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BRIEF REPORT

Clinical course and outcomes of COVID-19 in rheumatic disease patients: a case cohort study with a diverse population

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Abstract

Objective To determine clinical course and outcomes in rheumatic disease patients with coronavirus disease 2019 (COVID-19) and compare results to uninfected patients.

Methods We conducted a case cohort study of autoimmune disease patients with COVID-19 (confirmed by severe acute respiratory syndrome coronavirus 2 PCR) from February 1, 2020, to July 31, 2020, and compared them in a 1:3 ratio with uninfected patients who were matched based on race, age, sex, and comorbidity index. Patient demographics, clinical course, and outcomes were compared among these patient groups.

Results A total of 70 rheumatic disease patients with COVID-19 (mean age, 56.6 years; 64% African American) were identified. The 34 (49%) patients who were hospitalized used oral glucocorticoids more frequently than those treated as outpatients ($p < 0.01$). All 10 patients using anti-TNFα medications were treated as outpatients ($p < 0.01$). Those hospitalized with COVID-19 more often required ICU admission (17 (50%) vs 27 (26%), $p = 0.01$) and intubation (10 (29%) vs 6 (6%), $p < 0.01$) than uninfected patients and had higher mortality rates (6 (18%) vs 3 (3%), $p < 0.01$). Of the six COVID-19 patients who died, only one was of African ancestry ($p = 0.03$).

Conclusion Rheumatic disease patients infected with COVID-19 were more likely to require ICU admission, ventilation, and died more frequently versus uninfected patients with autoimmune disease. Patients on anti-TNFα medications were hospitalized less frequently, while those on chronic glucocorticoids were hospitalized more frequently. These findings have important implications for medication choice in rheumatic disease patients during the ongoing spread of COVID-19.

Key Points

- *We show that hospitalized rheumatic disease patients with COVID-19 have poorer outcomes including ICU admission, ventilation, and death compared to hospitalized rheumatic disease patients not infected with COVID-19.*
- *This study adds further support regarding protective effects of anti-TNFα medications in COVID-19 disease course, with 0 of 10 of these patients required hospitalization.*

Keywords Immunosuppressive agents · Rheumatic diseases · SARS-CoV-2 · Tumor necrosis factor inhibitors

Introduction

Data on COVID-19 in patients with immune-mediated rheumatic diseases using immunosuppressive medications such as biologic and conventional disease-modifying anti-rheumatic drugs (DMARDs), chronic glucocorticoids, and others is limited. Recent literature suggests that DMARDs may provide protective effects by disrupting the cytokine storm reaction that leads to serious disease [1, 2], while analysis of chronic glucocorticoid use shows increased rates of hospitalization from COVID-19 due to compromised immunity [3]. We aim to leverage our large rheumatic disease population with high

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prevalence of African American patients infected with COVID-19 to further characterize outcomes based on immunosuppressive medication.

Patients with rheumatic disease on immunosuppressive medications are considered at higher risk for contracting severe COVID-19 disease [3–5]. A potential confounder is that uninfected, admitted rheumatic disease patients experience poor outcomes regardless of COVID-19 infection, with up to 1/3 requiring ICU admission [6, 7]. We aim to further characterize the impact of COVID-19 infection by comparing infected, admitted COVID-19 patients to uninfected, admitted patients.

Methods

Study design

We conducted a case cohort study on rheumatic disease patients with a positive PCR test result for COVID-19 through the Emory Healthcare System using a data warehouse search. Patients tested between February 1, 2020 and July 31, 2020, were considered. PCR-positive patients were compared to matched control patients in a 1:3 ratio and were matched based on sex, age, race, and Elixhauser comorbidity index. Matches were prioritized based on Elixhauser score, followed by age. More detailed methodology can be found in Online Resource 1.

Selection criteria

Patients were considered if they had a diagnosed autoimmune condition and were on chronic immunosuppressants. Search criteria were based on a standardized list of autoimmune diseases (Online Resource 2) and immunosuppressive medications (Online Resource 3). Diagnoses were confirmed by study authors. Control patients were selected among hospitalized patients with no clinical concern for COVID-19 or who received a negative PCR test. Patients were excluded if they received a transplanted organ or were hospitalized for elective procedures or psychiatric conditions.

