

## Incidence and Clinical Course of COVID-19 in Patients with Connective Tissue Diseases: A Descriptive Observational Analysis

To the Editor:

The outbreak of COVID-19 in December 2019 in China has very quickly become a global health emergency, with almost 2 million infected patients worldwide<sup>1</sup>. Along with the spread of the pandemic, there has been growing concern about the management of fragile patients with rheumatic conditions. There are still very few data available on this aspect. In particular, subjects affected by connective tissue diseases (CTD) are known to have an increased infectious risk compared to the healthy population because of 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<sup>2,3</sup>. 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 common in rheumatology to also treat COVID-19<sup>4</sup>.

As rheumatologists operating in one of the major epicenters of the pandemic (Milan, Italy), we conducted a survey to investigate the effect of COVID-19 on patients with CTD 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 February 25 and March 25, 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 CTD (n = 9), or Sjögren syndrome (n = 10). The mean age ( $\pm$  SD) 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 (HCQ), 22 mycophenolate, 11 methotrexate, 8 azathioprine, and 1 cyclosporine], 25 patients were receiving biological agents [18 belimumab, 5 rituximab (RTX), and 2 tocilizumab (TCZ)], and 64.2% were also taking corticosteroids (mean dose 5.3 mg daily). The only recorded patient with a COVID-19 positive swab was a 32-year-old woman with SSc and pulmonary involvement treated with HCQ and RTX. She developed a severe pattern of COVID-19 interstitial pneumonia requiring hospitalization in intensive care, where, despite intubation and treatment with TCZ, the patient died. In the same period of observation, the incidence of COVID-19 positivity in our region (Lombardy) was consistent with what we observed in our cohort (0.62 vs 0.81%, respectively)<sup>5</sup>. 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 taking HCQ 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<sup>6</sup>. However, it is important to point out that to date, preliminary data have demonstrated the efficacy of antimalarials in the treatment of COVID-19<sup>7</sup>, while at the moment no evidence is yet available about their potential prophylactic effect in the prevention of contagion<sup>8</sup>.

Overall, of 123 patients, only 5 have discontinued their current rheumatological therapy (2 for fear of contagion and 3 upon indication of a

non-rheumatologist consultant) and 115 have maintained stable disease activity without experiencing flares.

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%), and 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 patients with CTD compared with the general population.

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

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First Release May 15 2020; *J Rheumatol* 2020;47:8;  
doi:10.3899/jrheum.200507