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SARS-CoV-2 infection among patients with systemic autoimmune diseases

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ABSTRACT

Objectives: This study aimed to evaluate the prevalence of clinically overt SARS-CoV-2 infection (COVID-19) among patients with systemic autoimmune diseases residing in Tuscany, and to compare it with that observed in the general Tuscan population.

Methods: In this cross-sectional study, Tuscan outpatients with systemic autoimmune diseases followed at a tertiary referral centre were telephonically interviewed between April 1st-14th 2020 to collect demographic and clinical data, information on ongoing immunomodulating/immunosuppressive treatments, and on the presence of symptoms suspected of SARS-CoV-2 or of a confirmed infection.

Results: 458 patients were interviewed [74% female, median age 56 years (IQR 43–68)]; 56% of them were receiving corticosteroids, 44% traditional disease-modifying anti-rheumatic drugs (DMARDs), of whom 23% hydroxychloroquine, 5% colchicine, while 41% were on biologic DMARDs (of whom 9% on tocilizumab). Thirteen patients reported symptoms suggesting SARS-CoV-2 infection. Of them, 7 had undergone nasopharyngeal swab and only one was positive and developed severe SARS-CoV-2 complications. Within our cohort, the prevalence of SARS-CoV-2 infection was therefore 0.22% (0.01–1.21%), comparable to that observed in the general population of Tuscany [0.20% (0.20–0.21%), $p = .597$].

Conclusions: Patients with systemic autoimmune diseases do not seem to carry an increased risk of SARS- CoV-2 infection as compared to the general population.

1. Introduction

The infection mediated by SARS-CoV-2 (severe acute respiratory coronavirus 2), also known as COVID-19 (Coronavirus disease 2019), is a new viral infection characterized by dry cough, fever, dyspnea, fatigue, and lymphopenia, which can be complicated by interstitial pneumonia leading to severe acute respiratory distress syndrome (ARDS) [1]. A cytokine storm syndrome might occur, eventually leading to multi-organ failure and death [2].

The highest case-fatality rates (CFR) have been reported in elderly and comorbid patients, particularly in those with cardiovascular or chronic respiratory diseases, diabetes, hypertension and cancer [3]. Moreover, a high CFR has been reported in transplant patients, particularly in those with long-term immunosuppressive regimens [4].

Since the outbreak of the pandemic, concerns have been raised on the risk of SARS-CoV-2 infection and related complications among patients affected by systemic autoimmune diseases [5]. On the one hand, these patients carry a higher risk of infections due to immunosuppression [6,7]. On the other hand, immunosuppression itself may dampen the abnormal immune response that seems to be responsible for the most severe disease complications such as interstitial pneumonia [8]. Indeed, two immune-modulating drugs largely used for immune-mediated disorders, hydroxychloroquine (HCQ) and chloroquine, have demonstrated some antiviral activity against SARS–CoV-2 in vitro and in small clinical studies [9]. Similarly, tocilizumab – an anti-interleukin (IL)-6 receptor antibody approved for different rheumatic diseases – proved effective in severe SARS-CoV-2 cases [10], although these data warrant confirmation by controlled trials.

Data on the occurrence of SARS-CoV-2 infection in patients with systemic autoimmune diseases, and on the risks and benefits of maintaining immunosuppression in this population, are scarce [11]. The SARS-CoV-2 infection deeply affected Italy, and Tuscany is the fifth

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most affected Region in Italy [12,13]. Herein, we evaluated the prevalence of SARS-CoV-2 infection among Tuscan patients with systemic autoimmune diseases followed at a tertiary referral center, and compared it to that observed in the general Tuscan population.

2. Methods

This cross-sectional study was performed at the Interdisciplinary Internal Medicine Unit of Careggi University Hospital, Firenze (Tuscany, Italy), and was approved by the local Ethics Committee. All outpatients with systemic autoimmune diseases, actively followed at our Unit and residing in Tuscany were eligible. Starting from April 1th 2020, two weeks after the beginning of the epidemiologic peak recorded in Tuscany, we systematically contacted by telephone our patients with planned follow-up visits in April or May 2020, to investigate their health status, with particular reference to their disease manifestations, the presence of symptoms suggesting SARS-CoV-2 infection (either current or in the past month), the results of nasopharyngeal swabs where available, and the ongoing pharmacological treatments. All patients with follow-up data collected between April 1st and 14th 2020 were included in the study.