Main outcome variable

Variables were extracted from the EHR using manual review. Main outcome variables included hospitalization status, immunosuppressive medications, and outcomes among those hospitalized, including hospitalization length, ICU admission, ventilator use, discharge disposition, and death. Data was also collected on demographics, primary rheumatic disease, medical comorbidities, symptoms at time of PCR test date or admission, and peak laboratory values among those hospitalized.

Statistical analysis

Continuous variables were analyzed using a two-tailed Welch *t* test assuming unequal variance and are presented as mean (95% CI). Categorical variables were analyzed using a 2-tailed Fisher test and are presented as number (percentage).

Results

From February 1, 2020, to July 31, 2020, 6536 patients tested positive for COVID-19. Of these, seventy had been diagnosed with rheumatic disease with immunosuppressive medication treatment (Table 1). The most common autoimmune diagnoses included rheumatoid arthritis (26, 37%), systemic lupus erythematosus (SLE) (8, 11%), polymyalgia rheumatica (PMR) or giant cell arteritis (GCA) (7, 10%), irritable bowel disease (IBD) (6, 9%), and sarcoidosis (5, 7%). Forty-five (64%) of the COVID-19-positive patients were African American.

Admitted, COVID-19 versus outpatient, COVID-19 patients

As seen in Table 1, 34 (49%) of the COVID-19 patients were hospitalized. Compared to those treated outpatient, sex and race distribution were similar ($p = 1.00$ and $p = 0.77$, respectively), but hospitalized patients were older with mean ages of 65.2 versus 48.4 ($p < 0.01$). African American patients were hospitalized at similar rates, with 22 of 45 (49%) being admitted. Hospitalized patients were more likely to have comorbidities of renal disease and congestive heart failure ($p < 0.01$ and $p = 0.02$, respectively). All seven PMR or GCA patients were hospitalized, while all six IBD patients were treated as outpatients ($p < 0.01$ and $p = 0.03$, respectively). Hospitalized patients were more likely to receive chronic glucocorticoids and were less likely to take a biologic DMARD (bDMARD) ($p < 0.01$ and $p = 0.02$, respectively). Of those using bDMARDs, none of the ten patients receiving anti-TNFα treatment were admitted ($p < 0.01$). The use of hydroxychloroquine (HCQ) and other chronic immunosuppressive medications did not differ between groups. Admitted patients more frequently experienced fever and dyspnea ($p = 0.02$ and $p = 0.01$, respectively) as presenting symptoms. Other symptoms did not differ between groups.

Admitted, COVID-19 versus admitted, uninfected patients

Admitted COVID-19 patients were compared to matched uninfected comparators as seen in Table 2. The distribution of sex, age, and race were similar ($p = 1.00$, $p = 0.52$, and $p = 0.78$, respectively). The frequency of comorbidities, including the Elixhauser comorbidity indices, was similar between groups.

Table 1 Baseline characteristics and manifestations in rheumatic disease patients with COVID-19 who were hospitalized (*n*=34) versus treated outpatient (*n*=36)

