Outcomes Among HIV-Positive Patients Hospitalized With COVID-19

Savannah Karmen-Tuohy, BS,[a] Philip M. Carlucci, BS,[a] Fainareti N. Zervou, MD,[a] Ioannis M. Zacharioudakis, MD,[a] Gabriel Rebick, MD,[a] Elizabeth Klein, BS,[a] Jenna Reich, BS,[a] Simon Jones, PhD,[b,c] and Joseph Rahimian, MD[a]

Background: SARS-CoV-2 infection continues to cause significant morbidity and mortality worldwide. Preliminary data on SARS-CoV-2 infection suggest that some immunocompromised hosts experience worse outcomes. We performed a retrospective matched cohort study to characterize outcomes in HIV-positive patients with SARS-CoV-2 infection.

Methods: Leveraging data collected from electronic medical records for all patients hospitalized at NYU Langone Health with COVID-19 between March 2, 2020, and April 23, 2020, we matched 21 HIV-positive patients with 42 non-HIV patients using a greedy nearest-neighbor algorithm. Admission characteristics, laboratory test results, and hospital outcomes were recorded and compared between the 2 groups.

Results: Although there was a trend toward increased rates of intensive care unit admission, mechanical ventilation, and mortality in HIV-positive patients, these differences were not statistically significant. Rates for these outcomes in our cohort are similar to those previously published for all patients hospitalized with COVID-19. HIV-positive patients had significantly higher admission and peak C-reactive protein values. Other inflammatory markers did not differ significantly between groups, although HIV-positive patients tended to have higher peak values during their clinical course. Three HIV-positive patients had superimposed bacterial pneumonia with positive sputum cultures, and all 3 patients died during hospitalization. There was no difference in frequency of thrombotic events or myocardial infarction between these groups.

Conclusions: This study provides evidence that HIV coinfection does not significantly impact presentation, hospital course, or outcomes of patients infected with SARS-CoV-2, when compared with matched non-HIV patients. A larger study is required to determine whether the trends we observed apply to all HIV-positive patients.

Key Words: HIV, COVID-19, SARS-CoV-2, coronavirus

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INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic, caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has resulted in significant morbidity and mortality around the world. Since first tracking the global outbreak in December 2019, researchers have reported worse outcomes for patients with pre-existing conditions, including diabetes, hypertension, cardiovascular disease, underlying respiratory disease, and cancer.[1,2] However, there are minimal data exploring the effect of SARS-CoV-2 infection on the world's estimated 37.9 million HIV-positive patients.[3] A single clinical case series of 5 patients and 1 case report have described the characteristics and outcomes of HIV-positive patients, but, to the best of our knowledge, nothing has been published to date comparing a cohort of HIV-positive patients with a matched non-HIV cohort.[4,5] This retrospective observational study aims to understand whether coinfection with HIV alters the initial presentation, hospital course, and outcomes of patients infected with SARS-CoV-2.

METHODS

Data were collected from electronic medical records (Epic Systems, Verona, WI) for all patients hospitalized with COVID-19 at any of 4 acute care NYU Langone Health hospitals in New York City between March 2, 2020, and April 23, 2020. Patients were included in the study if they had at least 1 positive COVID-19 polymerase chain reaction test, were admitted to the hospital, and had been discharged from the hospital, transitioned to hospice, or died at the time of analysis. Patients who did not test positive for COVID-19, who were never admitted to the hospital, and who had not yet completed their clinical course were excluded from the study. With an automated approach, we collected demographics, medical history, admission vitals and laboratory test results, and hospital outcomes. On generating our matched patients, manual chart review was performed to collect information, such as CD4 counts, HIV medications,

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From the [a]Department of Medicine, New York University Grossman School of Medicine, New York, NY; [b]Division of Healthcare Delivery Science, Department of Population Health, NYU Grossman School of Medicine, New York, NY; and [c]Center for Healthcare Innovation and Delivery Science, NYU Langone Health, New York, NY.

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S.K.-T. and P.M.C. contributed equally and share first authorship.

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Correspondence to: Joseph Rahimian, MD, Department of Medicine, NYU Grossman School of Medicine, 31 Washington Square West, Floor Number 4, New York, NY 10011 (e-mail: Joseph.Rahimian@nyulangone.org).

peak laboratory test results, culture results, thrombotic events, and imaging results.

