



COVID-19 and systemic sclerosis: analysis of lifestyle changes during the SARS-CoV-2 pandemic in an Italian single-center cohort

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Abstract

The outbreak of SARS-CoV-2 has changed the habits and lives of people worldwide. Patients affected by systemic sclerosis (SSc) experienced constant fear because of their immunocompromised status. The aim of this study was to investigate the prevalence of SARS-CoV-2 infection and to analyze the lifestyle changes in a single-center cohort of SSc patients and if these changes were more severe than in the general population. During the Italian lockdown, we supplied two surveys to our 184 SSc patients. In the first one, filled by 110 patients, we asked if SARS-CoV-2 had infected them or if they experienced signs and symptoms consistent with COVID-19. The second survey, performed by 79 SSc patients and 63 healthy subjects, included questions about the lifestyle adopted during this specific period. Among our patients, COVID-19 was diagnosed only in one case, while three other subjects reported signs and symptoms suggestive for the disease. Regarding the second survey, our patients greatly changed their lifestyle during the pandemic, adopting more restrictive isolation measures, because of their awareness of frailty. To date, we do not dispose of enough data to speculate about the risk of COVID-19 among immunocompromised patients, although in our SSc patients their frailty seems to have been their shelter. Pending more accurate epidemiological studies, it is essential to share as much data as possible to better understand the impact of COVID-19 on SSc patients' health.

Key points

- *The lifestyle adopted by SSc patients during the first months of COVID-19 pandemic was characterized by more stringent isolation rules than general population.*
- *The prudent behavior of patients with SSc during Italian lockdown should be considered as a possible bias when analyzing the risk of SARS-CoV-2 disease in these subjects, as well as a protective factor against infection.*

Keywords COVID-19 · Systemic Sclerosis · Lifestyle changes during SARS-CoV-2 pandemic

Introduction

Since the early time of SARS-CoV-2 infection outbreak, rheumatologists worldwide have expressed their concern about patients affected by autoimmune rheumatic diseases. It is well known how these diseases could increase the infective risk in several ways, because of the patients' immunosuppressed status due to the therapies and the

pathologies as well [1]. As regards coronavirus disease 2019 (COVID-19), to date, we do not dispose of enough data to assert if and in which way the virus impacts on patients with rheumatic diseases, including systemic sclerosis (SSc). SSc is a complex connective tissue disease associated with chronic multisystem involvement with frequently bad prognosis and impact on the quality of life [2].

The social distancing among patients affected by chronic diseases could have led to the development of more severe psychological distress in those subjects rather than in the general population. Besides, the media daily reports with conflicting data about the increased risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in immunosuppressed subjects could have forced our patients to take more severe isolation measures [3].

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Material and methods

During the first weeks of the outbreak of COVID-19 pandemic in Italy, we provided two different surveys among 184 patients, older than 18 years, fulfilling the SSc 2013 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria [4], followed in our Scleroderma Clinic. In the first one, filled by 110 patients, we telephonically asked if they had been infected by SARS-CoV-2, tested on the nasopharyngeal swab, or if they have shown the typical signs and symptoms of COVID-19. The second survey, sent by e-mail and performed by 79 SSc patients and 63 healthy subjects matched for sex and age living in the same geographical area, aimed to investigate the lifestyle adopted during this unique period. For all subjects an informed consent was obtained.

Frequencies and percentages were calculated for all observations. Mann-Whitney test was used for comparison among groups. Statistical analysis was performed with Prism GraphPad (Version 8).

Results

The main clinical, demographic, and treatment features of the whole group of SSc patients are shown in Table 1. Our patients presented hypertension in 19% (21 patients), diabetes in 6% (6 patients), and cardiovascular (CV) diseases in 10% (11 patients) of cases.

In our cohort, only one patient (0.9%), a 77-year-old woman with 6-year history of SSc characterized by limited cutaneous involvement and interstitial lung disease (ILD) treated with low-dose methyl-prednisolone and methotrexate, reported a positive throat and nasopharyngeal swab test for SARS-CoV-2 on real-time reverse-transcription-polymerase chain reaction (PCR). She was clearly symptomatic and needed hospitalization as well as specific treatments. Other 3 SSc patients (2.72%) reported the presence of typical signs and symptoms suggestive of mild COVID-19, adopting quarantine measures although they could not perform nasopharyngeal swab or serological examination due to the emergency health situation of our country. Demographic and clinical characteristics of these 4 patients are shown in Table 2.

As regards our second survey on the lifestyle of SSc patients during the Italian lockdown phase, 87% (67 cases) of our patients declared to consider themselves as “subject at risk” for COVID-19 and 81% (63 cases) were afraid they would have a worse prognosis than the general population if infected. Therefore, we found that patients have gone out of home significantly less frequently (defined as the number of times they have left home in 2 weeks of time) than controls (2/3 vs 4/4 (median/interquartile range); p value 0.0007), adopting restrictive isolation measures in 60% of cases.

