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Characteristics, Comorbidities, and Outcomes in a Multicenter Registry of Patients With Human Immunodeficiency Virus and Coronavirus Disease 2019

Dima Dandachi,[1] Grant Geiger,[2] Mary W. Montgomery,[3] Savannah Karmen-Tuohy,[4] Mojgan Golzy,[5] Annukka A. R. Antar,[6] Josep M. Llibre,[7] Maraya Camazine,[2] Alberto Díaz-De Santiago,[8] Philip M. Carlucci,[4] Ioannis M. Zacharioudakis,[9] Joseph Rahimian,[9] Celestine N. Wanjalla,[10] Jihad Slim,[11] Folasade Arinze,[12] Ann Marie Porreca Kratz,[13] Joyce L Jones,[6] Shital M. Patel,[14] Ellen Kitchell,[15] Adero Francis,[12] Manoj Ray,[16] David E. Koren,[17] John W. Baddley,[18] Brannon Hill,[19] Paul E. Sax,[3] and Jeremy Chow[15]; the Human Immunodeficiency Virus–Coronavirus Disease 2019 (HIV–COVID-19) Consortium

[1]Division of Infectious Diseases, University of Missouri-Columbia, Columbia, Missouri, USA, [2]School of Medicine, University of Missouri-Columbia, Columbia, Missouri, USA, [3]Department of Infectious Diseases, Brigham and Women's Hospital, Boston, Massachusetts, USA, [4]School of Medicine, New York University Grossman School of Medicine, New York, New York, USA, [5]Department of Health Management and Informatics, University of Missouri-Columbia, Columbia, Missouri, USA, [6]Division of Infectious Diseases, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA, [7]Infectious Diseases and Fight AIDS Foundation, University Hospital Germans Trias, Badalona, Spain, [8]Internal Medicine Department, Human Immunodeficiency Virus (HIV) Infection Unit, Puerta de Hierro Majadahonda University Hospital, Madrid, Spain, [9]Division of Infectious Diseases and Immunology, New York University Grossman School of Medicine, New York, New York, USA, [10]Division of Infectious Diseases, Vanderbilt University Medical Center, Nashville, Tennessee, USA, [11]Division of Infectious Diseases, Saint Michael's Medical Center, Newark, New Jersey, USA, [12]Department of Internal Medicine, Wellstar Health System, Atlanta, Georgia, USA, [13]Department of Pharmacy, Tower Health, West Reading, Pennsylvania, USA, [14]Section of Infectious Diseases, Medicine, Baylor College of Medicine, Houston, Texas, USA, [15]Division of Infectious Diseases, University of Texas Southwestern Medical Center, Dallas, Texas, USA, [16]Division of Infectious Diseases, Santa Clara Valley Health and Hospital System, San Jose, California, USA, [17]Department of Pharmacy, Temple University Health System, Philadelphia, Pennsylvania, USA, [18]Division of Infectious Disease, University of Maryland, Baltimore, Maryland, USA, and [19]Department of Pharmacy, University of Arkansas for Medical Sciences, Little Rock, Arkansas, USA

Background. People living with human immunodeficiency virus (HIV) may have numerous risk factors for acquiring coronavirus disease 2019 (COVID-19) and developing severe outcomes, but current data are conflicting.

Methods. Health-care providers enrolled consecutively, by nonrandom sampling, people living with HIV (PWH) with lab-confirmed COVID-19, diagnosed at their facilities between 1 April and 1 July 2020. Deidentified data were entered into an electronic Research Electronic Data Capture (REDCap) system. The primary endpoint was a severe outcome, defined as a composite endpoint of intensive care unit (ICU) admission, mechanical ventilation, or death. The secondary outcome was the need for hospitalization.

Results. There were 286 patients included; the mean age was 51.4 years (standard deviation, 14.4), 25.9% were female, and 75.4% were African American or Hispanic. Most patients (94.3%) were on antiretroviral therapy, 88.7% had HIV virologic suppression, and 80.8% had comorbidities. Within 30 days of testing positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), 164 (57.3%) patients were hospitalized, and 47 (16.5%) required ICU admission. Mortality rates were 9.4% (27/286) overall, 16.5% (27/164) among those hospitalized, and 51.5% (24/47) among those admitted to an ICU. The primary composite endpoint occurred in 17.5% (50/286) of all patients and 30.5% (50/164) of hospitalized patients. Older age, chronic lung disease, and hypertension were associated with severe outcomes. A lower CD4 count (<200 cells/mm^3) was associated with the primary and secondary endpoints. There were no associations between the ART regimen or lack of viral suppression and the predefined outcomes.

Conclusions. Severe clinical outcomes occurred commonly in PWH with COVID-19. The risks for poor outcomes were higher in those with comorbidities and lower CD4 cell counts, despite HIV viral suppression.

Clinical Trials Registration. NCT04333953.

Keywords: HIV; COVID-19; SARS-CoV-2; AIDS.

The patients with severe coronavirus disease 2019 (COVID-19) who require hospital admission are more likely to be older, male, and have underlying comorbidities [1–3]. Additionally, immunocompromising conditions, such as malignancy and solid organ transplantation, may increase patients' risks for severe COVID-19 and death [4–8]. Data are conflicting regarding whether people with human immunodeficiency virus (HIV) are also at increased risk.