Statistical Analysis

We identified 21 HIV-positive patients and 2617 non-HIV patients who met the inclusion criteria. Greedy 1:2 nearest-neighbor matching was employed using the MatchIt package, Version 3.0.2, in RStudio, Version 1.2.5042, to generate 42 matched non-HIV patients for our comparison group.[6] Patients were matched by admission date, age, body mass index, gender, tobacco history, and a history of chronic kidney disease, hypertension, asthma, chronic obstructive pulmonary disease, and heart failure. Descriptive statistics are presented as mean and SD or median and interquartile range for continuous variables and frequencies for categorical variables. Normality of distribution for continuous variables was assessed by measures of skewness and kurtosis. A 2-tailed Student *t* test was used for parametric analysis, and a Mann–Whitney *U* test was used for nonparametric data analysis. A Pearson χ^2 test was used to compare categorical characteristics. Logistic regression was used to test associations among variables. All analyses were performed using STATA/SE 16.0 software (STATA Corp.).

Study Approval

The study was approved by the NYU Grossman School of Medicine Institutional Review Board. A waiver of informed consent and a waiver of the Health Information Portability Privacy Act were granted.

RESULTS

HIV-positive patients (N = 21) and matched non-HIV patients (N = 42) did not differ significantly in age, sex, race, tobacco use, or medical history (see Table 1, Supplemental Digital Content, http://links.lww.com/QAI/B494). In the HIV-positive cohort, 19 patients and 17 patients had CD4 count and viral load results, respectively, recorded before or on the first day of admission. Patients in the HIV-positive cohort had a median last CD4 count of 298/μL, and only 6 of the 19 patients had a last measured CD4 count less than 200/μL. Fifteen of 17 patients had a viral load less than 50 copies/mL, and all patients in the HIV-positive cohort were on highly active antiretroviral therapy before admission. HIV-positive and non-HIV groups did not differ statistically on initial white blood cell count, hemoglobin, absolute neutrophil count, ferritin, D-dimer, troponin, creatine phosphokinase, procalcitonin, or creatinine. HIV-positive patients had a higher absolute lymphocyte count (mean ± SD, HIV+: 1.09 ± 0.53 vs. non-HIV: 0.88 ± 0.39, *P* value: 0.043) and higher C-reactive protein (CRP) (HIV+: 154.48 ± 94.44 vs. non-HIV: 96.1 ± 90.0, *P* value: 0.020) on initial laboratory test results than non-HIV patients (Table 1).

A greater percentage of HIV-positive patients had an abnormal finding of consolidation, infiltrate, or opacity on initial chest imaging than non-HIV patients [HIV+: 19 (90.5%) vs non-HIV: 27 (64.3%)], although no statistical difference was seen between the groups when analyzing the finding of bilateral consolidation, opacity, or infiltrate ever present on chest imaging during this hospitalization (Table 2). When analyzing COVID-related treatments received, there

