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BRIEF REPORT

Characteristics and Outcomes of People With Gout Hospitalized Due to COVID-19: Data From the COVID-19 Global Rheumatology Alliance Physician-Reported Registry

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Objective. To describe people with gout who were diagnosed with coronavirus disease 2019 (COVID-19) and hospitalized and to characterize their outcomes.

Methods. Data on patients with gout hospitalized for COVID-19 between March 12, 2020, and October 25, 2021, were extracted from the COVID-19 Global Rheumatology Alliance registry. Descriptive statistics were used to describe the demographics, comorbidities, medication exposures, and COVID-19 outcomes including oxygenation or ventilation support and death.

Results. One hundred sixty-three patients with gout who developed COVID-19 and were hospitalized were included. The mean age was 63 years, and 85% were male. The majority of the group lived in the Western Pacific Region (35%) and North America (18%). Nearly half (46%) had two or more comorbidities, with hypertension (56%), cardiovascular disease (28%), diabetes mellitus (26%), chronic kidney disease (25%), and obesity (23%) being the most common. Glucocorticoids and colchicine were used pre-COVID-19 in 11% and 12% of the cohort, respectively. Over two thirds (68%) of the cohort required supplemental oxygen or ventilatory support during hospitalization. COVID-19-related death was reported in 16% of the overall cohort, with 73% of deaths documented in people with two or more comorbidities.

Conclusion. This cohort of people with gout and COVID-19 who were hospitalized had high frequencies of ventilatory support and death. This suggests that patients with gout who were hospitalized for COVID-19 may be at risk of poor outcomes, perhaps related to known risk factors for poor outcomes, such as age and presence of comorbidity.

INTRODUCTION

Gout is the most common inflammatory joint disease (1) and is caused by monosodium urate crystal deposition leading to episodic arthritis (gout flare), tophus formation, and joint destruction.

The views expressed here are those of the authors and participating members of the COVID-19 Global Rheumatology Alliance and do not necessarily represent the views of the American College of Rheumatology (ACR), the European Alliance of Associations for Rheumatology (EULAR), the (UK) NHS, the National Institute for Health Research (NIHR), the (UK) Department of Health, or any other organization.

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Gout is associated with male gender, advanced age, and several comorbidities, including cardiovascular disease, chronic kidney disease, and obesity (2). These demographic factors and comorbidities are also associated with death related to coronavirus

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SIGNIFICANCE & INNOVATIONS

- The outcomes of patients with gout who develop coronavirus disease 2019 (COVID-19) have not been described well in the literature to date.
- Patients with gout often have significant comorbidity and therefore could be expected to be at risk of poor outcomes from COVID-19.
- This report describes the characteristics of and outcomes in 163 patients with gout who developed COVID-19 and were admitted to hospital and were reported to the COVID-19 Global Rheumatology Alliance physician registries.
- Patients with gout who were hospitalized commonly also had comorbidity, and a majority required oxygen therapy, noninvasive ventilation, or mechanical ventilation, with a high proportion of subsequent death.

disease 2019 (COVID-19) in the general population (3) and in people with rheumatic diseases (4,5). People with gout may therefore be at a higher risk of severe COVID-19 outcomes (6,7). Colchicine has been associated with lower rates of death and hospitalization from COVID-19 in the general population (8). Exposure to 10 or more mg/day of prednisone, usually used sporadically in patients with gout who do not respond to non-steroidal antiinflammatories or have contraindications, has been associated with COVID-19 hospitalization and death in people with rheumatic diseases, although this observation may be because of channeling bias (4,9,10). Despite the potential influence of gout on COVID-19 outcomes, recommendations for COVID-19 developed by international rheumatology societies do not directly address people with gout, perhaps because of limited direct evidence about gout and COVID-19 (11–13).

Characteristics of people with gout and COVID-19 have not been comprehensively described. A recent study using data from the UK Biobank explored the association between gout and

COVID-19 diagnosis and death (14). In this study, 117 people with gout were diagnosed with COVID-19, but their rheumatic disease clinical characteristics and medication exposure were not specifically described.

