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COMMENTARY

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COVID-19 in HIV-infected patients: A case series and literature review

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Abstract

During the current COVID pandemic, there is growing interest to identify subsets of the population that may be at a higher than average risk of infection. One such group includes people living with HIV.

KEYWORDS
coronavirus, COVID, HIV, SARS-CoV-2

1 | INTRODUCTION

During the current COVID pandemic, there is a growing interest to identify subsets of the population that may be at a higher than average risk of infection. One such group includes people living with HIV (PLWH). While immune deficiency could increase the risk of acquiring viral infections, reports suggest that defective cellular immunity could paradoxically bode better outcomes in COVID-associated cytokine dysregulation. Furthermore, antiretroviral drugs (protease inhibitors [PIs]), are being tested as a therapeutic option owing to their potential to inhibit the 3-chymotrypsin-like protease of COVID.[1-3] This case series reviews the clinical and laboratory characteristics of COVID in PLWH admitted to a community hospital.

COVID in PLWH raises certain unique concerns because older PLWH have a higher risk of comorbidities compared with uninfected individuals of the same age, while younger PLWH are more likely to be noncompliant with antiretroviral therapy (ART), thereby leading to reduced HIV viral suppression.[4] It may also multiply pre-existent issues in PLWH, such as access and adherence to ART, mental health burden, substance use, food insecurity, and so forth.[4] While social isolation slows the spread of COVID, its implications on the above-mentioned issues remains to be seen. Socioeconomic and ethnic disparities can affect clinical outcomes and there is a need for more data to make any definitive conclusions.[4] This retrospective analysis identified PLWH among all COVID inpatients in our institution from March to April 2020. HIV diagnosis was based on prior testing within the health system and COVID was confirmed by reverse-transcriptase polymerase chain reaction (RT-PCR). At admission, patients were categorized as mild, moderate, severe, or critical based on the NIH guidelines as follows:

1. Mild—any signs/symptoms of COVID without dyspnea/abnormal chest imaging.
2. Moderate—lower respiratory disease by clinical assessment or imaging and SpO_2 ≥94% on room air.
3. Severe—respiratory frequency >30/min, SpO_2 <94% on room air, PaO_2/FiO_2 <300 mmHg, or lung infiltrates >50%.
4. Critical—respiratory failure, septic shock, or multiorgan dysfunction (https://www.covid19treatmentguidelines.nih.gov/overview/management-of-COVID/).

We compiled demographics, clinical, and laboratory characteristics of all patients. Descriptive statistics like simple frequencies, percentages, and mean were calculated. This study was approved by the institutional review board. All six patients were African-American, reflecting the majority demographic that our hospital caters to. One patient was female, while the rest identified as male. The average BMI was 24 and the mean age was 64 years. All patients had at least one comorbidity. Half the patients had an active mental health problem/cognitive impairment and 33% had an active substance use problem. Five of the six were noted to be compliant with their ART preadmission. Majority of the patients were on INSTIs.

Abbreviations: BMI, body mass index; NIH, National Institutes of Health; PaO_2/FiO_2, ratio of arterial partial pressure of oxygen to fraction of inspired oxygen; RT-PCR, reverse-transcriptase polymerase chain reaction; SpO_2, saturation of oxygen.

TABLE 1 Patient demographics

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
General demographics						
Age	62	59	45	74	57	87
Sex	Male	Female	Male	Male	Male	Male
Race	African American	African American	African American	African American	African American	African American
Body mass index	25	21	21	22	32	24
Sick contact	+	+	–	–	+	–
Past medical history						
Active mental health problems	Dementia	–	Depression	–	–	Dementia
Active substance use	–	Tobacco	Cocaine	–	–	–
Chronic obstructive pulmonary disease	–	+	–	–	+	–
Diabetes mellitus	+	–	–	+	–	+
End-stage renal disease on dialysis	+	–	–	–	–	–
Coronary artery disease	–	+	+	–	–	–
Hypertension	+	+	–	+	–	+
Hyperlipidemia	–	+	–	+	+	+
Peripheral vascular disease	–	+	–	–	–	-
HIV-related values						
Last CD4 (cells/mm^3)	491	1500	500	772	678	651
HIV viral load (copies/ml)	10,000	Undetectable	Undetectable	Undetectable	Undetectable	Undetectable
ART regimen adherence	+	+	+	+	+	-
ART regimen preadmission	RPV/RAL/3TC	ABC/EFV/3TC	BIC/TAF/FTC	BIC/TAF/FTC	EVG-c/TAF/FTC	EFV/TDF/FTC
ART regimen during admission	ART held	Same continued	Same continued	Same continued	Same continued	Same continued

Abbreviation: ART, antiretroviral therapy.