People living with HIV (PWH) may have numerous factors that could increase their risk of exposure to and acquisition of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). First, PWH are aging and have high rates of smoking, chronic cardiovascular and lung disease, and obesity [9]. In addition, racial and ethnic minorities are disproportionately affected by both HIV and COVID-19. Ongoing research aims to

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Correspondence: D. Dandachi, Assistant Professor of Medicine, Medical Director of the HIV/AIDS Program, University of Missouri Health Care, Division of Infectious Diseases, Department of Medicine, University of Missouri-Columbia, 1 Hospital Drive, Columbia, MO, 65212 (dandachid@health.missouri.edu).

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determine the impact of structural racism in COVID-19 outcomes. While the causes of health disparities are multifaceted, lack of access to health care, differences in socioeconomic factors, and prevalences of chronic diseases are potential contributors [10, 11].

Several case series have described clinical characteristics of PWH and patients with COVID-19. Many have been limited to single-center studies or hospitalized patients, or included patients with suspected but not confirmed COVID-19. Most were also limited by small numbers of patients or lacked important HIV-specific variables, such as CD4 cell counts, antiretroviral therapy (ART) history, and plasma HIV viral load [12–15]. Some of these studies reported that PWH with COVID-19 had similar clinical characteristics and comparable risks of severe disease to the general population [16–21]. However, other studies found higher rates of SARS-CoV-2 infection and worse outcomes among PWH [22–24].

Because current data are conflicting and limited, further investigation in HIV and COVID-19 is warranted. We aim to describe the clinical characteristics and outcomes of COVID-19 in PWH and to characterize those PWH at the highest risk for severe COVID-19–associated outcomes using an extensive, multicenter registry.

METHODS

The COVID-19 in PWH Registry was sponsored by the University of Missouri, Columbia. The study was reviewed by the University of Missouri Institutional Review Board and considered to be exempt. Anonymized patient data were collected without the need for informed consent.

Study Design

This multicenter registry was for PWH who had COVID-19 and received care between 1 April and 1 July 2020. The study was listed on ClinicalTrials.gov (NCT04333953) and the Infectious Diseases Society of America (IDSA) website and was open to enrollment in the United States and internationally. The registry was promoted in the IDSA and HIV Medical Association discussion forums, and invitation emails were sent to Infectious Disease departments and HIV clinics across the United States.

Patients aged 18 years and older with a known diagnosis of HIV and laboratory-confirmed COVID-19 in both inpatient and outpatient settings were eligible for study inclusion.

Health-care providers collected study data by chart review of PWH with COVID-19 diagnosed at their facilities, and entered anonymous information into a secure, electronic Research Electronic Data Capture (REDCap) system [25, 26]. Patients were enrolled consecutively by nonrandom sampling. Study variables included patient demographics, HIV-associated variables, underlying medical problems, COVID-19 clinical presentation as reported by patients, laboratory values, treatment, and clinical outcomes.

Providers certified that the information submitted was accurate to the best of their knowledge. The data were cross-validated by 2 reviewers for duplicity by age, gender, race, location, and HIV-1 RNA (viral load).

Study Definitions

Laboratory-confirmed COVID-19 was defined as positive reverse-transcriptase polymerase chain reaction (RT-PCR) in respiratory samples or serum SARS-CoV-2–specific immunoglobin G or M.

The US geographical region of residence was based on the Centers for Disease and Prevention's National HIV Surveillance System region distribution [27].

Chronic lung disease included asthma and chronic obstructive pulmonary disease. Cardiovascular disease included coronary artery disease and congestive heart failure. Chronic liver disease included cirrhosis, chronic hepatitis B, and chronic untreated hepatitis C. Active malignancy excluded nonmelanoma skin cancer. We defined obesity as a body mass index ≥30 [28]. We defined virologic suppression as HIV-1 RNA (viral load) <200 copies/mL [29]. We collected the most recent HIV viral load measured before or at the time of COVID-19 presentation. ART categorizations were mutually exclusive.

Study Outcomes

The primary endpoint was the prevalence of severe clinical outcomes, defined as a composite endpoint of ICU admission, use of mechanical ventilation, or death [1]. Outcomes for survival analyses were the time from a positive SARS-CoV-2 test to ICU admission or death. The secondary outcome of interest was hospitalization.

Statistical Analysis

We used descriptive statistics to summarize patient data. For categorical variables, we used frequency and calculated proportions using the number of patients with data available as the denominator. For continuous variables, we used the mean with the standard deviation (SD) or the median with the interquartile range (IQR).

We analyzed the association between baseline variables with the defined outcomes by univariate analysis, using the chi-square test, Fisher's exact test, or *t*-test, as indicated. A multivariable logistic regression model was used to assess the association between each outcome of interest, severe outcome and hospitalization, and independent variables. To obtain the parsimonious model for each multivariable analysis, we identified the significant independent variables using the backward selection method. Variables with a *P* value ≤ .2 were included in the model, in addition to clinically relevant variables. To adjust for within-region differences, we fitted a generalized estimating

equation logistic regression model, assuming an exchangeable correlation structure and regions as clusters, for each outcome.

To test whether there were differential effects of CD4 count on ICU-free survival and overall survival, we used the Kaplan-Meier method to analyze survival outcomes and log-rank statistics to compare the survival distributions of the CD4 groups (<200, 200–500, and >500 cells/mm^3) with respect to the time from a positive SARS-CoV-2 test to ICU admission or death.

