OPEN

Descriptive Analysis of Patients Living With HIV Affected by COVID-19

Smitha Gudipati, MD, Indira Brar, MD, Shannon Murray, MHS, John E. McKinnon, MD, Nicholas Yared, MD, and Norman Markowitz, MD

Background: COVID-19 disease has spread globally and was declared a pandemic on March 11, 2020, by the World Health Organization. On March 10, the State of Michigan confirmed its first 2 cases of COVID-19, and the number of confirmed cases has reached 47,182 as of May 11, 2020, with 4555 deaths.

Setting: Currently, little is known if patients living with HIV (PLWH) are at a higher risk of severe COVID-19 or if their antiretrovirals are protective. This study presents epidemiologic and clinical features of COVID-19 infected PLWH in Detroit, Michigan.

Methods: This is a case series that included 14 PLWH with laboratory-confirmed COVID-19 infection who were evaluated at Henry Ford Hospital in Detroit, Michigan, between March 20, 2020, and April 30, 2020.

Results: Fourteen PLWH were diagnosed with COVID-19. Twelve patients were men and 2 were women; 13 patients were virally suppressed. Eight patients were hospitalized, and 6 patients were told to self-quarantine at home after their diagnoses. Three patients who were admitted expired during their hospital stay. No patient required bilevel positive airway pressure or nebulizer use in the emergency department, and none developed acute respiratory distress syndrome, pulmonary embolism, deep venous thrombosis, or a cytokine storm while on therapy for COVID-19.

Conclusion: Although the clinical spectrum of COVID-19 among PLWH cannot be fully ascertained by this report, it adds to the data that suggest that HIV-positive patients with SARS-CoV-2 infection are not at a greater risk of severe disease or death as compared to HIV-negative patients.

Key Words: HIV, COVID-19, SARS-CoV-2, cART, tenofovir

(*J Acquir Immune Defic Syndr* 2020;85:123–126)

INTRODUCTION

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a novel coronavirus first detected in December 2019 in Wuhan, Hubei Province, China.[1] Many of the initial cases had a common exposure to the Huanan Wholesale Seafood Market that also traded live animals.[2] SARS-CoV-2 was then identified on January 7, 2020, by the Chinese Center for Disease Control and Prevention, which then disclosed the genomic sequence on January 11, 2020.[3] The World Health Organization named the infection caused by SARS-CoV-2, COVID-19. Since the initial detection of COVID-19, the disease has spread globally and was declared a pandemic on March 11, 2020, by the World Health Organization.[4] In the United States, Detroit, Michigan, had become a "hotspot" of COVID-19 infected patients with the number of confirmed cases reaching 47,182 as of May 8, 2020, with 4555 deaths in Michigan (fourth most deaths in the United States).[5]

Currently, little is known if patients living with HIV (PLWH) are at a higher risk of severe COVID-19 or if antiretroviral medications used to treat HIV are protective against severe COVID-19. Tenofovir has been shown in vitro to tightly bind to the SARS-CoV-2 RNA-dependent RNA polymerase.[6] Alternatively, lopinavir–ritonavir has already been shown to have no benefit beyond standard care in a large randomized control trial.[7,8] In addition, little is known if and how frequently PLWH mount the intense cytokine response leading to cytokine storm and severe COVID-19. We describe our single-center experience in Detroit, Michigan, of COVID-19 in patients infected with HIV-1. We reviewed patients' demographics, clinical characteristics of both their HIV and COVID-19 coinfections, the antiviral and antiretroviral treatments they received, and their clinical outcomes.

METHODS

This is a case series that included 14 PLWH who were evaluated in the Henry Ford Hospital (HFH) emergency department for laboratory-confirmed COVID-19 infection, between March 20, 2020, and April 30, 2020. A confirmed case of COVID-19 was defined by a positive result on a reverse transcriptase polymerase chain reaction assay of a nasopharyngeal swab sample. Patients were identified, and clinical data were collected from electronic medical records. All laboratory tests and radiological assessments were performed at the discretion of the treating physician.

From the Department of Infectious Disease, Henry Ford Hospital, Detroit, MI.
The authors have no funding or conflicts of interest to disclose.
Correspondence to: Smitha Gudipati, MD, 2799 W Grand Blvd, Detroit, MI 48202 (e-mail: Sgudipa2@hfhs.org).

Categorical variables were analyzed using the χ^2 test. Approval from the Henry Ford Health System Institutional Review Board was obtained.

