Arthritis Care & Research
Vol. 75, No. 1, January 2023, pp 53–60
DOI 10.1002/acr.25039

AMERICAN COLLEGE of RHEUMATOLOGY
Empowering Rheumatology Professionals

HEALTH DISPARITIES AND HEALTH EQUITY IN THE RHEUMATIC DISEASES

Association Between Race/Ethnicity and COVID-19 Outcomes in Systemic Lupus Erythematosus Patients From the United States: Data From the COVID-19 Global Rheumatology Alliance

Manuel F. Ugarte-Gil,[1] Graciela S. Alarcón,[2] Andrea M. Seet,[3] Zara Izadi,[3] Anna D. Montgomery,[3] Alí Duarte-García,[4] Emily L. Gilbert,[5] Maria O. Valenzuela-Almada,[4] Leanna Wise,[6] Jeffrey A. Sparks,[7] Tiffany Y.-T. Hsu,[7] Kristin M. D'Silva,[8] Naomi J. Patel,[8] Emily Sirotich,[9] Jean W. Liew,[10] Jonathan S. Hausmann,[11] Paul Sufka,[12] Rebecca Grainger,[13] Suleman Bhana,[14] Zachary Wallace,[8] Lindsay Jacobsohn,[3] Anja Strangfeld,[15] Elsa F. Mateus,[16] Kimme L. Hyrich,[17] Laure Gossec,[18] Loreto Carmona,[19] Saskia Lawson-Tovey,[17] Lianne Kearsley-Fleet,[20] Martin Schaefer,[21] Pedro M. Machado,[22] Philip C. Robinson,[23] Milena Gianfrancesco,[3] and Jinoos Yazdany[3]

Objective. To determine the association between race/ethnicity and COVID-19 outcomes in individuals with systemic lupus erythematosus (SLE).

Methods. Individuals with SLE from the US with data entered into the COVID-19 Global Rheumatology Alliance registry between March 24, 2020 and August 27, 2021 were included. Variables included age, sex, race, and ethnicity (White, Black, Hispanic, other), comorbidities, disease activity, pandemic time period, glucocorticoid dose, antimalarials, and immunosuppressive drug use. The ordinal outcome categories were: not hospitalized, hospitalized with no oxygenation, hospitalized with any ventilation or oxygenation, and death. We constructed ordinal logistic regression models evaluating the relationship between race/ethnicity and COVID-19 severity, adjusting for possible confounders.

Results. We included 523 patients; 473 (90.4%) were female and the mean ± SD age was 46.6 ± 14.0 years. A total of 358 patients (74.6%) were not hospitalized; 40 patients (8.3%) were hospitalized without oxygen, 64 patients (13.3%) were hospitalized with any oxygenation, and 18 (3.8%) died. In a multivariable model, Black (odds ratio [OR] 2.73 [95% confidence interval (95% CI) 1.36–5.53]) and Hispanic (OR 2.76 [95% CI 1.34–5.69]) individuals had higher odds of more severe outcomes than White individuals.

Conclusion. Black and Hispanic individuals with SLE experienced more severe COVID-19 outcomes, which is consistent with findings in the US general population. These results likely reflect socioeconomic and health disparities and suggest that more aggressive efforts are needed to prevent and treat infection in this population.

INTRODUCTION

In the US, Hispanic and Black individuals have been shown to experience more severe COVID-19 outcomes; this disparity has been observed in the general population and the larger group of individuals with systemic rheumatic diseases included in the COVID-19 Global Rheumatology Alliance (C19-GRA) registry (1,2). In a systematic review evaluating the impact of race and ethnicity on COVID-19–related infections, hospitalization, and deaths, the research showed higher infection, hospitalization, and mortality

Supported by the American College of Rheumatology and the European Alliance of Associations for Rheumatology.

[1]Manuel F. Ugarte-Gil, MD, MSc: Universidad Cientifica del Sur and Hospital Guillermo Almenara Irigoyen, EsSalud, Lima, Peru; [2]Graciela S. Alarcón, MD, MPH: Heersink School of Medicine, University of Alabama at Birmingham, and School of Medicine, Universidad Peruana Cayetano Heredia, Lima, Peru; [3]Andrea M. Seet, MPH, Zara Izadi, MPharm, PhD, Anna D. Montgomery, MPH, Lindsay Jacobsohn, BA, Milena Gianfrancesco, MPH, PhD, Jinoos Yazdany, MD, MPH: University of California, San Francisco; [4]Alí Duarte-García, MD, MSc, Maria O Valenzuela-Almada, MD: Mayo Clinic, Rochester, Minnesota; [5]Emily L. Gilbert, MD, PhD: Mayo Clinic, Jacksonville, Florida; [6]Leanna Wise, MD: Keck School of Medicine, University of Southern California, Los Angeles; [7]Jeffrey A. Sparks, MD, MMSc, Tiffany Y.-T. Hsu, MD, PhD: Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts; [8]Kristin M. D'Silva, MD, Naomi J. Patel, MD, Zachary Wallace, MD, MSc: Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts; [9]Emily Sirotich, BSc: McMaster University, Hamilton, and Canadian Arthritis Patient Alliance, Toronto, Ontario, Canada; [10]Jean W. Liew, MD, MS: Boston University School of Medicine, Boston, Massachusetts; [11]Jonathan S. Hausmann, MD: Beth Israel Deaconess Medical Center

