Factors influencing the course of COVID-19 in the inflammatory rheumatic diseases

Sirs,

Coronavirus disease 2019 (COVID-19), is a severe acute respiratory syndrome coronavirus-2 (SARS-COV-2) disease, which emerged in China in December 2019 and then spread rapidly around the world (1). Over time, it is observed that the pathophysiology of this disease differs from other common viral infections and has the potential of disabling multiple organ systems as a result of hyperinflammation. Initially, drugs necessary to treat multiple organ failures during the course of COVID-19 have gained the attention of rheumatologists due to their common-place in the treatment of rheumatic diseases. There is now a growing interest in the course of COVID-19 in the setting of rheumatologic diseases (2). In this retrospective cohort study, we investigated the effect of the vaccination status and the period of various dominant variants on the course of COVID-19 in patients with autoimmune/autoinflammatory rheumatic disease (AIRD). The following data was recorded in AIRD patients, aged 18 years and older, under routine follow-up: COVID-19, vaccination status, clinical characteristics, and comorbid diseases. Patients diagnosed with COVID-19 after the 1st of December 2021, were designated as "Omicron period" patients. Our study was approved by the local ethics committee and informed consent was obtained from the patients. Demographic and clinical characteristics and vaccination status of study patients are summarised in Table I.

Myalgia, loss of taste and smell, and lung involvement were observed more frequently in unvaccinated patients ($p<0.05$ for all). Lung involvement and hospitalisations were found more frequently in patients treated with corticosteroids or rituximab or who had necrotising vasculitis ($p<0.05$ for all). The frequency of lung involvement was also significantly higher in the presence of diabetes mellitus and hypertension ($p<0.001$ for all). In multivariate analysis, old age, male sex, fever, cough, and dyspnea were determined as risk factors for lung involvement and hospitalisation and the use of corticosteroids increased the risk for hospitalisation ($p<0.05$ for all). Fever (67% *vs*. 57%), cough (57% *vs*. 42%), dyspnea (34% *vs*. 20%), myalgia (76% *vs*. 62%), loss of taste and smell (54% *vs*. 21%), and lung involvement (28% *vs*. 14%) were found to be significantly lower in the omicron period patients ($p<0.05$ for all).

Our results are in line with previous studies on this subject (3-9). Santos *et al*. from Spain, reported the presence of rheumatic disease activity, dyslipidaemia, and cardiovascular disease as risk factors for mortality in a study they conducted in the first months of the pandemic (3). Cordtz *et al*. reported that AIRD patients were hospitalised more often, especially patients with rheumatoid arthritis on corticosteroid therapy had a poorer prognosis, but TNF inhibitors were not associated with hospitalisation (5). Our data shows that the full dose vaccination in AIRD patients prevents the development of serious disease as reported in the healthy population (10). Eight patients died in our cohort and 4 of them were under rituximab therapy. Possibly, rituximab reduces the effectiveness of vaccines by decreasing antibody responses and leads to a more severe disease course in patients with AIRD (10). The existence of comorbidities has been reported as one of the most important factors affecting the course of COVID-19. In addi-

Table I. Distribution of clinical and demographic characteristics, comorbidities and vaccine status of the patients.