TABLE 1. Admission Characteristics Among HIV-Positive and Non-HIV Patients

	HIV-Positive, N = 21	Non-HIV, N = 42	*P*
Admission characteristics			
Respiratory rate, respirations per minute	20 (18–25)	20 (18–22)	0.779
Baseline systolic BP, mm Hg	126 (115–139)	137 (128–147)	**0.047**
Baseline diastolic BP, mm Hg	74.43 ± 10.98	79.69 ± 12.50	0.053
Temperature, °C	37.57 ± 0.76	37.64 ± 0.99	0.390
White blood cell count, 10^3/μL	7.2 (4.9–10.15), N = 20	6.25 (4.7–8.1), N = 38	0.365
Hemoglobin, g/dL	12.70 ± 2.19, N = 20	13.48 ± 1.96, N = 38	0.079
Absolute neutrophil count, 10^3/μL	5.8 (3.9–8.7), N = 21	4.4 (3–6.4), N = 41	0.186
Absolute lymphocyte count, 10^3/μL	1.09 ± 0.53, N = 21	0.88 ± 0.39, N = 41	**0.043**
Ferritin, ng/mL	679 (338–1446), N = 19	698 (232–1603), N = 34	0.905
D-dimer, ng/mL	333 (210–452), N = 17	330 (202–466), N = 31	0.911
Troponin, ng/mL	0.02 (0.01–0.05), N = 18	0.015 (0.01–0.03), N = 33	0.308
Creatine phosphokinase, U/L	239 (58–423), N = 14	161 (83–415), N = 23	0.728
Procalcitonin, ng/mL	0.2 (0.09–0.24), N = 19	0.08 (0.05–0.23), N = 36	0.095
Creatinine, mg/dL	1.14 (0.87–1.7), N = 20	1.09 (0.9–1.41), N = 38	0.830
CRP, mg/L	154.48 ± 94.44, N = 18	96.1 ± 90.0, N = 35	**0.020**
Lactate dehydrogenase, U/L	449.4 ± 239.8, N = 5	411.27 ± 229.6, N = 11	0.383
Last measured absolute CD4 count, /μL	298 (135–542), N = 19	—	—
Last measured CD4%	24 (16–28), N = 19	—	—

Data are represented as median (IQR), mean ± SD, or N (%). Sample size is reported where it differed due to laboratory tests not performed. *P* values were calculated using a 2-sided *t* test for parametric variables and a Mann–Whitney *U* test for nonparametric continuous variables. A Pearson χ^2 test was used for categorical comparisons. $P < 0.05$ (in bold) was deemed significant. All laboratory test results, except CD4 count, represent the first result found on admission.

BP, blood pressure; IQR, interquartile range.

was a significant difference in the use of corticosteroids between HIV-positive and non-HIV patients. Four HIV-positive patients received corticosteroids, whereas no patient from the non-HIV group received this treatment. None of the HIV-positive patients received corticosteroids at the time of their last T-cell measurement, and therefore, we do not expect this to have had any impact on the measured CD4 count for these patients.

Although there was a trend toward HIV-positive patients experiencing longer hospital stays and higher rates of intensive care unit (ICU) admission, mechanical ventilation, and discharge to hospice or mortality, we did not find a statistically significant difference between the HIV-positive and non-HIV cohort on these measures. Supplemental oxygen characteristics, such as average or maximum O2 flow rate and FiO2, were not statistically different between these groups, although HIV-positive patients trended toward higher O2 flow rates when compared with non-HIV patients. Although not statistically significant, HIV-positive patients had a nominally higher peak lactate dehydrogenase, ferritin, procalcitonin, and D-dimer. HIV-positive patients had statistically significant higher peak CRP values than non-HIV patients (HIV+: 185.13 ± 107.35 vs. non-HIV: 128.06 ± 99.29, *P* value: 0.024). Because HIV-positive patients had significantly higher admission and peak CRP values, we performed a logistic regression to see whether CRP predicted mortality among HIV-positive patients and found no association with mortality using admission CRP [odds ratio: 1.007, 95% confidence interval (CI): 0.998 to 1.015, N = 18]. However, we did observe a weakly significant association between the highest peak CRP values and mortality among HIV-positive patients (odds ratio: 1.026, 95% CI: 1.002 to 1.051, N = 20). A similar weak association was found among non-HIV patients (odds ratio: 1.018, 95% CI: 1.006 to 1.029, N = 38). Last measured CD4 count did not associate with mortality in HIV-positive patients (odds ratio: 0.996, 95% CI: 0.992 to 1.11).

Both groups were evaluated for complications of stroke, myocardial infarction, pulmonary embolism, and deep vein thrombosis. No patients included in this study experienced a stroke. Two patients, 1 each from the HIV-positive and non-HIV groups, experienced both pulmonary embolism and ST-segment elevation myocardial infarction documented on imaging, electrocardiogram, or clinical record.

The presence of a superimposed bacterial pneumonia was also evaluated. Twelve total patients (6 HIV-positive and 6 non-HIV) had sputum cultures performed because of clinical suspicion of bacterial superinfection. Four patients had positive sputum cultures, 3 of whom were HIV-positive.

