Clinical Characteristics and Outcomes in People Living With Human Immunodeficiency Virus Hospitalized for Coronavirus Disease 2019

Elijah D LaSota, Jason Zucker, Magdalena E Sobieszczyk, Matthew Scherer, Michael T Yin, Noga Shalev, Pantelis Antoniou

Clinical Infectious Diseases

BRIEF REPORT

Clinical Characteristics and Outcomes in People Living With Human Immunodeficiency Virus Hospitalized for Coronavirus Disease 2019

Noga Shalev,[1,a] Matthew Scherer,[1,a] Elijah D. LaSota,[1] Pantelis Antoniou,[2] Michael T. Yin,[1] Jason Zucker,[1] Magdalena E. Sobieszczyk[1]

[1]Division of Infectious Diseases, Columbia University Medical Center, New York, New York, USA and [2]Comprehensive Health Program, New York Presbyterian Hospital, New York, New York, USA

We describe the characteristics of 31 people living with human immunodeficiency virus hospitalized for severe acute respiratory syndrome coronavirus 2 infection. All patients were on antiretroviral therapy and virologically suppressed at the time of admission. Clinical course and outcomes were similar to those reported in other hospitalized cohorts.

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

Since the identification of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as the causal agent of coronavirus disease 2019 (COVID-19), approximately 4.2 million cases and 290 000 deaths have been reported worldwide [1]. The clinical manifestations of COVID-19 range from mild upper respiratory infection to fulminant respiratory failure and death. Older patients and those with medical comorbidities are at higher risk of severe COVID-19 [2, 3].

Little is known about the interaction between human immunodeficiency virus (HIV) type 1 (HIV-1) infection and SARS-CoV-2 pathogenesis. The US Centers for Disease Control and Prevention designates immunocompromised individuals as a high-risk population, with specific mention of people living with uncontrolled HIV or AIDS [4]. A recent case series of 5 people living with HIV (PLWH) and COVID-19 suggests a younger age at hospitalization but overall good clinical outcomes [5].

Epidemiological and clinical data about the overlapping HIV and SARS-CoV-2 pandemics remain sparse. In this study, we present data on all PLWH hospitalized for COVID-19 between 15 March and 15 April 2020 at a large tertiary care medical center in New York City.

Received 27 April 2020; editorial decision 19 May 2020; accepted 21 May 2020; published online May 30, 2020.

Correspondence: N. Shalev, 180 Ft Washington Ave, Harkness Pavilion, 6th Floor, New York, NY 10032 (ns2413@cumc.columbia.edu).

[a]The first two authors contributed equally to the study.

Clinical Infectious Diseases® 2020;XX(XX):1–4

DOI: 10.1093/cid/ciaa635

METHODS

Data were extracted from institutional HIV and COVID-19 registries. The hospital's COVID-19 registry was created at the onset of the pandemic and was designed to capture demographic, clinical, and laboratory data on all hospitalized COVID-19 patients. The HIV registry predates the COVID-19 pandemic and captures all PLWH seeking care within our hospital system utilizing *International Classification of Diseases, Tenth Revision* codes, laboratory data, and pharmacy records. We cross-referenced both registries to assure that all PLWH admitted with COVID-19 were included in our analysis. HIV diagnosis was ascertained by any history of positive HIV-1 antibody/antigen testing, detectable HIV-1 RNA, hospital and pharmacy records, or patient self-report. All medical records were reviewed manually by the 2 first authors (N. S. and M. S.) to ensure accuracy of the data.

We included all adults >18 years of age with confirmed COVID-19. A confirmed case was defined by a positive result on SARS-CoV-2 polymerase chain reaction (PCR) assay from nasopharyngeal sampling. All SARS-CoV-2 PCR assays were performed in a single hospital laboratory using either the Roche Cobas SARS-CoV-2 assay (Roche Diagnostics) or the Xpert Xpress SARS-CoV-2 assay (Cepheid). Patients admitted between 15 March and 15 April 2020 to Columbia University Irving Medical Center and Allen Hospital, 2 closely affiliated campuses of New York Presbyterian Hospital, were included in the analysis. Data were censored on 12 May 2020.

The institutional review board of Columbia University Medical Center approved the study protocol. Informed consent was waived. All data were deidentified prior to the planned analysis.

