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**BRIEF REPORT**

# Autoimmune and Chronic Inflammatory Disease Patients with COVID-19

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**Objective.** There are limited data on the impact of coronavirus disease 2019 (COVID-19) on hospitalized patients with autoimmune and chronic inflammatory disease (AICID) compared with patients who do not have AICID. We sought to evaluate whether patients with AICID who have confirmed COVID-19 presenting to the hospital are at higher risk of adverse outcomes compared with those patients without AICID who are infected with COVID-19 and whether immunosuppressive medications impact this risk.

**Methods.** We performed a multicenter retrospective cohort study with patients presenting to five hospitals in a large academic health system with polymerase chain reaction–confirmed COVID-19 infection. We evaluated the impact of having an AICID and class of immunosuppressive medication being used to treat patients with AICID (biologics, nonbiologic immunosuppressives, or systemic corticosteroids) on the risk of developing severe COVID-19 defined as requiring mechanical ventilation (MV) and/or death.

**Results.** A total of 6792 patients with confirmed COVID-19 were included in the study, with 159 (2.3%) having at least one AICID. On multivariable analysis, AICIDs were not significantly associated with severe COVID-19 (adjusted odds ratio [aOR] 1.3, 95% confidence interval [CI]: 0.9-1.8). Among patients with AICID, use of biologics or nonbiologic immunosuppressives did not increase the risk of severe COVID-19. In contrast, systemic corticosteroid use was significantly associated with an increased risk of severe COVID-19 (aOR 6.8, 95% CI: 2.5-18.4).

**Conclusion.** Patients with AICID are not at increased risk of severe COVID-19 with the exception of those on corticosteroids. These data suggest that patients with AICID should continue on biologic and nonbiologic immunosuppression but limit steroids during the COVID-19 pandemic.

## INTRODUCTION

Coronavirus disease 2019 (COVID-19) has rapidly become an international pandemic that can result in severe disease requiring hospitalization. COVID-19 fatality rates among hospitalized patients are significant, ranging from 10% to 24.5% (1,2). The vast majority of patients with COVID-19 who require hospitalization have at least one comorbidity, and nearly 80% of patients who end up in the intensive care unit have an underlying chronic condition (3). Risk factors for severe COVID-19 have included age, high fever, cardiovascular disease, diabetes, obesity, chronic obstructive pulmonary disease (COPD), and chronic kidney disease (CKD) (4–7).

Autoimmune and chronic inflammatory diseases (AICIDs), prevalent in 5% to 7% of developed countries, are associated with an increased risk of infection related to immunosuppression and disease activity (8,9). However, immunosuppressive medications frequently used by patients with AICID may decrease

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the risk of adverse COVID-19 outcomes by limiting the cytokine storm characteristic of severe COVID-19 (10). Current data on the impact of COVID-19 on patients with AICID are primarily case series or registry based, and there are limited data on hospitalized patients and AICID patient outcomes compared with those of patients without AICIDs (11–14). We therefore aimed to evaluate whether patients with AICID who had confirmed COVID-19 presenting to the hospital are at higher risk of adverse outcomes compared with patients without AICIDs who are infected with COVID-19.

## MATERIALS AND METHODS

We performed a retrospective, multicenter cohort study using data from the Mount Sinai Health System, an academic health network in New York City. Data were extracted from the electronic health record (EHR) system of five hospitals (Mount Sinai Hospital, Mount Sinai Brooklyn, Mount Sinai Queens, Mount Sinai Morningside, and Mount Sinai West). We retrieved data for all patients who were evaluated in the emergency department and/or hospitalized with a positive nasopharyngeal swab polymerase chain reaction (PCR) test for COVID-19 between March 1, 2020, and May 12, 2020.

Patient data extracted from the EHR included demographics, comorbidities, and hospitalization outcomes, such as mechanical ventilation (MV) and death. Obesity was defined as body mass index (BMI) greater than 30 kg/m$^2$. Smoking was defined as a record of past or present smoking. We defined AICID as any of the following autoimmune and inflammatory diseases: ankylosing spondylitis, autoimmune hepatitis, autoimmune pancreatitis, Bechet disease, inflammatory bowel disease (IBD), psoriasis/psoriatic arthritis, rheumatoid arthritis (RA), scleroderma, Sjögren

