COVID-19 outcomes in patients with systemic autoimmune diseases treated with immunomodulatory drugs

We read with great interest the paper published by Gianfrancesco and colleagues in *Annals of the Rheumatic Diseases* in 2020.[1] They examined demographic and clinical factors associated with COVID-19 hospitalisation status in people with rheumatic disease using 600 cases from 40 countries. In their multivariable model, it was found that prednisone dose ≥10 mg/day (OR: 2.05, 95% CI 1.06 to 3.96) and anti-tumour necrosis factor inhibitor use (OR: 0.40, 95% CI 0.19 to 0.81) were associated with odds of hospitalisation.[1]

Patients with autoimmune diseases (AD) are at an increased risk of infectious diseases due to the effects of the disease on the immune system function, much comorbidity caused by various comorbidities such as kidney and lung damage, diabetes mellitus and hypertension, as well as the chronic use of immunomodulatory drugs.[2 3] Patients treated with immunomodulatory drugs are vulnerable to viral infections,[3 4] and worse prognosis of COVID-19 is probable in patients with ADs[5] that need to be studied. Here, we would like to share our study results that were conducted on patients with ADs treated with immunomodulatory drugs.

In our single-centre retrospective study, charts of patients diagnosed with COVID-19 who were admitted to Imam Reza Hospital and were discharged or deceased were reviewed. Imam Reza Hospital is a referral centre for COVID-19 in the East Azerbaijan province, which is one of the high-risk areas in Iran.

In this centre, patients with symptoms suggestive of COVID-19 who had oxygen saturation lower than 90% were admitted. Diagnosis was made using positive PCR or findings consistent with COVID-19 pneumonia based on chest CT scan and ruling out other causes of pneumonia. Disease outcomes were assessed based on the level of care, the time interval between the onset of symptoms and intubation, duration of intubation, duration of admission in intensive care unit (ICU) and the number of patients who died.

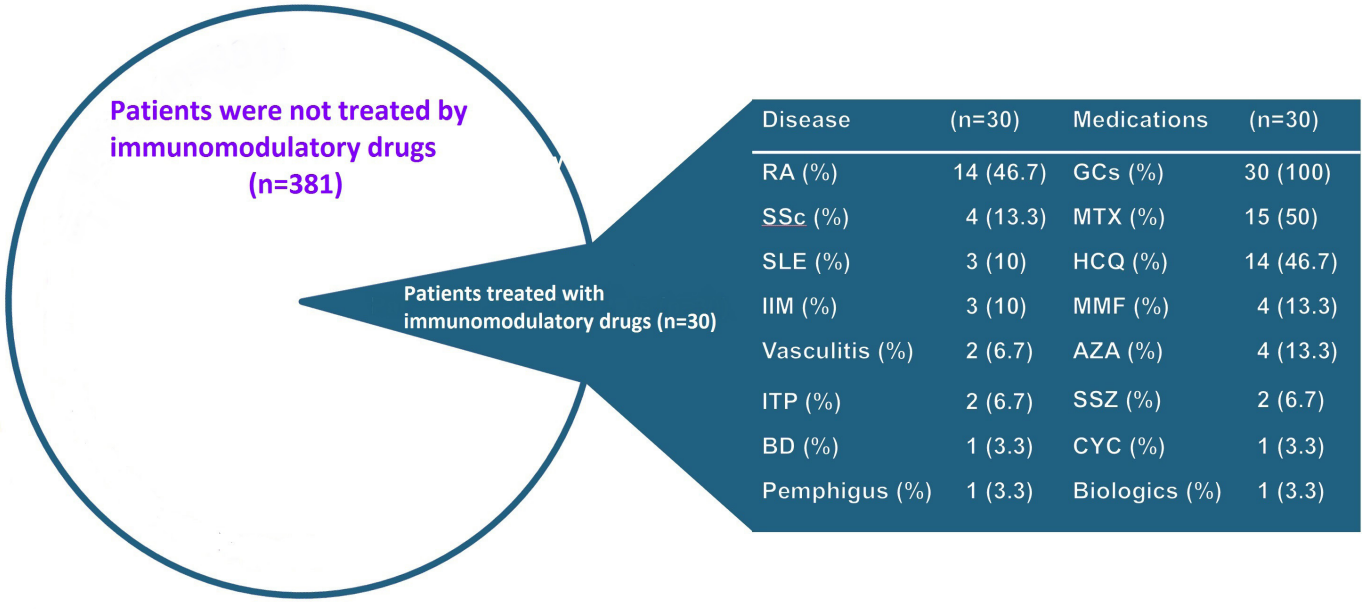
For statistical analysis, we used SPSS V.16 software. Continuous variables with normal distribution were reported as mean±SD and non-normally distributed continuous variables were reported as median (25%–75% IQR). Categorical variables were reported as frequency and percentage. χ^2 and independent samples t-test/Mann-Whitney U test were used to assess differences between groups of patients treated with or without immunomodulatory drugs.

Four hundred and eleven patients who were diagnosed with COVID-19 pneumonia were included in this study. Thirty of these patients had ADs (figure 1). In the immunomodulatory drugs-naïve and treated with immunomodulatory drugs groups 69.9% and 62.5% of patients were PCR positive for COVID-19, respectively (p=0.615). The frequency of some clinical manifestations such as malaise, dyspnoea, myalgia, anosmia and taste loss was significantly higher in patients with ADs treated with immunomodulatory drugs compared with immunomodulatory drugs-naïve patients (p<0.05) (table 1). In addition, lymphopenia was found to be less prevalent in patients treated with immunomodulatory drugs (p=0.015).

