Incidence and clinical course of COVID-19 in patients with connective tissue diseases: a descriptive observational analysis

Ennio Giulio Favalli, Elena Agape and Roberto Caporali

DOI: 10.3899/jrheum.200507
http://www.jrheum.org/content/early/2020/04/24/jrheum.200507

Incidence and clinical course of COVID-19 in patients with connective tissue diseases: a descriptive observational analysis

Ennio Giulio Favalli, MD[1], Elena Agape, MD[1], Roberto Caporali, MD[1,2]

[1] Division of Clinical Rheumatology, ASST Gaetano Pini-CTO Institute, Milan, Italy

[2] Department of Clinical Sciences and Community Health, Research Center for Adult and Pediatric Rheumatic Diseases, Università degli Studi di Milano, Milano, Italy

Key indexing terms: rheumatic diseases, COVID-19, management, coronavirus, organization

Funding: No specific funding was received from any funding bodies in the public, commercial or not-for-profit sectors to carry out the work described in this manuscript

Competing interests: Authors declare no competing interest

CORRESPONDING AUTHOR:

Ennio Giulio Favalli, MD

Division of Clinical Rheumatology, ASST Gaetano Pini-CTO Institute, Milan

Via Gaetano Pini, 9

20122 Milan - Italy

email address: enniofavalli@me.com

Phone: +39 0258296421

Mobile: +39 3289659778

FAX: +39 0258296315

Running title: COVID-19 and CTD

Ethics board approval: the current analysis is part of a project to collect observational data from rheumatological patients followed at the ASST Gaetano Pini-CTO. The project was approved by the Ethics Committee of the Geatano PIni Institute with approval number 141/2010. All included patients have signed an informed consent to data collection.

Dear Editor,

The outbreak of COVID-19 in December 2019 in China has very quickly become a global health emergency with almost two million of infected patients worldwide.[1] Along with the spread of the pandemic, there has been a growing concern about the management of fragile rheumatic patients, for whom there is still very little data available. In particular, subjects affected by connective tissue diseases (CTD) are known to have an increased infectious risk compared to the healthy population due to a general impairment of the immune system intrinsic to the autoimmune disease itself, the iatrogenic effect linked to the use of immunosuppressive drugs, and the high number of comorbidities that often complicate the clinical picture.[2,3] On the other hand, the progressive increase in the knowledge about the pathogenesis of the infection is paving the way for the use of certain drugs used in rheumatology to treat also COVID-19.[4]

As rheumatologists operating in one of the major epicenters of the epidemic (Milan, Italy), we conducted a survey to investigate the impact of COVID-19 in CTD patients followed at the Research Center for Adult and Pediatric Rheumatic Diseases of the ASST Gaetano Pini-CTO. The survey included demographics, clinical information on the rheumatic disease, the incidence of COVID-19 confirmed by nasopharyngeal swab, the frequency of respiratory symptoms of suspected viral infections, and how the outbreak affected the patient's behavior and the course of CTD. In the period between 25th February and 25th March 2020 the survey was administered face-to-face to patients who were assessed in the outpatient CTD clinic of our center or by telephone to those who missed an appointment scheduled for the same period.

The overall study population included 123 adult patients (110 females) with systemic lupus erythematosus (n=61), systemic sclerosis (SSc, n=43), undifferentiated connective tissue disease (n=9), or Sjoegren syndrome (n=10). The mean age (± standard deviation) was 49.3 (±14.4) years and the mean disease duration 10.2 (±8.7) years. About 60% of patients were treated with

conventional synthetic disease-modifying drugs (31 hydroxychloroquine, 22 mycophenolate, 11 methotrexate, 8 azathioprine, and 1 cyclosporine), 25 patients were receiving biological agents (18 belimumab, 5 rituximab, and 2 tocilizumab), and 64.2% were also taking corticosteroids (mean dose 5.3 mg daily). The only recorded patient with COVID-19 positive swab was a 32-year-old woman with SSc and pulmonary involvement treated with hydroxychloroquine and rituximab. She developed a severe pattern of COVID-19 interstitial pneumonia requiring hospitalization in intensive care, where, despite intubation and an attempt with tocilizumab, the patient died. In the same period of observation, the incidence of COVID-19 positivity in our region (Lombardy) was consistent with that we observed in our cohort (0.62 versus 0.81%, respectively).(5) A further 14 patients reported respiratory symptoms consistent with a viral infection but they did not have access to the swab. In these patients we observed a mild clinical course of infectious disease with a rapid resolution of symptoms. They did not require the discontinuation of ongoing rheumatological therapy and did not experience a CTD relapse. Among the latter group, 44.4% were on hydroxychloroquine therapy versus 24.2% of patients who did not develop respiratory symptoms. These data were not consistent with the proposed protective effect of the drug against COVID-19 infection.(6) However, it is important to point out that to date preliminary data have demonstrated the efficacy of antimalarials in the treatment of COVID-19,(7) while at the moment no evidence is yet available about their potential prophylactic effect in the prevention of contagion.(8)

Overall, of 123 patients, only 5 have discontinued their current rheumatological therapy (two for fear of contagion and three upon indication of a non-rheumatologist consultant) and 115 have maintained stable disease activity without experiencing flare-ups.

The vast majority of the study population (84.1%) reported to have adopted specific precautions to prevent the contagion such as social distancing (55.2%), use of masks (58.1%), non-working or home-working (60.1% of workers) since the outbreak began. This positive propensity is likely to

depend on the very fact of being carriers of a disease with increased infection risk and should certainly be taken into account when assessing the overall incidence of COVID-19 in the cohort of CTD patients compared with the general population.

In conclusion, these preliminary data seem to suggest that our approach of encouraging CTD patients to maintain ongoing rheumatological therapy and adhere strictly to the norms to prevent infection has avoided rheumatic disease relapse without increasing the risk of COVID-19. Waiting for our results to be confirmed on larger samples, this information can certainly be useful to all rheumatologists worldwide facing the pandemic.

References

1. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395:497-506.

2. Goldblatt F, Chambers S, Rahman A, Isenberg D. Serious infections in British patients with systemic lupus erythematosus: hospitalisations and mortality. Lupus 2009;18:682-9.

3. Alarcón GS. Infections in Systemic Connective Tissue Diseases: Systemic Lupus Erythematosus, Scleroderma, and Polymyositis/Dermatomyositis. Infect Dis Clin N Am 2006;20:849-75.

4. Favalli EG, Ingegnoli F, Lucia OD, Cincinelli G, Cimaz R, Caporali R. COVID-19 infection and rheumatoid arthritis: Faraway, so close! Autoimmun Rev 2020;102523.

5. https://www.regione.lombardia.it/wps/portal/istituzionale/. Accessed 10th April 2020

6. Touret F, Lamballerie X de. Of chloroquine and COVID-19. Antivir Res 2020;177:104762.

7. Gao J, Tian Z, Yang X. Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. Biosci Trends 2020;2020.01047.

8. Spinelli FR, Ceccarelli F, Franco MD, Conti F. To consider or not antimalarials as a prophylactic intervention in the SARS-CoV-2 (Covid-19) pandemic. Ann Rheum Dis 2020;annrheumdis-2020-217367.