In one patient, ART was discontinued as per the discretion of the supervising physician; others were continued on their home ART regimen. The mean CD4 count was 765, with only one patient having a detectable viral load. The distribution of COVID severity was one mild, three moderate, one severe, and one critical. Two patients expired due to post-cardiac arrest syndrome and worsening hypoxic respiratory failure, respectively. Of the remaining four, two required supplemental oxygen during admission and the other two did not. One patient was discharged on home-oxygen. The average duration of hospitalization was 7.5 days. Other clinical/diagnostic findings are in Tables 1-3. Our case series was set in a community hospital in Philadelphia from March to April 2020 and this period was picked because it had a rapid increase in COVID cases. To date, Philadelphia has had approximately 25,000 cases and 1500 deaths, with a peak of 603 new cases in a single day on April 15, 2020.[5] With regard to impact in immunosuppression/immunodeficiency, a systematic review demonstrated that both had increased severity of COVID illness, 3.29- and 1.55-fold, respectively, but this difference was not statistically significant.[6] With regard to HIV, Table 4 summarizes the available evidence.[1-3,7-11]

Available data does not point to HIV being an independent risk factor for poor prognosis in COVID but PLWH are at a higher risk for the noncommunicable comorbidities that are associated with worse clinical outcomes.[4] In our case series, we noted that the two patients who died had more medical comorbidities. These two patients also had elevated procalcitonin. Although both received broad-spectrum antibiotics, there was no growth in their blood/sputum cultures. Hence, it is difficult to assess if they truly had a superadded bacterial infection making them sicker or if it was a nonspecific finding.

Richardson et al.[15] looked at an exclusive inpatient COVID population in New York and found that mortality was 21% overall but as high as 88% in critically ill patients with underlying comorbidities. COVID mortality in PLWH has been noted to be highly variable, ranging anywhere from 3% to 77%.[1-3,7-11] This variability is due to the heterogeneity of the patients studied, differing in key elements, such as inpatients/outpatients, age group, and baseline characteristics. In our case series, limited to inpatients, the mortality rate was 33%, which seems higher than the average of 20%–21% but this should be interpreted with caution as both the patients that died required significant ventilatory support and had more comorbidities. The mean age in our case series (64 years) was notably higher than that described in the aforementioned studies,[1-3,7-11] which ranged from 38 to 60 years. When adjusted for higher mean age, severity of

TABLE 2 Admission laboratory values

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Hemoglobin (g/dl)	12.3	7.1	13.6	13.9	12.2	8.6
Leukocyte count (x1000/μl)	5.72	20.64	6.1	7.03	3.3	8.55
Neutrophil (%)	60.9	88.2	65	81.4	72.7	84.4
Lymphocyte (%)	17.7	8.6	20	11.2	17	7.3
Absolute lymphocyte count (x1000/μl)	1.01	1.77	1.22	0.78	0.56	0.62
Platelets	275	560	170	278	124	268
Baseline creatinine (mg/dl)	8	1	NA	1.6	0.8	1
Creatinine (mg/dl)	8.6	1	1.2	3.1	1.1	1.8
Peak creatinine (mg/dl)	11.9	1.9	1.2	3.1	1.1	1.8
LDH	338	520	214	508	499	258
Ferritin (ng/ml)	1944	171	NA	NA	7469	241
Peak ferritin (ng/ml)	2879	171	NA	NA	7469	347
AST (IU/ml)	24	72	NA	52	73	38
ALT (IU/ml)	6	42	NA	22	67	22
Total bilirubin (mg/dl)	0.2	0.2	NA	0.8	1.1	0.4
Direct bilirubin (mg/dl)	0.1	0.1	NA	0.4	0.7	0.3
INR	1.3	1.7	NA	NA	1.2	1.2
D-dimer (ng/ml)	1970	12,940	340	NA	2690	1170
Fibrinogen (mg/dl)	586	341	NA	NA	NA	677
CRP (mg/L)	274	243.8	NA	178.6	74	277.2
Procalcitonin (ng/ml)	5.83	2.74	NA	NA	0.1	0.42
Lactate (mmol/L)	1.8	11.19	NA	1.1	1.2	1.8

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; INR, international normalized ratio; LDH, lactate dehydrogenase.

illness, and ventilator needs, the mortality rate in our case series is comparable with other studies.