SIGNIFICANCE & INNOVATIONS

- Black and Hispanic individuals with systemic lupus erythematosus experienced more severe COVID-19 outcomes.
- The association between race and ethnicity and COVID-19 outcomes is likely to reflect socioeconomic and health disparities

rates (deaths due to diagnosis and undiagnosed COVID-19) in Black and Hispanic patients, but the case-fatality rate (deaths among those with confirmed COVID-19) was similar across groups. This finding suggests that the differences observed likely derive from the fact that Black and Hispanic individuals were more frequently exposed to the infection and may have experienced a delay in accessing the health care system. These data strongly suggest that differences in exposures and health care rather than genetic or other biologic factors explain the disparate outcomes (2).

In systemic lupus erythematosus (SLE), non-White individuals have a higher risk of developing SLE, experience more severe disease manifestations, and have higher mortality (3–5). However, studies also show that the relationship between race and ethnicity and disease outcomes is significantly confounded by social determinants of health in SLE (3,4). During the COVID-19 pandemic, many existing health disparities have been exacerbated in vulnerable populations who are more likely to have high-risk exposures, poor access to health care, and inequitable treatment. Although COVID-19 outcomes in people with SLE have been reported, differential outcomes by race and ethnicity in this vulnerable population have not been comprehensively assessed.

Recently, we reported that worse COVID-19–related outcomes in individuals with SLE were associated with sociodemographic characteristics like age and sex, comorbidities, active disease, untreated disease, and glucocorticoid use (6). The aim of this study was to determine the association between race and ethnicity and COVID-19 outcomes in individuals with SLE in the US.

MATERIALS AND METHODS

Data source. Individuals with rheumatic disease and COVID-19 from the C19-GRA registry entered by US rheumatologists were included in these analyses. The study included data collected between March 12, 2020 and August 27, 2021. The registry database was hosted by the University of California, San Francisco (UCSF) (7,8). There were 116 unique institutions (ranging from private clinics to large health care institutions) across 32 states plus the District of Columbia and Puerto Rico. Cases were entered into the registry by treating clinicians. Only individuals with SLE were included in this study. A prior study using C19-GRA data included some individuals who were also reported in this study (1), but the number of individuals in the current analysis is significantly larger than the number reported in the previous publication. Data quality was assessed by the data coordinating center at UCSF and included procedures to identify and remove any duplicate cases.

The C19-GRA physician-reported registry was determined to be not human subjects research by the UK Health Research Authority and the University of Manchester, as well as under US federal guidelines assessed by the UCSF Institutional Review Board. Due to the de-identified and noninterventional nature of the study, it was determined to be exempt by each institutional review board.

Racial and ethnic categorization. Race and ethnicity were reported by the physician entering the case, and multiple categories could be selected among the following: Arab, African American, East Asian, South Asian, West Asian/Middle Eastern, Pacific Islander, Latin American, White, Native American/Aboriginal/First Nations, other, unknown, or prefer not to answer. Physicians recorded race and ethnicity with the data available to them, which typically includes information in the electronic health record (EHR) on patient-reported race and ethnicity. In this study, race and ethnicity were categorized in mutually exclusive groups as either White (reference group), Black (African American), Hispanic (Latin American), or other/mixed race (including all other ethnic or racial groups). In a previous report using this data source, a chart review of a subsample of patients from 2 sites (n = 273;

and Harvard Medical School, Boston, Massachusetts; [12]Paul Sufka, MD: Healthpartners, St. Paul, Minnesota; [13]Rebecca Grainger, MBChB, BMedSci, PhD: University of Otago, Wellington, New Zealand; [14]Suleman Bhana, MD, FACR: Crystal Run Health, Middletown, New York; [15]Anja Strangfeld, MD, PhD: German Rheumatism Research Center, Berlin, Germany; [16]Elsa F. Mateus, PhD: Portuguese League Against Rheumatic Diseases, Lisbon, Portugal, and European League Against Rheumatism Standing Committee of People with Arthritis/Rheumatism in Europe, Kilchberg, Switzerland; [17]Kimme L. Hyrich, MD, PhD, Saskia Lawson-Tovey, BA: University of Manchester, National Institute of Health Research Manchester Biomedical Research Centre, Manchester University NHS Foundation Trust, and Manchester Academic Health Science Centre, Manchester, UK; [18]Laure Gossec, MD, PhD: Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique, and Pitié-Salpêtrière Hospital, AP-HP, Paris, France; [19]Loreto Carmona, MD, PhD: Instituto de Salud Musculoesquelética, Madrid, Spain; [20]Lianne Kearsley-Fleet, PhD: University of Manchester and Manchester Academic Health Science Centre, Manchester, UK; [21]Martin Schaefer, PhD: German Rheumatism Research Center, Berlin, Germany; [22]Pedro M. Machado, MD, PhD: University College London, National Institute for Health Research University College London Hospitals Biomedical Research Centre, University College London Hospitals NHS Foundation Trust, and Northwick Park Hospital, London North West University Healthcare NHS Trust, London, UK; [23]Philip C. Robinson, MBChB, PhD: University of Queensland School of Clinical Medicine, Herston, and Royal Brisbane and Women's Hospital, Metro North Hospital and Health Service, Queensland, Australia.