Parameters	All patients n=610	Behçet's syndrome n=17	FMF[1] n=72	Rheumatoid arthritis n=165	Sjögren's syndrome n=35	SLE[2] n=38	SpA[3,4] n=195	Necrotising vasculitis[5] n=22	Others[6] n=66
Age: mean±SD, (ranges), years	45.6 ± 13.5 (18-83)	40.9 ± 6.5 (32-51)	39.8 ± 12.9 (18-69)	51 ± 13 (24-80)	51.3 ± 12.2 (28-79)	38.2 ± 11 (18-65)	41.3 ±11.4 (18-81)	59.8 ± 16.6 (25-83)	48.4 ± 12.6 (27-71)
Female: n (%)	392 (64)	9 (53)	47 (65)	132 (80)	32 (91)	34 (90)	90 (46)	9 (41)	39; (59)
Vaccine status:									
No vaccination: n (%)[7]	126 (21)	4 (24)	19 (26)	32 (19)	6 (17)	12 (32)	34 (17)	4 (18)	15 (23)
Two doses: n (%)	300 (49)	9 (53)	39 (54)	75 (46)	23 (66)	17 (45)	99 (51)	11 (50)	27 (41)
Booster doses: n (%)	184 (30)	4 (24)	14 (19)	58 (35)	6 (17)	9 (24)	62 (32)	7 (32)	24 (36)
Co-morbidities:									
Hypertension: n (%)	152 (25)	3 (18)	11 (15)	55 (33,5)	5 (19)	5 (16)	41 (21)	13 (59)	19 (29)
Diabetes mellitus: n (%)	87 (14)	0	7 (10)	36 (22)	5 (14)	1 (3)	24 (18)	10 (15)	7 (11)
Ischaemic heart disease: n (%)	43 (7)	1 (6)	3 (4)	15 (9)	2 (6)	0 ()	14 (7)	3 (14)	5 (8)
Chronic lung disease: n (%)	37 (6.1)	1 (6)	4 (6)	15 (9)	3 (9)	2 (5)	6 (3)	4 (18)	2 (3)
Smoking									
Never smoker: n (%)	15 (88)	15 (88)	49 (72)	128 (78)	30 (81)	33 (87)	100 (53)	19 (86)	54 (82)
Ever smoker: n (%)	179 (29)	2 (12)	20 (28)	36 (22)	7 (19)	5 (13)	94 (47)	3 (14)	12 (18)
COVID-19 period:									
Before full vaccination[8]: n (%)	468 (77)	14 (82)	59 (82)	131 (80)	25 (71)	32 (84)	141 (72)	14 (64)	52 (79)
Omicron period: n (%)	111 (18)	3 (18)	9 (13)	27 (16)	5 (13.5)	4 (10.5)	42 (23)	9 (41)	12 (18)
Clinical features related to COVID-19									
Fever: n (%)	396 (65)	11 (65)	50 (69)	109 (66)	22 (68)	21 (55)	128 (66)	12 (55)	43 (65)
Cough: n (%)	310 (51)	8 (47)	34 (50)	94 (57)	15 (43)	19 (50)	90 (46)	17 (77)	33 (50)
Dyspnea: n (%)	190 (31)	6 (35)	26 (38)	56 (33.5)	5 (13.5)	15 (39.5)	54 (28)	10 (45.5)	18 (27)
Sore throat: n (%)	312 (51)	5 (31)	39 (56)	84 (51)	20 (57)	20 (53)	100 (51)	10 (45.5)	34 (51.5)
Myalgia: n (%)	447 (73)	13 (76.5)	56 (78)	118 (71)	30 (84)	27 (71)	146 (75)	12 (55)	45 (68)
Loss of taste/smell: n (%)	290 (38)	14 (82)	44 (61)	78 (48)	18 (54)	17 (45)	86 (44)	2 (9)	31 (47)
Lung involvement: n (%)	156 (26)	4 (24)	15 (21)	52 (32)	8 (24)	8 (21)	41 (21)	10 (45)	18 (27)
Hospitalisation: n (%)	108 (18)	3 (18)	9 (13)	35 (21)	5 (13.5)	5 (13)	22 (11)	13 (59)	16 (24)

1: FMF: familial Mediterranean fever; **2:** SLE: systemic lupus erythematosus; **3:** SPA: spondyloarthropathies; **4:** 19 patients were with psoriatic arthritis in this group; **5:** this group included (eosinophilic granulomatosis with polyangiitis: 2; giant cell arteritis: 2; granulomatous polyangiitis: 14; polyarteritis nodosa:1; Takayasu arteritis: 3); **6:** patients in this group included are adult onset Still's disease: 4; antiphospholipid syndrome: 9; discoid lupus erythematosus: 2; dermatomyositis:3; gout: 13; IGG4 related disease: 7; livedoid vasculit:1; morphea:2; polymyalgia rheumatica: 8; sarkoidosis:3; systemic sclerosis:14 cases; **7**: 7 patients received only one shot of approved vaccines and the others were not vaccinated until the last visit. 8: patients with at least two doses of an approved vaccine, *i.e*: CoronaVac or BNT162Bb2 vaccines

tion, the male sex and advanced age appear to be associated with poor prognosis (6, 7). As we have shown in our study, male patients, patients with comorbidities, elderly patients and patients using rituximab and corticosteroids need closer follow-up.

In conclusion, COVID-19 among AIRD cases seems to have a less severe course over time. The likelihood of lung involvement decreases in vaccinated AIRD patients. Old age, male patients with fever, cough, dyspnea, and the use of corticosteroids constitute the highest risk for hospitalisation.

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