Contrary to the concern for worse outcomes in HIV, some data suggest favorable outcomes for COVID in PLWH, perhaps due to the protective effect of ART.[1] However, PIs (lopinavir–ritonavir, darunavir) tested in clinical trials did not show increased efficacy compared with standard supportive care. Current guidelines do not recommend any change in ART to boosted PI-containing regimen.[7] In vitro studies show that remdesivir was the most effective against COVID when compared against medications like tenofovir, lamivudine, emtricitabine, and so forth. Tenofovir though has anti-RNA-dependent RNA polymerase activity akin to remdesivir and hence its protective effect cannot entirely be ruled out.[1,8]

Despite the largely reassuring data regarding COVID in PLWH in terms of disease severity and mortality, there are many aspects that are yet to be studied. Some data demonstrates that there is a more pronounced decline of CD4 count in the PLWH population with severe COVID and that the lymphopenia can take several weeks to return to baseline. It is unclear if this translates into an increased risk of opportunistic infections and need to be studied.[3] Studying these long-term effects is challenging, given the variable degree of control in PLWH. The spectrum includes viral suppression to a degree that it is undetectable and untransmittable (U = U), HIV-associated comorbidities/virological failure, and severe immunodeficiency/AIDS-defining illnesses. Larger studies are needed to ensure adequate representation of all these categories of PLWH.

TABLE 3 Clinical course

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
FiO_2 at admission	21	100	21	21	28	21
Chest radiograph at admission	+, <50% infiltrates	+, >50% infiltrates	-	+, <50% infiltrates	+, >50% infiltrates	+, <50% infiltrates
COVID severity at admission	Moderate	Critical	Mild	Moderate	Severe	Moderate
Highest FiO_2 during admission	100%	100	21	21	35	28
New supplemental O_2 during admission	+	+	–	–	+	+
Length of stay (days)	14	6	3	4	8	10
Intubation	–	6 days	–	–	–	–
NRB/high flow	6 days	–	–	–	–	–
Discharged on new O_2	Expired	Expired	–	–	+	–
Disseminated intravascular coagulation	–	–	–	–	–	–
New deep vein thrombosis/pulmonary embolism	–	–	–	–	–	+
Gastrointestinal bleed	–	–	–	–	–	–
Required pressors	–	4 days	–	–	–	–
Hydroxychloroquine (HCQ)	+	+	–	–	+	+
Steroids	–	+	–	–	–	–
Tocilizumab	–	–	–	–	–	–
Remdesivir	–	–	–	–	–	–
Azithromycin	–	–	–	+	+	–
Other antibiotics	+	+	–	+	+	–
Outcome	Expired	Expired	Discharged	Discharged	Discharged	Discharged

Abbreviation: NRB, non-rebreather mask.