No statistical sample size calculation was performed a priori. Continuous variables are presented as median (interquartile range, IQR), and categorical variables as number (%). The prevalence of SARS-CoV-2 infection was expressed as the percentage (with 95% confidence interval (CI)) of cases with SARS-CoV-2 infection confirmed by nasopharyngeal swab on the total number of patients included in the study. The proportion of patients with confirmed SARS-CoV-2 infection in our cohort was compared to those reported for the general population of Tuscany, using the Fisher exact test. Statistical significance was defined as $P < .05$.

3. Results

Out of 2074 patients with systemic autoimmune diseases actively followed at our unit, 527 were telephonically contacted, and all responded. Of them, 458 lived in Tuscany and were included in this study (Fig. 1). Table 1 shows their demographic and clinical characteristics. Most patients were female (74%); the median age was 56 years (43–68). The most common diseases were systemic lupus erythematosus (SLE), giant cell arteritis, and Behçet's syndrome. A minor proportion of patients reported active disease based on clinical and/or available laboratory data.

Fifty-six percent of the patients were receiving corticosteroids, at a median prednisone dose of 5 mg/day (2.5–5); 23% were receiving HCQ, 10% mycophenolate, and 24 (5%) colchicine. Biologic DMARDs were used in 41% of patients, mainly TNF alpha inhibitors (10%) and tocilizumab (9%).

Thirteen patients reported symptoms compatible with SARS-CoV-2 infection (2.8%; 95% CI 1.5–4.8%) (Fig. 2; Table 1); a considerable proportion of them had active disease ($n = 5$, 39% vs 6% in the patients free of SARS-CoV-2 symptoms).