In a post hoc subanalysis, we included patients from the United States to examine the clinical presentation and study outcomes, excluding international locations.

User-defined missing values were treated as missing and not imputed. All tests were 2-sided, with a level of significance defined as ≤0.05. SAS software was used for the statistical analysis of data.

RESULTS

Between 1 April and 1 July 2020, we identified 286 unique PWH and laboratory-confirmed COVID-19 cases. The data included cases from 36 institutions across 21 states and 3 international locations; 5 duplicate cases were removed.

Demographics and Baseline Characteristics

The mean age was 51.4 years (SD, 14.4), 74 (25.9%) patients were female, 133 (47.5%) were African American, and 78 (27.9%) were Hispanic. The greatest percentage of patients in the United States was from the South (47.0%), followed by the Northeast (35.4%), Midwest (5.3%), and West (4.9%); 7.4% were from international locations. Most patients (77.9%; 180/231) had been living with HIV for more than 5 years, had achieved virologic suppression (88.7%; 235/265), and were on ART at the time of their COVID-19 diagnosis (94.3%; 263/279). The mean CD4 count was 531 cells/mm^3 (SD, 340). The most common ART regimen was an integrase inhibitor with 2 nucleoside reverse transcriptase inhibitors (61.3%; 171/279). Hypertension (46.5%), obesity (32.3%), and diabetes (21.3%) were the most common underlying medical problems. When stratified by hospitalization status, older age, lower CD4 counts, the number of years living with HIV, not being on ART or virally suppressed, and a high comorbidity burden were associated with higher hospitalization rates (Table 1).

SARS-CoV-2 Diagnosis and Clinical Presentation

A SARS-CoV-2 RT-PCR test was used to diagnose all but 1 patient, who was diagnosed based on serologic testing. The most frequently reported symptoms within 72 hours of diagnostic testing were cough (76.2%; 205/269), fever (70.7%; 198/280), and fatigue (66.0%; 140/212). PWH hospitalized with COVID-19 were significantly more likely to have fever, fatigue, dyspnea, gastrointestinal symptoms, and altered mental status. In contrast, PWH who were not hospitalized were more likely to have upper respiratory symptoms, such as sore throat and nasal congestion, and headache. At presentation, all patients with a peripheral oxygen saturation of <94% on room air (30.6%; 72/235) and a Quick Sequential Organ Failure Assessment (q-SOFA) score of ≥2 (8.3%;17/206) were hospitalized. Chest X-rays were obtained in 194 (67.8%) patients, of whom 77.8% had abnormal findings; computerized tomography scans were performed for 44 (15.4%) patients, of whom 86.4% had abnormal findings. Patients who were hospitalized were more likely to have imaging done and to have abnormal findings (Table 2).

Treatment and Clinical Course

Within 30 days of testing positive for SARS-CoV-2, 164 (57.3%) patients were hospitalized. Among hospitalized PWH, potential SARS-CoV-2 targeted treatments, excluding placebo-controlled clinical trials, were given to 99 (60.4%) patients, with the most common medication being hydroxychloroquine (40.9%; Tables 3 and 4).

There were 47 (28.7%) patients who required ICU admission, with a median time of 2.0 days (IQR, 0–9.0) from the time of testing to admission; 35 (21.3%) patients who required vasopressors; 37 (22.6%) patients who required invasive mechanical ventilation; and 27 (16.5%) patients who died, with a median time of 16 days (IQR, 8–24) from the time of testing to death. When stratified by age groups (<40, 40–60, and >60 years), the relative risk for all poor outcomes was more than 1 for older age groups when compared to those less than 40 years old. Patients who were older than 60 years were significantly more likely to require respiratory support, develop acute kidney injury, and die, compared to patients who were less than 40 years old (Tables 3 and 4).

Study Outcomes

A multivariable analysis identified higher age, lower CD4 counts, chronic kidney disease, and chronic lung disease as independent predictors of hospitalization. PHW with 3 or more comorbidities, compared to those living with HIV only, were also more likely to be hospitalized (Table 5).

Severe clinical outcomes occurred in 17.5% (50/286) of all patients and 30.5% (50/164) of hospitalized patients. When comparing patients who experienced severe outcomes to those who did not, there were statistically significant differences in age (median age 59.3 in severe outcome group vs 49.7 without; $P < .01$), CD4 count (severe outcomes seen in 25.5% of patients with CD4 count <200cells/mm^3 vs 13.1% in patients >500cells/mm^3; P = .02), hypertension (72.0% vs 41.1%; $P< .01$), diabetes (32.0% vs 19.1%; $P = .04$), chronic lung disease (32.0% vs 14.0%; $P < .01$), and chronic kidney disease (30.0% vs 14.0%; $P < .01$). We further evaluated these associations with univariate and multivariate analysis. In univariate analysis, statistically significant associations with severe outcomes were seen with older age, lower CD4 count, hypertension, diabetes, chronic lung

