15th Annual Congress of Iranian Rheumatology Association

Clinical Coarse, CT Severity Score and Prognosis of COVID-19 in Patients with Rheumatoid Arthritis

Esalatmanesh Kamal[1] ,Azadchehr Mohammad Javad[2] , Azadbakht Javid[3]

1. Autoimmune Diseases Research Center, Kashan University of Medical Sciences, Kashan, I.R.Iran
2-Infectious Diseases Research Center, Kashan University of medical sciences , Kashan, Iran
3-Radiology Department, , Kashan University of medical sciences , Kashan, Iran
*email: esalat.kamal@yahoo.com Tel:+989131616775

Introduction

In December 2019, a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), led to an outbreak of coronavirus disease 2019 (COVID-19) pneumonia in China that rapidly spread across the planet, confirmed cases crossing 100 million globally, with more than 3 million casualties.[1] SARS-CoV-2 is the seventh member of the family of coronaviruses that infects mostly the human upper respiratory tracts, causing dry cough and shortness of breath.[2] Patients with various rheumatic diseases because of the effects of the immune system dysfunction, various comorbidities such as end organ damage, diabetes mellitus, and hypertension as well as the chronic use of immunosuppressants are in danger of infectious diseases.[3,4] Ferri et al. reported a higher frequency of COVID-19 in patients with various systemic autoimmune diseases compared with general population of Italy.[5] Meta-analysis of case–controlled studies showed a higher risk of COVID-19 in patients with autoimmune diseases.[6] Despite general agreement that COVID-19 is more prevalent in patients with rheumatic diseases, there is less consensus on the course and prognosis of COVID-19 in these patients. To improve our knowledge in this field, we conducted this multi-center cross sectional study.

Material & Methods

Study population

In a multicenter cross-sectional study, patients with rheumatic diseases who developed COVID-19 were recruited. These patients were followed at the rheumatology clinics of Kashan University of Medical Sciences .This study was approved under the ethical code of IR.KAUMS.MEDNT.REC.1399.166, while requirement to provide patients with informed consents was waived. The study was performed according to the Helsinki humanity research declaration (2008). Inclusion criteria were i) having been diagnosed with rheumatic diseases according to the clinical criteria, ii) age ≥ 16, iii) diagnosis of COVID-19 according to clinical manifestations consistent with COVID-19 plus positive polymerase chain reaction (PCR) or chest computerized tomography (CT) scan findings of COVID-19 pneumonia and ruling out of the other causes of pneumonia.

Data collection

Demographic, clinical and medications data of patients were extracted using a questionnaire for patients receiving outpatient care and review of electronic medical records in hospitalized patients. Patients with a diagnosis of COVID-19 were invited to visit in a multidisciplinary clinic. Disease activity was assessed by a rheumatologist and diagnosis of COVID-19 was evaluated by an infectious disease specialist. Two radiologists confident and experienced with thoracic imaging, blinded to the demographic and clinical data, reviewed the chest CT images on a same diagnostic monitor independently and discrepancies were resolved in consensus. The CT images were reviewed on both lung and mediastinal windows. Based on the parenchymal involvement extension, semi-quantitative CT severity score (CT-ss) was calculated and assigned to each patient following instructions in previous studies.[7,8] According to the extension of the diseased lung (involved with ground glass opacity, consolidation and crazy-paving pattern), each lung lobe (according to the anatomical definition provided by the Fleischner Society glossary of terms for thoracic imaging) scored a point between 0-5 as the following: score 0, no parenchymal involvement; score 1, 0-5 % parenchymal involvement; score 2, 5-25% parenchymal involvement; score 3, 25-50% parenchymal involvement; score 4, 50-75% parenchymal involvement; and score 5, 75-100% parenchymal involvement.[9] The summation of the scores were considered as CT-ss (on a scale of 0-25). Finally, patients were stratified based on their CT-ss into four groups: i) patients with normal CT scan (CT-ss of 0), ii) patients with mild pneumonia (CT-ss of 1-10), iii) patients with moderate pneumonia (CT-ss of 10-15), and iv) patients with severe pneumonia (CT-ss of 15-25).

Outcomes

COVID-19 outcomes were assessed based on the level of care, the number of patients who died and flare of Rheumatoid Arthritis disease. Four levels of care were identified including outpatient care, hospitalization, need to intensive care unit (ICU) care and need to mechanical ventilation.