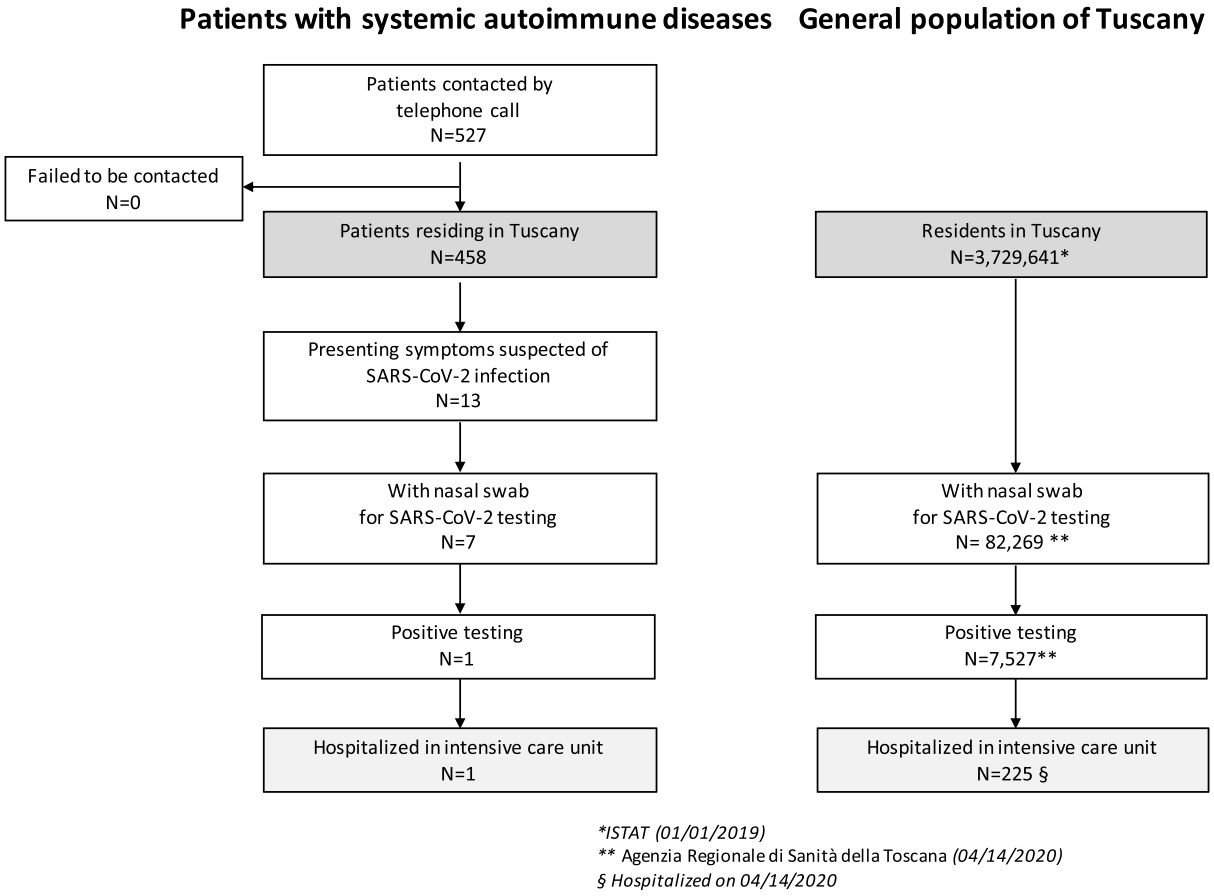

Fig. 1. Flow chart of SARS-CoV-2 cases in patients with systemic autoimmune diseases and in the general population of Tuscany.

Table 1
Demographic and clinical characteristics of the patients.

	Patients with systemic autoimmune diseases N (%)	Patients with symptoms suspected of SARS-CoV-2 N (%)
N obs	458	13
Sex		
Female	339 (74.0)	11 (84.6)
Male	119 (26.0)	2 (15.4)
Age, years*	56 (43–68)	42 (36–48)
Systemic autoimmune diseases		
Connective tissue diseases		
SLE	117 (25.6)	4 (30.8)
Sjogren disease	37 (8.1)	1 (7.7)
Systemic sclerosis	18 (3.9)	–
Antiphospholipid syndrome	17 (3.7)	1 (7.7)
Myositis	10 (2.2)	–
Arthritis		
Spondyloarthritis	40 (8.7)	2 (15.4)
Rheumatoid arthritis	24 (5.2)	–
Vasculitis		
Giant cell arteritis/Takayasu	63 (13.8)	–
Behçet's syndrome	41 (9.0)	4 (30.8)
EGPA/GPA/MPA	40 (8.7)	–
Cryoglobulinemia	3 (0.7)	–
Henoch–Schönlein purpura	2 (0.4)	–
Autoinflammatory diseases		
Familial Mediterranean Fever	15 (3.3)	1 (7.7)
Recurrent idiopathic pericarditis	9 (2.0)	–
Others		
Uveitis	14 (3.1)	–
Retroperitoneal fibrosis	4 (0.9)	–
Sarcoidosis	4 (0.9)	–
Active disease		
Yes	30 (6.6)	5 (38.5)
No	428 (93.4)	8 (61.5)
Ongoing treatments		
Corticosteroids	254 (55.5)	9 (69.2)
Prednisone equivalent dose, mg/day*	5 (2.5–5)	5 (1.5–5)
DMARDs	201 (43.9)	8 (61.5)
Hydroxychloroquine	107 (23.4)	3 (23.1)
Mycophenolate	47 (10.3)	1 (7.7)
Methotrexate	33 (7.2)	1 (7.7)
Azathioprine	33 (7.2)	4 (30.8)
Cyclosporine	7 (1.5)	–
Leflunomide	2 (0.4)	–
Cyclophosphamide	1 (0.2)	–
Colchicine	24 (5.2)	1 (7.7)
Biologics	189 (41.2)	7 (53.9)
Anti-TNF alpha #	46 (10.0)	4 (30.8)
Tocilizumab	42 (9.2)	–
Belimumab	35 (7.6)	3 (23.1)
Anti-IL5 §	22 (4.8)	–
Rituximab**	17 (3.7)	–
Anti-IL1 °°	13 (2.8)	–
Secukinumab	10 (2.2)	–
Ustekinumab	4 (0.9)	–
IvIg	41 (9.0)	3 (23.1)

