasting at least three months) were noted if there was.

Definition of COVID-19

We identified the SARS-CoV-2 infection according to diagnosis guideline of the Turkish Ministry of Health [10]. We noted the results of polymerase chain reaction (PCR) from the nasopharyngeal swab, which is regarded as the gold standard laboratory technique diagnosing SARS-CoV-2 infection [11]. We noted the high-resolution chest computed tomography (HRCT) results as positive if a patient had Coronavirus Disease 2019 Reporting and Data System (CO-RADS) Score ≥3. In asymptomatic individuals, a CO-RADS score of 3 or greater detects SARS-CoV-2 infection with low sensitivity but high specificity [12]. A confirmed diagnosis was defined as a positive test result from nasopharyngeal swab or chest CT. We divided patients with a positive history of SARS-CoV-2 into three groups according to treatment completing area; home isolation, hospitalization at service, or hospitalization at the intensive care unit (ICU).

Statistical analysis

Data were assessed using SPSS 21.0 (Statistical Package for the Social Science, version 21.0). Descriptive statistics were frequency (n) and percentage (%). The chi-square test was used to determine whether the difference between the observed and expected frequencies was significant. Univariate and multivariate regression analyses assessed the relationship between demographic data and COVID-19. A p-value less than 0.05 was considered statistically significant. The Ethics Committee of the University where the study was conducted approved our study.

Results

We analyzed 833 patients with axSpA; 54.3% of patients were male, and the mean age was 42 years. In the study population, 64.5% of patients had been diagnosed with AS, and the mean disease duration was nearly 10 years. Biologic agent use was 59.4%; adalimumab was the most commonly chosen with a rate of 20.8%. COVID-19 history in patients with axSpA was 23%, and 2.5% were hospitalized. Twelve patients with COVID-19 had negative PCR test results, and four of them had positive CT results, so 184 (95.8%) patients had confirmed diagnosis. Demographic, comorbidity, diagnosis, and treatment characteristics shown in Table 1.

We didn't find any relationship between variables and the frequency of COVID-19. COVID-19 frequency was 22.1% and 23.9% in smoker and non-smoker group respectively; 22.8% and 23.4% in biological agent user and non-user group respectively, but differences were not statistically significant.

Advanced age, HT, and DM were significantly higher in patients with pulmonary involvement in HRCT (p:0.02, p:0.01, and p<0.001, respectively). Pulmonary involvement in HRCT was 20.4% and 24.1% in biological agent user and non-user groups respectively; 27.5% and 17.9% in disease duration time ≥10 years and <10 years respectively, differences were not statistically significant. Female sex, HT, DM, and disease duration time ≥10 years were significantly higher in the hospitalized patients (p:0.03, p:0.011, p<0.001 ve p:0.014, respectively). The hospitalization rate was 15.8% and 8% in biological agent user and non-user groups respectively, but the difference was not statistically significant. Univariate analysis between variables and COVID-19 outcomes was given in Table 2. In multivariate analysis, only DM was found as an independent risk factor of pulmonary involvement in HRCT (p:0.029) and hospitalization (p:0.001).

COVID-19 frequency was statistically higher in non-steroidal anti-inflammatory drugs (NSAID) users than drug-free group (p:0.016) in univariate analyses but pulmonary involvement and hospitalization rates were similar. The frequency, pulmonary involvement, and hospitalization rates were similar between sulfasalazine and NSAID groups. There were no significantly differences in COVID-19 outcomes between biological agents; results were shown in Table 3.

Table 1. Demographic, comorbidity, diagnosis and treatment characteristics

Patient, (n)	833
Male sex %, (n)	54.3 (452)
Female sex %, (n)	45.7 (381)
Age, mean, years (range)	42 (23-82)
Body-mass index, mean, (kg/m^2), (range)	26.4 (16-46)
Smoking, %, (n)	45.1 (376)
Diabetes mellitus, %, (n)	9.2 (77)
Hypertension, %, (n)	16.3 (136)
Chronic kidney disease, %, (n)	2.3 (19)
Ankylosing spondylitis, %, (n)	64.5 (537)
Non-radyographic axial spondyloarthritis, %, (n)	35.5 (296)
Disease duration time, mean, month, (range)	109 (1-504)
Non-biological treatment %, (n)	40.6 (337)
***Drug-free follow-up**	14.8 (123)
***Non-steroidal anti-inflammatory drugs**	15.5 (129)
***Sulfasalazine**	9.7 (81)
***Methotrexate**	0.6 (5)
Biological treatment, %, (n)	59.4 (495)
***Adalimumab**	20.8 (173)
***Infliximab**	10 (83)
***Etanercept**	9 (75)
***Golimumab**	8.5 (71)
***Certolizumab pegol**	4.9 (41)
***Secukinumab**	6.2 (52)
COVID-19 history, %, (n)	23 (192)
***Home isolation**	20.5 (171)
***Hospitalization at service**	1.9 (16)
***Hospitalization at intesive care unit**	0.6 (5)
PCR positivity in COVID-19 cases %, (n)	93.8 (180)
Pulmonary involvement on HRCT in COVID-19 cases %, (n)	21.9 (42)