No significant differences were observed in the admission level, time interval between the onset of symptoms and intubation, duration of intubation, duration of admission in ICU and number of deceased patients in the two groups (table 1).

Pablos *et al* reported 1.3-fold higher prevalence of hospital PCR+COVID-19 in patients with rheumatic diseases.[6] Grasselli *et al* reported inflammatory diseases and suppression of immune system as the most common comorbidities in patients younger than 40 years with COVID-19 admitted to the ICU.[7]

To the best of our knowledge, no study has been conducted to assess the outcomes of COVID-19 in patients with ADs treated with immunomodulatory drugs in comparison with other patients. Our preliminary findings suggest that the severity and mortality of COVID-19 in patients with ADs treated with immunomodulatory drugs are probably not significantly different from the general population.



Disease	(n=30)	Medications	(n=30)
RA (%)	14 (46.7)	GCs (%)	30 (100)
SSc (%)	4 (13.3)	MTX (%)	15 (50)
SLE (%)	3 (10)	HCQ (%)	14 (46.7)
IIM (%)	3 (10)	MMF (%)	4 (13.3)
Vasculitis (%)	2 (6.7)	AZA (%)	4 (13.3)
ITP (%)	2 (6.7)	SSZ (%)	2 (6.7)
BD (%)	1 (3.3)	CYC (%)	1 (3.3)
Pemphigus (%)	1 (3.3)	Biologics (%)	1 (3.3)

Figure 1 Patients admitted with diagnosis of COVID-19. AZA, azathioprine; BD, Behcet's disease; CYC, cyclophosphamide; GC, glucocorticoid; HCQ, hydroxychloroquine; IIM, idiopathic inflammatory myopathy; ITP, idiopathic thrombocytopenia; MMF, mycophenolate mofetil; MTX, methotrexate; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; SSc, systemic sclerosis; SSZ, sulfasalazine.

Table 1 Demographic, clinical and laboratory characteristics and outcomes of studied groups

	Immunomodulatory drugs-naïve patients (n=381)	Patients with ADs treated with immunomodulatory drugs (n=30)	P value
Age (mean±SD), years	62.6±17.1	55.1±13.6	0.020
Gender (female/male)	0.64	3.28	0.001
Clinical and laboratory manifestations			
Fever (%)	85 (22.3)	8 (26.7)	0.519
Dyspnoea (%)	274 (71.9)	24 (80.0)	0.036
Cough (%)	223 (58.57)	16 (53.3)	0.129
Myalgia (%)	124 (32.5)	17 (56.7)	0.006
Malaise (%)	117 (30.7)	15 (50.0)	0.001
Nausea/vomiting/ diarrhoea (%)	63 (16.5)	7 (23.3)	0.085
Anorexia (%)	57 (14.9)	10 (33.3)	0.050
Taste loss (%)	38 (10)	6 (20.0)	0.001
Anosmia (%)	32 (8.4)	7 (23.3)	0.001
Sore throat (%)	30 (7.9)	4 (13.3)	0.080
Lymphopenia (%)	278 (72.9)	13 (43.3)	0.015
High C-reactive protein (%)	328 (86.1)	21 (70.0)	0.078
Level of care			
Admitted in ward (%)	155 (40.7)	11 (36.7)	0.889
Admitted in ICU (%)	89 (23.4)	7 (23.3)	
Intubated and mechanically ventilated (%)	137 (36.0)	12 (40.0)	
The time interval from the onset of symptoms to admission, median (IQR) days	7 (3, 10)	6 (3.5, 11)	0.912
The time interval from the onset of symptoms to mechanical ventilations, median (IQR) days	0 (0, 2)	2.5 (0, 6.75)	0.096
Duration of admission in ICU, median (IQR) days	9 (5, 16)	12.5 (4, 18)	0.711
Duration of intubation, median (IQR) days	4 (2, 10)	5 (1.5, 13.5)	0.889
Death (%)	95 (24.9)	8 (26.7)	0.491

AD, autoimmune disease; ICU, intensive care unit.;

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REFERENCES

1 Gianfrancesco M, Hyrich KL, Al-Adely S, *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;79:859–66.
2 Memoli MJ, Athota R, Reed S, *et al*. The natural history of influenza infection in the severely immunocompromised vs nonimmunocompromised hosts. *Clin Infect Dis* 2014;58:214–24.
3 Jeong SJ, Choi H, Lee HS, *et al*. Incidence and risk factors of infection in a single cohort of 110 adults with systemic lupus erythematosus. *Scand J Infect Dis* 2009;41:268–74.
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 Venerito V, Lopalco G, Iannone F. COVID-19, rheumatic diseases and immunosuppressive drugs: an appeal for medication adherence. *Rheumatol Int* 2020;40:827–8.
6 Pablos JL, Abasolo L, Álvaro-Gracia JM, *et al*. Prevalence of hospital PCR-confirmed COVID-19 cases in patients with chronic inflammatory and autoimmune rheumatic diseases. *Ann Rheum Dis* 2020. doi:10.1136/annrheumdis-2020-217763
7 Grasselli G, Zangrillo A, Zanella A, *et al*. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy region, Italy. *JAMA* 2020;323:1574–81.