Table 1. Patient Demographics and Baseline Characteristics

Variables	n (%)	Nonhospitalized	Hospitalized	*P* value
Mean age, years, n = 286	51.4 (SD 14.4)	45.4 (SD 12.7)	55.8 (SD 14.0)	<.01
Age in years	…	…	…	<.01
<40	66 (23.1%)	42 (34.4%)	24 (14.6%)	
40–60	146 (51.0%)	64 (52.5%)	82 (50.0%)	
>60	74 (25.9%)	16 (13.1%)	58 (35.4%)	
Sex, n = 286	…	…	…	.23
Female	74 (25.9%)	36 (29.5%)	38 (23.2%)	
Male	212 (74.1%)	86 (70.5%)	126 (76.8%)	
Race/ethnicity, n = 280	…	…	…	.89
African American	133 (47.5%)	59 (49.2%)	74 (46.3%)	
Hispanic	78 (27.9%)	32 (26.7%)	46 (28.8%)	
White	48 (17.1%)	19 (15.8%)	29 (18.1%)	
Asian/other	21 (7.5%)	10 (8.3%)	11 (6.9%)	
Years with HIV, n = 231	…	…	…	<.01
<1 year	14 (6.1%)	5 (4.6%)	9 (7.3%)	
1–5 years	37 (16.0%)	26 (24.1%)	11 (8.9%)	
>5 years	180 (77.9%)	77 (71.3%)	103 (83.7%)	
CD4 count, n = 268	…	…	…	<.01
<200 cells/mm^3	41 (15.3%)	5 (4.5%)	36 (23.1%)	
200–500 cells/mm^3	98 (36.6%)	33 (29.5%)	65 (41.7%)	
>500 cells/mm^3	129 (48.1%)	74 (66.1%)	55 (35.3%)	
Viral load suppression,[a] n = 265	235 (88.7%)	107 (93.9%)	128 (84.8%)	.02
Antiretroviral therapy, n = 279	…	…	…	.04
INI + 2 NRTI	171 (61.3%)	85 (70.8%)	86 (54.1%)	
NNRTI + 2 NRTI	20 (7.2%)	8 (6.7%)	12 (7.5%)	
PI + 2 NRTI	20 (7.2%)	9 (7.5%)	11 (6.9%)	
Dual ART regimen	22 (7.9%)	7 (5.8%)	15 (9.4%)	
Other	30 (10.8%)	8 (6.7%)	22 (13.8%)	
Not on ART	16 (5.7%)	3 (2.5%)	13 (8.2%)	
Underlying medical problems, n = 286				
Hypertension	133 (46.5%)	43 (35.2%)	90 (54.9%)	<.01
Diabetes	61 (21.3%)	19 (15.6%)	42 (25.6%)	.04
Chronic lung disease[b]	49 (17.1%)	11 (9.0%)	38 (23.2%)	<.01
Chronic kidney disease[c]	48 (16.8%)	9 (7.4%)	39 (23.8%)	<.01
Cardiovascular disease[d]	30 (10.5%)	5 (4.1%)	25 (15.2%)	<.01
Chronic liver disease[e]	28 (9.8%)	10 (8.2%)	18 (11.0%)	.43
Active malignancy[f]	13 (4.5%)	2 (1.6%)	11 (6.7%)	.04
Obesity: BMI ≥30, n = 257	83 (32.3%)	37 (34.3%)	46 (30.9%)	.57
Comorbidity burden, n = 286	…	…	…	<.01
HIV disease with no other known comorbidity	41 (14.3%)	24 (19.7%)	17 (10.4%)	
HIV with 1 or 2 comorbidities	168 (58.7%)	82 (67.2%)	86 (52.4%)	
HIV with 3 or more comorbidities	77 (26.9%)	16 (13.1%)	61 (37.2%)	
Smoking history,[g] n = 275	105 (38.2%)	38 (31.9%)	67 (42.9%)	.06

Data are stratified by hospitalization (n = 286).

Abbreviations: ART, antiretroviral therapy; BMI, body mass index; COPD, chronic obstructive pulmonary diseases; HIV, human immunodeficiency virus; INI, integrase inhibitor; NNRTI, nonnucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; SD, standard deviation.

[a]Virologic suppression defined as HIV RNA <200 copies/mL.

[b]Chronic lung disease including asthma and COPD.

[c]Chronic kidney disease includes end-stage renal disease.

[d]Cardiovascular disease includes coronary artery disease and congestive heart failure.

[e]Chronic liver disease includes cirrhosis, chronic hepatitis B, and chronic untreated hepatitis C.

[f]Active malignancy excludes nonmelanoma skin cancer.

[g]Current or former smokers.

disease, and chronic kidney disease. In a multivariable analysis, older age, a lower CD4 count, chronic lung disease, hypertension, and a high comorbidity burden were significantly associated with severe outcomes (Table 5).

Survival Analysis of Time from Test to ICU Admission and Death

Based on 47 patients admitted to an ICU and 27 deceased patients, CD4 cell count had a significant effect on survival. The pairwise comparison showed significant differences between

Table 2. Clinical Presentation and Characteristics Within 72 Hours of Severe Acute Respiratory Syndrome Coronavirus 2 Testing