This study aims to characterize hospitalized people with gout and COVID-19 by their demographics, comorbidities, medication exposure, COVID-19 treatment, and outcomes, using data from the COVID-19 Global Rheumatology Alliance (C19-GRA) registry (15,16).

MATERIALS AND METHODS

Population and databases. All adult patients from the C19-GRA registry with rheumatology physician-diagnosed gout who were hospitalized for COVID-19 between March 12, 2020, and October 25th, 2021, were included in the analysis. Patients who had an additional rheumatic disease or those who were on disease-modifying antirheumatic drugs (DMARDs) were excluded from the analysis.

Providers entered data on patients with rheumatic diseases and COVID-19 into the C19-GRA registry via two parallel online portals, the European Alliance of Associations for Rheumatology (EULAR) COVID-19 portal, which was limited to European countries (hosted by The University of Manchester, UK), and the C19-GRA portal, which included all other countries (hosted by the University of California, San Francisco, California). The design and development of these registries has been described elsewhere (15,17).

Data quality was assessed by the University of California, San Francisco, and the University of Manchester, UK, who both confirmed that there were no duplicate data entries. Data were entered anonymously into both registries, so the GRA and EULAR are unable to trace data back to individual patients. It was therefore determined by the local institutional review boards that patient consent was not required.

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Variables and outcomes. Demographic data included age at COVID-19 diagnosis, sex (male or female), ethnicity, and region based on World Health Organization category (Africa, the Americas, Eastern Mediterranean, Europe, Southeast Asia, and Western Pacific), with the Americas further divided into North and South. Number of comorbidities was recorded as none, one, and two or more. Specific comorbidities were recorded as categorical variables (yes or no) including hypertension, cardiovascular disease, diabetes mellitus, chronic kidney disease, interstitial lung disease (ILD), lung disease (chronic obstructive pulmonary disease, asthma, or other conditions other than ILD), cancer, obesity (body mass index >30), and smoking status (never or ever).

Gout disease activity was categorized as in remission, low, moderate, or high (physician global assessment). Baseline (preinfection) use of colchicine and glucocorticoids were extracted and reported as categorical variables. Daily prednisone-equivalent glucocorticoid doses at the time of COVID-19 diagnosis were further categorized as 0 mg/day, 1 to 5 mg/day, 6 to 9 mg/day, and 10 mg/day or more.

For the COVID-19 diagnostic method, clinicians selected from the following options: polymerase chain reactions, antibody testing, metagenomic testing, computed tomographic scan, laboratory assay, or a presumptive clinical diagnosis. Date of COVID-19 diagnosis was categorized into the following three time periods: June 15, 2020, and earlier; from June 16 to September 30, 2020; and October 1, 2020, onward. These cutoffs were chosen as the Oxford University RECOVERY Trial released data demonstrating the efficacy of dexamethasone in COVID-19 treatment on June 16, 2020 (18). COVID-19 severity was classified based on requirement for oxygenation or ventilatory support as follows: no oxygenation, any oxygenation, mechanical ventilation or extracorporeal membrane oxygenation (ECMO), and death.

Statistical analysis. Descriptive statistics were used to characterize people with gout and COVID-19. Categorical variables were reported as number and percentage and continuous variables as mean and SD. Glucocorticoid dose was additionally reported as median and interquartile range. Missing data were reported as separate categories. Prevalence of death, a major COVID-19-related outcome, was reported for the overall cohort and stratified by number of comorbidity (none, one, and two or more). The data were further compared with the prevalence of death in hospitalized people with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), also stratified by number of comorbidities, from the C19-GRA registry during the same time frame. Statistical analyses were conducted using R version 4.0.2.

