Psychological Fragility in an Italian Cohort of Systemic Sclerosis Patients During COVID-19 Pandemic Category: Short Communication

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Objective: This work aims to evaluate the prevalence of anxiety and COVID-19-related fear in systemic sclerosis (SSc) patients during the second and third waves of the SARS-CoV-2 pandemic in Italy and their possible associated factors.

Methods: A cohort study was carried out on 114 SSc patients referred to our Scleroderma Clinic, matched for sex and age. Twenty-eight of them had missed scheduled examinations during the October 2020–March 2021 period and 86 had attended regular outpatient visits during the same period. Both groups were administered (by telephone for cases and in-person for controls) the Generalized Anxiety Disorder Scale-7 (GAD-7) questionnaire and the validated on SSc patients COVID-19 Fears Questionnaire for Chronic Medical Conditions (COVID-19 Fears). Concurrent factors related to higher scores were investigated in patients who did not have an outpatient follow-up.

Results: The missing group had significantly more patients scoring ≥8 on the GAD-7 questionnaire [22 (78.6%) vs 16 (18.6%), p < 0.0001] and significantly higher scores on the COVID-19 Fears questionnaire (median [quartiles] 31.5 [26.25;37.25] vs 20 [13.75;28], p < 0.0001) than the attending group. Multivariate analysis performed on the missing patients group showed a significant association of the lack of work and ongoing therapy for anxiety/depression with GAD-7 (p = 0.0275 and p = 0.0188) and COVID-19 Fears score (p = 0.0016 and p = 0.0099).

Conclusion: Anxiety disorder and COVID-19-related fear were greater in SSc patients who missed regular follow-ups and are associated with a lack of work activity. These findings aim to identify a subgroup deserving attention regarding risk factors for missed periodic controls.

Keywords: systemic sclerosis, anxiety, COVID-19 fear

Introduction

Since the beginning of the COVID-19 pandemic, social distancing had a major impact on the mental health of the general population,1,2 with an increase in symptoms related to anxiety, depression, and post-traumatic stress disease (PTSD) compared with before the pandemic outbreak.3–5 Such was associated primarily with young age, female gender, and previous psychiatric illness,6 but also with loneliness, COVID-19-specific worry, and low distress tolerance.7 Other studies on the Chinese population showed how the prevalence of acute stress symptoms gradually declined with the progression of the epidemic, although that of anxiety and depression symptoms still stayed at high levels.8

Systemic sclerosis (SSc) is a chronic autoimmune disease characterized by fibrosis of skin and internal organs and vasculopathy, leading to severe physical impairment.9

A state of psychological fragility was notably found in people with chronic conditions during COVID-19 pandemic,10 including SSc patients. In such a population, a substantial increase in anxiety, but not depression symptoms compared to before the COVID-19 pandemic emerged, inversely related to adequacy of financial resources.11
Another crucial element for this population is fear due to COVID-19, as reported in a cohort of SSc patients from the United States, Canada, France, and the United Kingdom (UK) by a validated questionnaire. Higher levels of COVID-19-related fear were found in UK SSc patients and were associated with low economic intake and with a previous anxiety condition. Pandemic fear was described by patients as a major cause of missed outpatient visits, as emerged from a tele-survey of Indian Progressive Systemic Sclerosis Registry.

For SSc patients, assiduous follow-up is essential to prevent or limit disease multi-organ involvement through appropriate diagnostic and therapeutic tools to achieve a better disease outcome. Anxiety and fear due to COVID-19 thus emerged as marking psychological fragility in SSc patients in the course of the current pandemic. Therefore, the aim of the present work is to assess their prevalence among SSc patients during the second and third waves of the SARS-CoV-2 pandemic in Italy using validated questionnaires, and to investigate possible associated factors.