**Table 1.** Characteristics of study cohort comparing patients with and without AICIDs

| Characteristic | Non-AICID patients (n = 6633) | AICID patients (n = 159) | *p* value |
|---|---|---|---|
| *Demographics* | | | |
| Age in years, median (IQR) | 62.0 (49.0-74.0) | 63.0 (51.0-73.0) | 0.775 |
| Male, n (%) | 3706 (55.9) | 54 (34.0) | <0.001 |
| Race | | | |
| African American, n (%) | 1723 (26.0) | 30 (18.9) | 0.053 |
| White, n (%) | 1553 (23.4) | 54 (34.0) | 0.003 |
| *Comorbidities* | | | |
| HTN, n (%) | 3708 (55.9) | 93 (58.5) | 0.569 |
| CD, n (%) | 1086 (16.4) | 26 (16.4) | 0.919 |
| DM, n (%) | 2499 (37.7) | 50 (31.4) | 0.128 |
| CHF, n (%) | 695 (10.5) | 21 (13.2) | 0.329 |
| CKD, n (%) | 967 (14.6) | 26 (16.4) | 0.609 |
| COPD, n (%) | 473 (7.1) | 14 (8.8) | 0.514 |
| Asthma, n (%) | 823 (12.4) | 30 (18.9) | 0.021 |
| History of malignancy, n (%) | 775 (11.7) | 28 (17.6) | 0.031 |
| Smoking, n (%) | 1332 (20.1) | 44 (27.7) | 0.024 |
| Obesity, n (%) | 1802 (27.2) | 55 (34.6) | 0.047 |
| BMI, median (IQR) | 27.5 (24.0-32.5) | 27.1 (23.2-32.8) | 0.306 |
| *Outcomes* | | | |
| Admitted to hospital, n (%) | 4517 (68.1) | 134 (84.3) | <0.001 |
| Mortality, n (%) | 1445 (21.8) | 36 (22.6) | 0.872 |
| Intubation and MV, n (%) | 1018 (15.3) | 31 (19.5) | 0.187 |
| Mortality/Intubation and MV, n (%) | 1711 (25.8) | 45 (28.3) | 0.534 |
| *AICID*[a] | | | |
| Autoimmune hepatitis, n (%) | n/a | 5 (3.1) | |
| Ankylosing spondylitis, n (%) | n/a | 4 (2.5) | |
| Sjögren syndrome, n (%) | n/a | 9 (5.7) | |
| Scleroderma, n (%) | n/a | 4 (2.5) | |
| Psoriasis/psoriatic arthritis, n (%) | n/a | 22 (13.8) | |
| Systemic lupus erythematosus, n (%) | n/a | 29 (18.2) | |
| Rheumatoid arthritis, n (%) | n/a | 45 (28.3) | |
| Inflammatory bowel disease, n (%) | n/a | 41 (25.8) | |
| Systemic vasculitis, n (%) | n/a | 6 (3.8) | |
| Myositis, n (%) | n/a | 2 (1.3) | |

Abbreviations: AICID, autoimmune and chronic inflammatory disease; BMI, body mass index; CAD, coronary artery disease; CHF, congestive heart failure; CKD chronic kidney disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; HTN, hypertension; IQR, interquartile range; MV, mechanical ventilation; n/a, not applicable.

[a] Percentages and n from each subcategory may not add up to the exact number of total reported cases because of nonmutually exclusive variables.

**Table 2.** Multivariable model for severe COVID-19 among entire study cohort

| Variable | aOR (95% CI)[a] | *p* value |
|---|---|---|
| Age > 70 years | 3.1 (2.7-3.5) | <0.001 |
| Male sex | 1.3 (1.2-1.5) | <0.001 |
| Race, White | 1.1 (0.9-1.2) | 0.376 |
| CVD | 1.7 (1.5-2.0) | <0.001 |
| DM | 1.6 (1.4-1.8) | <0.001 |
| CKD | 2.0 (1.7-2.4) | <0.001 |
| COPD | 1.4 (1.2-1.9) | <0.001 |
| Obesity | 1.4 (1.2-1.6) | <0.001 |
| AICID | 1.3 (0.9-1.8) | 0.235 |

Abbreviations: AICID, autoimmune and chronic inflammatory disease; aOR, adjusted odds ratio; CI, confidence interval; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease (composite of coronary artery disease, congestive heart failure and hypertension); DM, diabetes mellitus.
[a] The model was adjusted for age over 70, male sex, White race, known comorbidities associated with severe COVID-19 outcome, and AICID status. CVD was defined as either coronary artery disease or congestive heart failure.

syndrome, systemic lupus erythematosus (SLE), systemic vasculitis, or myositis. AICID diagnoses were confirmed through review of outpatient and inpatient physician notes. Patients required prior visits at relevant subspecialty outpatient clinics. Home immunosuppressive treatments at time of presentation among patients with AICID were determined through review of medication reconciliation record. Home immunosuppressive treatments were categorized as biologics, nonbiologic immunosuppressives, or systemic corticosteroids (Supplementary Table 1). These categorizations were nonmutually exclusive. The Institutional Review Board of Mount Sinai approved this study.

