Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Clinical course of COVID-19 in 41 patients with immune-mediated inflammatory diseases: Experience from humanitas center, Milan

Dear Sir

The risk of infection from Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and the outcomes of the COronaVIrus Disease 19 (COVID-19) in patients with immune mediated inflammatory diseases (IMIDs) remains challenging. Whether treatments with immunosuppressive and biologic therapies may increase the risk of infection, its severity and outcome is poorly investigated and, as a result, the discontinuation of these treatments has been suggested [1]. Earlier studies did not find a correlation between immunomodulating treatments and the prognosis of COVID-19 [2,3], while drugs used in IMIDs are being tested to block the cytokine release syndrome associated with COVID-19 [4].

We report a prospective case series of 41 patients with IMIDs and concomitant COVID-19 infection. The diagnosis of COVID-19 infection was either confirmed with a positive PCR nasopharyngeal swab; or highly suspected in the presence of typical symptoms, including fever, dry cough, shortness of breath, or a lung computed tomography image consistent with COVID-19 pneumonia.

The clinical characteristics of the 41 IMID patients are summarized in Table 1. Twelve patients had ulcerative colitis (UC), 9 Crohn's disease (CD), 8 psoriasis (Pso), 4 psoriatic arthritis (PsA), 5 rheumatoid arthritis (RA), and 3 had other related conditions. Twenty-four percent of patients were taking immunosuppressants, 17 % steroids, and 68 % a biologic. Thirteen patients (32 %) had relevant comorbidities, including hypertension, diabetes, obesity, chronic lung disease and malignancy. All patients developed COVID-19 symptoms, pneumonia was observed in 16 patients (40 %). Fourteen patients (34 %) were hospitalized with a median (IQ range) stay of 13 days (7–22). Ten patients (24 %) needed non-invasive ventilation while no patient was admitted to the intensive care unit but one died due to respiratory failure. This patient was a 79 year-old woman, with a diagnosis of RA since eight years, under concomitant prednisone 5 mg and methotrexate 12.5 mg daily. She had hypertension and chronic obstructive polmonary disease, and had a history of past tuberculosis. She was hospitalized for pneumonia and died two days after hospitalization.

The patients that were hospitalized were older than the non-hospitalized patients [median (IQ range) age was 55 (46–74) compared to 43 (30–53), $p = 0.02$]. No differences in terms of IMID was found in the hospitalized population ($p = 0.30$). However, those subjects with rheumatological diseases needed more oxygen therapy compared to patients with a diagnosis of inflammatory bowel diseases (IBD) or psoriasis ($p = 0.03$). The subjects with comorbidities were more frequently hospitalized ($p = 0.0003$), and needed more oxygen supplementation ($p = 0.0001$). Finally, therapy with steroids increased the risk for the need of oxygen ($p = 0.007$). No association was found

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Table 1
Characteristics of thePatients with IMID and concomitant COVID-19 (n = 41).

Age at diagnosis of COVID-19	48 (31.0 – 57.5)
Female	24 (59)
Region	
Lombardy	29 (71)
Other	12 (29)
IMID diagnosis	
Ulcerative colitis	12 (29)
Crohn's disease	9 (22)
Psoriasis	8 (20)
Psoriatic arthritis	4 (10)
Rheumatoid arthritis	5 (12)
Ankylosing spondylitis	1 (2.0)
Systemic sclerosis	1 (2.0)
Systemic lupus erythematosus	1 (2.0)
Long-term medications	
Any immunosuppressants	10 (24)
Prednisone	7 (17)
Azathioprine	1 (2.0)
Methotrexate	6 (15)
Hydroxychloroquine	3 (7.0)
Any biologic therapy	28 (68)
Tumor necrosis factor inhibitors	13 (32)
Adalimumab	10 (24)
Infliximab	2 (4)
Etanercept	1 (2)
Interleukin-12/23 blocker (Ustekinumab)	6 (15)
Interleukin-23 blockers	2 (5.0)
Guselkumab	1 (2)
Risankizumab	1 (2)
Interleukin-17 blocker (Ixekizumab)	2 (5.0)
Rituximab	1 (2.0)
Belimumab	1 (2.0)
Vedolizumab	1 (2.0)
Baricitinib	1 (2.0)
Apremilast	1 (2.0)
Clinical trial partecipants	2 (5.0)
Exposure risk	
High risk work*	9 (22)
Contact with confirmed or suspected COVID patients	23 (58)
No strict adherence to oprevention measures	23 (56)
In- out-patient visits (within 14 days from COVID infection)	9 (23)
Smoking	
Past	10 (24)
Active	3 (7.0)
Comorbidities	13 (32)
Hypertension	3 (7.0)
Metabolic disorders §	6 (15)
Chronic lung diseases	2 (5.0)
Malignancy §§	2 (5.0)
Positive rhinopharyngeal swabs	25 (61)
COVID-related symptoms	41 (100)
Gastro-intestinal symptoms	16 (39)
COVID-related pneumonia	16 (40)
Discontinuation of IMID therapy	24 (59)
Hospitalization	14 (34)
Use of supplementary oxigen	10 (24)
Intensive Care Unit	0 (0.0)
Death	1 (2.0)

IMID Immuno-Mediated Inflammatory Diseases; Data are presented as medians (interquartile range) or percentages when appropriate.