**Materials and Methods**

We performed a cohort study on 114 consecutive patients with SSc referring to the Scleroderma Clinic of Policlinico Umberto I in Rome, Italy. During the period from October 2020 to March 2021, a new rise in the $R_t$ index (the average number of new infections caused by a single infected individual at time $t$ in the susceptible population) was registered and stricter lockdown measures have been applied. We selected 28 patients who had not attended the scheduled examination and 86 subjects who had performed regular outpatient visits during the same period, matched for sex and age. Both groups were administered (respectively by telephone or in-person) the Generalized Anxiety Disorder Scale-7 (GAD-7) questionnaire, used in patients with pre-existing medical conditions during the COVID-19 pandemic, and the COVID-19 Fears Questionnaire for Chronic Medical Conditions (COVID-19 Fears), developed and validated on SSc patients of Scleroderma Patient-centered Intervention Network (SPIN) COVID-19 cohort study. The GAD-7 is a 7-item scale reporting score from 0 to 3 on all the questions. It investigates how often the patient has been bothered by seven different symptoms of anxiety during the last 2 weeks with response options such as “not at all”, “several days”, “more than half the days”, and “nearly daily” scored as 0, 1, 2, and 3, respectively. The scores of 5, 10, and 15 are taken as cut-off points for mild, moderate, and severe anxiety, respectively. A score of 8 points or more is a reasonable cut-off for needing further evaluation to determine the presence and type of anxiety disorder. The GAD-7 has been found to have great psychometric properties and is short and easy to administer (Table 1). The COVID-19 fears is a 10-item scale measure assessing pandemic-related fears among vulnerable patients due to pre-existing illnesses. It evaluates fears of social isolation, adequate care of chronic conditions during the pandemic, greater risk of the COVID-19 complications due to medical conditions and fear of COVID-19 infection (Table 2).

Finally, an analysis of possible factors associated with higher questionnaire scores in patients who

**Table 1** Generalized Anxiety Disorder Scale-7 (GAD-7) Questionnaire.

| Over the Last 2 Weeks, How Often Have You Been Bothered by the Following Problems? | Not at All | Several Days | More Than Half the Days | Nearly Every Day |
|---|---|---|---|---|
| 1) Feeling nervous, anxious or on edge | 0 | 1 | 2 | 3 |
| 2) Not being able to stop or control worrying | 0 | 1 | 2 | 3 |
| 3) Worrying too much about different things | 0 | 1 | 2 | 3 |
| 4) Trouble relaxing | 0 | 1 | 2 | 3 |
| 5) Being so restless that it is hard to sit still | 0 | 1 | 2 | 3 |
| 6) Becoming easily annoyed or irritable | 0 | 1 | 2 | 3 |
| 7) Feeling afraid as if something awful might happen | 0 | 1 | 2 | 3 |

**Note:** A score ≥8 is a reasonable cut-off for needing further identifying evaluation to determine presence and type of anxiety disorder. GAD-7 score obtained by adding score for each question (total points).
did not have outpatient follow-up was conducted, such as age, disease activity reported by patients, ongoing therapy for anxiety/depression, current work status, and living alone.

This study complies with the Declaration of Helsinki. The Sapienza University of Rome–Policlinico Umberto I ethic committee has approved (institutional review board approval n° 6364) the study, and informed consent has been obtained from the subjects.

**Statistical Analysis**

Statistical analysis of the result was performed using GraphPad Prism 8 for Windows. Qualitative variables were described as frequencies and percentages, continuous variables as medians and interquartile ranges, and assessed by chi-square test ($\chi^2$ test) and Fisher’s exact test, as appropriate. For the comparison of ordinal values between independent sample Mann–Whitney test for paired or unpaired samples was used. Multivariate linear regression analysis was used to adjust the association between a continuous dependent variable and independent variables for potential confounders.

**Results**

The study population consisted of 114 consecutive SSc patients. Of the 28 patients who did not perform outpatient visits during the selected period, 27 were female and the median age [quartiles] was 64 [55.25;70] years. Among 86 patients who performed regular follow-up, 78 were female and the median age [quartiles] was 60 [61.5;67] years. The first group had statistically significant more patients scoring ≥8 on the GAD-7 questionnaire (22/78.6% vs 16/18.6%, p<0.0001) and recorded higher scores both on GAD-7 (median [quartiles] 10.5 [8.25;14] vs 4 [0;7], p<0.0001) and COVID-19 Fears (median [quartiles] 31.5 [26.25;37.25] vs 20 [13.75;28], p<0.0001) than the second group. More attending group patients self-reported a worsening of SSc symptoms than missing group ones (26/30.3% vs 3/10.7, p=0.0039) (Table 3). On multivariate analysis performed on missing group patients, lack of work and ongoing therapy for anxiety/depression showed a significant association with GAD-7 (p=0.0275 and p=0.0188) and COVID-19 Fears.