RESULTS

We identified 348 people diagnosed with gout and COVID-19 in the C19-GRA registry. One hundred eighty-one

Table 1. Baseline characteristics of the people diagnosed with gout and hospitalized with COVID-19

Characteristics	Results (N = 163)
Demographics	
Age, y, mean (SD)	63.0 (16.0)
Female, n (%)	25 (15.0)
Race or ethnicity, n (%)	
White	63 (38.6)
East Asian	45 (27.6)
South Asian	20 (12.3)
Hispanic	14 (8.6)
Black	9 (5.6)
Southeast Asian	3 (1.8)
Unknown	9 (5.6)
Regions, n (%)	
Western Pacific region	87 (53.7)
North America	30 (18.5)
Eastern Mediterranean region	21 (13.0)
South America	16 (9.9)
South-East Asia	4 (2.5)
Europe	3 (1.8)
Africa	2 (1.2)
Time period of COVID-19 diagnosis, n (%)	
June 15, 2020, or earlier	80 (49.1)
June 16, 2020, to September 30, 2020	32 (19.6)
October 1, 2020, to October 25, 2021	51 (31.3)
Number of comorbidities, n (%)	
None	42 (25.8)
One	46 (28.2)
Two or more	75 (46.0)
Comorbidities, n (%)	
Hypertension	91 (55.8)
Cardiovascular disease	45 (27.6)
Diabetes mellitus	42 (25.8)
Chronic kidney disease	41 (25.1)
Obesity	38 (23.3)
Lung disease ^a	25 (15.3)
Cancer	15 (9.2)
Interstitial lung disease	0 (0.0)
Smoking (ever), n (%)	73 (44.8)
Gout disease activity, n (%)	
Remission	95 (58.3)
Low	34 (20.9)
Moderate	14 (8.6)
High	11 (6.7)
Unknown	9 (5.5)
Death, n (%)	26 (15.9)
Ventilation status, n (%)	
No oxygenation	45 (27.6)
Supplemental oxygenation or noninvasive ventilation	89 (54.6)
Invasive ventilation or ECMO	21 (12.9)
Not reported	8 (4.9)

Abbreviations: COVID-19, coronavirus disease 2019; ECMO, extracorporeal membrane oxygenation.

^aLung disease includes chronic obstructive pulmonary disease, asthma, and other conditions, excluding interstitial lung disease.

patients were not hospitalized and therefore, were excluded (Supplementary Table 1). Four patients were excluded because of concomitant rheumatic diseases and/or DMARD use. The final cohort consisted of 163 hospitalized patients with physician-diagnosed gout. The demographics and clinical characteristics

Table 2. Baseline medications used by people with gout who were hospitalized for COVID-19

Medications	Results
Colchicine, n (%)	20 (12.3)
Glucocorticoids, n (%)	18 (11.0)
Glucocorticoid dosage in people taking glucocorticoids (n = 18)	
Mean (SD)	18.3 (16.0)
Median (min, max)	15 (2, 60)
Categories of glucocorticoid dosage in prednisone daily equivalents (n = 18), n (%)	
No use of glucocorticoids	145 (90.0)
1 to 5 mg/d	6 (3.7)
6 to 9 mg/d	0 (0.0)
10 or more mg/d	11 (6.7)
Not reported	1 (1.6)

Abbreviation: COVID-19, coronavirus disease 2019.

of patients are shown in Table 1. The cohort was predominantly male (85%), and the mean age was 63 years (SD = 16.0 years). The majority of people were from the Western Pacific region (54%), followed by North America (19%) and the Eastern Mediterranean region (13%). Hypertension was the most common comorbidity (56%) followed by cardiovascular disease (28%), diabetes mellitus (26%), chronic kidney disease (25%), and obesity (23%). More than 46% of patients had two or more comorbidities.

Gout disease activity was reported as in remission or low activity in the majority of the cohort (79%), with the remaining 21% reported as having moderate or high disease activity (Table 1). Medication exposure in the cohort is shown in Table 2. Twenty people (12%) were taking colchicine. Eighteen people (11%) were taking glucocorticoids, with the majority at daily dosages of prednisone 10 mg or higher (11/18 people, 61%). Over half of people with gout hospitalized for COVID-19 required oxygenation or noninvasive ventilation (55%) (Table 1). Invasive ventilation or ECMO was required in 21 (13%) people.