Author disclosures are available at https://onlinelibrary.wiley.com/action/downloadSupplement?doi=10.1002%2Facr.25039&file=acr25039-sup-0001-Disclosureform.pdf.

Address correspondence via email to Manuel F. Ugarte-Gil, MD, MSc, at mugarte@cientifica.edu.pe.

Submitted for publication April 4, 2022; accepted in revised form October 4, 2022.

approximately 21% of the total analytic sample) indicated 81% concordance between EHR- and registry-entered race and ethnicity. Misclassification largely occurred with Hispanic/Latino ethnicity being characterized as "other" in the patient's EHR. Therefore, the current registry data collection may potentially be more accurate than standard EHR-based assessment of race and ethnicity (1).

COVID-19 outcomes. We used an ordinal severity outcome in the analyses, with mutually exclusive categories, including not hospitalized, hospitalized with no oxygenation, hospitalized with any ventilation or oxygenation, or death. These outcomes were chosen so that the analyses could reflect the full spectrum of disease associated with COVID-19 and are analogous to outcome measures used in many trials evaluating COVID-19 therapeutics. Only the highest severity level of the outcome occurring during the patient's disease course was included, and all individuals were required to have a resolved clinical course, meaning that the ultimate outcome of their COVID-19 infection was recorded; if an individual was entered into the registry before the ultimate outcome, an update was requested in all cases.

Covariates, including medication exposure. Covariates included demographic characteristics (age and sex) as well as clinical characteristics: the number of comorbidities (lung, liver or neurologic diseases, cancer, diabetes mellitus, obesity, among others), specific comorbidities (chronic renal insufficiency or end stage renal disease and hypertension or cardiovascular disease), disease activity (assessed by a physician global assessment categorized as remission, low, moderate, or high), dose of glucocorticoids (entered as daily oral prednisone equivalents), and use of immunosuppressive or immunomodulating medications. Additionally, the date of the case report was examined in 3 time periods: from March 24, 2020 to June 15, 2020, from June 16, 2020 to September 30, 2020, and from October 1, 2020 to August 27, 2021. The first time period was before the publication of the RECOVERY trial, which changed COVID-19 treatment protocols to incorporate glucocorticoids (9). The second time period was between the publication of the RECOVERY trial and the beginning of the second wave in the US, and the third time period was between the beginning of the second wave and the last visit included in this analysis.

Medications taken by patients prior to COVID-19 were categorized as conventional synthetic drugs (antimalarials [hydroxychloroquine, chloroquine], conventional disease-modifying monotherapies generally considered to represent less intensive immunosuppression [sulfasalazine, methotrexate, and leflunomide], conventional disease-modifying monotherapies with more intense immunosuppressive drugs [mycophenolate mofetil (MMF), tacrolimus, cyclophosphamide, cyclosporine, azathioprine]); biologics (abatacept, belimumab, rituximab, interleukin [IL]-6 inhibitors, IL-17 inhibitors, tumor necrosis factor inhibitors, and targeted synthetic drugs, specifically JAK inhibitors); and glucocorticoids. In analyses, we divided medications into 5 groups: no SLE medications, antimalarials only, less intense conventional disease-modifying monotherapies (including sulfasalazine, methotrexate, and leflunomide), more intense conventional disease-modifying monotherapies (including MMF, tacrolimus, cyclophosphamide, cyclosporine, azathioprine), biologic/targeted synthetic drug monotherapy, and finally combination therapy with conventional and biologic disease-modifying immunosuppressive drugs. Glucocorticoids were categorized into 4 groups by dose: prednisone dose = 0 mg/day, >0 to 5 mg/day, >5 to <10 mg/day, and ≥10 mg/day. Vaccination status was reported in the registry starting in January 2021, which was approximately 1 month after Food and Drug Administration emergency use authorization for the first COVID-19 vaccine manufactured by Pfizer.