**Table 2** 10-Item COVID-19 Fears Questionnaire for Chronic Medical Conditions (COVID-19 Fears), Validated on Population of Patients with Systemic Sclerosis

| Question                                                                 | Not at All | Slightly | Moderately | Very | Extremely |
|--------------------------------------------------------------------------|------------|----------|------------|------|-----------|
| 1) I will become infected when I have to leave the house to get supplies or when supplies are brought to me |            |          |            |      |           |
| 2) I will not be able to access health care that I need for my condition |            |          |            |      |           |
| 3) I will need to be isolated for longer than others because of my condition |            |          |            |      |           |
| 4) I will be infected and experience more severe complications because of my condition |            |          |            |      |           |
| 5) I will be infected and will not receive the medical treatment I need |            |          |            |      |           |
| 6) I will be infected and healthcare professionals will not be familiar with the needs of a person with my condition |            |          |            |      |           |
| 7) People close to me (eg, family, close friends) will be infected and become ill |            |          |            |      |           |
| 8) I will not be able to access medications I need for my condition due to shortages |            |          |            |      |           |
| 9) I will not be able to obtain basic supplies (eg, food, other household necessities) |            |          |            |      |           |
| 10) I will be infected with the virus |            |          |            |      |           |

Notes: This table contains a list of statements that are related to COVID-19 and possible fears you may have about its consequences. Please select the response that reflects how much each statement describes your experience on a typical day in the last week. You may choose among not at all, slightly, moderately, very, extremely. Please do not skip any questions. Because of the COVID-19 pandemic outbreak, I am afraid that. COVID-19 Fears Questionnaire for Chronic Medical Conditions reprinted from Journal of Psychosomatic Research, Vol 139, Authors: Yin Wu, Linda Kwoikkenbos, Richard S. Henry, Lydia Tao, Sami Harb, Angelica Bourgeault, Marie-Eve Carrier, Brooke Levis, YingSun, Parash Mani Bhandari, Andrea Carboni-jiménez, MariaGagarina, Chen He, Ankur Krishnan, Zelalem F. Negere, Dipika Neupane, Luc Mouton et al. Validation of the COVID-19 Fears Questionnaires for Chronic Medical Conditions: A Scleroderma Patient-centered Intervention Network COVID-19 Cohort study. page 110271. Copyright (2020), with permission from Elsevier, license number 5315350257568.
The multivariate analysis performed on all the 114 patients, considering GAD-7 and COVID-19 Fear scores as dependent variables, showed statistically significant associations with anxiety/depression therapy assumption (p=0.0010 and p=0.0137, respectively).

Table 3 Characteristics of Study Population

|                | Patients Who Missed Scheduled Appointment | Patients Who Regularly Performed Follow-Up |
|----------------|------------------------------------------|-------------------------------------------|
| Female:Male ratio | 28:1                                      | 78:8                                      |
| Mean age ± SD     | 63 ± 12.3                                 | 60 ± 13                                   |
| Current job, n (%) | 11 (39.3)                                 | 30 (34.8)                                 |
| No cohabitant, n (%) | 6 (21.4)                                | 15 (17)                                   |
| Worsening of SSc symptoms, n (%) | 3 (10.7)                             | 26* (30.3)                                 |
| Taking medications for anxiety/depression, n (%) | 8 (28.6)                              | 16 (18.6)                                  |
| Median GAD-7 score [quartiles] | 10.5 [8.25;14]**           | 4 [0;7]                                    |
| GAD-7 score ≥8, n (%) | 22 (78.6)**                  | 16 (18.6)                                  |
| Median COVID-19 Fears score [quartiles] | 31.5 [26.25;37.25]******          | 20 [13.75;28]                               |