Characteristic	Inpatient COVID-19 (*n*=34)	Outpatient COVID-19 (*n*=36)	*P* value
Female *n* (%)	27 (79%)	29 (81%)	1.00
Age in years, mean [95% CI]	65.2 [59.1–71.2]	48.4 [44.1–52.7]	0.00
Race, *n* (%)			0.94*
Caucasian	9 (26%)	11 (31%)	
Black or African American	22 (65%)	23 (64%)	
Other[†]	3 (9%)	2 (6%)	
Comorbidities, *n* (%)			
Pulmonary disease[‡]	8 (24%)	3 (8%)	0.11
Diabetes	10 (29%)	6 (17%)	0.26
Renal disease	12 (35%)	2 (6%)	0.00
Cancer	2 (6%)	5 (14%)	0.43
Hypertension	24 (71%)	19 (53%)	0.22
Coronary artery disease	6 (18%)	1 (3%)	0.22
Congestive heart failure	9 (26%)	2 (6%)	0.02
Obesity, BMI 30+ kg/m2	13 (38%)	15 (42%)	0.81
Smoking	10 (29%)	11 (31%)	1.00
AI diagnosis, *n* (%)			
RA	13 (38%)	13 (36%)	1.00
SLE	5 (15%)	3 (8%)	0.47
PMR or GCA	7 (21%)	0 (0%)	0.00
IBD	0 (0%)	6 (17%)	0.03
Sarcoidosis	2 (6%)	3 (8%)	1.00
Vasculitis	2 (6%)	1 (3%)	0.61
ILD	2 (6%)	0 (0%)	0.23
Sjogren's syndrome	1 (3%)	1 (3%)	1.00
Mixed SLE and MCTD	0 (0%)	2 (6%)	1.00
Castleman disease/TAFRO	1 (3%)	0 (0%)	1.00
MCTD	1 (3%)	0 (0%)	0.49
Scleroderma	0 (0%)	1 (3%)	1.00
Psoriatic arthritis	0 (0%)	1 (3%)	1.00
Adult-onset still's disease	0 (0%)	1 (3%)	1.00
Autoimmune hepatitis	0 (0%)	1 (3%)	1.00
Antisynthetase syndrome	0 (0%)	1 (3%)	1.00
Spondyloarthropathy	0 (0%)	1 (3%)	1.00
Ankylosing spondylitis	0 (0%)	1 (3%)	1.00
Medications, *n* (%)			
Oral glucocorticoid	24 (71%)	13 (36%)	0.00
>10mg/day	14 (41%)	7 (19%)	0.07
Hydroxychloroquine	10 (29%)	10 (28%)	1.00
bDMARDs	3 (9%)	12 (33%)	0.02
anti-TNFα	0 (0%)	10 (28%)	0.00
Rituximab	3 (9%)	2 (6%)	0.67
csDMARDs	12 (35%)	15 (42%)	0.63
Methotrexate	5 (15%)	7 (19%)	0.75
Mycophenolate mofetil	4 (12%)	1 (3%)	0.19
Leflunomide	2 (6%)	0 (0%)	0.23
Azathioprine	1 (3%)	7 (19%)	0.06

Table 1 (continued)

Characteristic	Inpatient COVID-19 (*n*=34)	Outpatient COVID-19 (*n*=36)	*P* value
tsDMARDs	0 (0%)	1 (3%)	1.00
Tofacitinib	0 (0%)	1 (3%)	1.00
Cyclophosphamide	1 (3%)	0 (0%)	0.49
Sirolimus	1 (3%)	0 (0%)	0.49
Presenting symptoms, *n* (%)			
Fever	25 (74%)	19 (53%)	0.02
Cough	24 (71%)	27 (75%)	0.78
Dyspnea	18 (53%)	8 (22%)	0.01
Myalgias	10 (29%)	17 (47%)	0.23
Diarrhea	9 (26%)	8 (22%)	0.59
Loss of taste or smell	5 (15%)	14 (39%)	0.07

**P* value for Race was computed by merging "Caucasian" and "Other" race categories and comparing to "Black or African American"

† "Other" race includes American Indian or Alaska Native, Native Hawaiian or other Pacific Islander and not reported

‡ Pulmonary disease includes asthma or COPD

§ *RA*, rheumatoid arthritis; *SLE*, systemic lupus erythematosus; *PMR*, polymyalgia rheumatica; *GCA*, giant cell arteritis; *IBD*, irritable bowel disease; *ILD*, interstitial lung disease; *MCTD*, mixed connective tissue disease; *bDMARDs*, biologic disease modifying anti-rheumatic drugs; *TNF*, tumor necrosis factor; *csDMARDs*, conventional synthetic disease modifying anti-rheumatic drugs; *tsDMARDs*, targeted synthetic disease modifying anti-rheumatic drugs

There were more PMR or GCA patients in the COVID-19 group ($p = 0.04$), but there were no other differences in frequency in autoimmune diagnoses between groups. Uninfected patients more frequently received HCQ ($p = 0.03$), but medication use was otherwise similar between the groups. COVID-19 patients more frequently experienced fever, cough, myalgias, and loss of taste or smell versus their comparators ($p < 0.01$ for all). As seen in Table 2, frequency of dyspnea was similar ($p = 0.47$). COVID-19 patients had higher maximum C-reactive protein (CRP) values and lower minimum albumin values during their first hospitalization ($p < 0.01$ and $p = 0.02$, respectively), while other laboratory values were similar between groups.