Statistical analysis. We used ordinal logistic regression with severity as the dependent variable and covariates as described below. This practice is similar to using binary logistic regression for each of the 3 possible dichotomizations of the 4-category dependent variable, with the assumption that the odds ratio (OR) is the same for each cutoff. The assumption for proportional odds was assessed by the test of parallel lines, which confirmed that this assumption was not violated and that the slope coefficients in the model were the same across response categories. We assumed that missing data were missing at random, and missing data were handled using multiple imputation, with 20 imputed data sets.

In the model, covariates included sex, age, time period (March 24, 2020 to June 15, 2020 [9], June 16, 2020 to September 30, 2020, and October 1, 2020 to August 27, 2021), comorbidities (including specific comorbidities [renal disease and hypertension/cardiovascular disease] and number of other comorbidities), disease activity (remission, low, moderate, and high), glucocorticoids as a categorical variable (0, 1–5, ≥6 mg/day) and the immunosuppressive medication category. The COVID-19 diagnosis date was also included as a continuous variable in the model as a random intercept. Time variables were included to capture the significant variability in recommended masking and other mitigation strategy regulations enforcing personal protective equipment, hospital resource allocation, and quarantine procedures over the course of the pandemic. A sensitivity analysis to evaluate the association with the binary outcome of hospitalization was done using a multivariable logistic regression model including the same confounders as in the analysis described above. To remove any impact of vaccination on COVID-19 outcomes, the same analyses were repeated excluding vaccinated individuals and those with missing vaccination status but who had a COVID-19 diagnosis date after November 30, 2020

Table 1. Characteristics of SLE patients at the time of COVID-19 diagnosis, up to August 27, 2021, by race and ethnicity*

Characteristics	Total (n = 469)†	White (n = 161)	Black (n = 126)	Hispanic (n = 154)	Other/mixed (n = 28)
Age, mean ± SD years	46.4 ± 13.7	50.4 ± 14.5	45.8 ± 13.1	43.2 ± 12.0	42.9 ± 15.2
Female	425 (90.6)	147 (91.3)	116 (92.1)	138 (89.6)	24 (85.7)
Date of COVID-19 diagnosis					
Prior to June 15, 2020	184 (39.2)	52 (32.3)	73 (57.9)	50 (32.5)	9 (32.1)
June 16 to Sept. 30, 2020	69 (14.7)	19 (11.8)	21 (16.7)	27 (17.5)	2 (7.1)
Oct. 1, 2020 to Aug. 27, 2021	216 (46.1)	90 (55.9)	32 (25.4)	77 (50.0)	17 (60.7)
Comorbidities					
0	208 (44.4)	81 (50.3)	48 (38.1)	67 (43.5)	12 (42.9)
1	159 (33.9)	55 (34.2	43 (34.1)	51 (33.1)	10 (35.7)
≥2	102 (21.8)	25 (15.5)	35 (27.8)	36 (23.4)	6 (21.4)
Specific comorbidities					
Chronic renal insufficiency or ESRD	64 (13.7)	10 (6.2)	20 (15.9)	25 (16.2)	9 (32.1)
Hypertension or cardiovascular disease	172 (36.7)	51 (31.7)	58 (46.0)	54 (35.1)	9 (32.1)
Disease activity					
Remission	97 (20.7)	38 (23.6)	22 (17.5)	31 (20.1)	6 (21.4)
Minimal or low	274 (58.4)	93 (57.8)	80 (63.5)	86 (55.8)	15 (53.6)
Moderate	71 (15.1)	19 (11.8)	16 (12.7)	30 (19.5)	6 (21.4)
Severe or high	10 (2.1)	3 (1.9)	5 (4.0)	2 (1.3)	0 (0.0)
Missing	17 (3.6)	8 (5.0)	3 (2.4)	5 (3.3)	1 (3.6)
Prednisone dose, mg/day‡					
0	284 (60.6)	114 (70.8)	79 (62.7)	76 (49.4)	15 (53.6)
1–5	102 (21.8)	19 (11.8)	26 (20.6)	50 (32.5)	7 (25.0)
≥6–9	74 (15.8)	24 (14.9)	21 (16.7)	23 (14.9)	6 (21.4)
Missing	9 (1.9)	4 (2.5)	0 (0.0)	5 (3.3)	0 (0.0)
Medication category					
Antimalarial monotherapy	152 (32.4)	69 (42.9)	35 (27.8)	42 (27.3)	6 (21.4)
No SLE therapy	49 (10.5)	16 (9.9)	11 (8.7)	19 (12.3)	3 (10.7)
Oral synthetic drug monotherapy with mycophenolate/ mycophenolic acid, tacrolimus, cyclophosphamide, cyclosporine, OR azathioprine§	29 (6.2)	13 (8.1)	8 (6.4)	5 (3.3)	3 (10.7)
Oral synthetic drug monotherapy with methotrexate, leflunomide, OR sulfasalazine only§	155 (33.1)	30 (18.6)	51 (40.5)	64 (41.6)	10 (35.7)
Biologic/targeted synthetic monotherapy	17 (3.6)	2 (1.2)	5 (4.0)	7 (4.6)	3 (10.7)
Biologic/targeted and immunosuppressive drug combination therapy§	67 (14.3)	31 (19.3)	16 (12.7)	17 (11.0)	3 (10.7)

* Values are the number (%), unless indicated otherwise. ESRD = end-stage renal disease; SLE = systemic lupus erythematosus.
† Data on outcome available.
‡ All glucocorticoids were converted to prednisone-equivalent doses.
§ These patients could also receive antimalarials.