	Nonhospitalized	Hospitalized	*P* value
Symptoms			
Cough, n = 269	87 (73.7%)	118 (78.1%)	.40
Fever, chills, n = 279	75 (64.1%)	123 (75.9%)	.03
Fatigue, n = 212	53 (55.2%)	87 (75.0%)	<.01
Myalgia, arthralgia, n = 229	51 (49.5%)	77 (61.1%)	.08
Dyspnea, n = 267	33 (29.5%)	113 (72.9%)	<.01
Headache, n = 219	40 (40.4%)	29 (24.2%)	.01
Sore throat, n = 216	35 (34.0%)	21 (18.6%)	.01
Nausea, vomiting, n = 24	20 (20.6%)	47 (32.9%)	.04
Diarrhea, n = 245	12 (12.2%)	51 (34.7%)	<.01
Chest pain, n = 242	20 (19.8%)	34 (24.1%)	.43
Nasal congestion, n = 205	23 (24.7%)	14 (12.5%)	.02
Anosmia, ageusia, or dysgeusia, reported as other symptoms, n = 286	12 (9.8%)	11 (6.7%)	.54
Altered mental status, n = 272	0 (0%)	21 (13.4%)	<.01
Initial laboratory values, median (IQR)			
White blood cell count, 10^9/L, n = 204	5.6 (4.2–7.0)	6.4 (4.8–8.5)	.03
Neutrophil percentage, n = 201	57.0 (46.5–72.5)	69.9 (59.7–79.0)	<.01
Lymphocyte count, 10^9/L, n = 201	30.0 (17.7–41.9)	19.0 (12.0–28.1)	<.01
Creatinine, mg/dL, n = 201	1.0 (.8–1.3)	1.1 (.9–1.5)	.20
Alanine aminotransferase, units/L, n = 195	23.0 (17.0–37.5)	27.5 (19.7–44.2)	.11
SpO2 on room air	…	…	<.01
SpO2 ≥94%, n = 163	78 (100%)	85 (54.1%)	
SpO2 <94%, n = 72	0 (0%)	72 (45.9%)	
q-SOFA score	…	…	<.01[a]
0, n = 119	63 (94.0%)	56 (40.3%)	
1, n = 70	4 (6.0%)	66 (47.5%)	
2, n = 14	0 (0%)	14 (10.1%)	
3, n = 3	0 (0%)	3 (2.2%)	
Chest X-ray obtained, n = 194	35 (28.7%)	159 (97.0%)	<.01
CXR findings[b]			
Normal, n = 43	20 (57.1%)	23 (14.5%)	<.01
Multifocal or patchy opacities, n = 104	11 (31.4%)	93 (58.5%)	<.01
Interstitial abnormalities, n = 39	3 (8.6%)	36 (22.6%)	.06
Other findings, n = 18	2 (5.7%)	16 (10.1%)	.54[a]
Lobar consolidation, n = 9	1 (2.9%)	8 (5.0%)	1.0[a]
Chest CT obtained, n = 44	5 (4.1%)	39 (23.8%)	<.01
CT findings[b]			
Normal, n = 6	1 (20%)	5 (12.8%)	.54[a]
Multifocal patchy or ground-glass opacities, n = 29	3 (60.0%)	26 (66.7%)	1.0[a]
Interstitial abnormalities, n = 6	0 (0%)	6 (15.4%)	1.0[a]
Lobar consolidation, n = 6	0 (0%)	6 (15.4%)	1.0[a]

n = 286.

Abbreviations: CT: computed tomography; CXR, chest X-ray; IQR, interquartile range; q-SOFA, Quick Sequential Organ Failure Assessment; SpO2, peripheral oxygen saturation.

[a]Using Fisher's exact test.

[b]Findings on CXR and CT chest are not mutually exclusive.

Table 3. Treatment of Hospitalized Patients

Received experimental targeted therapy	99 (60.4%)
Hydroxychloroquine	67 (40.9%)
Azithromycin	36 (22.0%)
Interleukin-6 receptor antagonist, tocilizumab or sarilumab	14 (8.5%)
Remdesivir	12 (7.3%)
Convalescent plasma	8 (4.9%)
Lopinavir/ritonavir	6 (3.7%)

Data are from patients with HIV and COVID-19 (n = 164).

Abbreviations: COVID-19, coronavirus disease 2019; HIV, human immunodeficiency virus.

those with CD4 counts <200 and >500 cells/mm^3 for both ICU-free survival (P = .04) and overall survival (P = .05; Figure 1).

In a post hoc analysis, we included PWH diagnosed with COVID-19 from the United States (n = 265) and excluded those from international locations (n = 21). There were no significant differences in presentation or predictors of outcomes, except for hypertension. Hypertension was not significantly associated with severe outcomes, after adjusting for other variables. An analysis is presented in Supplementary Tables 1–4.

Table 4. Clinical Course of Hospitalized Patients

	n (%)	<40 yrs,[a] n = 24	40–60 yrs, n = 82	RR	>60 yrs, n = 58	RR	*P* value
ICU admission	47 (28.7%)	4 (16.7%)	22 (26.8%)	1.6	21 (36.2%)	2.2	.11
Vasopressor use	35 (21.3%)	4 (16.7%)	14 (17.1%)	1.0	17 (29.3%)	1.8	.26
Respiratory support use	123 (75.0%)	12 (50.0%)	63 (76.8%)	1.5	48 (82.8%)	1.7	.02
Highest level of respiratory support							
NC or face mask	69 (42.1%)	7 (29.2%)	42 (51.2%)	1.8	20 (34.5%)	1.2	.65
High-flow NC or NRB	17 (10.4%)	1 (4.2%)	7 (8.5%)	2.0	9 (15.5%)	3.7	.20
Invasive mechanical ventilation[b]	37 (22.6%)	4 (16.7%)	14 (17.1%)	1.0	19 (32.8%)	2.0	.17
Acute kidney injury[c]	62 (38.0%)	5 (20.8%)	26 (32.1%)	1.5	31 (50.0%)	2.6	.02
Liver injury[d]	46 (28.9%)	7 (30.4%)	19 (24.1%)	.8	20 (35.1%)	1.1	.69
Death	27[e] (16.5%)	1 (4.2%)	8 (9.8%)	2.3	18 (31.0%)	7.4	.04
Severe outcome	50 (30.5%)	4 (16.7%)	22 (26.8%)	1.6	24 (41.4%)	2.5	.06

Data are from patients with HIV and COVID-19, stratified by age (n = 164).