TABLE 4 Summary of evidence regarding COVID in PLWH

Design, duration, and authors of the study	Number of cases	Mean age and demographics	Mean CD4 and immune status	Severity of COVID illness	Deaths	Home ART regimen	Other treatment (Rx)	Other findings
Gervasoni et al.[1] Italy February 21–April 16, 2020 Retrospective	47 28 confirmed	51 ± 11 years 76% male	636 ± 290/mm^3 3 detectable viral load	13 admitted 6 severe 2 ventilation	2	80% INSTI 11% PI 42% tenofovir	<50% received hydroxychlorquine/ azithromycin/ lopinavir–ritonavir 1 tocilizumab and remdesivir 1 tocilizumab	64% patients—at least 1 comorbidity Mean age was 10 years lower than HIV-negative population
Blanco et al.[2] Spain February to March 9, 2020 Retrospective	5 cases	38 years 3 male 2 transgenders	563.6/mm^3	2 ICU 1 NIV 1 ventilation	0	1 patient was not on ART 1 PI 3 INSTI	2 interferon 4 hydroxychloroquine 2 steroids 1 tocilizumab 3 azithromycin 3 broad-spectrum antibiotics	All five patients were put on a boosted PI regimen during admission
Harter et al.[3] Germany March 11–April 17, 2020 Retrospective; 12 centers	33 cases	48 years 30 male	670/mm^3 2 detectable viral load 4 CD4 count < 350	14 admitted 6 ICU 4 ventilation 1 NIV 76% mild, 24% severe/ critical	3	All patients were on ART NRTIs 31 INSTI 20 NNRTIs 9 PIs 4 NRTI –tenofovir/ emtricitabine/ lamivudine	Unknown	60% patients had at least 1 comorbidity 5, HBV coinfection; 4 resolved/1 chronic Hep B 1 cured HCV
Ozlem et al.[10] Turkey March–April 2020 Retrospective	4 patients	37 years All male	627 cells/mm^3 1 detectable viral load	1 ICU	1	1 newly started on TDF/ FTC + LPV/r 2 PI 1 INSTI	1 patient got PCP Rx with TMP–SMX as well and discharged on PCP and MAC prophylaxis 1 HCQ, azithromycin	1 HBV coinfection 1 DM, COPD, HTN
Suwanwongse et al.[11] New York March 25–April 20, 2020 Retrospective	9 patients	58 years 7 male 2 female	616 cells/mm^3 (excluding one patient with unknown CD4)	5 ventilation 6 INSTI 1 PI All patients were on tenofovir and emtrici-tabine	7	8/9 were on ART	6/9 got antibiotics 4 azithromycin 4 got HCQ	All patients had at least 1 other medical comorbidity 5 hypertension 3 diabetes mellitus 4 COPD
Karmen-Tuohy et al.[12] New York March 2–April 23, 2020	21 HIV 42 non-HIV	60 years 19 male	298 cells/m^3 (2 unknown CD4) 1 CD4 < 200 and viral load > 50	6 - ICU 5- ventilation	6 died/ transfer-red to hospice	All patients were on HAART 1 PI	3 HIV and 1 non-HIV patient received antibiotics for superimposed bacterial pneumonia	HIV patients- higher absolute lymphocyte count ($p = .043$) and higher CRP

(Continues)

TABLE 4 (Continued)

Design, duration, and authors of the study	Number of cases	Mean age and demographics	Mean CD4 and immune status	Severity of COVID illness	Deaths	Home ART regimen	Other treatment (Rx)	Other findings
4 hospitals Retrospective, observational Matched with non-HIV patients								Greater % of HIV patients had an abnormal chest radiograph Trend toward HIV-positive patients having longer hospital stay, higher ICU admission, mechanical ventilation but not statistically significant No significantly worse outcomes in HIV compared with matched non-HIV patient
Shalev et al.[13] New York March 15–April 15, 2020 Retrospective	31 patients	60.7 years 24 male	396 cells/mm^3 30 patients with viral load < 200	2 ICU	8	All patients were on ART NRTI 20 17 got tenofovir 7 PI	24 hydroxychlorquine 16 azithromycin 8 corticosteroids 2 tocilizumab 1 remdesivir 1 sarilumab	At least 1 comorbidity in 22 patients, most common included HTN, DM, obesity 13 current or former smokers 8 asthma or COPD
Vizcarra et al.[14] Spain Until April 30, 2020 Observational prosepective study	51 patients	53 years 8 female	Unknown mean 24 patients with nadir < 200, 21(41%) between 200-499, 6(12%) > 500	28 admitted 23 ambulatory 6 ICU 5 ventilation	2	41 INSTI 11 PI 8 NNRTI 37 tenofovir	30 HCQ 19 azithromycin 14 lopinavir 1 remdesivir 15 steroids 4 tocilizumab	38 (75%) mild/moderate disease, 13 (25%) severe disease 32 patients with at least 1 comorbidity, mostly HTN and DM

Abbreviations: ART, antiretroviral therapy; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; DM, diabetes mellitus; HAART, highly active antiretroviral therapy; HCQ, hydroxychloroquine; HBV, hepatitis B virus; HCV, hepatitis C virus; HTN, hypertension; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; PCP, pneumocystis pneumonia; PLWH, people living with HIV; SMX, sulfamethoxazole; TMP, trimethoprim.

This case series shows that despite a higher mean age and all our patients having at least one other medical illness, the morbidity and mortality were comparable to other previously conducted studies. The limitation of this study is that it is a single-center retrospective analysis and bigger prospective studies with longer follow-up are needed to assess the effect of HIV and ART in COVID and also look at its other long-term sequelae.

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