Clinical characteristics and outcomes in people living with HIV hospitalized for COVID-19

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Abstract

We describe the characteristics of 31 people living with HIV (PLWH) hospitalized for Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-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.

Introduction

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 ([i]). 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 ([ii,iii]).

Little is known about the interaction between Human Immunodeficiency Virus-1 (HIV-1) infection and SARS-CoV-2 pathogenesis. The US Center for Disease Control and Prevention designates immune-compromised individuals as a high-risk population, with specific mention of people living with uncontrolled HIV or AIDS ([iv]). A recent case series of five people living with HIV (PLWH) and COVID-19 suggests a younger age at hospitalization but overall good clinical outcomes ([v]).

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

Methods

Data was 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 ICD10 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 charts were reviewed manually by the two first authors (NS and MS) 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 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, Inc.). Patients admitted between March 15 and April 15, 2020 to Columbia University Irving Medical Center and Allen Hospital, two closely affiliated campuses of New York Presbyterian Hospital, were included in the analysis. Data were censored on May 12, 2020.

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

The primary outcome of interest was vital status at the time of analysis: death, ongoing hospitalization and alive 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 Excel (Microsoft Corp).

Results

Baseline demographics, clinical characteristics and outcomes are presented in the Table. Between March 15 and April 15, 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); 24 (77%) were men and 7 (22.4%) women. Race/ethnicity was available in 30 subjects: 16 (51.6%) non-Hispanic black, 9 (29%) Hispanic of any race and 5 (9.1%) non-Hispanic white. At least one comorbidity was identified in 22 (71.0%) patients. The most common comorbidities were hypertension in 21 (67.7%), diabetes mellitus 13 (41.9%), and obesity 9 (33.3%). Mean BMI was 28.0 kg/m2 (range 14.2-43.8 kg/m2). Thirteen (42%) patients were current or former smokers and 8 (25.8%) were diagnosed with asthma or COPD.

All subjects were taking antiretroviral therapy (ART) at the time of admission. HIV-1 viral load and T cell panel data was available in 30 patients. Virological suppression, defined as an HIV-1 RNA <200 copies/ml, was observed in 30 (100%) subjects; 28 (90.3%) had a viral load <37 copies/ml. Mean absolute and percent CD4+ T cell counts were 396 cells/ul and 28.7%, respectively. Twenty-four (80%) had a CD4+ T cell count >200 cells/ul, and 27 (90%) had a CD4+ T cell percent above 14. The most commonly prescribed ART was integrase inhibitor-based triple therapy in 20 (64.5%) patients. Antiretroviral regimens containing

tenofovir prodrugs or protease inhibitors (PI) were prescribed in 17 (54.8%) and 7 (22.6%) patients, respectively. No patient was prescribed lopinavir/ritonavir.

Twenty-three patients (74.3%) 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 12.1. Twenty-eight (90.3%) patients received supplemental oxygen and 8 (25.7%) 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 ([vi]). 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 IL6-receptor 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-6 receptor 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 two patients still hospitalized remain in intensive care units. The death rate observed in subjects with a known outcome (i.e. no longer alive or hospitalized) was 27.6%. Four deaths occurred in subjects over 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. 7 of the 8 deceased patients were receiving a tenofovir prodrug as part of their antiretroviral 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 ([vii]), 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% ([viii]). Baseline characteristics and outcomes were comparable to those described in large cohorts of HIV-uninfected patients with COVID-19 ([3,4,ix]).

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 percent above 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 ([x]). 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 ([xi]).

Certain antiretroviral agents, including tenofovir and lopinavir, have shown antiviral activity against SARS-CoV-2 *in vitro* ([xii,xiii]). The *in vitro* antiviral activity of tenofovir prodrugs has led to speculation about a protective effect of TDF- and TAF-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 PIs. 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 ([xiv]).

This study has multiple limitations. The data represent findings from a small group of subjects admitted to two 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/ul 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.

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None

Notes

The authors report no financial conflicts of interest.

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Table: Baseline demographics, clinical characteristics and outcomes

	Total patients n=31^
Age, years mean (range)	60.7 (23-89)
Gender n, (%)	
Female	7 (22.5)
Male	24 (77.4)
Race/ethnicity n (%)	
Non-Hispanic Black	16 (51.6)
Non-Hispanic White	5 (16.1)
Hispanic, Any Race	9 (29)
Unknown	1 (3.3)
Comorbidities n (%)	
Hypertension	21(67.7)
Diabetes Mellitus	13 (41.9)
Chronic kidney disease	7 (22.6)
Asthma/COPD	8 (25.8)
Obesity (BMI>30 kg/m2)*	9 (33.3)
>=1 comorbidity	22 (71.0)
Current or former smoker n (%)	13 (42)

HIV-related variables	
CD4+ T cells, cells/ul mean (range)	396 (89-924)
CD4+ T cells % (range)	28.7 (7-49)
HIV-1 viral load <37 copies per ml, n (%)	28 (90.3)
Viral load <200 copies/ml, n (%)	30 (96.8)
Antiretroviral regimen, n (%)	
INSTI+2NRTI	20 (64.5)
NNRTI+2NRTI	3 (9.7)
PI/b+2NRTI	4 (12.9)
Other	4 (12.9)
Contains TDF/TAF	17 (54.8)
Contains PI	7 (22.6)
Fever	
Temperature >38.0°C during admission	23 (74.2)
CXR abnormalities on admission**	20 (64.5)
Pharmacologic treatment n (%)	
None	3 (9.7)
Hydroxychloroquine	24 (77.4)
Azithromycin	16 (51.6)
Corticosteroids	8 (25.8)

IL6 Receptor inhibitor	3 (9.7)
Laboratory values mean (range)	
Lymphocyte % nadir	12.6 (3.8-31.9)
C-reactive protein max, µg/mL	182.2 (1.1->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 n (%)	
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)

*BMI data missing for 4 patients; **One patient did not undergo chest radiography; ^Missing laboratory data as follows: HIV viral load and T cell data missing in 1 patient, lymphocyte% and CRP, 1; ferritin, 2; procalcitonin, 3; d-dimer, 4.

BMI, body mass index; INSTI, integrase strand transfer inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI/b, pharmacologically enhanced protease inhibitor; TDF, tenofovir disoproxil fumarate; TAF, tenofovir alafenamide fumarte.

CXR, chest radiography; ICU, intensive care unit.