PCR: polymerase chain reaction (PCR) from nasopharangeal swab, HRCT: high-resolution computed tomography of lungs

Table 2. Univariate analysis between variables and COVID-19 outcomes

Variable	**Frequency of COVID-19**	**Pulmonary involvement on HRCT**	**Hospitalization**
Age, years (≥50, <50)	-	**+**	-
Gender	-	-	**+**
BMI, kg/m^2 (>25, ≤25)	-	-	-
Smoking	-	-	-
Hypertension	-	**+**	+
Diabetes mellitus	-	**+**	+
Diagnosis (AS, nr-axSpA)	-	-	-
Disease duration time, years (≥10, <10)	-	-	+
Biologic agent use	-	-	-

BMI: body-mass index; AS: ankylosing spondylitis; nr-axSpA: non-radyographic axial spondyloarthritis
HRCT: high-resolution computed tomography of the lungs; '-', $p>0.05$; '+', $p\leq0.05$

Table 3. Comparison of biologic agents and COVID-19 outcomes HRCT, high- resolution computed tomography of lungs

Biologic agent	COVID-19 frequency (%), (n/total patient)	Hospitalization (%), (n/total patient)	Pulmonary involvement on HRCT (%), (n/total patient)
Adalimumab	25.4 (44/173)	9.0 (4/44)	15.9 (7/44)
Infliximab	15.7 (13/83)	15.4 (2/13)	53.8 (7/13)
Etanercept	18.7 (14/75)	7.1 (1/14)	21.4 (3/14)
Golimumab	31.0 (22/71)	0 (0/22)	13.6 (3/22)
Certolizumab pegol	22.0 (9/41)	11.1 (1/9)	11.1 (1/9)
Secukinumab	21.2 (11/52)	9.1 (1/11)	18.2 (2/11)
Total	22.8 (113/495)	8 (9/113)	20.4 (23/113)

Discussion

Previous studies usually included patients with a pooled inflammatory rheumatic disease (IRD) groups. However, in this multi-centric study, we defined the COVID-19 outcomes in a homogenous axSpA study group; 23% of patients had SARS-CoV-2 infection in an one-year period, but variables did not affect the frequency of infection. Advanced age, HT, and DM were statistically higher in patients with pulmonary involvement in HRCT; female sex, HT, DM, and disease duration time ≥10 years were statistically higher in hospitalized patients in univariate analysis. In multivariate analysis, we found that only DM was the independent risk factor of pulmonary involvement in HRCT and hospitalization. Biologic agent use did not affect the frequency or severity of COVID-19. Serious complications such as venous thromboembolism, cerebral or myocardial infarction, acute renal failure, or mechanical ventilation were not observed in hospitalized patients.

Raiker et al. [13] showed that patients with axSpa had better COVID-19 outcomes such as severity, hospitalization, and mortality but worsened results for venous thromboembolism (VTE) and cerebral infarction than propensity score matched controls, but we didn't observe these complications; anti-TNF agents did not affect poor COVID-19 outcomes as our study. Rosenbaum et al. [14] reported that both Spa and its treatment, including cDMARDs or bDMARDs (anti-TNF agents and IL-17 inhibitors), had no unfavourable impact on COVID-19 frequency and severity; 83.5% of study patients were AS and 7% were nr-axSpa, but results didn't include subgroup analysis. Turk et al. [15] performed a study with AS patients before the vaccination against SARS-CoV-2 infection as our study (77 were TNFi users, 49 were non-users; age, sex, and comorbidities were similar between the two groups) and defined that anti-TNF agents weren't associated with frequency and severity of COVID-19; our results supported that small sample sized study.