Patients infected with COVID-19 had longer hospital stays of 12.9 days versus 8.0 days ($p = 0.03$). Admitted COVID-19 patients required ICU admission (17 (50%) vs 27 (26%), $p = 0.01$) and intubation (10 (29%) vs 6 (6%), $p < 0.01$) at higher frequencies. Admitted COVID-19 patients remained on ventilators for 12.9 days versus 4.3 days for uninfected patients ($p = 0.02$). COVID-19 patients were less likely to be discharged under self-care (14 (41%) vs 69 (68%), $p < 0.01$) and were more likely to die while hospitalized (6 (18%) vs 3 (3%), $p < 0.01$) (Table 2).

Admitted COVID-19: patients who died versus patients who survived

Six of the 70 COVID-19 patients died, resulting in a 9% mortality rate. The mortality rate among hospitalized COVID-19 patients was 18%. The distribution of sex was similar between patients who died and survived, but patients who died were older with a mean age of 76.5 vs 62.8 ($p < 0.01$) (Table 3). Hospitalized patients who died were less likely to be African American, with one of 22 African American patients dying, three of nine Caucasian patients dying, and two of three patients of another race dying ($p = 0.03$). There were no differences in comorbid medical conditions between those who died and survived. Of the six patients who died, three had rheumatoid arthritis, two had PMR or GCA, and one had interstitial lung disease secondary to connective tissue disease. Autoimmune disease frequency was similar to surviving patients. All patients who died used glucocorticoids, with five on doses of 10 mg/day or greater. One patient who died took rituximab, while one other patient took mycophenolate mofetil. As seen in Table 3, reported symptom frequency and laboratory values were similar between groups. All six patients who died were admitted to the ICU with four requiring ventilation ($p < 0.01$ and $p = 0.03$, respectively).

Discussion

In this study, we evaluated patients with rheumatic conditions on chronic immunosuppressive medications who developed COVID-19 infections.

Among COVID-19 patients, those hospitalized were more likely to be older, have heart failure, and have renal disease. These are known risk factors for severe COVID-19 outcomes and are supported in other studies [3–5, 8, 9]. Gianfrancesco et al.'s study found additional risk factors including

Table 2 Baseline characteristics and outcomes in rheumatic disease patients with COVID-19 (*n*=34) and age, sex, race, and comorbidity index matched rheumatic disease comparators without COVID-19 (*n*=102)

