Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Correspondence

Are there any association between COVID-19 severity and immunosuppressive therapy?

Dear Editor,

The novel coronavirus, formerly called SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), is a health threating disease that has so far spread from China to all around the world [1–3]. So far, no study has been performed to support the benefits of immunosuppressive drugs in patients with Coronavirus disease 2019 (COVID-19) decisively. In current study, we investigate whether receiving these drugs can either mitigate or stop the severity of symptoms in confirmed COVID-19 patients. Therefore, we retrospectively collected and analyzed detailed clinical data from both inflammatory bowel disease (IBD) and autoimmune hepatitis (AIH) patients with the history of receiving immunosuppressive drugs for treating gastrointestinal (GI) disorders. After the outbreak of COVID-19 in Iran, we evaluated these patients in our gastroenterology clinic in Shahid Beheshti Hospital, Qom province. The total of 200 patients (aged 30–65 years, with a BMI of 17.5–22 Kg/m^2) enrolled in this study, had received Azathioprine 50–150 mg or one of anti-TNF drugs (Infliximab 300 − 400 mg every 8 weeks or Adalimumab 40 mg every two weeks) as mono-therapy or co-therapy with Prednisolone 10 mg (for 150 IBD patients) and Azathioprine 50–150 mg as mono-therapy or co-therapy with Prednisolone 10 mg (for AIH patients) for 1–2 years (Table 1). The majority of patients reported that they resided at the high risk areas of the city. The follow-up plan was to assess suspected patients who presented COVID-19 symptoms (30 cases with cough and mild fever) through laboratory real-time reverse-transcriptase polymerase chain reaction (rRT-PCR) tests in order to confirm their infection with SARS-CoV-2. For more evaluation, patients that were positive in (rRT-PCR) test (11 cases), chest CT scan were performed (Table 1). In comparison to normal population without the immunosuppressive drugs use in their medication history and without any significant demographic characterizations with infected patients, IBD and AIH patients, exhibited low potential for infection, and also surprisingly laboratory-confirmed COVID-19 patients presented mild symptoms and showed minimal lung involvement in chest CT scan image (more than 90 % of the total 11 COVID-19 patients, showed ground glass opacity). No mortality occurred in this group and all symptoms subsided faster than in immunocompetent COVID-19 patients. Additionally, radiologic findings disappeared sooner in immunocompromised patients compared to immunocompetent cases. The interesting finding of our study is that there was a significant difference between patients who had mono-therapy and co-therapy in term of COVID-19 prevalence and/or severity. In both groups of IBD and AIH patients with mild fever and cough symptoms, five patients received co-therapy and the rest received mono-therapy (16 % *v.s* 83 %). Also, among laboratory-confirmed COVID-19 patients, three patients received co-therapy and the rest received mono-therapy (27 % *v.s* 72 %).

This study further verified the disease responses to immunosuppressive drugs (especially when used as a combination therapy) in patients confirmed to have COVID pneumonia. There is no proven or approved treatment for COVID-19, the administration of immunosuppressive drugs after taking consent from the patient (if possible) or his/her family, may be final decision to reduce the respiratory symptoms of COVID pneumonia. This approach (treatment using immunosuppressant drugs) was applied in 3 critical patients who were under the treatment with Prednisolone 10 mg & Infliximab 300 − 400 mg in Shahid Beheshti Hospital. Two of them exhibited better condition and also respiratory tract symptoms were subsided with acceptable saturation (from 66 % before treatment to 84 % after treatment). Also, not only CRP level get closer to its normal level, but also in continual chest CT following, we noticed that radiologic findings disappeared. One case of death was related to a patient that was older than the other two patients.

Previously Xu X and *et.al.*, reported that tocilizumab (IL-6 receptor blocker used for both rheumatoid arthritis and cytokine release syndrome) improved CT scan abnormalities and oxygen saturation, and normalized CRP levels and lymphocytes count in most of the patients [4]. In this regard, phase II study has been approved by Italian Regulatory Drug Agency (AIFA). In the end, we concluded that there is relation between corona virus severity symptoms and immunosuppressive therapy. It seems that symptoms of COVID infection are partly associated with the inflammatory cascade and hyperinflammatory syndrome, which may be the leading cause of mortality [5]. Therefore, our findings further validated the immunosuppressive drug benefits, especially IL-6 receptor antagonist for the emergency use in critical infected COVID-19 patients.

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Table 1
Characteristics of IBD and AIH patients according to outcome and related treatment protocols. The majority of patients reported that they resided at the high risk areas of the city.

Total (N = 200) Survivor (N = 200) Non-Survivor *(N = 0)* Variable	IBD (N = 150) n (%)	AIH (N = 50) n (%)
Basic Characteristics		
Age, Mean ± SD (year)	48.4 ± 11	42.5 ± 6.5
[a]BMI; Mean ± SD	19.7 ± 1.6	20.1 ± 0.7
Clinical presentation		
Cough with mild fever (≤38°c)	21 (14)	9 (18)
Sore Throat	9 (6)	4 (8)
rRT-PCR results		
Positive	8 (5.3)	3 (6)
CT scan finding		
Ground Glass opacity	8 (72.7)	2 (18.1)
Patchy infiltration	1 (9.1)	0
Medication history during 1 − 2 years		
Only AZA (50–150 mg)	60 (40)	2(4)
AZA (50–150 mg) & Prednisolone (10 mg)	30 (20)	48 (96)
AZA (50–150 mg) & Anti-TNF[b]	45 (30)	No
Only Anti-TNF	15 (10)	No

Abbreviation: IBD: Inflammatory bowel disease; **AIH**: Autoimmune hepatitis patients; **AZA** Azathioprine.

[a] BMI (body mass index) was calculated by using the square of the height (kg/m2) measurement.

[b] Infliximab (300 − 400 mg every 8 weeks) or Adalimumab (40 mg every two weeks).

Declaration of Competing Interest

The authors declare no conflicts of interest.

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