Notes: *p=0.0039; **p<0.0001; ***p<0.0001; ****p<0.0001.
Abbreviations: SSc, systemic sclerosis; SD, standard deviation; GAD-7, Generalized Anxiety Disorder Scale-7; COVID-19 Fears, COVID-19 Fears Questionnaire for Chronic Medical Conditions.

score (p=0.0016 and p=0.0099) (Tables 4 and 5). The multivariate analysis performed on all the 114 patients, considering GAD-7 and COVID-19 Fear scores as dependent variables, showed statistically significant associations with anxiety/depression therapy assumption (p=0.0010 and p=0.0137, respectively).

Table 4 Multivariate Analysis Performed on 28 Patients Who Missed Scheduled Appointments Considering GAD-7 Score as the Dependent Variable

| Variable                  | OR    | SE    | 95% CI            | P-value |
|---------------------------|-------|-------|-------------------|---------|
| Current job               | −0.3100 | 0.1406 | −0.5881 to −0.03634 | 0.0275* |
| Disease reported as “active” | 0.1014  | 0.1736 | −0.2493 to 0.4326  | 0.5591  |
| No cohabitant             | −0.08060 | 0.1441 | −0.3705 to 0.1953  | 0.5760  |
| Age                       | 0.002937 | 0.005284 | −0.007311 to 0.01341 | 0.5783  |
| Therapy for anxiety/depression | 0.2903  | 0.1235 | 0.04553 to 0.5302   | 0.0188* |

Note: *p<0.05.
Abbreviations: OR, odds ratio; SE, standard error; CI, confidence interval.

Table 5 Multivariate Analysis Performed on 28 Patients Who Missed Scheduled Appointments Considering COVID-19 Fears Score as the Dependent Variable

| Variable                  | OR    | SE    | 95% CI            | P-value |
|---------------------------|-------|-------|-------------------|---------|
| Current job               | −0.2615 | 0.08282 | −0.4245 to −0.09976 | 0.0016* |
| Disease reported as “active” | 0.06232 | 0.1078 | −0.1530 to 0.2697  | 0.5631  |
| No cohabitant             | −0.1367 | 0.08776 | −0.3116 to 0.03263 | 0.1192  |
| Age                       | 0.002224 | 0.003170 | −0.003949 to 0.008479 | 0.4829  |
| Therapy for anxiety/depression | 0.1943  | 0.07531 | 0.04560 to 0.3409   | 0.0099* |

Note: *p<0.05.
Abbreviations: OR, odds ratio; SE, standard error; CI, confidence interval.
Discussion
Patients with SSc represent a high-risk population for complications related to COVID-19 due to the presence of fragility and immunosuppressant drug use,\textsuperscript{20,21} where a higher prevalence of SARS-CoV-2 infection related to lung involvement resulted.\textsuperscript{22} The presence of interstitial lung disease and ongoing immunosuppressive treatment may place patients with SSc at risk of developing more severe disease and higher mortality when infected with SARS-CoV-2.\textsuperscript{23,24} Since the beginning of the pandemic, the need to balance patients’ safety with the necessity for frequent medical check-ups became apparent, as well as a growing interest in the psychological fragility of SSc patients emerged.\textsuperscript{25} In Italy, during the pandemic progression, additional waves of the epidemic occurred, making it necessary the reintroduction of stricter restrictive measures. Of note, psychological consequences showed a correlation with the length of isolation time.\textsuperscript{26}

Our study shows that anxiety disorder and fear related to COVID outbreak are greater in patients with SSc who have not attended scheduled appointments, and they are associated with lack of work activity and ongoing therapy for anxiety/depression. Our results are in line with the multicentric Scleroderma Patient-centred Intervention Network (SPIN) COVID-19 cohort study, in which SSc patients presented a rise in anxiety symptoms compared to pre-COVID-19 era, with no significant increase in depression symptoms and with the adequacy of financial resources associated with a better outcome.\textsuperscript{11} Similar results emerged from Indian Progressive Systemic Sclerosis Registry, where the pandemic fear was a cause of missed outpatients visits and job loss was found associated to a self-reported worsening of disease.\textsuperscript{14} Another work from the SPIN COVID-19 cohort showed that variables associated with COVID-19 fear were interference of breathing problems in daily activities, financial resources inadequacy, and high levels of previous anxiety.\textsuperscript{13}