Characteristics	Inpatient COVID-19 (*n*=34)	Inpatient comparators (*n*=102)	*P* value
Female sex, *n* (%)	27 (79%)	81 (79%)	1.00
Age in years, mean [95% CI]	65.2 [59.1–71.2]	62.9 [61.3–64.6]	0.52
Race, *n* (%)			0.92*
Caucasian	9 (26%)	31 (30%)	
Black or African American	22 (65%)	67 (66%)	
Other†	3 (9%)	4 (4%)	
Comorbidities, *n* (%)			
Elixhauser index, mean [95% CI]	10.2 [6.8–13.5]	9.5 [8.6–10.3]	0.72
Pulmonary disease‡	8 (24%)	23 (23%)	1.00
Diabetes	10 (29%)	30 (29%)	1.00
Renal disease	12 (35%)	38 (37%)	1.00
Cancer	2 (6%)	13 (13%)	0.36
Hypertension	24 (71%)	76 (75%)	0.66
Coronary artery disease	6 (18%)	17 (17%)	0.66
Congestive heart failure	9 (26%)	34 (33%)	0.53
Obesity, BMI 30+ kg/m2	13 (38%)	32 (31%)	0.53
Smoking	10 (29%)	38 (37%)	0.53
AI diagnosis, *n* (%)			
RA	13 (38%)	38 (37%)	1.00
SLE	5 (15%)	30 (29%)	0.11
PMR or GCA	7 (21%)	7 (7%)	0.04
Sarcoidosis	2 (6%)	5 (5%)	1.00
ILD	2 (6%)	1 (1%)	0.15
Vasculitis	2 (6%)	1 (1%)	0.15
Sjogren's syndrome	1 (3%)	4 (4%)	1.00
MCTD	1 (3%)	2 (2%)	1.00
Anti-synthetase syndrome	0 (0%)	3 (3%)	0.57
Castleman disease/TAFRO	1 (3%)	0 (0%)	0.25
Irritable bowel disease	0 (0%)	1 (1%)	1.00
Inflammatory myopathy	0 (0%)	1 (1%)	1.00
Inflammatory arthritis	0 (0%)	1 (1%)	1.00
Mixed RA and SLE	0 (0%)	4 (4%)	0.57
SLE, RA, and Sjogren's disease	0 (0%)	1 (1%)	1.00
Scleroderma	0 (0%)	1 (1%)	1.00
Takayasu arteritis	0 (0%)	1 (1%)	1.00
Medications, *n* (%)			
Oral glucocorticoid	24 (71%)	59 (58%)	0.23
>10mg/day	14 (41%)	38 (38%)	0.84
HCQ	10 (29%)	52 (51%)	0.03
bDMARDs	3 (9%)	11 (11%)	1.00
Rituximab	3 (9%)	3 (3%)	0.16
anti-TNF	0 (0%)	3 (3%)	0.57
Infliximab	0 (0%)	2 (2%)	1.00
Tocilizumab	0 (0%)	2 (2%)	1.00
Ustekinumab	0 (0%)	1 (1%)	1.00
csDMARDs	12 (35%)	43 (42%)	0.55
Methotrexate	5 (15%)	20 (20%)	0.62

Table 2 (continued)

Characteristics	Inpatient COVID-19 (*n*=34)	Inpatient comparators (*n*=102)	*P* value
MMF	4 (12%)	10 (10%)	0.75
Azathioprine	1 (3%)	6 (6%)	0.68
Leflunomide	2 (6%)	2 (2%)	0.26
Mesalamine/sulfasalazine	0 (0%)	5 (5%)	0.33
tsDMARDs	0 (0%)	1 (1%)	1.00
Tofacitinib	0 (0%)	1 (1%)	1.00
Cyclophosphamide	1 (3%)	0 (0%)	0.25
Sirolimus	1 (3%)	0 (0%)	0.25
Vedolizumab	0 (0%)	1 (1%)	1.00
Tacrolimus	0 (0%)	1 (1%)	1.00
Presenting symptoms			
Fever	25 (74%)	16 (16%)	0.00
Cough	24 (71%)	27 (27%)	0.00
Dyspnea	18 (53%)	42 (42%)	0.17
Myalgias	10 (29%)	1 (1%)	0.00
Diarrhea	9 (26%)	12 (12%)	0.03
Loss of taste or smell	5 (15%)	0 (0%)	0.00
Laboratory values, mean [95% CI]			
Creatinine	2.35 [1.03–3.68]	2.64 [1.99–3.29]	0.69
C-reactive protein	160.99 [117.35–204.63]	76.09 [42.74–109.45]	0.00
D Dimer	3180.8 [1781.8–4579.7]	4422.3 [1788.1–7056.5]	0.40
Ferritin	1004.57 [346.69–1662.45]	1406.48 [469.94–2343.03]	0.47
Lactate dehydrogenase	466.15 [305.40–626.90]	408.71 [211.19–606.23]	0.65
Absolute neutrophil count	8.08 [6.45–9.72]	8.79 [7.61–9.96]	0.48
Absolute lymphocyte count	1.51 [1.24–1.78]	1.48 [1.31–1.64]	0.86
Neutrophil-to-lymphocyte ratio	10.58 [7.54–13.62]	9.65 [7.68–11.62]	0.61
White blood cell count	12.06 [9.53–14.58]	12.47 [11.04–13.90]	0.77
Minimum albumin	2.89 [2.69–3.09]	3.17 [3.05–3.29]	0.02
Outcomes, n (%) or mean [95%CI]			
Intensive Care Admission	17 (50%)	27 (26%)	0.01
Intubation	10 (29%)	6 (6%)	0.00
Days of intubation	12.9 [7.8–18.0]	4.3 [1.1–7.4]	0.02
CRRT	1 (3%)	2 (2%)	0.44
Days hospitalized	12.9 [9.4–16.3]	8.0 [5.5–10.4]	0.03
Disch to home self-care	14 (41%)	69 (68%)	0.01
Disch with home health	8 (24%)	20 (20%)	0.63
Disch to rehabilitation	3 (9%)	8 (8%)	1.00
Disch to hospice	3 (9%)	3 (3%)	0.16
Patients re-hospitalized	4 (11%)	30 (29%)	0.04
Death	6 (18%)	3 (3%)	0.01