RESULTS

From March 20, 2020, to April 30, 2020, 7372 people tested positive for COVID-19 at HFH. Of this group, 14 were PLWH. Twelve patients were men and 2 were women. Twelve were African American and 2 were Hispanic. Six patients were discharged from the emergency department to self-quarantine. Eight patients were admitted to the general practice unit, one of whom required supplemental oxygenation. Two of the 8 patients were admitted to the intensive care unit and required invasive mechanical ventilation. The average duration of symptoms before admission was 12 days. The most common presenting complaints were fever (N = 7; 50%), shortness of breath (N = 7; 50%), cough (N = 10; 70%), diarrhea (N = 4; 29%), and loss of taste and smell (N = 4; 29%). One patient endorsed previous travel to Texas and 2 patients endorsed exposure as health care workers. Baseline characteristics of the patients are shown in Table 1. The most common comorbidities included obesity (N = 8; 57%), hypertension (N = 8; 57%), diabetes (N = 6; 43%), chronic kidney disease (N = 5; 36%), and end-stage renal disease requiring hemodialysis (N = 2; 14%). Past or present smoking and alcohol use was noted in the medical histories of 7 patients. One patient was previously on an angiotensin-converting enzyme inhibitor, 2 patients were on an angiotensin II receptor blocker, and 4 patients were on inhaled steroids for either chronic obstructive pulmonary disease or asthma.

Thirteen patients had suppressed HIV viral loads (Table 1) on combination antiretroviral therapy (cART) regimens. One patient was not on cART at presentation. All patients but one on cART had a regimen with a tenofovir component, and only 1 patient was on a protease inhibitor–based regimen with cobicistat-boosted darunavir. Two patients had a history of an AIDS defining illness in the past.

In the emergency department, antibiotics for community-acquired pneumonia were initiated for 4 of the 14 patients, intravenous fluids were given to 3 patients, and systemic corticosteroids were given to 3 patients. No patient required bilevel positive airway pressure or nebulizer use in the emergency department, and none developed acute respiratory distress syndrome, pulmonary embolism, deep venous thrombosis, or a cytokine storm while on therapy for COVID-19. Two patients were transferred to the intensive care unit during their admission and both expired; one from respiratory failure secondary to multifocal pneumonia, and the second one from cardiac arrest and had an extensive history of congestive heart failure. The third patient died while on the general practice unit from cardiac arrest. Five patients were discharged home. All admitted patients received hydroxychloroquine 400 mg per os twice a day for 2 doses, followed by 200 mg per os twice a day for 4 days. The administration of hydroxychloroquine was consistent with our institution's treatment guidelines during that period. At 30 days after their COVID-19 diagnoses, 11 of the 14 PLWH were still alive.

Because of cardiac-associated mortality concern in the 3 patients who expired, a further medical record review was undertaken with a focus on COVID-19 and hydroxychloroquine-associated causes. Patient 13 died from worsening heart failure that was severe before a COVID-19 diagnosis. The patient expired in the intensive care unit from pulseless electrical activity arrest with no documentation of torsades de pointes noted on cardiac monitoring. Patient 9 expired on the general practice unit from a cardiac arrest. He was found pulseless and unresponsive by a nurse. This patient had multiple comorbidities, including metastatic cancer, heart

TABLE 1. Characteristics Among Our Coinfected COVID-19 and HIV Patients at Presentation

Patient	Age, yrs	Gender	Race/ Ethnicity	CD4 cells/ mm^3	BMI, kg/m^2	HIV-1 Viral Load (copies/mL)	CRP, mg/dL	ALC, K/μL	Comorbidities	Disposition From ED
1	74	Male	Black	523	28.8	<20	21.5	0.2	HTN, DM, CKD	GPU to ICU*
2	57	Male	Black	982	55.82	<20	2.1	2.1	COPD, HTN, DM, CHF	GPU
3	65	Female	Black	21	33.32	1646	5.1	1	DM	GPU
4	58	Female	Black	482	33.45	<20	N/A	N/A	DM, CKD	Home
5	39	Male	Black	1291	28.7	<20	N/A	N/A	None	Home
6	64	Male	Black	523	34	<20	11.3	0.3	HTN	GPU
7	48	Male	Hispanic	516	36.26	<20	11.4	1.5	None	GPU
8	54	Male	Hispanic	280	32.92	<20	N/A	0.4	HTN, DM, CKD	Home
9	63	Male	Black	242	20.71	26	20.7	0.3	COPD on 2L O2, HTN, CHF, ESRD on HD	GPU*
10	45	Male	Black	1756	25.73	<20	N/A	N/A	None	Home
11	56	Male	Black	806	31.2	<20	14.4	0.8	CKD, DM, HTN	GPU
12	36	Male	Black	463	23.9	<20	N/A	N/A	None	Home
13	64	Male	Black	145	31.2	35	11.9	1.1	HTN, ESRD on HD, COPD, CHF	GPU to ICU*
14	64	Male	Black	540	23	<20	N/A	N/A	HTN	Home

ALC, absolute lymphocyte count; BMI, body mass index; COPD, chronic obstructive pulmonary disease; CHF, congestive heart failure; CKD, chronic kidney disease; CRP, C-reactive protein; DM, diabetes mellitus; ED, emergency department; ESRD on HD, end-stage renal disease on hemodialysis; GPU, general practice unit; HTN, hypertension; ICU, intensive care unit; N/A, not available.