Abbreviations: COVID-19, coronavirus disease 2019; HIV, human immunodeficiency virus; ICU, intensive care unit; NC, nasal cannula; NRB, non-rebreather mask; RR, relative risk.

[a]RR calculated based on <40-year age group as a reference.

[b]Invasive mechanical ventilation includes 2 patients on extracorporeal membrane oxygenation.

[c]Acute kidney injury, defined as creatinine increase of 0.3 mg/dL above baseline, including 7 patients who required new renal replacement therapy.

[d]Liver injury, defined by an increase of over 2 times from baseline in serum alanine aminotransferase.

[e]Including 2 deaths: 1 after hospital discharge to hospice and 1 in the emergency department.

Table 5. Multivariable Analysis

		Logistic Regression Analysis		Generalized Estimating Equation (GEE)	
Outcome	Clinical Characteristics	Odds ratio (95% CI)	*P* value	Odds ratio (95% CI)	*P* value
Hospitalization	Age, years	1.04 (1.01–1.08)	.01	1.08 (1.04–1.07)	.03
	CD4 count				
	<200 cells/mm^3	5.22 (1.28–21.35)	.02	3.67 (1.64 – 17.1)	<.01
	200–500 cells/mm^3	1.47 (.7–3.08)	.30	1.12 (1.1–12.22)	.03
	>500 cells/mm^3	1.00 (reference)			
	Chronic kidney disease	5.12 (1.60–16.85)	<.01	4.08 (1.45 – 11.52)	<.01
		1.00 (reference)			
	Chronic lung disease	4.54 (1.58–13.01)	<.01	4.06 (1.87 – 8.81)	<.01
		1.00 (reference)			
	Comorbidity burden				
	HIV with no other known comorbidity	1.00 (reference)			
	HIV with 1 or 2 comorbidities	1.19 (.56–2.55)	.65	1.13 (.49–2.6)	.78
	HIV with 3 or more comorbidities	4.56 (1.81–11.48)	<.01	3.57 (1.29–9.9)	.01
Severe outcome[a]	Age, years	1.04 (1.01–1.07)	.02	1.04 (1.0–1.07)	.02
	CD4 count				
	<200 cells/mm^3	3.32 (1.11–9.93)	.03	2.8 (1.02–7.67)	.05
	200–500 cells/mm^3	1.75 (.76–4.02)	.19	1.93 (.73–5.06)	.18
	>500 cells/mm^3	1.00 (reference)			
	Hypertension	2.44 (1.01–5.55)	.03	2.43 (1.2–4.93)	.01
		1.00 (reference)			
	Chronic lung disease	3.65 (1.56–8.56)	<.01	3.37 (1.63–6.97)	<.01
		1.00 (reference)			
	Comorbidity burden				
	HIV with no other known comorbidity	1.00 (reference)			
	HIV with 1 or 2 comorbidities	2.58 (.56–11.91)	.23	2.21 (.42–11.7)	.35
	HIV with 3 or more comorbidities	5.09 (1.05–24.76)	.04	5.40 (1.02–28.54)	.05

The analysis examines the associations between hospitalization, severe outcomes, and clinical characteristics of patients with HIV and COVID-19 (n = 286). The model for hospitalization outcomes is adjusted for age, sex, race/ethnicity, years with HIV, CD4 count, HIV viral load suppression, antiretroviral regimen, hypertension, diabetes, chronic lung disease, chronic kidney disease, cardiovascular disease, active malignancy, and chronic liver disease. The model for severe outcomes is adjusted for age, sex, race/ethnicity, CD4 count, HIV viral load suppression, hypertension, diabetes, chronic lung disease, chronic kidney disease, and chronic liver disease. The model for the associations between hospitalization, severe outcomes, and the comorbidity burden is adjusted for age, sex, and race/ethnicity.

Abbreviations: CI, confidence interval; HIV, human immunodeficiency virus.

[a]Severe outcome is defined as a composite outcome of intensive care admission, invasive mechanical ventilation, or death.