In a study from Spain which included 820 patients with IRDs (25% was of them were AS) between 1st December 2019 and 1st December 2020, COVID-19 frequency was 4.3% in patients with AS, and bDMARDs (except for rituximab) weren't associated with frequency of SaRS-CoV-2 infection and serious COVID-19 manifestations also AS-specific results were absent [16]. The COVID-19 Global Rheumatology Alliance reported that axSpa, biologic agents, NSAIDs, and csDMARDs were not associated with increased hospitalization; age >65 years, DM, HT, and lung disease were associated with higher hospitalization ratio, but only 8% of the study population had diagnose with axSpA. Their hospitalization rate was (33%) higher than our study, which could be a result of exclusion criteria of our study, such as older age and chronic lung disease [17]. In a study from Turkey which included 535 patients with IRDs (35% was of them Spa, and 61.6% of patients achieved bDMARDs) between June 2020-March 2021, adalimumab (ADA), etanercept (ETA), and golimumab (GOL) were associated with lower SARS-CoV-2 infection rates than non-bDMARD group and ADA reduced the hospitalization ratio; but results weren't specific to axSpa [18]. Favalli et al. [19] showed that the incidence and severity of COVID-19 in patients with IRDs who were treated with csDMARDs or bDMARDs were not significantly different from the general population in the same region; the study population was heterogeneous, and only 19% was of them were AS.

A meta-analysis from China reported that anti-TNF agents had lower hospitalization risk and older age was associated with worse clinical outcomes in patients with IRDs during pandemic [20]. In a multi-centric study from Germany which included 468 patients with IRDs who had confirmed COVID-19 diagnosis between March 2020-November 2020, advanced age (especially >75 years), rheumatic disease activity, cardiovascular disease, ILD/COPD, glucocorticoid treatment (GC) >5 mg/day were the independent risk factors of hospitalization as the general population. Regarding the IRD diagnosis, RA was the most common with a rate of 48%, and axSpa was the third as 12%. The hospitalization rate was 16% in patients with Spa, which was lower than RA. Unlike our study, DM does not affect poor prognosis [21]. The hospitalization risk of COVID-19 in patients with immune-mediated inflammatory diseases (IMID) is higher than in the general population, but the hospitalization risk varies between IMIDs; iritis, multiple sclerosis, RA, and vasculitis have an increased risk but is not applicable for AS so we believe that each IMID should be assessed separately with a homogenous study group for the evaluation of COVID-19 outcomes [22]. In a prospective study with 103 COVID-19 patients who had a diagnosis with AS (54%) and RA (46%), hospitalized patients had a higher ratio of advanced age, HT, COPD, and GC use, but anti-cytokine therapy wasn't associated with worse COVID-19 outcomes [23].

Some predictive factors of acute respiratory distress syndrome (ARDS) in patients with rheumatic diseases such as age, daily glucocorticoid dose, pulmonary hypertension, interstitial lung disease, CKD, rituximab (RTX), DM, HT, active rheumatic disease, and morbid obesity existed in our exclusion criteria so it may be the reason why we didn't encounter the ARDS [24]. Obesity, male sex, HT, DM, and CKD are associated with poor prognosis in COVID-19. Still, we defined only DM, which could be a result of study design because other poor prognostic factors such as advanced age (>65 years), cardiovascular disease, CLD, transplantation or cancer were replaced in exclusion criteria [25]. Pablos et al. [26] showed that connective tissue disease had worsened outcomes than inflammatory arthritis during COVID-19 pandemic so rheumatologists should keep in mind both of disease type and comorbidities [26].

Pulmonary involvement in HRCT and hospitalization rates were 20.4% versus 24.1%, and 8% versus 15.2% in biological agent user and non-user groups, but the differences were not statistically significant. In patients with severe SARS-CoV-2 infection, the serum level of TNF-α is elevated, which causes cytokine storm and lung injury [27, 28]; potential beneficial effects of TNF-α blocking may be a result of this mechanism. Systemic GC and RTX use have harmful effects on COVID-19 in patients with IRD, but GC is not widely used, and RTX is not licensed for the treatment of axSpa [16, 17, 21, 23, 24, 29]. Thus, the treatment of axSpa is safe during COVID-19 pandemic.

There were some limitations in our study. First, we didn't perform SARS-CoV-2 antibody testing because of technical insufficiency, so that we couldn't detected the asymptomatic COVID-19 cases; a serologic study, which was based on anti-SARS-CoV-2 antibodies, demonstrated that COVID-19 cases were higher than reported based on symptoms or PCR test form nasopharyngeal swabs [30]. Second, we didn't had mortality results because the study included the patients who visited to the hospital. Third, we didn't had disease activity indexes during the pandemic because of the communal isolation rules. Four, biological agent users were more isolated than the non-biologic group in daily life because they had legal permission to work.

