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Letter to the Editor

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# Are Patients With Autoimmune Disease at Greater Risk of Developing Severe COVID-19?

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## To the Editor

The novel coronavirus disease 2019 (COVID-19) outbreak caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection was declared a pandemic in early 2020, affecting mostly middle-aged and older population irrespectively of their medical background. Individuals with autoimmune inflammatory diseases are at greatly morbidity and mortality risk due to infectious diseases, so it was hypothesized that they would be at increased risk of severe complications from SARS-CoV-2 infection as well. These individuals are considered to be at high risk for developing serious infections due to their underlying conditions and the use of targeted immune-modulating drugs such as biologic agents. In particular, data on COVID-19 patients with immune-mediated inflammatory disease are scarce [1-3].

We report a retrospective case series referring to patients who were diagnosed with COVID-19 infection and had known autoimmune inflammatory disease. All infected patients who visited the Emergency Department of University Hospital of Patras, Western Greece, during the first month period since the recording of the first case, were enrolled in the study. The study period was from March 3, 2020 until April 3, 2020.We recorded the demographic characteristics, clinical findings, laboratory parameters and outcome of patients who had immune-mediated inflammatory disease with symptomatic COVID-19 infection and compared them with the age and gender matched group of patients who visited our hospital due to symptomatic COVID-19 infection and did not suffer from any autoimmune disease. All the above parameters are shown in Table 1. This study was conducted in compliance with the ethical standards of the responsible institution on human subjects as well as with the Helsinki Declaration.

Ten patients with autoimmune inflammatory disease presented to the Emergency Department with clinical symptoms of SARS-CoV-2 infection. Seven of them, due to disease severity were hospitalized (group 1); three patients had a diagnosis of multiple sclerosis (MS), two had rheumatoid arthritis (RA), four with Hashimoto thyroiditis and one with psoriatic arthritis. Of these patients, four were receiving immune-modulatory therapies (interferon α, anti-tumor necrosis factor (TNF)-α, anti-interleukin 6 (IL-6)), and one was receiving hydroxychloroquine. All patients with Hashimoto thyroiditis were treated with levothyroxine. At the same period, an age and gender matched group of 14 patients without any known history of immune disease were hospitalized with SARS-CoV-2 infection (group 2). No significant differences were identified on clinical examination of the two group patients. All patients were alert and orientated, were cardiovascular stable and expressed a similar clinical pattern from the respiratory system with mild dyspnea (oxygen saturation ($SaO_2$) 92-95% in room air), fever (37.8 - 38.6 °C), non-productive cough and chest pain.

Most of the hospitalized patients with autoimmune inflammatory disease (6/7) were treated with supplemental oxygen, either with simple nasal cannula or Venturi face mask, and only one received non-invasive ventilation for acute respiratory distress syndrome. Parameters from peripheral blood samples including lymphocyte absolute count (ALC), fibrinogen, D-dimers, lactate dehydrogenase (LDH) and ferritin levels were measured. We also calculated the duration of hospitalization and the mortality rate in both groups.

Our study did not reveal any statistically significant longer hospitalization for the group of patients with immune-mediated inflammatory disease ($P = 0.771$). In regards to the laboratory parameters that have been suggested as prognostic factors for COVID-19 infection (ferritin, D-dimers, lymphocytes, fibrinogen and LDH), we did not find statistically significant differences between the two groups ($P = 0.800$, $P = 0.667$, $P = 0.445$, $P = 0.114$ and $P = 0.945$, respectively). Furthermore, the presence of lung infiltrates as well as the need for oxygen treatment was not significantly different in the comparison of the two groups ($P = 0.552$ and $P = 0.626$, respectively). All of the patients with immune-mediated inflammatory disease who were hospitalized had a good outcome and were discharged. The mean duration of hospitalization was not longer for patients receiving immunomodulatory therapies compared to those who were not ($7.14 \pm 2.6$ vs $8 \pm 3.1$ days).

Patients with respiratory distress caused by SARS-CoV-2 display hyper-inflammatory responses with features of either

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**Table 1.** Comparison of Outcome and Laboratory Values on Admission Between COVID-19 Patients With Comorbid Autoimmune Disease and COVID-19 Patients Without Autoimmune Disease in a Single Center in Western Greece

| | Inpatients with comorbid autoimmune disease (n = 7) | Inpatients without comorbid autoimmune disease (n = 14) | Normal range of parameters compared | P value |
|---|---|---|---|---|
| Sex (male/female), % | 0/100 | 14.3/85.7 | - | 0.481 |
| Age, years (mean ± SD) | 57 ± 21 | 64.6 ± 6.8 | - | - |
| Immune-modulatory therapies | Yes: interferon α, anti-TNF-α, anti-IL-6 | No | - | - |
| Duration of hospitalization, days (mean ± SD) | 7.14 ± 2.6 | 8 ± 3.1 | - | 0.771 |
| Serum ferritin (mean ± SD) | 442 ± 200 | 319.7 ± 88 | 12 - 300 mg/dL (male); 12 - 150 mg/dL (female) | 0.800 |
| Plasma D-dimers (mean ± SD) | 762.5 ± 104.2 | 1,090 ± 1,131.4 | < 500 µg/dL | 0.667 |
| Lactate dehydrogenase (mean ± SD) | 307.5 ± 92.3 | 277.7 ± 55.07 | 120 - 220 U/L | 0.945 |
| Plasma fibrinogen (mean ± SD) | 424.5 ± 104 | 624 ± 135.6 | 200 - 400 mg/dL | 0.114 |
| Lymphocyte count (mean ± SD) | 1,806.5 ± 897.6 | 1,242.1 ± 355.8 | 20-50% of WBC, k/µL | 0.445 |
| Mortality (n) | 0 | 0 | - | |

COVID-19: coronavirus disease 2019; SD: standard deviation; WBC: white blood cell; TNF: tumor necrosis factor; IL: interleukin.

immune dysregulation or macrophage activation syndrome, both of which are characterized by an extensive release of pro-inflammatory cytokines[4, 5]. Although this is a case series with a small sample size, our data reveal an almost similar clinical, laboratory and radiological pattern between COVID-19 patients with a known underlying chronic inflammatory immune disease and a group of patients without such a disorder. These findings may suggest that the overall course of the COVID-19 disease is not far worse, as was initially assumed, in patients with a known autoimmune inflammatory disease. Taking into account that progression to acute respiratory distress syndrome (ARDS) is associated with the up-regulation of pro-inflammatory cytokines and chemokines, a condition known as cytokine release syndrome (CRS), a question is raised whether patients with autoimmune diseases, especially these receiving immune-modulatory medication have a worse outcome or not.

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## Conflict of Interest

The authors declare no conflict of interest.

## Informed Consent

Not applicable.

## Author Contributions

ML, OK and AK collected the data; ML and NZ wrote the paper; DV corrected the paper.

## Data Availability

The authors declare that data supporting the findings of this study are available within the article.

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