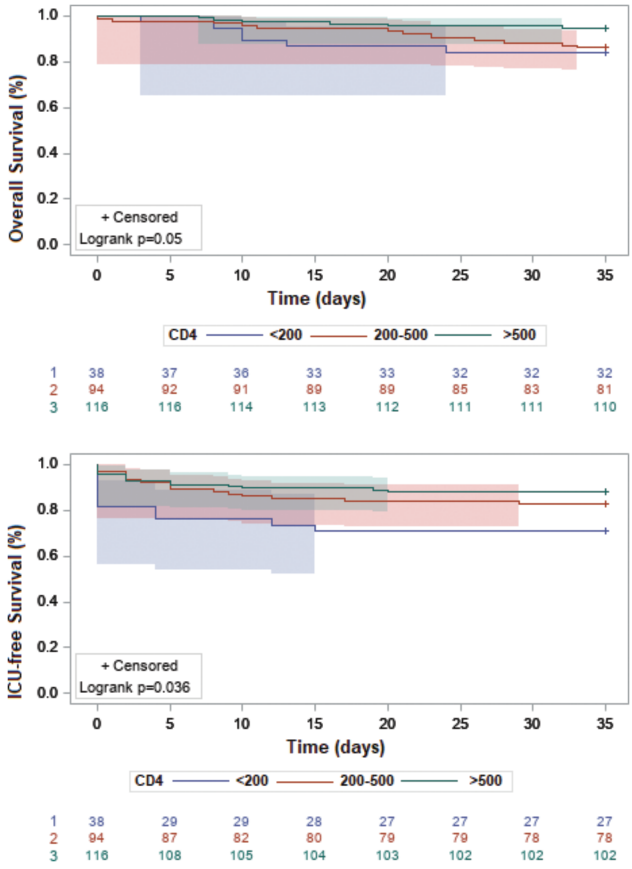

Figure 1. *A*, Overall survival curves by CD4 groups (<200, 200–500, and >500 cells/mm^3; $P = .05$). *B*, ICU-free survival curves by CD4 groups ($P = .04$). Abbreviation: ICU, intensive care unit.

DISCUSSION

In this multicenter analysis, severe clinical outcomes occurred commonly in PWH with COVID-19. As reported in multiple other studies in people without HIV, we found that age, chronic lung disease, and a comorbidity burden were associated with increased rates of severe outcomes. In addition, among HIV-specific factors, we found that a lower CD4 count (<200 cells/mm^3) was associated with poor outcomes, including higher hospitalization rates, lower ICU-free survival, and lower overall survival. Our study is the first to characterize outcomes in a large number of geographically diverse PWH with laboratory-confirmed COVID-19.

The clinical and radiologic presentations of the PWH in our study were similar to those reported in other studies of patients with COVID-19, whether living with or without HIV [1, 17, 22, 30].

Our study confirms the unequal racial and gender distributions of PWH and COVID-19. It mirrors the demographics of PWH in the United States, with higher proportions of men and of African American and Hispanic patients [31]. However, we did not find that race and gender were associated with worse outcomes in this cohort. Our findings demonstrate a high prevalence of comorbidities among PWH with COVID-19. Consistent with other studies [22, 32], we found that underlying comorbidities constitute significant risk factors for hospitalization and poor outcomes in PWH.

Available data indicate considerable variability in mortality rates, ICU admission rates, and the need for invasive mechanical ventilation among PWH diagnosed with COVID-19 [16, 18–20, 22]. Based on our analyses, rates of ICU admission, mechanical ventilation use, and death among PWH and COVID-19 were consistent with the general US data [30].

We did not identify HIV viremia (a proxy for not taking ART) as a risk factor for severe COVID-19, but the proportion of study participants with HIV viremia was small, and more than 90% of our study enrollees were receiving ART. Hence, our ability to compare the outcomes between those with and without HIV control was limited.

It has been postulated that patients with advanced HIV, low CD4 counts, and severe immunosuppression cannot mount the robust inflammatory response responsible for COVID-19–associated complications [15, 16, 18, 21]. Our study does not support this hypothesis for those who are virologically suppressed but have low CD4 cell counts. Although we did not collect information about nadir CD4 cell counts or durations of ART, this population (low CD4 but virally suppressed) usually has a history of severe immunosuppression, recent ART initiation, or both. Our findings show a significant association between low CD4 counts and poor outcomes, contrasting with recently published cases series. The study by Karmen-Tuohy et al [19] showed that 6 patients out of 19 had CD4 counts <200 cells/mm^3, and the CD4 count was not associated with mortality in PWH. In comparison, the study from Collins et al [21] from GA, had 20 PWH with COVID-19 and showed that all 3 who died had CD4 counts >200 cells/mm^3. In our study, there were deaths among PWH with CD4 counts >200 cells/mm^3, but our larger sample size was possibly able to detect a difference between PWH with CD4 counts <200, 200–500, and >500 cells/mm^3.

A recent study from Spain suggested that PWH receiving tenofovir disoproxil fumarate (TDF) in combination with emtricitabine as part of their ART regimen have a lower risk for SARS-CoV-2 acquisition and related hospitalizations than those on other ART regimens [33]. Although the data we gathered were not specific enough to address the differences between those on TDF and other nucleoside reverse transcriptase inhibitors, in our study, we did not find an association between the class of ART or the use of darunavir-containing regimens and predefined outcomes.

This study has several limitations. First, this study cannot comment on the prevalence of SARS-CoV-2 infection among PWH. Second, COVID-19 testing, treatment, and hospitalization were all done at the discretion of individual health-care providers and may have varied widely between sites, as well as between different time points during the pandemic, reflective of local test availability and policies. There may also be selection bias, as contributors entered cases voluntarily and may not have entered every case from their institution or clinic. However,

17 out of 36 institutions (accounting for 246 patients out of 286), have included systematically all PWH with COVID identified through the search performed in their corresponding centers during the study period. We could not control for COVID-19 therapies because we did not collect data on steroid use and clinical trial participation, and also because of the small number of patients in each treatment group. We also did not collect data on social determinants of health that may have impacted the clinical course of COVID-19. Future studies should assess whether specific socioeconomic factors impart a greater risk related to COVID-19 for PWH. Finally, death is counted as all-cause mortality; we did not verify the exact cause of death. Despite these limitations, evaluating outcomes for PWH with COVID-19 who were hospitalized or nonhospitalized from multiple sites and settings (community hospitals, clinics, and large academic centers) make these results more generalizable.