(as the first emergency use authorization for a COVID-19 vaccine occurred on December 11, 2020).

Results were considered statistically significant using a 2-sided *P* value less than 0.05. Analyses were conducted in R software, version 4.0.2. Due to the de-identified and noninterventional nature of the study, the C19-GRA physician registry was defined as not human subjects research by the UCSF Institutional Review Board.

Table 2. COVID-19 outcomes as a function of race and ethnicity*

Outcome	Total (n = 469)	White (n = 161)	Black (n = 126)	Hispanic (n = 154)	Other/mixed (n = 28)
Not hospitalized	351 (74.8)	139 (86.3)	80 (63.5)	110 (71.4)	22 (71.0)
Hospitalized with no oxygenation	38 (8.1)	6 (3.7)	18 (14.3)	11 (7.1)	3 (10.7)
Hospitalized with any ventilation/oxygenation	62 (13.2)	11 (6.8)	22 (17.5)	27 (17.5)	2 (7.1)
Death	18 (3.8)	5 (3.1)	6 (4.8)	6 (3.9)	1 (3.6)

* Values are the number (%).

Table 3. Multivariable ordinal and binary regression analyses of the association between race/ethnicity and COVID-19 outcomes in US individuals with systemic lupus erythematosus*

	Ordinal outcome (n = 469)†		Hospitalization (n = 497)	
Race/ethnicity	OR (95% CI)	*P*	OR (95% CI)	*P*
White	Ref.	–	Ref.	–
Black	2.73 (1.36–5.53)	<0.01	2.15 (1.16–3.99)	0.02
Hispanic	2.76 (1.34–5.69)	<0.01	1.73 (0.94–3.16)	0.08
Other	1.13 (0.34–3.77)	0.85	1.22 (0.42–3.49)	0.71

* 95% CI = 95% confidence interval; OR = odds ratio; Ref. = reference.
† This model included 4 mutually independent outcomes: 1) not hospitalized, 2) hospitalized with no oxygenation, 3) hospitalized with any ventilation or oxygenation, or 4) death. Both models were adjusted by sex, age, region, time period, comorbidities (including specific comorbidities [renal disease and hypertension/cardiovascular disease] and number of other comorbidities), disease activity (remission, low, moderate, or high), glucocorticoids as a categorical variable (0, 1–5, ≥6 mg/day), and immunosuppressive medication category.

RESULTS

As of August 27, 2021, 536 individuals with SLE and COVID-19 in the US were entered into the registry. Of our 536 patients, 429 (80.0%) were documented as having COVID confirmed from polymerase chain reaction, 22 (4.1%) were confirmed by laboratory assay (type unknown), 16 (3.0%) were presumptive diagnosis based on symptoms only, 16 (3.0%) were from antibody tests, 2 (0.4%) were from metagenomic testing, and 51 (9.5%) were other/unknown. We excluded 13 individuals who did not have data on race and ethnicity, leaving a final cohort of 523 people. Data regarding final COVID-19 outcomes were available in 469 individuals; among them the mean ± SD age at diagnosis of COVID-19 was 46.4 ± 13.7 years, and 425 (90.6%) were female. Race and ethnicity were reported as 161 (34.3%) White, 126 (26.9%) Black, 154 (32.8%) Hispanic, and 28 (6.0%) other/mixed. Demographic and disease characteristics are shown in Table 1. Individuals included in the analyses were similar to the global population, and both groups are shown in Supplementary Table 1, available on the *Arthritis Care & Research* website at http://onlinelibrary.wiley.com/doi/10.1002/acr.25039. Data regarding final COVID-19 outcomes were available in 469 individuals and regarding hospitalization status in 497 individuals. Among those with outcomes, there were 351 individuals (74.8%) not hospitalized, 38 (8.1%) hospitalized with no oxygenation, 62 (13.2%) hospitalized with any ventilation or oxygenation, and 18 (3.8%) who died (Table 2). Black and Hispanic patients were more likely than White patients to be hospitalized without oxygen or hospitalized with any ventilation or oxygenation. Compared to other racial/ethnic groups, Black patients were more likely to die.