Our study identifies for the first-time higher amounts of COVID-19-related fear and generalized anxiety disorder symptoms in the subgroup of SSc patients who missed regular visits, evidenced by validated questionnaires. These patients deserve attention regarding the presence of risk factors for missed periodic check-ups, whose regularity should be ensured as recommended by the World Scleroderma Foundation.\textsuperscript{27} As emerged in the Taiwan population, high anxiety and COVID-19 worry resulted associated with non-attendance to the scheduled appointment.\textsuperscript{28} Such result stressed the need for intervention strategies regarding the mental health of this patient’s group. An example in this way is the SPIN COVID-19 Home-Isolation Activities Together (SPINCHAT) Program, a group-based intervention delivered by video conference and intended to reduce anxiety among at-risk people with SSc, whose results are in progress.\textsuperscript{29} Other strategies to address patient concerns were and still are applied, such as telemedicine or home delivery drugs.\textsuperscript{30}

A partially encouraging finding is that more regular attendees reported a worsening of SSc symptoms, and this gives hope that, at least for this group of at-risk patients, regular check-ups will be guaranteed. Maybe patients who are worse off are keener to comply than controls and more worried about their current autoimmune disease than about the risk of viral infection.\textsuperscript{31} Besides, the reason for this behaviour can be also due to the more difficult management of their clinical state remotely.

Conclusion
A limitation of the present work is the small size of the cohort of missing patients, with the impossibility to make a further stratification. On the other hand, strengths are the choice of a homogeneous population and the application of a questionnaire validated for SSc patients.

On that note, what we learned from our present study is that the possible arising of psychosocial disabilities and deterioration in the quality of life should be taken into account. We expect that the results obtained so far will allow focusing on the psychological fragility of SSc patients, to provide the necessary follow-up and treatment, thus preventing their disease from worsening during such a particular long-lasting historical period.

Data Sharing Statement
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.


**Ethics Statement**

This study complies with the Declaration of Helsinki. The Sapienza University of Rome – Policlinico Umberto I ethic committee has approved (institutional review board approval n° 6364) the study and written (or oral for patients reached by telephone) informed consent has been obtained from the subjects.

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**Author Contributions**

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

**Disclosure**

The authors declare they have no conflicts of interest.