In conclusion, our study adds to existing reports of the clinical characteristics of COVID-19 among PWH. The strengths of this analysis include a relatively large sample size and a population broadly representative of the PWH in the United States. Although we did not have a comparison group, our results suggest comparable outcomes and non-HIV risk factors for severe disease as those observed in people without HIV. Among HIV-related factors, our observation that those with lower CD4 cell counts are at higher risk for poor outcomes despite viral suppression suggests that people with a history of advanced HIV-related immunosuppression or relatively recent ART initiation may warrant closer observation and monitoring. The results of the study can also help prioritize interventions in PWH in areas with an ongoing high incidence of SARS-CoV-2 infection, to mitigate the impact of COVID-19.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

The Human Immunodeficiency Virus–Coronavirus Disease 2019 (HIV–COVID-19) Consortium includes many contributors who helped with this work by enrolling their patients, collecting data, and providing a critical revision to the manuscript. The following order is based on the number of patients enrolled for each institution:

1. New York University Grossman School of Medicine, New York: Fainareti N. Zervou, MD; Gabriel Rebick, MD; Anna Stachel, PhD; Shini Tang, BS; and Dan Ding, MA.
2. Johns Hopkins University, Maryland: Jason E. Farley, PhD, MPH; Kelly E. Dooley, MD, PhD; Barbara E. Wilgus, MSN, CRNP; and Michael Sanchez, DNP, CRNP, FNP-BC, FAANP.
3. University of Texas Southwestern Medical Center/Parkland Memorial Hospital, Texas: Shannon Koh, MD; Daniel Maxwell, MD; Abby Lau, MD; Shamika Brooks APRN, FNP-C, AAHIVS; Jessica Chu, PA-C; Joshua Estrada, PA-C, AAHIVS; and Susana M. Lazarte, MD.
4. Wellstar Kennestone Regional Medical Center, Georgia: Neha Paranjape, MD, MPH.
5. Brigham and Women's Hospital, Massachusetts.
6. Vanderbilt University Medical Center, Tennessee: Asghar N. Kheshti; Samuel Bailin, MD; John R. Koethe, MD; Sean G. Kelly, MD; and Stephen P. Raffanti, MD.
7. Baylor College of Medicine, Texas: Teena Huan Xu, MD; and Melanie Goebel, MD.
8. Infectious Diseases and Fight AIDS Foundation, University Hospital Germans Trias, Badalona, Spain.
9. Puerta de Hierro Majadahonda University Hospital, Madrid, Spain.
10. Santa Clara Valley Medical Center, California: Carol Hu, MD.
11. Saint Michael's Medical Center, New Jersey.
12. Tower Health, Pennsylvania.
13. Temple University Health System, Pennsylvania: Kayla Hiryak, PharmD.
14. The University of Arkansas for Medical Sciences, Arkansas: Ryan K Dare, MD, MS; Stacie Bordelon, PharmD, AAHIVP; and Brett Bailey, PharmD.
15. University of Maryland, Maryland.
16. University of Kansas Medical Center, Kansas: D. Matthew Shoemaker, DO.
17. AMITA Health Saint Francis Hospital, Illinois: Guillermo Rodriguez-Nava, MD.
18. Mayo Clinic College of Medicine, Rochester, Minnesota: F. N. U. Shweta, MBBS.
19. The University of California, San Francisco Medical Center, California: Carolyn Chu, MD, MSc; and Catherine Pearson, MD.
20. The Polyclinic, Washington: Amy Treakle, MD.
21. Case Western Reserve University, Ohio: Jennifer J. Furin, MD, PhD.
22. MetroHealth Medical Center, Ohio: Milana Bogorodskaya, MD.
23. Hackensack University Medical Center, New Jersey: Samit Desai, MD.
24. Hurley Medical Center/Michigan State University College of Human Medicine, Michigan: Danielle Osterholzer, MD.
25. San Joaquin General Hospital, California: Jered Arquiette, PharmD, BCPS-AQ ID.
26. University of Washington, Washington: Emily S. Ford, MD.
27. University of Maryland Medical Center Midtown Campus, Maryland: Patrick R. Ching, MD, MPH.
28. Alexandra Hospital, National University Health System (NUHS), Singapore: Louisa Sun, MBBS, MRCP.
29. Washington University, Missouri.
30. Advocate Aurora St. Luke's Medical Center, Wisconsin: Brian P. Buggy, MD.
31. Indiana University Health, Indiana: Amir Tirmizi, MD.
32. Mount Sinai Hospital, Illinois: Sarah Argentine, NP.
33. SOVAH Health (Southern Virginia Health Center), VA: Balaji Desai, MD.
34. Icahn School of Medicine at Mount Sinai, New York: Talia H. Swartz, MD, PhD.
35. Callen Lorde Community Health, New York: Dusty Latimer, PA-C.
36. University of Missouri, Columbia, Missouri: Andres Bran, MD.

Author contributions. As principal investigator, D. D. had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. D. D. provided administrative, technical, or material support, and supervised the study. D. D. and G. G. conceived of and designed the study. D. D., G. G., and J. C. drafted the manuscript. D. D., M. G., and M. C. conducted the statistical analysis. All authors participated in the data acquisition, analysis and interpretation of data, and critical revision of the manuscript for important intellectual content.

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