Table 1 Comprehensive clinical, demographic, and therapeutic features of all the investigated 110 SSc patients

Features	Patients ($N = 110$)
Women ($n/\%$)	102/93
Age, years, median (IQR range)	62 (49.75–68)
Disease duration, years, median (IQR range)	9 (5–15)
lcSSc-dcSSc-no cutaneous involvement ($n/\%$)	80/72–27/25–3/3
ILD ($n/\%$)	39/35
PAH ($n/\%$)	0/0
Associated chronic disease	
Cardiovascular disease ($n/\%$)	11/10
Diabetes ($n/\%$)	6/6
Arterial hypertension ($n/\%$)	21/19
Chronic kidney impairment ($n/\%$)	4/4
Smoker ($n/\%$)	19/17
Treatment	
Hydroxychloroquine ($n/\%$)	22/20
Methotrexate ($n/\%$)	13/12
Mycophenolate mofetil ($n/\%$)	16/15
Azathioprine ($n/\%$)	4/4
Prednisone ($n/\%$)	29/26
Prednisone ≥ 10 mg per day ($n/\%$)	3/3
Tocilizumab ($n/\%$)	2/2
Antiplatelet drug ($n/\%$)	49/45
Oral Anticoagulant ($n/\%$)	3/3
ACE inhibitors and/or ARBs ($n/\%$)	9/8

lcSSc limited cutaneous systemic sclerosis, dcSSc diffuse cutaneous systemic sclerosis, ILD interstitial lung disease, PAH pulmonary arterial hypertension, ACE angiotensin-converting enzyme, ARBs angiotensin receptor blockers

Discussion

In relation to the risk of COVID-19 in immunocompromised patients, our data are similar to those previously described in other reports. It is interesting to note that, although accurate data on the real incidence of COVID-19 cannot be derived due to the small sample size, our results are consistent with those from other rheumatologic centers in different Italian area. In our cohort, only one SSc patient was diagnosed by SARS-CoV-2 infection, such as in two Northern Italian cohorts described by Bellan et al. [5] and Zen et al. [6]. This is in line with those reports sustaining that patients with rheumatic diseases do not seem to have an increased risk of SARS-CoV-2 infection [7, 8]. In contrast, data from two Italian reports showed a higher incidence of COVID-19 among different rheumatic disease patients. They both showed an incidence of 2.5%, although in patients affected by systemic lupus erythematosus and large-vessel vasculitis, respectively [9, 10]. It has been hypothesized by others that patients suffering from

Table 2 Details on the four SSc cases presenting signs and symptoms consistent with COVID-19 infection

Features	Patient 1	Patient 2	Patient 3	Patient 4
Age (years)	77	69	66	67
Gender	Female	Female	Female	Female
Disease duration (years)	6	15	13	23
SSc form	lcSSc	lcSSc	lcSSc	lcSSc
ILD	Yes	No	Yes	No
PAH	No	No	No	No
CV disease	No	No	No	No
Other comorbidities	Arterial hypertension	None	Arterial hypertension; diabetes	Hashimoto's thyroiditis; primary biliary cirrhosis
Treatment for SSc	Methylprednisolone Methotrexate	Acetylsalicylic acid	Mycophenolate mofetil	Methylprednisolone, acetylsalicylic acid
Nasopharyngeal swab for SARS-CoV-2	Positive	Not performed	Not performed	Not performed
Hospitalization	Yes	No	No	No
Signs and symptoms	Fever (37.7 °C), fatigue	Fever (38.5 °C), myalgia, dry cough	Fever (37.7°), myalgia, arthralgia, dysgeusia, conjunctivitis, dry cough, dyspnea	Fever (37.8°), headache, fatigue, rhinitis, dry cough, dyspnea
Treatment for COVID-19	Methylprednisolone, hydroxychloroquine, azithromycin, tocilizumab	None	None	None
Outcome	Full recovery	Full recovery	Full recovery	Full recovery

lcSSc limited cutaneous systemic sclerosis, dcSSc diffuse cutaneous systemic sclerosis, ILD interstitial lung disease, PAH pulmonary arterial hypertension, CV cardiovascular

connective tissue diseases could run a higher risk of COVID-19 than those with inflammatory arthritis [11]. Thus, considering the demographic data of the different cohorts, the relevant element seems to be the belonging geographical area of the patients. Our patients mainly came from Central and Southern Italy, while most of those interviewed in the other studies came from Lombardy, the Italian area with the highest rate of SARS-CoV-2 infections between March and May 2020 [12].