**References**

1. Wang C, Pan R, Wan X, et al. A longitudinal study on the mental health of the general population during the COVID-19 epidemic in China. *Brain Behav Immun*. 2020;87:40–48. PMID: 32298802; PMCID: PMC7153528. doi:10.1016/j.bbi.2020.04.028
2. Dubey S, Biswas P, Ghosh R, et al. Psychosocial impact of COVID-19. *Diabetes Metab Syndr*. 2020;14(5):779–788. PMID: 32526627; PMCID: PMC7255207. doi:10.1016/j.dsx.2020.05.035
3. Castellini G, Rossi E, Cassioli E, et al. A longitudinal observation of general psychopathology before the COVID-19 outbreak and during lockdown in Italy. *J Psychosom Res*. 2021;141:110328. PMID: 33316632; PMCID: PMC7716728. doi:10.1016/j.jpsychres.2020.110328
4. Di Crosta A, Palumbo R, Marchetti D, et al. Individual differences, economic stability, and fear of contagion as risk factors for PTSD symptoms in the COVID-19 emergency. *Front Psychol*. 2020;11:567367. PMID: 33013604; PMCID: PMC7506146. doi:10.3389/fpsyg.2020.567367
5. Georgieva I, Lepping P, Bozey V, et al. Prevalence, new incidence, course, and risk factors of PTSD, depression, anxiety, and panic disorder during the covid-19 pandemic in 11 Countries. *Healthcare*. 2021;9(8):664. PMID: 34284925; PMCID: PMC9227861. doi:10.3390/healthcare9060664
6. Xiong J, Lipsitz O, Nasri F, et al. Impact of COVID-19 pandemic on mental health in the general population: a systematic review. *J Affect Disord*. 2020;277:55–64. PMID: 32799105; PMCID: PMC7413844. doi:10.1016/j.jad.2020.08.001
7. Liu CH, Zhang E, Wong GTF, Hyun S, Hahm HC. Factors associated with depression, anxiety, and PTSD symptomatology during the COVID-19 pandemic: clinical implications for U.S. young adult mental health. *Psychiatry Res*. 2020;290:113172. PMID: 32512357; PMCID: PMC7263263. doi:10.1016/j.psychres.2020.1113172
8. Li W, Zhang H, Zhang C, et al. The prevalence of psychological status during the COVID-19 epidemic in China: a systemic review and meta-analysis. *Front Psychol*. 2021;12:614964. PMID: 34017278; PMCID: PMC8129549. doi:10.3389/fpsyg.2021.614964
9. Denton CP, Khanna D. Systemic sclerosis. *Lancet*. 2017;390(10103):1685–1699. PMID: 28413064. doi:10.1016/S0140-6736(17)30933-9
10. Bunevicius I, Bunevicius R, Bagdonas S, Bunevicius A. The impact of pre-existing conditions and perceived health status on mental health during the COVID-19 pandemic. *J Public Health*. 2021;fdab248. PMID: 34179996. doi:10.1093/pubmed/fdb248
11. Thombs BD, Kwakkenbos L, Henry RS, et al. Changes in mental health symptoms from pre-COVID-19 to COVID-19 among participants with systemic sclerosis from four countries: a Scleroderma Patient-centered Intervention Network (SPIN) Cohort study. *J Psychosom Res*. 2020;139:110262. PMID: 33070843; PMCID: PMC7532799. doi:10.1016/j.jpsychres.2020.110262
12. Wu Y, Kwakkenbos L, Henry RS, et al. Validation of the COVID-19 fears questionnaires for chronic medical conditions: a scleroderma patient-centered intervention network COVID-19 cohort study. *J Psychosom Res*. 2020;139:110271. PMID: 33096402; PMCID: PMC7539345. doi:10.1016/j.jpsychres.2020.110271
13. Wu Y, Kwakkenbos L, Henry RS, et al. Factors associated with fears due to COVID-19: a Scleroderma Patient-centered Intervention Network (SPIN) COVID-19 cohort study. *J Psychosom Res*. 2021;140:110314. PMID: 33271402; PMCID: PMC7685938. doi:10.1016/j.jpsychres.2020.110314
14. Kavadichanda C, Shobha V, Ghosh P, et al. Clinical and psychosocioeconomic impact of COVID-19 pandemic on patients of the Indian Progressive Systemic Sclerosis Registry (IPSSR). *Rheumatol Adv Pract*. 2021;5(2):rkab027. PMID: 34095747; PMCID: PMC8135468. doi:10.1093/rap/rkab027
15. Allanore Y, Simms R, Distler O, et al. Systemic sclerosis. *Nat Rev Dis Primers*. 2015;1(1):15002. PMID: 27189141. doi:10.1038/nrdp.2015.2
16. Rodpothong P, Auewarakul P. Viral evolution and transmission effectiveness. *World J Virol*. 2012;1(5):131–134. PMID: 24175217; PMCID: PMC3782273. doi:10.5501/wjv.v1.i5.131
17. Available from: https://covid19.infn.it/sommario/rt.html. COVIDSTAT INFN - Istituto Nazionale di Fisica Nucleare. Accessed July 5, 2022.
18. Sapra A, Bhandari P, Sharma S, Chanpura T, Lopp L. Using Generalized Anxiety Disorder-2 (GAD-2) and GAD-7 in a primary care setting. *Cureus*. 2020;12(5):e8224. PMID: 32582485; PMCID: PMC7306644. doi:10.7759/cureus.8224
19. Xu Z, Zhang D, Xu D, et al. Loneliness, depression, anxiety, and post-traumatic stress disorder among Chinese adults during COVID-19: a cross-sectional online survey. *PLoS One.* 2021;16(10):e0259012. PMID: 34673812; PMCID: PMC8530321. doi:10.1371/journal.pone.0259012

20. Orlandi M, Lepri G, Damiani A, et al. One year in review 2020: systemic sclerosis. *ClinExpRheumatol.* 2020;38(3):3–17.