DMARDs: Disease-Modifying Anti-Rheumatic Drugs; EGPA: Eosinophilic Granulomatosis with Polyangiitis; GPA: Granulomatosis with Polyangiitis; IvIg: Intravenous Immunoglobulin; MPA: Microscopic Polyangiitis; SLE: Systemic Lupus Erythematosus.

* Data are reported as median value and IQR.
# Infliximab, Adalimumab, Etanercept, Golimumab, Certolizumab.
§ Mepolizumab, Benralizumab.
** Within the previous 3 months.
°° Anakinra, Canakinumab.

Of the 13 patients, seven had undergone nasopharyngeal swab, and one tested positive for SARS-CoV-2 (Fig. 1). She was a 68-year-old woman affected by Sjögren syndrome treated with prednisone (5 mg/day) and HCQ (200 mg/day) at time of SARS-CoV-2 confirmation. The patient initially had fever, fatigue, cough and dyspnea. As her general condition rapidly worsened, she was admitted to ICU due to interstitial pneumonia complicated by ARDS. She improved after antiviral treatment and tocilizumab and is currently in a sub-intensive care unit (Fig. 2).

No other patient had confirmed SARS-CoV-2 positivity. Within our cohort, the prevalence of SARS-CoV-2 infection was 0.22% (95% CI 0.01–1.21%). Data from the general Tuscan population (updated April 14th 2020) indicate a prevalence of SARS-CoV-2 infection of 0.20% (95% CI 0.20–0.21%). There was no significant difference in the proportion of patients with confirmed SARS-CoV-2 infection between our cohort and the general population ($p = .597$).

4. Discussion

In this study, SARS-CoV-2 infection was evaluated among 458 patients with systemic autoimmune diseases residing in Tuscany, an Italian Region with an incidence of SARS-CoV-2 infection comparable to that observed in other European countries [13]. Only one case of confirmed SARS-CoV-2 infection was found, resulting in a prevalence of SARS-CoV-2 infection similar to that observed in the general population.

A previous study on 320 Italian patients with chronic arthritis receiving immunosuppressive therapies reported four cases of confirmed infection and another four highly suggestive of SARS-CoV-2; no case developed severe complications or died [11]. However, the study did not compare the frequency of SARS- CoV-2 infection with that of the general population in Lombardy.

Our findings suggest that patients with systemic autoimmune diseases do not carry an increased risk of SARS-CoV-2 infection; additionally, as most patients were on treatment, it can be speculated that immunosuppressive treatments should not be discontinued in such cases. These results are not surprising, as a prominent immune response seems to mediate the most severe complications of SARS-CoV-2-induced.

tissue injury. Furthermore, also the female predominance of systemic autoimmune diseases might represent a protective feature, as growing studies suggest gender differences in the SARS-CoV-2 infection, with women being less (severely) affected than men [14]. Of interest, a high proportion of patients with symptoms compatible with SARS-CoV-2 had an active disease, further suggesting that active immune responses might be associated with a higher susceptibility to the infection, which however could not be confirmed in most symptomatic patients.

Our results do not allow any conclusion on the association between immunosuppressive treatments, particularly HCQ, colchicine and tocilizumab, and SARS-CoV-2 infection in these patients. Moreover, the lack of nasopharyngeal swab for all (at least symptomatic) patients, and the still ongoing pandemic, with new cases possibly occurring after our evaluation, represent major limitations of this study. Pending the results of further investigations coming from an ongoing international alliance of SARS-CoV-2 cases with rheumatic diseases [15,16], our experience shows that patients with chronic systemic autoimmune diseases do not seem to be at increased risk of SARS-CoV-2 infection or complications compared with the general population.