In conclusion, we performed a study with a homogenous study group including only patients with axSpa (not including other IRDs). Only DM was an independent predictor of pulmonary involvement in HRCT and hospitalization in patients with axSpa. During an one-year period, hospitalization and ICU requirement rate was 2.5% and 0.6%, respectively; serious complications were absent. We didn't detect a red flag for the treatment of axSpa during COVID-19 pandemic; cDMARDs or bDMARDS showed a good safety profile. No differences existed between biological agents but larger studies were needed comparing head-to-head results.

Conflict of interest: The authors declared no conflict of interest.

References

1. World Health Organization (WHO) https://www.who.int (World Health Organization official website)
2. Sieper J, Poddubnyy D. Axial spondyloarthritis. Lancet 2017;390:73-84. https://doi.org/10.1016/S0140-6736(16)31591-4
3. Lopez Medina C, Molto A. Update on the epidemiology, risk factors, and disease outcomes of axial spondyloarthritis. Best Pract Res Clin Rheumatol 2018;32:241-253. https://doi.org/10.1016/j.berh.2018.10.006
4. Van der Heijde D, Ramiro S, Landewé R, et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. Ann Rheum Dis 2017;76:978-991. https://doi.org/10.1136/annrheumdis-2016-210770
5. Evangelatos G, Bamias G, Kitas GD, Kollias G, Sfikakis PP. The second decade of anti-TNFa therapy in clinical practice: new lessons and future directions in the COVID-19 era. Rheumatol Int 2022;42:1493-1511. https://doi.org/10.1007/s00296-022-05136-x
6. Aparicio M, Guillén Astete CA, López Medina C, Sastre C, Rodríguez Martínez FJ. Evidence for the use of secukinumab in patients with radiographic and non-radiographic axial spondyloarthritis in the last 5 years. Rheumatol Ther 2022;9:73-94. https://doi.org/10.1007/s40744-021-00400-1
7. Sun WT, He YH, Dong MM, et al. The comparative safety of biological treatment in patients with axial spondylarthritis: a meta-analysis of randomized controlled trials with placebo. Eur Rev Med Pharmacol Sci 2020;24:9824-9836. https://doi.org/10.26355/eurrev_202010_23192
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;27:361-368. https://doi.org/10.1002/art.1780270401
9. Rudwaleit M, van der Heijde D, Landewe 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;68:777-783. https://doi.org/10.1136/ard.2009.108233
10. The guidelines published by the Turkish Ministry of Health's Scientific Committee. URL: https://covid19.saglik.gov.tr
11. Tahamtan A, Ardebili A. Real-time RT-PCR in COVID-19 detection: issues affecting the results. Expert Rev Mol Diagn 2020;20:453-454. https://doi.org/10.1080/14737159.2020.1757437
12. De Smet K, De Smet D, Ryckaert T, et al. Diagnostic performance of Chest CT for SARS-CoV-2 infection in individuals with or without COVID-19 symptoms. Radiology 2020;298:30-37. https://doi.org/10.1148/radiol.2020202708
13. Raiker R, Pakhchanian H, Kavadichanda C, Gupta L, Kardes S, Ahmed S. Axial spondyloarthritis may protect against poor outcomes in COVID19: propensity score-matched analysis of 9766 patients from a nationwide multicentric research network. Clin Rheumatol 2022;41:721-730. https://doi.org/10.1007/s10067-021-05979-y
14. Rosenbaum JT, Weisman MH, Hamilton H, et al. The interplay between COVID-19 and spondyloarthritis or its treatment. J Rheumatol 2022;49:225-229. https://doi.org/10.3899/jrheum.210742
15. Türk SM, Öztürk Z, Karataş D, Erkorkmaz Ü, Gönüllü E. Evaluation of the frequency and intensity of COVID-19 in patients with ankylosing spondylitis under anti-TNF therapy. Turk J Med Sci 2022;52:522-523. https://doi.org/10.55730/1300-0144.5341
16. Santos CS, Férnandez XC, Moriano Morales C, et al. Biological agents for rheumatic diseases in the outbreak of COVID-19: friend or foe? RMD Open 2021;7:e001439. https://doi.org/10.1136/rmdopen-2020-001439
17. Gianfrancesco M, Hyrich KL, Al Adely S, et al. Characteristics associated with hospitalization for COVID-19 in people with rheumatic disease: data from the COVID-19 Global Rheumatology Alliance physician-reported registry. Ann Rheum Dis 2020;79:859-866. https://doi.org/10.1136/annrheumdis-2020-217871
18. Pehlivan Ö, Aydın T. Clinical outcomes of patients with COVID-19 and inflammatory rheumatic diseases receiving biological/targeted therapy. Ann Saudi Med 2022;42:155-164. https://doi.org/10.5144/0256-4947.2022.155
19. Favalli EG, Monti S, Ingegnoli F, Balduzzi S, Caporali R, Montecucco C. Incidence of COVID-19 in patients with rheumatic diseases treated with targeted immunosuppressive drugs: what can we learn from observational data? Arthritis Rheumatol 2020;72:1600-1606. https://doi.org/10.1002/art.41388
20. Wang Q, Liu J, Shao R, Han X, Su C, Lu W. Risk and clinical outcomes of COVID19 in patients with rheumatic diseases compared with the general population: a systematic review and metaanalysis. Rheumatol Int 2021;41:851-861. https://doi.org/10.1007/s00296-021-04803-9
21. Hasseli R, Mueller Ladner U, Hoyer BF, et al. Older age, comorbidity, glucocorticoid use, and disease activity are risk factors for COVID-19 hospitalization in patients with inflammatory rheumatic and musculoskeletal diseases. RMD Open 2021;7:e001464.
22. Eder L, Croxford R, Drucker AM, et al. COVID-19 hospitalizations, intensive care unit stays, ventilation, and death among patients with immune-mediated inflammatory diseases compared to controls. J Rheumatol 2022;49:523-530. https://doi.org/10.3899/jrheum.211012