In the multivariable ordinal logistic regression model, Black race and Hispanic ethnicity were associated with increased odds of experiencing more severe outcomes (OR 2.73 [95% confidence interval (95% CI) 1.36–5.53] and OR 2.76 [95% CI 1.34–5.69], respectively) compared to patients who were White. In the binary logistic regression model with hospitalization as the outcome, Black patients had a higher odds of hospitalization (OR 2.15 [95% CI 1.16–3.99]) compared with White patients. Hispanic ethnicity had a higher odds of hospitalization (1.73 [95% CI 0.94–3.16]) compared to patients who were White. These models are shown in Table 3. Complete outputs from these models including odds ratios corresponding to covariates are provided in Supplementary Tables 2 and 3, available on the *Arthritis Care & Research* website at http://onlinelibrary.wiley.com/doi/10.1002/acr.25039.

We were not able to evaluate the impact of vaccination on the outcome of these individuals, as most cases occurred prior

Table 4. Sensitivity analysis excluding patients who were vaccinated or who had unknown vaccination status once vaccines became available (November 30, 2020)*

	Ordinal outcome (n = 380)†		Hospitalization (n = 380)	
Race/ethnicity	OR (95% CI)	*P*	OR (95% CI)	*P*
White	Ref.	–	Ref.	–
African American	2.74 (1.31–5.74)	<0.01	3.35 (1.57–7.16)	0.02
Hispanic	2.54 (1.18–5.47)	0.02	2.57 (1.18–5.57)	0.02
Other	1.64 (0.45–5.97)	0.75	2.24 (0.58–8.68)	0.24

* 95% CI = 95% confidence interval; OR = odds ratio; Ref. = reference.
† This model included 4 mutually independent outcomes: 1) not hospitalized, 2) hospitalized with no oxygenation, 3) hospitalized with any ventilation or oxygenation, or 4) death. Both models were adjusted by sex, age, region, time period, comorbidities (including specific comorbidities [renal disease and hypertension/cardiovascular disease] and number of other comorbidities), disease activity (remission, low, moderate, or high), glucocorticoids as a categorical variable (0, 1–5, ≥6 mg/day), and immunosuppressive medication category.

to vaccine availability (142 individuals had a diagnosis date after November 30, 2020, and of those, vaccination was reported in 68 cases). These data are shown in Supplementary Table 4, available on the *Arthritis Care & Research* website at http://onlinelibrary.wiley.com/doi/10.1002/acr.25039.

In the subanalyses excluding vaccinated patients as well as those with missing vaccination status who had a diagnosis date after November 30, 2020, the results were very similar; individuals with Black race and Hispanic ethnicity had a higher odds of experiencing more severe outcomes (OR 2.75 [1.31–5.74] and OR 2.54 [1.18–5.4], respectively) compared to patients who were White, and Black and Hispanic patients also had a higher odds of hospitalization (OR 3.36 [1.56–7.16] and OR 2.57 [1.18–5.57], respectively). These models are shown in Table 4.

DISCUSSION

To our knowledge, this is the first study to examine racial and ethnic differences in COVID-19 outcomes among individuals with SLE in the US. White populations tended to be older than individuals in the other groups, had a lower number of comorbidities, used prednisone less frequently, and more frequently used antimalarial monotherapy, biologics, and immunosuppressive drug combination therapy; nevertheless, Black and Hispanic individuals experienced poorer outcomes compared to White individuals, even after adjustment for demographic and disease-specific features and comorbidities. In the US, in an analysis using COVID-19 mortality data for the entire 2020 calendar year provided by the US Centers for Disease Control and Prevention (CDC) in the 50 states and the District of Columbia, cumulative mortality rates per 100,000 population adjusted for age were 116.4 for the White population, 265.2 for the Hispanic or Latin population, and 237.9 for the Black population (10). Furthermore, in an analysis including the 50 states and the District of Columbia, the CDC evaluated the incidence of COVID-19 at a county level in three 2-week periods (April 1–14, 2020, August 5–18, 2020, and December 9–22, 2020), taking into consideration the percentage of the county population from each racial and ethnic minority group.

In the first period, high COVID-19 incidence was reported in 11.4% of the counties (27.9% and 12.5% of counties with large Black and Hispanic populations), in the second period, high COVID-19 incidence was reported in 64.7% of the counties (92.4% and 74.5% of counties with large Black and Hispanic populations), and in the third period, 99.1% of the counties reported high COVID-19 incidence, including >95% of counties with large populations of each racial and ethnic minority group (11). These data suggest significant disparities in disease prevalence for COVID-19. Although our study was not designed to examine differences in COVID-19 prevalence among different racial and ethnic groups, our work adds to the literature suggesting significant disparities in this disease outcome.