Our primary exposures of interest were history of AICID for the entire study population and immunosuppressive treatments among patients with AICID. Our primary outcome was severe COVID-19 defined as death or need for MV. Categorical variables were compared using $\chi^2$ test. Continuous variables were compared using one-way analysis of variance. We used multivariable logistic regression to assess the association of AICIDs with severe COVID-19, adjusting for previously reported risk factors including age greater than 70, sex, race (White vs. non-White), cardiovascular disease, diabetes mellitus, CKD, COPD, and obesity. Cutoff age value was determined using Youden index. A second multivariable logistic regression model was applied only to patients with AICIDs to evaluate the association of medication class with severe COVID-19, adjusting for risk factors noted above. A correlation matrix was constructed to assess possible collinearity between covariates in the model. All correlations were below $r = 0.5$. Adjusted odds ratios (aOR) with 95% confidence intervals (CI) are reported. All analyses were performed with Python (version 3.6.5, 64 bits). Two-sided values of $p < 0.05$ were considered statistically significant.

## RESULTS

A total of 6792 patients with PCR-confirmed COVID-19 were included. Of the total, 159 (2.3%) had at least one AICID (Table 1). The most frequent AICIDs in our cohort were RA, IBD, and SLE. Patients with AICIDs were more likely to be female, White, have obesity, have a history of asthma, and have prior or current malignancy. Patients with AICIDs were also more likely to be admitted to the hospital compared with those without an AICID. There were no significant differences in unadjusted rates of death or MV. Among patients with AICIDs who required MV, the number of intubation days ranged from 0 to 43, with a mean of 9.1 days (standard deviation [SD] 11.3). On multivariable analysis, controlling for all variables in Table 2, AICIDs were not significantly associated with severe COVID-19 (aOR 1.3, 95% CI: 0.9-1.8).

We next examined the association of immunosuppressive medications with severe COVID-19 among patients with AICID. Twenty-one patients (13%) were on a biologic, 46 (30%) were on a nonbiologic immunosuppressive, and 42 (26%) were on systemic corticosteroids (Supplementary Table 2). Patients on corticosteroids had a higher crude rate of mortality or MV (corticosteroids 50.0% vs. other home medication groups 23.8%-28.3%) (Table 3). On multivariable analysis, both biologics and nonbiologic immunosuppressive agents were not significantly associated with severe COVID-19 (Table 4). However, systemic corticosteroid use was significantly associated with an increased risk of severe COVID-19 (aOR 6.8, 95% CI: 2.5-18.4).

## DISCUSSION

In a large, multicenter cohort of patients with confirmed COVID-19, we observed that, although patients AICIDs were more likely to be hospitalized, having an AICID was not an independent

**Table 3.** Rates of outcomes among patients with AICID by medication class[a]

| Medication Class | Death | MV | Death or MV |
|---|---|---|---|
| Not on immunosuppressive treatment | 16/79 (20.3%) | 12/79 (15.2%) | 19/79 (24.1%) |
| Nonbiologic immunosuppressive | 12/46 (26.1%) | 9/46 (19.6%) | 13/46 (28.3%) |
| Biologic | 3/21 (14.3%) | 4/21 (19.0%) | 5/21 (23.8%) |
| Systemic corticosteroids | 17/42 (40.0%) | 16/42 (38.1%) | 21/42 (50.0%) |

Abbreviations: AICID, autoimmune and chronic inflammatory disease; MV, mechanical ventilation.
[a] Percentages and n from each subcategory may not add up to the exact number of total reported cases because of nonmutually exclusive variables.

**Table 4.** Multivariable model for severe COVID-19 among patients with AICIDs

| Variable | aOR (95% CI)[a] | *p* value |
|---|---|---|
| Age > 70 | 3.6 (1.4-9.0) | 0.007 |
| Male sex | 0.6 (0.3-1.6) | 0.343 |
| Race white | 1.0 (0.4-2.5) | 0.957 |
| CVD | 1.3 (0.5-3.5) | 0.564 |
| DM | 4.2 (1.8-10.1) | 0.001 |
| CKD | 0.8 (0.3-2.4) | 0.730 |
| COPD | 1.2 (0.3-4.7) | 0.753 |
| Obesity | 1.0 (0.4-2.4) | 0.979 |
| Biologics | 1.0 (0.3-3.5) | 0.977 |
| Nonbiologic immunosuppressives | 0.7 (0.3-1.8) | 0.434 |
| Systemic corticosteroids | 6.8 (2.5-18.4) | <0.001 |