Twenty-six deaths (16%) were reported overall (Table 3). When stratified by the number of comorbidities, 25% of people

with two or more comorbidities died compared to 2% in those without comorbidity and 13% in those with one comorbidity. The overall prevalence of death in the gout cohort (16%) was comparable to hospitalized people with RA (18%) and SLE (17%) during the same period. In the subgroup of patients with gout who died, 73% had two or more comorbidities. However, the prevalence of having two or more comorbidities was 49% in hospitalized people with RA and 39% in hospitalized people with SLE who died of COVID-19.

DISCUSSION

We have characterized hospitalized patients diagnosed with gout and COVID-19 from an international provider-reported registry. The following characteristics of the cohort were as expected from prior studies of people with gout: older people, mostly men, with multiple comorbidities, including hypertension, cardiovascular disease, obesity, and chronic kidney disease (2,19). Similar to the general gout population, nearly half of individuals in our cohort had two or more comorbid conditions. These data from the C19-GRA registry support the hypothesis that people with gout and COVID-19 requiring hospitalization have several risk factors for poor COVID-19 outcomes, particularly older age (mean 63 years) and multiple comorbidities.

The majority of this hospitalized cohort (67%) required at least oxygen therapy, indicating at least moderate COVID-19. Invasive ventilatory support was required in 13% of the gout cohort, which was comparable to the general inpatient COVID-19 populations (13%–14%) (20,21), as well as patients with RA (13%) and those with connective tissue disease (11%) from the C-19-GRA registry (4).

The percentage of patients who died (16%) in our cohort of hospitalized people with gout was similar to the prevalence of death in RA (18%) and SLE (17%) cohorts collected during the same period (Table 3), as well as the prevalence of death in the general inpatient COVID-19 populations (16%–18%) (22,23). The majority (73%) of those who died in our gout cohort had two

Table 3. Prevalence of death in people with gout compared with people with rheumatoid arthritis and systemic lupus erythematosus stratified by number of comorbidities

Outcomes	No comorbidity	One comorbidity	Two or more comorbidities	Total
Gout				
Hospitalization, n (%)	42 (25.8)	46 (28.2)	75 (46.0)	163 (100.0)
Death, n (%)	1 (3.8)	6 (23.1)	19 (73.1)	26 (100.0)
Death in the same comorbidity subgroup, %	2	13	25	16
Rheumatoid arthritis				
Hospitalization, n (%)	640 (30.0)	707 (33.1)	788 (36.9)	2135 (100.0)
Death, n (%)	74 (18.9)	127 (32.4)	191 (48.7)	392 (100.0)
Death in the same comorbidity subgroup, %	12	18	24	18
Systemic lupus erythematosus				
Hospitalization, n (%)	220 (39.0)	194 (34.3)	151 (26.7)	565 (100.0)
Death, n (%)	26 (27.4)	32 (33.7)	37 (38.9)	95 (100.0)
Death in the same comorbidity subgroup, %	12	16	25	17

or more comorbid conditions, which was higher than the prevalence in RA (49%) and SLE (39%) in the same registry. However, only 2% of deaths in people with gout were in the no-comorbidity subgroup. These observations provided some support for the hypothesis that COVID-19 mortality in people with gout was driven at least partially by the presence of comorbid conditions.

The association between gout and poor COVID-19 outcomes remains uncertain. Research using data from the UK Biobank did not find statistically significant associations between gout and COVID-19 diagnosis or gout and COVID-19-related death, despite the presence of several risk factors for poor COVID-19 outcomes in the overall UK Biobank gout cohort (14). The UK Biobank cohort is, however, a voluntary cohort of predominantly older White participants in a high-income country, so results are not necessarily generalizable to other settings. The association between gout and other COVID-19 outcomes (eg, ventilatory support, hospitalization) has not been directly explored. Our data were able to confirm high rates of death and requirement for ventilatory support in a large proportion of people with gout hospitalized for COVID-19 in the C19-GRA registry but could not confirm whether there was a statistically significant association between gout and poor COVID-19 outcomes, owing to the small sample size. A larger data set with more detail is required to answer this question.