**P* value for Race was computed by merging "Caucasian" and "Other" race categories and comparing to “Black or African American”

† ”Other” race includes American Indian or Alaska Native, Native Hawaiian or other Pacific Islander and not reported

‡ Pulmonary disease includes asthma or COPD

§ *RA*, rheumatoid arthritis; *SLE*, systemic lupus erythematosus; *PMR*, polymyalgia rheumatica; *GCA*, giant cell arteritis; *IBD*, irritable bowel disease; *ILD*, interstitial lung disease; *MCTD*, mixed connective tissue disease; *bDMARDs*, biologic disease modifying anti-rheumatic drugs; *TNF*, tumor necrosis factor; *csDMARDs*, conventional synthetic disease modifying anti-rheumatic drugs; *tsDMARDs*, targeted synthetic disease modifying anti-rheumatic drugs

Table 3 Baseline characteristics and outcomes in rheumatic disease patients with COVID-19 who died (*n*=6) and survived (*n*=28) hospitalizations

Characteristic	COVID-19 Death (*n*=6)	COVID-19 Survive (*n*=28)	*P* value
Female sex, *n* (%)	4 (67%)	23 (82%)	0.58
Age in years, mean [95% CI]	76.5 [65.6–87.4]	62.8 [56.5–69.0]	0.01
Race			0.03*
Caucasian	3 (50%)	6 (21%)	
Black or African American	1 (17%)	21 (75%)	
Other †	2 (33%)	1 (4%)	
Comorbidities, *n* (%)			
Elixhauser index, mean [95% CI]	5.25 (0%)	10.96 (0%)	0.07
Pulmonary disease ‡	0 (0%)	8 (29%)	0.30
Diabetes	2 (33%)	8 (29%)	1.00
Renal disease	0 (0%)	12 (43%)	0.07
Cancer	0 (0%)	2 (7%)	1.00
Hypertension	4 (67%)	20 (71%)	1.00
Coronary artery disease	2 (33%)	4 (14%)	0.28
Congestive heart failure	1 (17%)	8 (29%)	1.00
Obesity, BMI 30+ kg/m2	0 (0%)	13 (46%)	0.06
Smoking	1 (17%)	9 (32%)	0.64
Former	1 (17%)	9 (32%)	
Current	0 (0%)	0 (0%)	
AI diagnosis, *n* (%)			
Rheumatoid arthritis	3 (50%)	10 (36%)	0.65
SLE	0 (0%)	5 (18%)	0.56
PMR or GCA	2 (33%)	5 (18%)	0.58
Sarcoidosis	0 (0%)	2 (7%)	1.00
Interstitial lung disease	1 (17%)	1 (4%)	0.33
Vasculitis	0 (0%)	2 (7%)	1.00
Sjogren's syndrome	0 (0%)	1 (4%)	1.00
MCTD	0 (0%)	1 (4%)	1.00
Castleman disease/TAFRO	0 (0%)	1 (4%)	1.00
Medications, *n* (%)			
Oral glucocorticoid	6 (100%)	18 (64%)	0.15
>10mg/day	5 (83%)	9 (32%)	0.06
Hydroxychloroquine	1 (17%)	9 (32%)	0.64
bDMARDs	1 (17%)	2 (7%)	0.45
Rituximab	1 (17%)	2 (7%)	0.45
csDMARDs	1 (17%)	11 (39%)	0.39
Methotrexate	0 (0%)	5 (18%)	0.56
MMF	1 (17%)	3 (11%)	0.56
Azathioprine	0 (0%)	1 (4%)	1.00
Leflunomide	0 (0%)	2 (7%)	1.00
Cyclophosphamide	0 (0%)	1 (4%)	1.00
Sirolimus	0 (0%)	1 (4%)	1.00
Presenting symptoms			
Fever	4 (67%)	21 (75%)	0.31
Cough	3 (50%)	21 (75%)	0.64
Dyspnea	2 (33%)	16 (57%)	1.00
Myalgias	2 (33%)	8 (29%)	0.36
Diarrhea	0 (0%)	9 (32%)	0.64