The primary outcome of interest was vital status at the time of analysis: death, ongoing hospitalization, and alive at discharge disposition. Secondary outcomes include laboratory and radiographic findings and clinical course. Descriptive statistics were used to summarize the data. Results are reported as means, proportions, and ranges. Analysis was performed with Microsoft Excel software.

RESULTS

Baseline demographics, clinical characteristics, and outcomes are presented in Table 1. Between 15 March and 15 April 2020, 2159 patients with laboratory-confirmed COVID-19 were admitted to our hospital. Of these, 31 were HIV-1 infected (1.4%). The mean age was 60.7 years (range, 23–89 years); 24 (77%) were men and 7 (22.6%) women. Race/ethnicity was available in 30 subjects: 16 (51.6%) non-Hispanic black, 9 (29%) Hispanic of

Table 1. Baseline Demographics, Clinical Characteristics, and Outcomes

Characteristic	Total Patients (N = 31)[a]
Age, y, mean (range)	60.7 (23–89)
Sex	
Female	7 (22.6)
Male	24 (77.4)
Race/ethnicity	
Non-Hispanic black	16 (51.6)
Non-Hispanic white	5 (16.1)
Hispanic, any race	9 (29)
Unknown	1 (3.3)
Comorbidities	
Hypertension	21 (67.7)
Diabetes mellitus	13 (41.9)
Chronic kidney disease	7 (22.6)
Asthma/COPD	8 (25.8)
Obesity (BMI >30 kg/m^2)[b]	9 (33.3)
≥1 comorbidity	22 (71.0)
Current or former smoker	13 (42)
HIV-related variables	
CD4$^+$ T cells, cells/μL, mean (range)	396 (89–924)
CD4$^+$ T-cell % (range)	28.7 (7–49)
HIV type 1 viral load <37 copies/mL	28 (90.3)
Viral load <200 copies/mL	30 (96.8)
Antiretroviral regimen	
INSTI + 2 NRTIs	20 (64.5)
NNRTI + 2 NRTIs	3 (9.7)
PI/b + 2 NRTIs	4 (12.9)
Other	4 (12.9)
Contains TDF/TAF	17 (54.8)
Contains PI	7 (22.6)
Temperature >38.0°C during admission	23 (74.2)
CXR abnormalities on admission[c]	20 (64.5)
Pharmacologic treatment	
None	3 (9.7)
Hydroxychloroquine	24 (77.4)
Azithromycin	16 (51.6)
Corticosteroids	8 (25.8)
IL-6 receptor inhibitor	3 (9.7)
Laboratory values, mean (range)	
Lymphocyte % nadir	12.6 (3.8–31.9)
CRP max, μg/mL	182.2 (1.1 to >300)
Ferritin max, μg/L	1356.7 (80–7490)
D-dimer max, μg/mL	6.9 (0.3–20)
Procalcitonin max, μg/mL	2.2 (0.04–26.9)
Maximal oxygenation support	
Room air	3 (9.7)
Low-flow nasal cannula	13 (41.9)
Non-rebreather mask	7 (22.6)
Mechanical ventilation	8 (25.8)
Vital status	
Alive	23 (74.2)
Discharged	21 (67.7)
Hospitalized	2 (6.5)
Deceased	8 (25.8)

Table 1. Continued

Data are presented as no. (%) unless otherwise indicated.

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; CXR, chest radiography; HIV, human immunodeficiency virus; IL-6, interleukin 6; INSTI, integrase strand transfer inhibitor; NNRTI, nonnucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI/b, pharmacologically enhanced protease inhibitor; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate.

[a]Missing laboratory data as follows: HIV viral load and T-cell data (n = 1); lymphocyte % and CRP (n = 1); ferritin (n = 2); procalcitonin (n = 3); D-dimer (n = 4).

[b]BMI data missing for 4 patients.

[c]One patient did not undergo chest radiography.

any race, and 5 (16.1%) non-Hispanic white. At least 1 comorbidity was identified in 22 (71.0%) patients. The most common were hypertension in 21 (67.7%), diabetes mellitus 13 (41.9%), and obesity 9 (33.3%). Mean body mass index was 28.0 kg/m^2 (range, 14.2–43.8 kg/m^2). Thirteen (42%) patients were current or former smokers and 8 (25.8%) were diagnosed with asthma or chronic obstructive pulmonary disease.