Statistical analysis

Data analysis was performed using SPSS 16.0 software (SPSS, Chicago, IL). The normal distribution of data was assessed using the Kolmogorov-Smirnov test. Continuous variables with normal distribution were presented as mean ± standard deviation (SD). Continuous variables with non-normal distribution were reported as median (25-75% interquartile range [IQR]). Categorical variables were presented as frequency (percentage). Continuous variables with normal distribution, continuous variables with non-normal distribution and categorical variables between groups were compared using the independent sample t-test, Mann-Whitney test and Chi-squared test, respectively. P<0.05 was considered statistically significant.

The parameters associated with hospitalization of patients were subjected to univariate analysis. The predictive factors of hospitalization with P-values of < 0.1 in univariate analysis were included in a multivariate regression analysis and were expressed as OR and 95% confidence interval (95% CI). We selected variable using a backward stepwise method based on P-value.

Results

Between Feb 2020 to March 2021, 107 adult patients with rheumatic diseases who developed COVID-19 were included in the study. Diagnosis was made according to positive PCR in 89 (83.1%) patients and clinical criteria in 18 (16.8%) of the cases. Obesity, hypertension and age ≥ 65 were the most common COVID-19 risk factors. Rheumatoid Arthritis was active in 47 (43.9%) patients at the time of developing COVID-19. Except for 3 patients the rest were treated with prednisolone and/or conventional or biologic disease-modifying anti-rheumatic drugs (DMARDs). Prednisolone, hydroxychloroquine and methotrexate were the most common medications used for the treatment of Rheumatoid Arthritis.

Myalgia, malaise and fever were the most common clinical manifestations of COVID-19. Pneumonia on CT scan occurred in 81 (75.7%) patients. Mild, moderate and severe pneumonia was observed in 27 (25.2%), 34 (31.7%) and 19 (17.7%) patients, respectively. Treatment with NSAIDs (OR 5.16, 95% CI 2.19-14.01, P=0.001) and glucocorticoids (OR 4.84, 95% CI 1.14-20.06, P=0.032), diabetes (OR 5.35, 95% CI 2.12-13.48, P=0.001) and underlying pulmonary disease (OR 3.25, 95% CI 1.09-9.72, P=0.049) were the independent factors associated with moderate to severe pneumonia in multivariate regression analysis.

We assessed the outcomes of COVID-19 in the studied patients. Forty-two (39.2%) participants were hospitalized, 12 (11.2%) cases received ICU care, and 7 (6.5%) patients underwent mechanical ventilation. Five (4.6%) patients died. Flare of Rheumatoid Arthritis occurred in 18 (16.8%) patients.

After multivariate analysis, treatment with NSAIDs (OR 2.8, 95% CI 1.15-2.77, P = 0.050), treatment with glucocorticoids (OR 5.34, 95% CI 1.93-14.78, P = 0.001) and diabetes (OR 4.62, 95% CI 1.65-12.91, P = 0.004) remained the independent predictors of hospitalization.

Table I. Predictors of moderate and severe pneumonia in CT scan in patients with Rheumatoid Arthritis who developed COVID-19 (N=107)
CT: computed tomography; OR: odds ratio; CKD: chronic kidney disease; NSAIDs; nonsteroidal anti-inflammatory drugs

Parameters	Univariate analysis		Multivariate analysis*	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Age > 65 years	3.61 (1.52-8.60)	0.004	2.05 (0.76-5.61)	0.158
Male sex	0.79 (0.35-1.77)	0.563		
Smoking	3.42 (0.67-17.38)	0.138		
Diabetes	6.33 (2.92-13.73)	0.001	5.35 (2.12-13.48)	0.001
Obesity	1.94 (1.09-3.45)	0.024	1.26 (0.64-2.51)	0.505
Hypertension	2.19 (0.95-5.03)	0.065	1.53 (0.55-4.27)	0.415
Pulmonary disease	4.67 (0.96-22.58)	0.055	3.25 (1.09-9.72)	0.049
Heart disease	0.53 (0.13-2.98)	0.474		
CKD	4.31 (1.36-13.61)	0.014	0.85 (0.20-3.56)	0.822
Treatment with NSAIDs	2.59 (1.21-5.54)	0.014	5.16 (2.19-14.01)	0.001
Treatment with prednisolone	3.01 (0.93-9.67)	0.066	4.84 (1.14-20.06)	0.032
Treatment with hydroxychloroquine	0.73 (0.41-1.32)	0.297		
Treatment with sulfasalazine	0.89 (0.47-1.72)	0.739		
Treatment with methotrexate	1.45 (0.82-2.59)	0.205		
Treatment with leflunomide	0.83 (0.29-2.31)	0.719		
Treatment with azathioprine	1.89 (0.81-4.42)	0.139		
Treatment mycophenolate mofetil	0.84 (0.27-2.40)	0.694		
Treatment with biologics	0.79 (0.35-1.77)	0.563		
Active disease at the time of COVID-19	1.55 (0.82-2.94)	0.177		