The strengths of our study include representation of people with gout from multiple diverse populations and physician confirmation of gout diagnosis. The results of this study, however, should be interpreted with caution because there are limitations to this study that may limit its generalizability. The inception of the C19-GRA registry was driven by concerns that people with rheumatic diseases may be at higher risk of SARS-CoV-2 infection and poor COVID-19 outcomes due to disease activity, comorbidities, and exposure to immunomodulatory or immunosuppressive agents (24). These assumptions may have led to selection bias in favor of rheumatic diseases typically treated with immunosuppressive agents. As a result, despite the high prevalence of gout in the general population, the registry was dominated by people with RA and autoimmune connective tissue diseases, including lupus and systemic sclerosis (4). In addition, because most patients with gout are managed in primary care, people with gout cared for by rheumatologists tend to have more severe disease and a higher frequency of comorbidity (for example, renal impairment or other rheumatic diseases). People with gout who did not develop flare during COVID-19 care could have been overlooked by their physicians, further adding to the selection bias of more severe gout cases or those with comorbid rheumatic disease (25). Some gout-specific variables were also not collected in the registry (eg, tophus, gout flare, serum urate levels), which leads to limitations in analysis of people with gout. The disease activity variable in the C19-GRA cohort was a global assessment of disease activity assessed by the reporting clinicians and was used for all cases regardless of diagnosis, limiting its applicability to gout because high activity could have indicated advanced

(tophaceous) gout or simply gout flare during COVID-19 care. Because COVID-19 immunization status was added later in the C19-GRA data collection, the study was unable to investigate the role of COVID-19 immunization status in clinical outcomes. Finally, the relatively small cohort size could not support secondary statistical modeling beyond a descriptive analysis.

Despite being the most common inflammatory arthritis in the general population, gout remains relatively neglected in COVID-19 guidelines and recommendations. Patients with gout have also reported difficulty with their disease management during the pandemic and both improvements and declines in quality of life (26,27). Data from the C19-GRA registry suggest that people with gout and COVID-19 have a high prevalence of established risk factors for poor COVID-19 outcomes, and many required ventilatory support or died. Future research should focus on exploring the possible connections between comorbid gout and COVID-19 diagnosis and outcomes. Such knowledge may help clinicians make the most informed decisions when managing people with gout during the ongoing COVID-19 pandemic.

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AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Robinson had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Jatuworapruk, Montgomery, Gianfrancesco, Conway, Durcan, Graef, Jayatilleke, Keen, Kilian, Young, Grainger, Robinson.

Acquisition of data. Jatuworapruk, Montgomery, Gianfrancesco, Conway, Durcan, Graef, Jayatilleke, Keen, Kilian, Young, Carmona, Cogo, Duarte-García, Gossec, Hasseli, Hyrich, Langlois, Lawson-Tovey, Malcata, Mateus, Schafer, Scirè, Sigurdardottir, Sparks, Strangfeld, Xavier, Bhana, Gore-Massy, Hausmann, Liew, Sirotych, Sufka, Wallace, Machado, Yazdany, Grainger, Robinson.

Analysis and interpretation of data. Jatuworapruk, Montgomery, Gianfrancesco, Conway, Durcan, Graef, Jayatilleke, Keen, Kilian, Young, Carmona, Cogo, Duarte-García, Gossec, Hasseli, Hyrich, Langlois, Lawson-Tovey, Malcata, Mateus, Schafer, Scirè, Sigurdardottir, Sparks, Strangfeld, Xavier, Bhana, Gore-Massy, Hausmann, Liew, Sirotych, Sufka, Wallace, Machado, Yazdany, Grainger, Robinson.

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