Letter to the Editor of *Journal of Crohns and Colitis*

IMPACT OF ANTI-TNFα ANTIBODIES ON THE RISK OF COVID-19 AND ITS SEVERITY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES

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Authors Contributions
A.T. and A.P.: Study design and data analysis;
A.T. and A.P.: Patient recruitment, data collection and writing up of the first draft of the paper

Funding
None.

Competing Interest
The authors declare any conflict of interest.

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Dear Editor,

Giovanni Monteleone e Sandro Ardizzone analyzed recently which are the risk of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus causing coronavirus disease 2019 (COVID-19), in Inflammatory Bowel Diseases (IBD) (1). Through an elegant analysis, they claimed that overall IBD population could not have an increased risk of developing SARS-CoV-2 infection. Of course, we have two main variables.

The first is that the older people could be equally at higher risk, at least in Italy. Mazza et al. recently reported a case of a 80-year-old female suffering from ulcerative colitis (UC) who died after an hospital-acquired SARS-CoV-2 infection (3). In those people, surveillance for COVID-19 should be mandatory and close due to the higher risk.

The second variable is the risk COVID-19 in patients under immunosuppressive therapies. As we know, a lot of our patients are under treatment with biologics in order to obtain and maintain remission in IBD not responsive to the standard treatments. In particular, most of them are under treatment with anti-Tumour Necrosis Factor (TNF) α antibodies. We know that SARS-CoV-2 comes into cells after binding to its functional receptor, angiotensin-converting enzyme 2 (ACE2) and causes enhanced TNFα-production and TNFα-converting enzyme (TACE)-dependent shedding of the ectodomain of ACE2, that facilitates viral entry (3). Since this process seems to be strictly coupled to TNFα production, we can postulated that the use of anti-TNFα antibodies may be effective used in IBD patients without a significant risk of IBD recurrence. This hypothesis is advised by an our recent case, in which a 30-year-old male suffering from ileal Crohn's disease (CD) in remission under treatment with adalimumab was infected by SARS-CoV-2. He developed only a mild pneumonia, with fast resolution of symptoms and fast hospital discharging (figure 1) (4). In particular, no sign of CD recurrence was recorded during the COVID-19 hospital stay (no diarrhea was recorded and fecal calprotectin was normal), and also the pulmonary disease recovered very quickly (within 5 days). The question is: do the clinical picture of the pneumonia in CD recovered *despite* adalimumab or do the clinical picture of the pneumonia in CD recovered *thanks to* adalimumab? Of course, the young age of our patient could explain this favorable course. However, an intriguing hypothesis is that adalimumab could inhibit the basic mechanisms of COVID-19 (3), and could be potentially useful in managing/preventing COVID-driven pneumonia. As a result, a study evaluating adalimumab injection in COVID-19 patients with severe pneumonia has recently been registered (5).

Thus, the risk of COVID-19 in IBD patients should be evaluated according to age and comorbidities. Moreover, adalimumab could be useful not only in maintain IBD remission during COVID-19, but also potentially useful in managing/preventing COVID-driven pneumonia.

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Figure legend

Figure1. Chest X-ray at the fifth day of hospital admission. No significant sign of pulmonary infiltrate can be seen.

Figure 1