23. Haberman RH, Castillo R, Chen A, et al. COVID-19 in patients with inflammatory arthritis: a prospective study on the effects of comorbidities and disease-modifying antirheumatic drugs on clinical outcomes. Arthritis Rheumatol 2020;72:1981-1989. https://doi.org/10.1002/art.41456

24. Izadi Z, Gianfrancesco MA, Aguirre A, et al. Development of a prediction model for COVID-19 acute respiratory distress syndrome in patients with rheumatic diseases: results from the global rheumatology alliance registry. ACR Open Rheumatol 2022;4:872-882. https://doi.org/10.1002/acr2.11481

25. Gallo Marin B, Aghagoli G, Lavine K, et al. Predictors of COVID-19 severity: a literature review. Rev Med Virol 2021;31:1-10. https://doi.org/10.1002/rmv.2146

26. Pablos JL, Galindo M, Carmona L, et al. Clinical outcomes of hospitalized patients with COVID-19 and chronic inflammatory and autoimmune rheumatic diseases: a multicentric matched cohort study. Ann Rheum Dis 2020;79:1544-1549. https://doi.org/10.1136/annrheumdis-2020-218296

27. Robinson PC, Richards D, Tanner HL, Feldmann M. Accumulating evidence suggests anti-TNF therapy needs to be given trial priority in COVID-19 treatment. Lancet Rheumatol 2020;2:653-655. https://doi.org/10.1016/S2665-9913(20)30309-X

28. Fara A, Mitrev Z, Rosalia RA, Assas BM. Cytokine storm and COVID-19: a chronicle of pro-inflammatory cytokines. Open Biol 2020;10:200160. https://doi.org/10.1098/rsob.200160

29. Bachiller Corral J, Boteanu A, Garcia Villanueva MJ, et al. Risk of severe COVID-19 infection in patients with inflammatory rheumatic diseases. J Rheumatol 2021;48:1098-1102. https://doi.org/10.3899/jrheum.200755

30. Ortolan A, Lorenzin M, Cosma C, et al. SARS-CoV-2 infection in spondyloarthritis patients treated with biotechnological drugs: a study on serology. Front Immunol 2021;12:682850. https://doi.org/10.3389/fimmu.2021.682850

Ethics committee approval: Permission was obtained from Hatay Mustafa Kemal University Non-Interventional Clinical Research Ethics Committee for the study (permission date 09.01.2022, number: 15).

Authors' contributions to the article

M.P. and M.K. constructed the main idea and hypothesis of the study. G.K. and E.K. developed the theory and arranged the material and method section. M.P., M.K., E.K. and G.K. have done the evaluation of the data in the results section. Discussion section of the article written by M.P. and E.K., M.K. and G.K. reviewed, corrected and approved. In addition, all authors discussed the entire study and approved the final version.