TABLE 2. Hospital Outcomes Among HIV-Positive and Non-HIV Patients

	HIV-Positive, N = 21	Non-HIV, N = 42	*P*
Length of hospital stay, d	6 (4–13), N = 21	5 (3–10), N = 42	0.262
O2 flow rate AVG, L/min	4.5 (2–16), N = 16	3.3 (2–12), N = 33	0.653
O2 flow rate MAX, L/min	11 (2–38), N = 16	4 (3–15), N = 33	0.681
Fraction of inspired oxygen AVG	79.1 ± 21.4, N = 7	71.88 ± 34.4, N = 12	0.313
Fraction of inspired oxygen MAX	90.0 ± 17.32, N = 7	81.25 ± 35.94, N = 12	0.278
Died or transferred to hospice	6 (28.6%)	10 (23.8%)	0.682
Needed ICU	6 (28.6%)	7 (16.7%)	0.271
Needed invasive ventilation	5 (23.8%)	5 (11.9%)	0.223
Lactate dehydrogenase peak, U/L	477.04 ± 210.37, N = 21	436.30 ± 223.02, N = 37	0.249
CRP peak, mg/L	185.13 ± 107.35, N = 20	128.06 ± 99.29, N = 38	**0.024**
Ferritin peak, ng/mL	1446 (493–2209), N = 20	1156 (314–2148), N = 36	0.617
Procalcitonin peak, ng/mL	0.22 (0.11–0.42), N = 20	0.11 (0.06–0.28), N = 35	0.227
White blood cell count peak, $10^3/\mu L$	8.3 (7.1–12.4), N = 21	7.3 (5.5–11.6), N = 41	0.125
White blood cell count low, $10^3/\mu L$	5.1 (4.3–5.6), N = 21	4.6 (3.6–6.1), N = 41	0.828
D-dimer peak, ng/mL	N = 19	N = 34	0.315
<1000	11 (57.9%)	26 (76.5%)	0.158
1000–6000	5 (26.3%)	6 (17.6%)	0.456
>6000	3 (15.8%)	2 (5.9%)	0.237
Abnormal initial chest x-ray*	19 (90.5%)	27 (64.3%)	**0.027**
Bilateral	18 (94.7%)	23 (85.2%)	
Unilateral	1 (5.3%)	4 (14.8%)	
Chest x-ray bilateral ever*	18 (85.7%)	29 (69.0%)	0.152
Myocardial infarction	1 (4.8%)	1 (2.4%)	0.611
Pulmonary embolism	1 (4.8%)	1 (2.4%)	0.611
Deep vein thrombosis	1 (4.8%)	1 (2.4%)	0.611

Data are represented as median (IQR), mean ± SD, or N (%). Sample size is reported where it differed due to laboratory tests not performed. *P* values were calculated using a 2-sided *t* test for parametric variables and a Mann–Whitney *U* test for nonparametric continuous variables. A Pearson χ^2 test was used for categorical comparisons. $P < 0.05$ (in bold) was deemed significant. Peak laboratory results represent the highest measured value during hospitalization.

*Chest x-rays were considered abnormal if a finding of consolidation, infiltrate, or opacity suggestive of pneumonia/pneumonitis was recorded.

IQR, interquartile range.

Of these patients with positive sputum results, 2 patients had polymicrobial infections, and cultures grew *Pseudomonas aeruginosa* (2 patients), *Stenotrophomonas maltophilia* (2 patients), *Klebsiella pneumoniae* (1 patient), *Staphylococcus aureus* (1 patient), and *Escherichia coli* (1 patient). All 4 patients with positive cultures were subsequently treated with antibiotics for bacterial pneumonia, and all 4 died in the hospital. Clinical suspicion of a superimposed pneumonia occurred at least 6 days or more before death in each case.