Discussion

We assessed the clinical, CT-ss and outcomes of COVID-19 in patients with Rheumatoid Arthritis. Myalgia, malaise and fever were the most common symptoms of COVID-19. Treatment with NSAIDs and glucocorticoids, diabetes and underlying pulmonary disease were the factors associated with moderate to severe pneumonia. Hospitalization rate and COVID-19-related death rate were 37% and 7.6%, respectively. Treatment with NSAIDs, glucocorticoids and diabetes were predictors of hospitalization.

Our findings on the prognostic factors of COVID-19 in patients with rheumatic diseases differ in some respects from reports in other countries. In data published by COVID-19 Global Rheumatology Alliance registry on 7263 patients with inflammatory rheumatic diseases, 76% of the patients were female and RA (41%) was the most common disease.[10] Most common symptoms of COVID-19 were fever (79%), cough (77%), shortness of breath (50%), myalgia (45%) and sore throat (37%).[11] Thirty one percent of the patients were hospitalized and 5.6% died.[10] In Haberman et al. report on 103 patients with inflammatory arthritis, 26% of patients were hospitalized.[12] In 62% of the cases rheumatic disease was active at the time of developing COVID-19.[12] Hospitalized patients were older, had higher BMI and comorbidities including hypertension and COPD.[12] Hospitalization rate in patients treated with glucocorticoids (OR 21) and JAK inhibitors (OR 6) was more common. RA patients hospitalized significantly more than SpA patients (38% versus 16%).[12] In Nunez et al. report on 123 patients with autoimmune rheumatic diseases, 44% of patients were hospitalized and 9.8% died.[13] Although having COVID-19 risk factors and treatment with NSAIDs, glucocorticoids and TNFα inhibitors in hospitalized patients was more common, in multivariate regression analysis only older age and having systemic autoimmune condition (vasculitis and SLE, and other CVDs) versus chronic inflammatory arthritis (RA, SpA and juvenile idiopathic arthritis) were significantly associated with hospitalization. Montero et al. reported a higher hospitalization rate in males, patients with underlying pulmonary disease and patients treated with prednisolone (doses ≥ 5 mg/d).[14] They did not find any association between baseline rheumatic disease and DMARDs with hospitalization rate. In a report from National registry for patients with inflammatory rheumatic diseases from Germany, 48% of patients were hospitalized.[15] Hospitalization rate in men, patients treated with GCs and patients with comorbidities was higher. However, in patients treated with bDMARDs hospitalization rate was lower. Although TNFα inhibitors has been shown to be protective against severe coronavirus, and in particular COVID-19 related outcomes and it has reduced hospitalization rate according to previous studies,[16,17] our data did not support a prognostic role for biologics. In agreement with our results, Bezzio et al. did not report any significant association between medications and COVID-19 pneumonia, in a cohort of patients with inflammatory bowel disease.[18]

The results of our study showed that patients with RA treated with NSAIDs or glucocorticoids and patients with underlying conditions including diabetes and pulmonary disease are in the danger of severe COVID-19 and they should probably be given priority over vaccination against COVID-19.

The results of this study should be interpreted with caution because of cross sectional design of the study and heterogenicity of various groups of rheumatic diseases with different demographic and clinical characteristics and medications that affect the analysis.

Interpretation & conclusions

In Rheumatoid Arthritis patients, treatment with NSAIDs or prednisolone, diabetes and pulmonary disease are risk factors of moderate to high CT-ss and hospitalization during COVID-19.