Since the beginning of the pandemic, a higher COVID-19 death rate has been reported in those US counties having greater income inequality, a higher prevalence of poverty, more household crowding, and a higher proportion of non-White individuals (12,13). These differences are explained, at least in part, due to the lack of access to adequate health care; for example, according to the New York City zip code tabulation areas, those areas with a high proportion of Black and Hispanic individuals had fewer licensed health facilities and intensive care unit (ICU) beds (14). In addition, individuals living in these areas are overrepresented in all essential service industries, including home health aides, nursing home staff, hospital janitorial services, and food services, among other sectors. The common denominator for these services is that they must be done in person, increasing the possible exposure to COVID-19 infection. Individuals of lower socioeconomic status are also more likely to live in crowded settings, limiting their ability to prevent household exposure to infected individuals (15). When each wave was evaluated independently, the differences between Black, Hispanic, and White individuals was more evident during the first wave of the pandemic than afterward, reflecting, perhaps, the impact of health policy changes and of immunity acquired through earlier infection (16). Similarly, in the UK, racial and ethnic minorities were more likely to be hospitalized, to be admitted to an ICU, and to die of COVID-19 (17). Taken together, these data support the negative impact of structural inequities, including racism, on health outcomes (18).

In SLE, Black and Hispanic populations have been found to have poorer outcomes, including higher disease activity, damage, and mortality, than White populations. This finding may be explained by gene-environment interactions between lupus-related (single-nucleotide polymorphisms, loci) (19,20) and social determinants of health (3). Among the socioeconomic factors, poverty, educational level, lack of health insurance, poor social support, and lower treatment adherence are associated with poorer outcomes, including higher disease activity, progression of lupus nephritis, damage accrual, and mortality (21). In addition, COVID-19 outcomes are associated with the presence of comorbidities, disease activity, and prednisone use (6), all of which are more common or severe in Black and Hispanic individuals.

Due to the low number of vaccinated individuals, we were not able to evaluate the impact of vaccination in COVID-19 outcomes, but based on previous reports (21–23), we would expect that vaccinated individuals with autoimmune diseases (in particular SLE) will do better than unvaccinated individuals. Nevertheless, in those individuals with a higher risk of poor outcomes (older individuals, those using a glucocorticoid dose ≥10 mg/day, and rituximab use, among others), alternative mitigation strategies like prophylaxis pre- and post-exposure or shielding practices are needed. Although the analysis of vaccinated individuals suggests that a possible association may exist between race and ethnicity and outcomes, independent of vaccination status,

no definitive conclusions can be drawn, since very few people were vaccinated.

This study has some limitations. First, the C19-GRA is a physician-reported registry and thus could have been skewed to include more severe COVID-19 cases that were more likely to come to medical attention; additionally, other forms of selection biases such as the exclusion of patients who face barriers to health care access and survival bias are likely to be present. Second, even though we were able to include several potential confounders, we could not include factors such as access to health care, poverty, or other social determinants of health that likely underlie the relationship between race and ethnicity and COVID-19 outcomes. Third, as we have included only people in the US, we cannot assume that these findings are generalizable to other countries; however, by performing this analysis in a single country, we were able to reduce the impact of other factors (like the country's gross-domestic product) on the examined associations. Fourth, race and ethnicity were categorized by the entering physician, which may not have been consistent with the individual's self-reported identity. Fifth, missing data on COVID-19 outcomes in 54 patients possibly would have had some impact on our results; however, as the characteristics of the entire population and those with missing outcomes data are very similar, this limitation is not expected to significantly skew our results. Sixth, due to the small numbers for some variables, the study maybe underpowered to identify significant associations between less frequent characteristics. Finally, due to the number of individuals for whom vaccination status was reported, we were unable to evaluate the impact of vaccination on outcomes.

In conclusion, Black race and Hispanic ethnicity were associated with more severe COVID-19 outcomes among SLE patients entered in the COVID-19 GRA registry. These results likely reflect health disparities that are at least in part mediated by social determinants of health. Achieving equitable health outcomes for socially disadvantaged SLE populations is likely to require the implementation of public health measures that directly address social disparities and mitigate social disadvantage.

ACKNOWLEDGMENT

The authors thank all rheumatology providers who entered data into the registry.

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 submitted for publication. Dr. Ugarte-Gil 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. Ugarte-Gil, Alarcón, Seet, Izadi, Montgomery, Gianfrancesco, Yazdany.

Acquisition of data. Ugarte-Gil, Seet, Izadi, Montgomery, Duarte-García, Gilbert, Valenzuela-Almada, Wise, Sparks, Hsu, D'Silva, Patel, Sirotich, Liew, Hausmann, Sufka, Grainger, Bhana, Wallace, Jacobsohn, Strangfeld, Mateus, Hyrich, Gossec, Carmona, Lawson-Tovey, Kearsley-Fleet, Schaefer, Machado, Robinson, Gianfrancesco, Yazdany.

Analysis and interpretation of data. Ugarte-Gil, Alarcón, Seet, Izadi, Montgomery, Duarte-García, Gilbert, Valenzuela-Almada, Wise, Sparks, Hsu, D'Silva, Patel, Sirotich, Liew, Hausmann, Sufka, Grainger, Bhana, Wallace, Jacobsohn, Strangfeld, Mateus, Hyrich, Gossec, Carmona, Lawson-Tovey, Kearsley-Fleet, Schaefer, Machado, Robinson, Gianfrancesco, Yazdany.