DISCUSSION

The impact of HIV coinfection on the clinical course of patients with COVID-19 has yet to be fully characterized. Overall, our findings suggest that HIV status did not significantly impact clinical outcomes in patients with SARS-CoV-2 infection. However, we did detect trends suggesting that outcomes may be worse in HIV-positive patients, as a greater percentage of HIV-positive patients required ICU level care, required mechanical ventilation, or died or were discharged to hospice, compared with the non-HIV cohort. A previous study investigating outcomes in all patients admitted to NYU Langone Health hospitals found that 28.1% of patients required mechanical ventilation, and 18.5% were discharged to hospice or died.[7] In our study, both cohorts had a lower rate of mechanical ventilation (23.8% of HIV-positive patients and 11.9% of non-HIV patients) and a higher rate of mortality (28.6% of HIV-positive patients and 23.8% of non-HIV patients), as compared to data from the larger study of all patients hospitalized at NYU Langone Health. In addition, a recent study reporting outcomes among patients in New York City found a 21% mortality rate for hospitalized patients, whereas a study from China reported a 28% mortality rate among hospitalized patients,[1,8] contributing to a wide range of published mortality data. The mortality rate of both cohorts in this study falls within this established range, and further investigation is merited into the impact of HIV coinfection on COVID-19 outcomes.

As reported in Table 1, Supplemental Digital Content, http://links.lww.com/QAI/B494, there was a trend toward a greater percentage of African American patients in the HIV-positive cohort, compared with the non-HIV cohort. In further analysis, none of the African American patients in either group died. These data suggest that the nonsignificant difference in the percentage of African American patients between cohorts did not have a significant effect on the mortality data presented.

T-cell subset labs were drawn for HIV-positive patients before admission or on admission, and patients did not have these tests repeated during their hospital course. No patient in the non-HIV cohort had T-cell subset labs performed. Data from Wuhan, China, suggest that patients with COVID infection demonstrate a drop in lymphocytes, specifically CD4 T cells, a finding that is more prevalent in patients with severe disease.[9] At the time of our data collection, it was not routine practice to perform T-cell subset labs on non-HIV patients in our hospitals, and, as such, none of the patients in the non-HIV had these labs performed. Further investigation into the impact of COVID infection on T-lymphocyte levels, specifically CD4 cells, is needed in both HIV and non-HIV patients.

We found an increased frequency of chest x-ray abnormalities on admission imaging in HIV-positive patients, and this trend persisted throughout the course of hospitalization. A previous study reported up to 84% of patients with COVID-19 present with abnormal chest x-rays on admission, an incidence similar to the HIV-positive cohort in our study.[10] Admission x-ray was not a reliable indicator of illness severity in HIV-positive patients, a similar finding to what has been reported in the general population.[10]

In this cohort, 4 patients were clinically treated for superimposed bacterial infection based on positive sputum culture results, 3 of whom were HIV-positive. All 3 HIV-positive patients with bacterial superinfection died in the hospital. Existing data highlight the higher incidence of bacterial pneumonias in HIV-positive patients compared with the general population, in addition to the significant mortality burden of non-AIDS bacterial infections in this population.[11–15] Risk factors associated with contracting severe non-AIDS bacterial infections include immunosuppression and a history of cancer and diabetes, comorbidities that have also been associated with worse prognosis in SARS-CoV-2 infection.[2,8,16] This study was not powered to conclude that superimposed bacterial infections were a predictor of mortality in HIV-positive patients with SARS-CoV-2 infection. However, all HIV-positive patients with a bacterial pneumonia died, and this finding should be considered when making clinical decisions about these patients. Future studies should investigate whether SARS-CoV-2 infection increases the risk of secondary bacterial infection in similar patients and whether bacterial pneumonia might serve as a predictor of mortality in the HIV-positive population.

All HIV-positive patients in the study were on highly active antiretroviral therapy before hospital admission, and only 1 patient in the HIV-positive cohort had both a CD4 count less than 200/μL and a viral load greater than 50 copies/mL. Therefore, these findings may not apply to a population with poorly controlled HIV or AIDS. Only one patient was taking a protease inhibitor, a class of drugs under investigation for potential therapeutic benefit in COVID-19 treatment.[17] Given the lack of data in our cohort, we are unable to comment on the clinical impact of protease inhibitor use in HIV-positive patients with SARS-CoV-2 infection. This was a retrospective study that is susceptible to confounding variables, and our limited sample size prevented us from detecting small differences among groups. Larger prospective studies should examine the impact of poorly controlled HIV on the SARS-CoV-2 clinical course. Taken together, our findings are reassuring that HIV-positive patients may not experience significantly worse outcomes in SARS-CoV-2 infection, as compared to matched non-HIV patients.

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