1. World Health Organization. Coronavirus disease (COVID-19) pandemic 2020 [Last updated 5 May 2021. Accessed 5 May 2021]. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019
2. Moore JB, and June CH Cytokine release syndrome in severe COVID-19. Science 2020; 368 : 473-474.
3 Jeong SJ, Choi H, Lee HS, Han SH, Chin BS, Baek JH, et al. Incidence and risk factors of infection in a single cohort of 110 adults with systemic lupus erythematosus. Scand J Infect Dis 2009; 41 : 268-274.
4. Dixon WG, Suissa S, Hudson M. The association between systemic glucocorticoid therapy and the risk of infection in patients with rheumatoid arthritis: systematic review and meta-analyses. Arthritis Res Ther 2011; 13 : R139.
5. Ferri C, Giuggioli D, Raimondo V, Andolina ML, Tavoni T, Cecchetti R, et al. COVID-19 and rheumatic autoimmune systemic diseases: report of a large Italian patients series. Clin Rheumatol 2020; 39 : 3195-3204.
6. Akiyama S, Hamdeh S, Micic D, Sakuraba A. Prevalence and clinical outcomes of COVID-19 in patients with autoimmune diseases: a systematic review and meta-analysis. Ann Rheum Dis 2020; Oct 13.
7. Pan F, Ye T, Sun P, Gui S, Liang B, Li L, et al. Time course of lung changes on chest CT during recovery from 2019 novel coronavirus (COVID-19) pneumonia. Radiology 2020; 295 : 715-721.
8. Chang YC, Yu CJ, Chang SC, Galvin JR, Liu HM, Hsia VH, et al. Pulmonary sequelae in convalescent patients after severe acute respiratory syndrome: evaluation with thin-section CT. Radiology 2005; 236 : 1067-75.
9. Hansell DM, Bankier AA, MacMahon H, McLoud TC, Müller NL, Remy J. Fleischner Society: glossary of terms for thoracic imaging. Radiology 2008; 246 : 697-722.
10. COVID-19. Global Rheumatology Alliance. https://rheum-covid.org/updates/combined-data.html. Last updated 14 April 2021. Accessed 3 May 2021
11. Gianfrancesco MA, Hyrich KL, Gossec L, Strangfeld A, Carmona L, Mateus EF, et al. Rheumatic disease and COVID-19: initial data from the COVID-19 Global Rheumatology Alliance provider registries. Lancet Rheumatol 2020; 2: e250-e253.
12. Haberman RH, Castillo R, Chen A, Yan D, Ramirez D, Sekar V, et al. COVID-19 in patients with inflammatory arthritis: a prospective study on the effects of comorbidities and disease-modifying antirheumatic. Arthritis Rheumatol 2020; 72 : 1981-1989.
13. Freites Nuñez DD, Leon L, Mucientes A, Rodriguez-Rodriguez L, Urgelles JF, García AF, et al. Risk factors for hospital admissions related to COVID-19 in patients with autoimmune inflammatory rheumatic diseases. Ann Rheum Dis 2020; 79 : 1393-1399.
14. Montero F, Martinez-Barrioˊ , Serrano- Benavente B, González T, Rivera J, Collada JM, et al. Coronavirus disease 2019 (COVID-19) in autoimmune and inflammatory conditions: clinical characteristics of poor outcomes. Rheumatol Int 2020; 40 : 1593-1598.
15. Hasseli R, Mueller-Ladner U, Schmeiser T, Hoyer BF, Krause A, Lorenz HM, et al. National registry for patients with inflammatory rheumatic diseases (IRD) infected with SARS-CoV-2 in Germany (ReCoVery): a valuable mean to gain rapid and reliable knowledge of the clinical course of SARS-CoV-2 infections in patients with IRD. RMD Open 2020; 6 : e001332.
16. Gianfrancesco M, Hyrich KL, Al- Adely S, Carmona L, Danila MI, Gossec L, 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; 79:859-866.
17. Tobinick E. TNF- alpha inhibition for potential therapeutic modulation of SARS coronavirus infection. Curr Med Res Opin 2004; 20 : 39-40.
18. Bezzio C, Saibeni S, Variola A, Allocca M, Massari A, Gerardi V, et al. Outcomes of COVID-19 in 79 patients with IBD in Italy: an IG-IBD study. Gut 2020; 69 : 1213-1217.