The role of risk factors for COVID-19 in patients affected by rheumatic disease is unclear, so we tried to analyze those already hypothesized or defined in previous reports [2, 13]. We learned that patients affected by COVID-19 are more frequently males, suffering from hypertension, diabetes, and CV and chronic pulmonary diseases [14], and hypertension and CV diseases seem to represent bad prognostic factors for more severe form [15]. Our data are similar to others where hypertension and CV diseases were found in 21%, and 8.4%, respectively, while the presence of diabetes slightly differs, 6 vs 9.7% of cases [14]. On the other hand, among all the rheumatic diseases, SSc is one of the most commonly affected by pulmonary involvement [16]. As underlined by Del Papa et al., pulmonary and CV manifestations during SSc need to be considered when we speculate about the risk of COVID-19 in these patients [2]. Thirty-nine patients (35% of cases) in our

cohort presented ILD, while none had pulmonary arterial hypertension; 11 (10%) patients had a history of CV disease. Similar data were published in the COVID-19 Global Rheumatology Alliance preliminary report where lung and CV diseases have been identified in the five main comorbidities among the patients with rheumatic diseases [17]. The only case of COVID-19 in our cohort had a history of arterial hypertension and presented ILD, but she experienced a disease course characterized by a good prognosis and she was discharged after a complete resolution of the symptoms. Despite these considerations, due to the slightness of our sample and the lack of a control group, we could not clearly demonstrate the relevance for any considered risk factor in the onset of COVID-19 in patients affected by SSc. Understanding whether and in which way the virus could impact on our patients remains the most compelling issue, especially in the light of the rising of contagions that we are experiencing in the last weeks. Most of the scientific reports published in the last months have shown that patients with rheumatic diseases, SSc included, could have the same risk of COVID-19 than the general population, but the reasons has not been elucidated yet [5, 6, 18].

Evolving knowledge about the mechanism of action of SARS-CoV-2 virus brought to include many agents, largely used in the treatment of rheumatic patients, for the

management of COVID-19. So far, starting from the initial issue on the potentially higher infectious risk for patients treated with immunosuppressant therapies, the rheumatologists' community began to question about a "protective role" of some of these drugs, when used chronically without reaching any clear conclusion [13, 19, 20]. Among our patients, sixty (54.4%) were under chronically use of immune-modifying drugs (Table 1); except for the case diagnosed with COVID-19, none of them discontinued chronic treatment for SSc as recommended in the preliminary advice for patient management [13]. This decision does not seem to have been of prognostic value on our patients, as already demonstrated in a large cohort of patients with rheumatic diseases treated with biological and targeted synthetic disease-modifying antirheumatic drugs [21]. In addition, some reports have started to notice that patients affected by autoimmune diseases had adopted more restrictive preventive strategies against COVID-19, as occurred in our SSc patients [18]. In fact, data from our second survey demonstrate for the first time that SSc patients, frightened by the potential consequences of the virus on their condition, have adopted more stringent rules than the control group. What has just been asserted constitutes a possible bias to take into account when analyzing the prevalence of COVID-19 in SSc, but it may have been the winning strategy during the first months of SARS-CoV-2 pandemic.

Our data, as well as those from other authors, seem to reassure about the risk of COVID-19 in immunosuppressed patients [5–8]. We do not actually know if our SSc patients do have an increased risk of COVID-19, but their related conditions make them "frail" and the effect of SARS-CoV-2 pandemic is supposed to have serious implications. Among the factors that may have contributed to making the risk of SARS-CoV-2 disease similar to that of the general population, we would consider their "frailty awareness" as a protective factor.

The pandemic COVID-19 was a lightning bolt from the blue with a significant impact on many aspects of our lives. Thus, we are conscious that our SSc patients have experienced the pandemic period with a lot of fear and concern and changed their lifestyle more than the general population. Their prudential behavior seems to have had a favorable development on their outcome.

However, our study has some limitations. In our cohort, only one patient with COVID-19 was identified, making difficult a clear definition of the epidemiologic data. Therefore, as already asserted, due to the small sample size and the lack of a control group, we cannot draw conclusion about the role of any risk factors in the occurrence of SARS-CoV-2 infection in SSc patients. There is a needed evidence from more extensive epidemiological studies to better define the real impact of specific disease features in increasing the risk of infection, if any. Being SSc a rare disease, it will be fundamental to join our preliminary experience on the effects of COVID-19

pandemic with all the international groups dedicated to the care of these frail patients.

Authors' contributions VR was responsible for data collection and analysis, drafted and revised the paper. GP collected the data, drafted and revised the paper. DMRB collected the data and revised the paper. CA, MC, KS, SM, and FC revised the paper.

Compliance with ethical standards

Declarations None.

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