What is the true incidence of COVID-19 in patients with rheumatic diseases?

After its emergence in December 2019 in Wuhan, China, the COVID-19 outbreak has now one of its main epicentres in Lombardy (Italy), with more than 50 000 confirmed cases and 9000 deaths. As rheumatologists operating in the same pandemic area (Milan), we read with great interest the letter published by Monti and colleagues[1] about the description of COVID-19 among patients with rheumatic diseases treated with biologic disease-modifying drugs (bDMARDs). Certainly, the quantification of the risk of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection and its evolution towards severe interstitial pneumonia leading to acute respiratory distress syndrome (ARDS) is crucial in such a population of fragile patients. To fill this gap, in the same period of health emergency between 25 February and 2 April 2020, we collected data from patients treated with bDMARDs afferent to the Research Center for Adult and Pediatric Rheumatic Diseases of the ASST Gaetano Pini-CTO in Milan, by using a survey investigating the impact of COVID-19. The survey was administered face-to-face to all patients who underwent an outpatient visit or by telephone in those who missed a scheduled visit during the period under review. The final study population included 530 patients (372 women, mean age 50.1 years), affected by rheumatoid arthritis (49.6%), spondyloarthritis/psoriatic arthritis (SpA/PsA, 36.8%), connective tissue diseases (3.3%), sarcoidosis (one patient only) or juvenile idiopathic arthritis (10.3%). Most patients were treated with antitumour necrosis factor agents (53.7%), 39.3% with other bDMARDs (mainly interleukin (IL)-6 blockers (11.5%) and abatacept (10%)) and 7% with JAK inhibitors.

We recorded only three patients with mild COVID-19 confirmed by positive nasopharyngeal swab. Of these, only a 56-year-old man with sarcoidosis treated with adalimumab required hospitalisation with oxygen therapy, whereas a 40-year-old man with axial SpA receiving infliximab and a 68-year-old woman with PsA treated with secukinumab were both managed at home without any respiratory complication. None of the 10 patients who reported contact with established cases of COVID-19 developed symptoms of infection. Along with the results reported by Monti and colleagues,[1] our findings could provide further reassurance about the incidence of life-threatening COVID-19 in patients with rheumatic diseases receiving bDMARDs. Pathogenetically, ARDS complicating the more severe cases of SARS-CoV-2 pneumonia is associated with a massive but late immune response resulting in a cytokine release syndrome (CRS) orchestrated mainly by IL-6, which is currently the only considered target to treat most serious COVID-19.[2] The role of drugs targeted on alternative pathways in the management of CRS and consequently in the potential prevention of ARDS in patients with rheumatic diseases still needs to be clarified.[3]

However, it should also be noted that about 90% of our patients declared that they had adopted a preventive strategy against COVID-19 based on social distancing and use of personal protective equipment such as gloves and masks since the beginning of the epidemic. This stringent approach, which is likely to arise from patients' awareness of an additional risk due to rheumatic disease may introduce a bias that would lead to underestimating the real incidence of COVID-19. On the other hand, severe cases of COVID-19 are only the tip of the iceberg, as the vast majority of cases are asymptomatic or oligosymptomatic.[4] For this reason, in our survey we extended the evaluation to the reporting of even mild symptoms of viral infection, which have been recorded in 81 (15.2%) patients, suggesting that the real overall incidence rate of COVID-19 in our population might be significantly higher.

Finally, in comparison with Monti *et al*'s cohort,[1] ours also included a portion of paediatric patients (n=54), in which no cases of COVID-19 positivity were reported. However, we observed a frequency of patients carrying mild symptoms of potential infection consistent with the adult subgroup (14.8%) as possible confirmation of the already described tendency of children to get a less aggressive subset of COVID-19.[5]

Ennio Giulio Favalli ,[1] **Francesca Ingegnoli** ,[1,2] **Rolando Cimaz**,[2,3] **Roberto Caporali**[1,2]

[1]Division of Clinical Rheumatology, Gaetano Pini-CTO, Milano, Lombardia, Italy
[2]Department of Clinical Sciences and Community Health, Research Center for Adult and Pediatric Rheumatic Diseases, Università degli Studi di Milano, Milano, Lombardia, Italy
[3]Division of Pediatric Rheumatology, Gaetano Pini-CTO, Milano, Lombardia, Italy

Correspondence to Dr Ennio Giulio Favalli, Division of Clinical Rheumatology, Gaetano Pini-CTO, Milano 20122, Italy; ennio.favalli@gmail.com

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ORCID iDs
Ennio Giulio Favalli http://orcid.org/0000-0003-1471-6467
Francesca Ingegnoli http://orcid.org/0000-0002-6727-1273

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