Table 3 (continued)

Characteristic	COVID-19 Death (*n*=6)	COVID-19 Survive (*n*=28)	*P* value
Loss of taste or smell	0 (0%)	5 (18%)	1.00
Laboratory values			
Creatinine	1.64 [0.78–2.50]	2.50 [0.02–3.25]	0.32
C-reactive protein	215.45 [79.72–351.18]	147.38 [168.01–262.89]	0.28
D Dimer	3402.2 [-2262.3–9066.6]	3123.0 [1995.8–4808.5]	0.91
Ferritin	1612.60 [-947.52–4172.72]	814.56 [962.23–2262.97]	0.46
Lactate dehydrogenase	456.50 [282.78–630.22]	468.90 [249.01–663.99]	0.92
Absolute neutrophil count	9.91 [4.02–15.80]	7.74 [8.13–11.69]	0.39
Absolute lymphocyte count	1.21 [0.60–1.81]	1.56 [0.90–1.52]	0.22
Neutrophil-to-lymphocyte ratio	9.26 [4.54–13.98]	10.82 [5.67–12.85]	0.53
White blood cell count	19.60 [9.88–29.32]	10.44 [8.22–12.66]	0.07
Minimum albumin	2.77 [2.13–3.41]	2.91 [2.54–2.99]	0.60
Outcomes, *n* (%) or mean [95% CI]			
Intensive Care Admission	6 (100%)	11 (39%)	0.00
Intubation	4 (67%)	6 (21%)	0.03
Days of intubation	15.0 [7.5–22.5]	11.2 [7.6–14.8]	0.39
CRRT	0 (0%)	1 (4%)	1.00
Days hospitalized	18.7 [10.0–27.4]	11.6 [15.0–22.4]	0.19

**P* value for Race was computed by merging "Caucasian" and "Other" race categories and comparing to "Black or African American"

† "Other" race includes American Indian or Alaska Native, Native Hawaiian or other Pacific Islander and not reported

‡ Pulmonary disease includes asthma or COPD

§RA, rheumatoid arthritis; *SLE*, systemic lupus erythematosus; *PMR*, polymyalgia rheumatica; *GCA*, giant cell arteritis; *IBD*, irritable bowel disease; *ILD*, interstitial lung disease; *MCTD*, mixed connective tissue disease; *bDMARDs*, biologic disease modifying anti-rheumatic drugs; *csDMARDs*, conventional synthetic disease modifying anti-rheumatic drugs

hypertension, cardiovascular disease, lung disease, and diabetes, although this study has a significantly larger COVID-19 population ($n = 600$).

Other studies claim that TNF is involved in the pro-inflammatory activity of the cytokine storm that occurs in COVID-19 infection, leading to end-organ damage and poor patient outcomes. Therefore, it is hypothesized that anti-TNFα medications play protective roles in COVID-19 infection [10, 11]. Another explanation for improved outcomes in patients using DMARDs is that these patients follow up with their rheumatologist more closely and have better control of their underlying disease [12]. Furthermore, these patients typically require less chronic steroid use which is a known risk factor for worse outcomes [3]. In our study, none of the ten COVID-19 patients taking anti-TNFα medications required hospitalization, while other DMARDs did not impact patient outcomes. In patients using rituximab, the other bDMARD included, three of five patients required hospitalization, and one patient died. Conventional synthetic DMARD (csDMARDs) use was also similar between those hospitalized and treated as outpatients. Therefore, this study supports that only anti-TNFα medications are protective in COVID-19 infection, rather than DMARD medications in general. Further studies including a quantitative measure of rheumatic disease control or activity may help to further distinguish reasons for patients having better outcomes on anti-TNFα medications.