ID	Reported symptoms									Nasal swab
	Fever	Dry cough	Fatigue	Myalgia	Headache	Sore throat	Diarrhoea	Anosmia/ dysgeusia	Dyspnoea at rest	
1	x	x	x			x				NA
2	x	x			x					NA
3	x	x	x							NA
4	x	x								NA
5	x		x	x	x					NA
6	x	x				x				NA
7	x	x			x		x			Negative
8	x	x	x	x						Negative
9	x	x			x			x		Negative
10	x	x	x	x	x	x				Negative
11	x	x	x				x			Negative
12	x	x		x		x				Negative
13	x	x	x						x	Positive

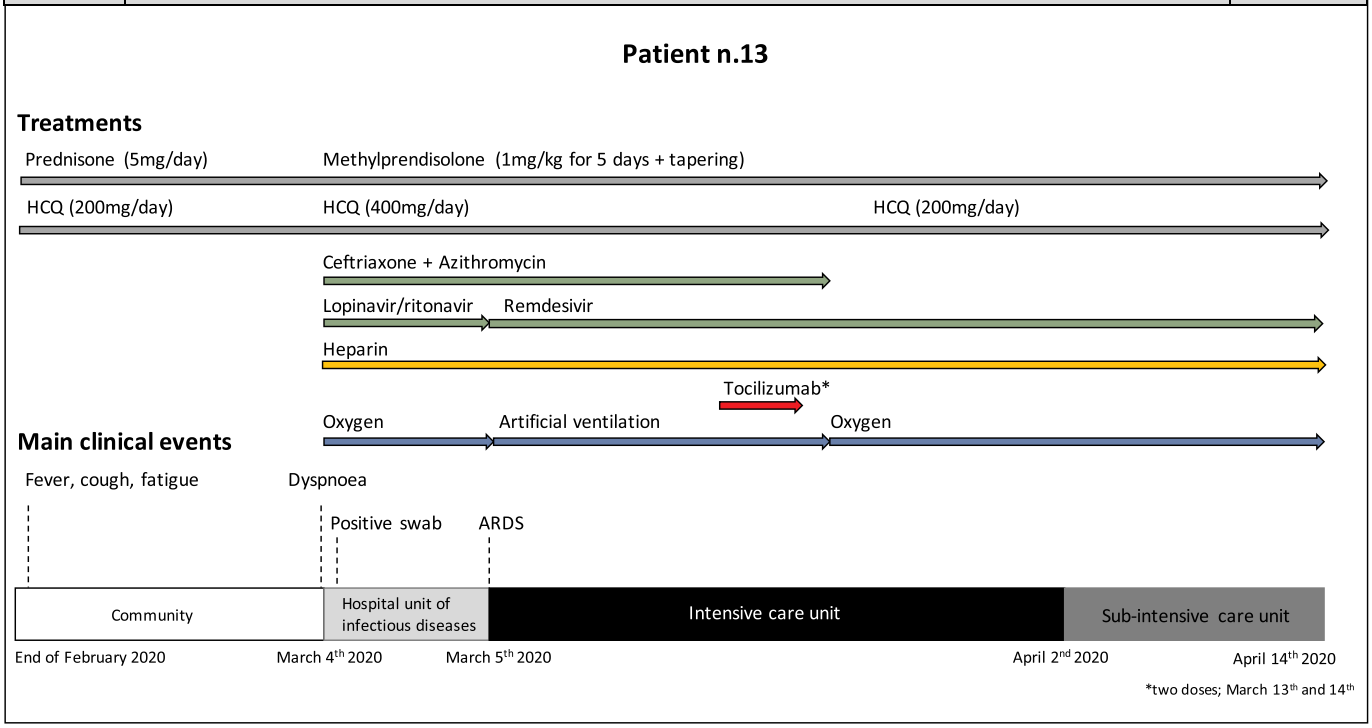

Fig. 2. Reported symptoms suspected of SARS-CoV-2 and results nasopharyngeal swab tests, and details of the main clinical events and treatments of the single case with confirmed SARS-CoV-2 infection found in our cohort. HCQ: hydroxychloroquine.

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Declaration of Competing Interest

None declared.

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