Abbreviations: AICID, autoimmune and chronic inflammatory disease; aOR, adjusted odds ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; CVD, cardiovascular disease (composite of coronary artery disease, congestive heart failure and hypertension); DM, diabetes mellitus.
[a] The model was adjusted for age over 70, male sex, white race, known comorbidities associated with severe COVID-19 outcome and AICID status. CVD was defined as either coronary artery disease or congestive heart failure.

risk factor for severe disease, defined as a composite of death or need for MV. However, patients with AICIDs who were on systemic corticosteroids at the time of infection had an eight-fold increased risk for severe COVID-19. In contrast, treatment with biologic or nonbiologic immunosuppressive agents did not significantly increase the risk of severe disease.

To our knowledge, these are the first data on COVID-19 outcomes comparing patients with AICIDs against those without AICIDs and AICID medication classes. A prior case series included primarily outpatient AICID patients with confirmed and unconfirmed COVID-19 and suggested a similar or lower hospitalization rate compared with a reference population in New York City (11). Our data suggest that patients with AICID presenting to the emergency department are more likely to be admitted, potentially because of concern about their underlying disease and immunosuppression, but are not more likely to die or require MV than other patients. We observed a higher proportion of patients with rheumatic disease being admitted to the hospital than in a large international registry but similar a hospitalization rate as in a case series from the United States and Canada, potentially reflecting differences in patient populations (comorbidities, disease severity) and/or thresholds for hospital admission in different health system settings (12,13). A prior study investigated outcomes in 52 patients with rheumatic disease compared with 104 matched controls and, similar to our findings, observed that patients with AICIDs were not more likely to die from COVID-19 (14). In contrast to the current study, patients with rheumatic disease in this study were more likely to require intensive care and/or MV. The reason for these differing outcomes is unclear but potentially could be related to differences in multivariable models (different covariates that were adjusted for including comorbidities, race, and medications), selection of controls, or sample size. Ultimately, further studies are needed to clarify whether there is a true difference in the risk of MV and intensive care for patients with AICIDs who are infected with COVID-19.

An important observation from our study is that biologic and nonbiologic immunosuppressive agents do not appear to increase the risk of severe COVID-19. Anticytokine therapies, including both biologics and small molecules, are currently in clinical trials as potential treatments for COVID-19, as they may dampen the excessive immune response in severe disease (15). These results are congruent with prior results from a large international registry that did not observe an increased risk of adverse events among patients on disease-modifying antirheumatic drugs and in fact found that tumor necrosis factor inhibitors were associated with decreased risk of hospitalization (13). In contrast, corticosteroids conferred a significantly increased risk of severe COVID-19. This finding is consistent with data from large rheumatology and IBD patient registries and may be due to an impact from corticosteroids themselves or reflect underlying disease severity (12,16). Corticosteroids have been linked to delayed viral clearance and have had mixed results when used as a treatment for coronaviruses (17,18). Overall, our data suggest that patients with AICIDs should stay on their medications during this pandemic with the exception of corticosteroids, which should ideally be tapered to the lowest possible dose weighing the risks and benefits of these therapies in the individual patient.

The limitations of this study include its retrospective design, lack of AICID activity data, and limited data on duration of time patient was taking medications. In addition, we could not reliably determine the dose of many medications (of note steroids) at the time of admission. Other limitations include potential differential use of medications by disease indication and lack of generalizability, as patients who presented to the emergency department may be different than the entire population of patients with AICIDs. Last, given the limitations of electronic medical record data, many patients did not have a specific race available (listed as Unknown or Other) and therefore we only examined White and African American race as a variable in these analyses as these were the two most commonly reported racial categories. Our study's strengths include utilization of a large cohort from a metropolitan area with AICID cases and non-AICID controls adjusting for potential confounders.

Patients with AICIDs do not appear to be at increased risk of severe COVID-19, with the exception of those on corticosteroids. Although further research is needed to determine the individual impact of specific immunosuppressive agents on COVID-19 disease course, our data suggest that patients with AICIDs should continue on biologic and nonbiologic immunosuppression but minimize use of steroids when feasible.

## AUTHOR CONTRIBUTIONS

All authors critically reviewed this manuscript.
**Study conception and design.** Ungaro, Twyman, Gulko, Klang.

**Acquisition of data.** Ungaro, Agrawal, Park, Hirten, Twyman.
**Analysis and interpretation of data.** Ungaro, Agrawal, Park, Hirten, Colombel, Twyman, Gulko, Klang.

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