21. Hyrich KL, Machado PM. Rheumatic disease and COVID-19: epidemiology and outcomes. *Nat Rev Rheumatol.* 2021;17(2):71–72. PMID: 33339986; PMCID: PMC7747184. doi:10.1038/s41584-020-00562-2

22. Ferri C, Giuggioli D, Raimondo V, et al. Covid-19 And rheumatic autoimmune systemic diseases: role of pre-existing lung involvement and ongoing treatments. *Curr Pharm Des.* 2021;27(41):4245–4252. PMID: 34477509. doi:10.2174/1381612827666210903103935

23. Avosue J, Airò P, Carlier N, Matucci-Cerinic M, Allanore Y. Severe COVID-19-associated pneumonia in 3 patients with systemic sclerosis treated with rituximab. *Ann Rheum Dis.* 2020. doi:10.1136/annrheumdis-2020-217864

24. Mariano RZ, Del Rio APT, Reis F. COVID-19 overlapping with systemic sclerosis. *Rev Soc Bras Med Trop.* 2020;53:1–6. doi:10.1590/0037-8682-0450-202014

25. Orlandi M, Lepri G, Bruni C, et al. The systemic sclerosis patient in the COVID-19 era: the challenging crossroad between immunosuppression, differential diagnosis and long-term psychological distress. *Clin Rheumatol.* 2020;39(7):2043–2047. PMID: 32514674; PMCID: PMC7276334. doi:10.1007/s10067-020-05193-2

26. Namdar P, Mojabi NA, Mojabi B. Neuropsychological and psychosocial consequences of the COVID-19 pandemic. *Neuropsychology.* 2021;1:1–10. PMID: 34400849; PMCID: PMC8357964. doi:10.1007/s11062-021-09903-7

27. Matucci-Cerinic M, Bruni C, Allanore Y, et al. Systemic sclerosis and the COVID-19 pandemic: world scleroderma foundation preliminary advice for patient management. *Ann Rheum Dis.* 2020;79(6):724–726. PMID: 32349982. doi:10.1136/annrheumdis-2020-217407

28. Hsieh YP, Yen CF, Wu CF, Wang PW. Nonattendance at scheduled appointments in outpatient clinics due to COVID-19 and related factors in Taiwan: a health belief model approach. *Int J Environ Res Public Health.* 2021;18(9):4445. PMID: 33922171; PMCID: PMC8122706. doi:10.3390/ijerph18094445

29. Thornbs BD, Kwakkenbos L, Carrier ME, et al. Protocol for a partially nested randomised controlled trial to evaluate the effectiveness of the sclerodermainpatient-centered intervention network COVID-19 home-isolation activities together (SPIN-CHAT) program to reduce anxiety among at-risk scleroderma patients. *J Psychosom Res.* 2020;135(110132). PMID: 32521338; PMCID: PMC7224675. doi:10.1016/j.jpsychores.2020.110132

30. Minniti A, Maglione W, Pignataro F, Cappadona C, Caporalì R, Del Papa N. Taking care of systemic sclerosis patients during COVID-19 pandemic: rethink the clinical activity. *Clin Rheumatol.* 2020;39(7):2063–2065. PMID: 32462423; PMCID: PMC7251048. doi:10.1007/s10067-020-05191-4

31. Pellegrino G, Mohammad Reza Beigi D, Angelelli C, et al. COVID-19 and systemic sclerosis: analysis of lifestyle changes during the SARS-CoV-2 pandemic in an Italian single-center cohort. *Clin Rheumatol.* 2021;40(4):1393–1397. PMID: 33188620; PMCID: PMC7666573. doi:10.1007/s10067-020-05504-7

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