All subjects were taking antiretroviral therapy (ART) at the time of admission. HIV-1 viral load and T-cell panel data were available in 30 patients. Virological suppression, defined as HIV-1 RNA <200 copies/mL, was observed in 30 (100%) of subjects for whom data was available, and in 96.8% of the total sample. Mean absolute and percentage CD4$^+$ T-cell counts were 396 cells/μL and 28.7%, respectively. Twenty-four (80%) had a CD4$^+$ T-cell count >200 cells/μL, and 27 (90%) had a CD4$^+$ T-cell percentage > 14%. The most commonly prescribed ART was integrase inhibitor–based triple therapy in 20 (64.5%) patients. ART regimens containing tenofovir prodrugs or protease inhibitors were prescribed in 17 (54.8%) and 7 (22.6%) patients, respectively. No patient was prescribed lopinavir/ritonavir.

Twenty-three patients (74.2%) presented with fever (defined as a temperature of >38.0°C) or developed fever during admission. Chest radiography was performed in 30 patients, 20 of whom (64.5%) displayed abnormalities consistent with viral pneumonia. Mean peak inflammatory marker concentrations were elevated and mean nadir lymphocyte percentage was 12.6%. Twenty-eight (90.3%) patients received supplemental oxygen and 8 (25.8%) required invasive mechanical ventilation. Disease severity was distributed as follows: mild, 1 (3.2%); moderate, 2 (6.5%); severe, 21 (67.7%); and critical in 7 (22.6%) patients [6]. Hydroxychloroquine was the most frequently prescribed antimicrobial agent, used in 24 patients (77.4%), followed by azithromycin in 16 (51.6%). Corticosteroids were used in 8 (25.8%) and the interleukin 6 receptor (IL-6R) antagonist tocilizumab in 2 (6.5%) patients. One patient was enrolled in a randomized clinical trial (RCT) of the antiviral drug remdesivir and another patient in an RCT of the IL-6R inhibitor sarilumab.

At the time of analysis, 8 (25.8%) patients had died, 21 (67.7%) were alive and discharged, and 2 (6.5%) were alive and hospitalized. Thirteen (41.9%) patients were discharged home and 8 (25.8%) to a care facility. The 2 patients still hospitalized remain in intensive care units. The death rate observed in subjects with a known outcome (ie, no longer alive or hospitalized) was 27.6%. Four deaths occurred in subjects >65 years of age and 4 in patients between 50 and 65 years of age. Four patients had do not resuscitate orders at the time of death. Seven of the 8 deceased patients were receiving a tenofovir prodrug as part of their ART regimen.

DISCUSSION

This is the largest case series to date describing the clinical characteristics and outcomes in PLWH hospitalized for COVID-19. Approximately 1.4% of COVID-19 patients hospitalized at our institution were HIV infected. Based on an estimated HIV-1 prevalence of 1.5% in our hospital catchment area [7], this finding does not suggest increased rates of hospitalization in this patient population. Similarly, a larger study of 5700 patients admitted with COVID-19 to a network of New York City hospitals demonstrated an HIV prevalence of 0.8% [8]. Baseline characteristics and outcomes were comparable to those described in large cohorts of HIV-uninfected patients with COVID-19 [3, 4, 9].

A striking finding of our series is the observation that all patients were virologically suppressed on ART at the time of admission and that 90% had $CD4^+$ T-cell percentage >14%. Although mean $CD4^+$ T-cell counts and percentages were slightly lower than the normal range, this reduction likely reflects SARS-CoV-2–associated $CD4^+$ T-cell lymphopenia as reported in other studies [10]. In an unadjusted comparison, mean nadir lymphocyte percentage did not differ between the HIV-infected and uninfected patients in our cohort. Thus far, no patient with uncontrolled HIV or AIDS has been admitted to our hospital during the COVID-19 outbreak. This finding is surprising since, during routine times, our hospital maintains an active inpatient teaching service for the care of people with uncontrolled HIV and AIDS-related complications. Furthermore, surveillance data show that nearly one-quarter of PLWH in New York City are not virologically suppressed [7]. These observations raise the possibility that uncontrolled HIV infection and poor $CD4^+$ T-cell function may limit SARS-CoV-2–related immune dysregulation and cytokine release. Absence of T-cell activation has been hypothesized to mitigate the severe immunopathological phenomena seen in COVID-19 [11].