REFERENCES

1. Gianfrancesco MA, Leykina LA, Izadi Z, et al. Association of race and ethnicity with COVID-19 outcomes in rheumatic disease: data from the COVID-19 Global Rheumatology Alliance Physician Registry. Arthritis Rheumatol 2021;73:374–80.
2. Mackey K, Ayers CK, Kondo KK, et al. Racial and ethnic disparities in COVID-19-related infections, hospitalizations, and deaths: a systematic review. Ann Intern Med 2021;174:362–73.
3. Gonzalez LA, Pons-Estel GJ, Toloza SMA, et al. Understanding risk factors for poor outcomes in a multiethnic longitudinal cohort: the LUMINA (Lupus in Minorities: Nature vs. Nurture) Experience (LUMINA LXXXII). Rheum Dis Clin North Am 2021;47:55–64.
4. Pons-Estel GJ, Ugarte-Gil MF, Alarcon GS. Epidemiology of systemic lupus erythematosus. Expert Rev Clin Immunol 2017;13:799–814.
5. Maningding E, Dall'Era M, Trupin L, et al. Racial and ethnic differences in the prevalence and time to onset of manifestations of systemic lupus erythematosus: the California Lupus Surveillance Project. Arthritis Care Res (Hoboken) 2020;72:622–9.
6. Ugarte-Gil MF, Alarcon GS, Izadi Z, et al. Characteristics associated with poor COVID-19 outcomes in individuals with systemic lupus erythematosus: data from the COVID-19 Global Rheumatology Alliance. Ann Rheum Dis 2022;81:970–8.
7. Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap): a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009;42:377–81.
8. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: building an international community of software platform partners. J Biomed Inform 2019;95:103208.
9. Recovery Collaborative Group, Horby P, Lim WS, et al. Dexamethasone in hospitalized patients with Covid-19. N Engl J Med 2021;384:693–704.
10. Feldman JM, Bassett MT. Variation in COVID-19 mortality in the US by race and ethnicity and educational attainment. JAMA Netw Open 2021;4:e2135967.
11. Lee FC, Adams L, Graves SJ, et al. Counties with high COVID-19 incidence and relatively large racial and ethnic minority populations: United States, April 1-December 22, 2020. MMWR Morb Mortal Wkly Rep 2021;70:483–9.
12. Chen JT, Krieger N. Revealing the unequal burden of COVID-19 by income, race/ethnicity, and household crowding: US county versus zip code analyses. J Public Health Manag Pract 2021;27 Suppl 1, COVID-19.
13. Tan AX, Hinman JA, Abdel Magid HS, et al. Association between income inequality and county-level COVID-19 cases and deaths in the US. JAMA Netw Open 2021;4:e218799.
14. Douglas JA, Subica AM. COVID-19 treatment resource disparities and social disadvantage in New York City. Prev Med 2020;141:106282.
15. Poteat T, Millett GA, Nelson LE, et al. Understanding COVID-19 risks and vulnerabilities among black communities in America: the lethal force of syndemics. Ann Epidemiol 2020;47:1–3.

16. Howland RE, Wang S, Ellen IG, et al. Not a new story: place- and race-based disparities in COVID-19 and influenza hospitalizations among Medicaid-insured adults in New York City. J Urban Health 2022;99:345–8.
17. Mathur R, Rentsch CT, Morton CE, et al. Ethnic differences in SARS-CoV-2 infection and COVID-19-related hospitalisation, intensive care unit admission, and death in 17 million adults in England: an observational cohort study using the OpenSAFELY platform. Lancet 2021; 397:1711–24.
18. Bailey ZD, Feldman JM, Bassett MT. How structural racism works: racist policies as a root cause of U.S. racial health inequities. N Engl J Med 2021;384:768–73.
19. Sanchez E, Nadig A, Richardson BC, et al. Phenotypic associations of genetic susceptibility loci in systemic lupus erythematosus. Ann Rheum Dis 2011;70:1752–7.
20. Carter EE, Barr SG, Clarke AE. The global burden of SLE: prevalence, health disparities and socioeconomic impact. Nat Rev Rheumatol 2016;12:605–20.
21. Fragoulis GE, Karamanakos A, Arida A, et al. Clinical outcomes of breakthrough COVID-19 after booster vaccination in patients with systemic rheumatic diseases. RMD Open 2022;8:e002279.
22. Cook C, Patel NJ, D'Silva KM, et al. Clinical characteristics and outcomes of COVID-19 breakthrough infections among vaccinated patients with systemic autoimmune rheumatic diseases. Ann Rheum Dis 2022;81:289–91.
23. Lawson-Tovey S, Hyrich KL, Gossec L, et al. SARS-CoV-2 infection after vaccination in patients with inflammatory rheumatic and musculoskeletal diseases. Ann Rheum Dis 2022;81: 145–50.