* 8 health workers, 1 police officer.

§ Metabolic disorders include diabetes, obesity, metabolic syndrome.

§§ 1 renal carcinoma, 1 prostate cancer.

between the use of biologic therapy and the risk of hospitalization and need for oxygen therapy. A logistic regression analysis was performed. The presence of risk of hospitalization and risk of oxygen need were the outcome variables (or dependent variable) (i.e. binomial variables taking the value 1 if hospitalization and/or need of oxygen were occurred, and the value 0 if they don't). All the parameters described in Table 2 were employed as explanatory variables (or independent variables). Univariable analysis was used to identify candidate predictors. Then, a multivariable model was fitted using a "backwards elimination procedure". All variables with $p < 0.05$ were retained in the model. Multivariable analysis revealed that only coexisting comorbidities were associated with increased risk of hospitalization and oxygen therapy **(**Table 2**).**

Immunosuppression is expected to weaken the immune system response in patients with COVID-19 infection and concomitant IMID and possibly lead to worse outcomes. However, some studies suggest that active disease, older age and comorbidities may also be associated with COVID-19 negative outcomes, such as pneumonia, hospitalization and death [5]. Our data confirm that the presence of comorbidities, such as hypertension, diabetes, obesity and chronic lung disease, may increase the risk of hospitalization and the need of oxygen supplementation [6]. Despite limitations created by a small sample size, our study suggests using caution especially when administering steroid therapy, wheras biologic therapy seems safe since no association between the use of biologic therapy and a worse pattern of COVID-19 infection was observed.

In conclusion, patients with IMID and on a stable steroid-free remission under immunosuppression are not at increased risk of worse outcomes from COVID-19. Caution should be paid to older patients with comorbidities and concomitant chronic glucocorticoid intake.

Authors' contributions

MA conceived and designed the study; MA, GMG, RGB, AN collected the data; MA and GF performed the data analysis; MA and GF drafted the manuscript; all Authors critically revised the manuscript; all Authors approved the final version of the manuscript.

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Declaration of Competing Interest

MA received consulting fees from Nikkiso Europe, Mundipharma, Janssen, Abbvie and Pfizer; RGB received consulting fees from Eli Lilly and Co, LEO Pharma, Novartis, Janssen, Almirall, Abbvie, Pfizer, ADC Therapeutics Sa, received grants from Celgene; GF received consultancy fees from Ferring, MSD, AbbVie, Takeda, Janssen, Amgen, Sandoz, Samsung Bioepis, Celltrion; SD served as a speaker, consultant and advisory board member for Schering-Plough,Abbott (AbbVie) Laboratories, Merck, UCB Pharma, Ferring, Cellerix, Millenium Takeda, Nycomed, Pharmacosmos, Actelion, Alfa Wasserman, Genentech, Grunenthal, Pfizer, AstraZeneca, Novo Nordisk, Cosmo Pharmaceuticals, Vifor and Johnson and Johnson. GMG, CS and AN, none to declare.

Table 2
Influence of baseline parameters on the probability of hospitalization and need of supplementary oxygen.

	Risk of hospitalization				Risk of oxygen need			
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
Parameters	OR (95 % CI)	*p*	OR (95 % CI)	*p*	OR (95 % CI)	*p*	OR (95 % CI)	*p*
Age at diagnosis	1.06 (1.00 – 1.11)	*0.01*			1.12 (1.03 – 1.21)	*0.003*		
Gender	4.27 (1.08 – 16.8)	*0.03*			1.58 (0.37 – 6.64)	0.53		
Use of steroids	6.94 (1.13 – 42.3)	*0.03*			14.5 (2.18 – 96.43)	*0.005*		
Immunosuppressants*	3.2 (0.60 – 16.9)	0.17			2.89 (0.52 – 16.0)	0.22		
Biologic therapy	0.63 (0.15 – 2.53)	0.51			0.52 (0.11 – 2.33)	0.39		
Comorbidities§	20.0 (3.76 – 106.1)	*0.0004*	13.8 (2.23 – 85.1)	*0.004*	60.7 (5.98 – 616.6)	*0.0005*	60.7 (5.98 – 616.6)	*0.0005*
IMID diagnosis IBD**	0.23 (0.05 – 0.95)	*0.04*			0.15 (0.02 – 0.87)	*0.03*		
Psoriasis	2.3 (0.47 – 11.0)	0.29			1.04 (0.17 – 6.22)	0.96		
Rheumatological diseases§§	2.62 (0.65 – 10.58)	0.17			6.25 (1.32 – 29.3)	*0.02*		

* Immunosuppressants: Azathioprine or Methotrexate.
** IBD, inflammatory bowel disease.
§ comorbidities included arterial hypertension, diabetes, obesity, metabolic syndrome, chronic lung disease, renal cancer and prostate cancer.
§§ rheumatological diseases included psoriatic arthritis, rheumatoid arthritis, ankylosing spondylitis, systemic sclerosis and systemic lupus erythematosus.

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