Our results also add to the body of evidence suggesting that chronic glucocorticoid use increases disease severity, with glucocorticoids being used at nearly twice the frequency among hospitalized COVID-19 patients (71% vs 36%) [3]. Furthermore, of the six COVID-19 patients who died, all received chronic glucocorticoids, and five of these six used 10 mg/day or more of prednisone. This reinforces that high-dose chronic steroid use prior to COVID-19 infection is associated with worse outcomes [3]. We speculate that with a larger study population, risk of poor outcomes with chronic steroid use may be further stratified using daily dosing and treatment duration.

Our study is unique as we compared outcomes among rheumatic disease patients with COVID-19 infection to a matched group without COVID-19 infection. This provides an important clarification among those hospitalized with COVID-19, as admitted rheumatic disease patients have poor outcomes irrespective of infection [6]. By comparing our infected patients to comparators, this study clarifies the degree to which COVID-19 infection impacts hospitalization

outcomes. The higher rate of ICU admission, ventilation, and death among COVID-19 patients is particularly concerning, as these results confirm the suspicion that rheumatic disease patients infected with COVID-19 are particularly susceptible to a severe disease course and do poorly clinically.

The statistically significantly lower minimum albumin concentrations and higher maximum CRP values seen in hospitalized COVID-19 patients are supported by other studies as increased CRP and decreased albumin have both been reported as prognostic indicators of disease progression and more severe COVID-19 infection [13].

One of our study's strengths is in comparing outcomes in a large healthcare system with a significantly diverse population. This study's racial is enriched with 65% African Americans, differing from similar studies looking at primarily Caucasian populations [4]. Appropriate racial representation is important as there is concern that African American populations face an excess disease burden [14]. Our study's overall hospitalization rate of 49% was slightly higher than those in similar studies with a hospitalization rate of 46% reported by Gianfrancesco and 44% reported by D'Silva [3, 4]. Our rates of ICU admission were similar between our study and D'Silva's study (50% vs 48%, respectively). Furthermore, our 9% mortality rate matched the mortality rate reported by Gianfrancesco and was higher than the 6% mortality rate reported by D'Silva. However, in our study, the hospitalization rate among African Americans was similar to the overall hospitalization rate, and only one of six patients who died was African American. Aside from differing racial composition among these studies, factors such as comorbid and rheumatic disease burden may impact the difference in the observed outcomes. Unlike D'Silva and Gianfrancesco's studies, this study only includes patients actively taking immunosuppressive medications. This may result in a self-selection for a higher proportion of active rheumatic disease. In addition, none of these studies specifies the severity of comorbid conditions. Given that each of these populations shares different demographic backgrounds, severity of comorbid conditions among each of these patient populations is likely to differ and confound the outcome results. More than half of our patients are from African ancestry who are known to have more severe autoimmune conditions [15].

The strength of this study is that it is the first to evaluate the outcomes of rheumatic disease patients on active treatment for their conditions with immunosuppressive medication among a significantly diverse population with many African American patients. It is also the first to compare infected, admitted rheumatic disease patients with their uninfected rheumatic disease counterparts.

This study's power is limited by the sample size, especially when comparing COVID-19 patients who died or survived. Furthermore, we do not account for rheumatic conditions or comorbidity severity, and do not account for dosage and duration of medication regimens. These factors likely contribute to clinical course and outcomes. This study builds on the growing body of information on risk factors and clinical course of COVID-19 in rheumatic disease patients.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10067-021-05578-x.

Data availability Due to privacy and ethical concerns, the supporting data is not publicly available.

Compliance with ethical standards

Conflict of interest Dr. Khosroshahi reports grant from Pfizer and personal fees from Viela Bio, outside of the submitted work.

Ethics approval and consent to participate The study was determined to be exempt by the Emory University eIRB.

Code availability N/A.

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