Certain antiretroviral agents, including tenofovir and lopinavir, have shown antiviral activity against SARS-CoV-2 in vitro [12, 13]. The in vitro antiviral activity of tenofovir prodrugs has led to speculation about a protective effect of tenofovir disoproxil fumarate– and tenofovir alafenamide–containing antiretroviral regimens against COVID-19 [8]. In our series, 17 subjects (54.8%) were prescribed tenofovir-containing antiretroviral regimens, and 7 (22.6%) were receiving protease inhibitors. While our cohort is too small to detect differences in outcomes by ART components, these data demonstrate that ART does not fully prevent severe COVID-19. A randomized clinical trial of lopinavir/ritonavir failed to show mortality benefit in severe COVID-19 [14].

This study has multiple limitations. The data represent findings from a small group of subjects admitted to 2 hospitals within a single academic medical center. Comparison to patients without HIV was not included in the analysis due to the difficulty of adequate matching. Data were extracted from the medical record, which may have contained omissions or errors.

CONCLUSIONS

PLWH hospitalized for COVID-19 share similar clinical characteristics and outcomes with other hospitalized cohorts. All patients in our series were virologically suppressed on ART and most had $CD4^+$ T-cell counts >200 cells/μL at admission. These data suggest that SARS-CoV-2 does not act as an opportunistic pathogen in patients with uncontrolled HIV or AIDS. The relationship between intact cellular immunity and COVID-19 severity in PLWH requires further study.

Note

Potential conflicts of interest. The authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

References

1. World Health Organization. Coronavirus disease (COVID-19) pandemic, **2020**. Available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019. Accessed 13 May 2020.
2. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA **2020**; 323:1239–42.
3. Onder G, Rezza G, Brusaferro S. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy [manuscript published online ahead of print 23 March 2020]. JAMA **2020**. doi:10.1001/jama.2020.4683.
4. Centers for Disease Control and Prevention. People who are at higher risk for severe illness. **2020.** Available at: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-at-higher-risk.html. Accessed 20 April 2020.
5. Blanco JL, Ambrosioni J, Garcia F, et al. COVID-19 in patients with HIV: clinical case series. Lancet **2020**; 7:e314–6.
6. National Institutes of Health. Management of persons with COVID-19. Available at: https://covid19treatmentguidelines.nih.gov/overview/management-of-covid-19. Accessed 13 May 2020.
7. New York City Department of Health and Mental Hygiene. HIV surveillance annual report, 2018. Available at: https://www1.nyc.gov/assets/doh/downloads/pdf/dires/hiv-surveillance-annualreport-2018.pdf. Accessed 21 April 2020.
8. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area [manuscript published online ahead of print 22 April 2020]. JAMA **2020**. doi:10.1001/jama.2020.6775.

9. Centers for Disease Control and Prevention. Severe outcomes among patients with coronavirus disease 2019 (COVID-19)—United States, February 12–March 16, 2020. MMWR Morb Mortal Wkly Rep **2020**; 69:343–6.
10. Chen G, Wu D, Guo W, et al. Clinical and immunological features of severe and moderate coronavirus disease 2019. J Clin Invest **2020**; 130:2620–9.
11. Mascolo S, Romanelli A, Carleo MA, Esposito V. Could HIV infection alter the clinical course of SARS-CoV-2 infection? When less is better [manuscript published online ahead of print 15 April 2020]. J Med Virol **2020**. doi:10.1002/jmv.25881.
12. Choy KT, Wong AY, Kaewpreedee P, et al. Remdesivir, lopinavir, emetine, and homoharringtonine inhibit SARS-CoV-2 replication in vitro. Antiviral Res **2020**; 178:104786.
13. Elfiky AA. Ribavirin, remdesivir, sofosbuvir, galidesivir, and tenofovir against SARS-CoV-2 RNA dependent RNA polymerase (RdRp): a molecular docking study. Life Sci **2020**; 253:117592.
14. Cao B, Wang Y, Wen D, et al. A trial of lopinavir-ritonavir in adults hospitalized with severe Covid-19. N Engl J Med **2020**; 382:1787–99.