*Patient expired.

failure, lung disease requiring oxygenation, and end-stage renal disease. It is unclear if COVID-19 contributed to his cardiac arrest. Patient 1 expired from multifocal pneumonia 14 days from a COVID-19 confirmed diagnosis; this death was potentially attributable to late complications from COVID-19 (Table 1).

DISCUSSION

Although the clinical spectrum of COVID-19 among PLWH cannot be ascertained by this report, the course of infection among those described in this report is similar to what has been described in the literature.[1] A case series from Germany presented 33 virally suppressed PLWH infected with COVID-19 with 76% having mild infection, 27% patients having severe infection, and 3% patients expiring.[9] These findings were also consistent with our results. An observational prospective study from Madrid, Spain, analyzed 51 PLWH diagnosed with COVID-19, of whom 69% required hospitalization, 63% had one comorbidity, and 12% were critically ill. The authors of this study noted that PLWH should not be considered to be protected from COVID-19 or to have a lower risk of severe disease. Therefore, they should receive the same treatment approach applied to the general public.[10] PLWH at HFH had similar comorbidities and hospital admissions compared with non-HIV patients admitted with COVID-19. In a recent publication of 463 patients infected with COVID-19, but without known HIV, the investigators from HFH found that the 3 most common comorbidities were hypertension (63.7%), obesity (57.6%), and diabetes (38.4%). Patients in the HFH study also had a 16% overall 30-day mortality rate.[11] These comorbidities were also the 3 most common in our population (57%, 57%, and 43%, respectively) with a 21% overall 30-day mortality rate. Our case series, the current published literature on HIV and SARS-CoV-2, and the published data from HFH on COVID-19 patients without known HIV supports the theory that there is not an excess morbidity and mortality among PLWH affected by COVID-19 compared with the general public.

There are many hypotheses as to why PLWH might have favorable outcomes to COVID-19. One hypothesis is that most of these patients are on tenofovir-based regimens. Tenofovir has been described as having the capacity to bind to SARS-CoV-2 RNA-dependent RNA polymerase.[6] This mechanism of action is similar to the antiviral drug remdesivir, which has been approved for treatment for COVID-19 through emergency use by the United States Food and Drug Administration. However, the affinity for the binding substrate was lowest in tenofovir, compared with galidesivir, remdesivir, and ribavirin.[6] Tenofovir–emtricitabine was also recently shown to reduce virus titers in a highly susceptible ferret infection model.[12] In a Spanish study, PLWH receiving emtricitabine and tenofovir disoproxil fumarate were found to have a lower risk for COVID-19 and related hospitalization than those receiving other nucleoside reverse transcriptase inhibitors.[13] Whether the tenofovir-based regimen resulted in a reduction in the severity of response to COVID-19 will need to be studied further, but this regimen did not protect our patients from acquiring the infection.

Early, cART can blunt the cytokine response in acute HIV infection.[14] In addition, tenofovir has been shown to have anti-inflammatory effects in cells and tissue from HIV-uninfected donors.[15,16] The impact on COVID-19 of ART, early therapy for SARS-CoV-2, or pre-existing immunodeficiency is unknown. However, none of these patients developed a clinical syndrome compatible with a cytokine storm. Although it is of interest that CD4 and CD8 counts fall with SARS-CoV-2 infection, it is unknown whether this change exacerbates or dampens the cytokine response associated with COVID-19 or leads to an increased risk of secondary infections.

The absence of reports of COVID-19 among immunosuppressed hosts is striking. The susceptibility, disease course, and outcome among PLWH have not been described. Given the role of the "cytokine storm" in the outcome of COVID-19 infection, some immunodeficient states may be protective in terms of reducing the severity of infection. However, Guan et al[17] in a review of 1590 patients found that any malignancy was associated with poor clinical outcomes regardless of an individual's HIV status. The COVID-19 outbreak in Detroit is at a plateau as of May 10, 2020, but the total number of PLWH who have been diagnosed with COVID-19 is unknown as universal testing is not consistently performed.[18] The Michigan Department of Health and Human Services reported that as of June 30, 2020, 278 of the 17,093 (1.6%) known PLWH in Michigan tested positive for COVID-19 with 8% expiring, 21% requiring hospitalization, and 5% requiring ventilation (Table 2) (J. B. Kent, personal communication, 2020). This is similar to the 1.7% prevalence of confirmed COVID-19 in Detroit.[5] Of the approximately 1500 PLWH followed in our HIV clinic in Detroit, MI, 14 HIV-positive individuals were diagnosed with COVID-19 in our laboratories. Others have self-reported to have been diagnosed elsewhere, but because of a lack of

TABLE 2. Summary of Total Number of COVID-19 Cases in Michigan With and Without HIV

Characteristic	COVID-19 Patients	PLWH	Coinfection with COVID-19 and HIV
Total cases	65,271	17,093	278
Gender			
Males	47%	79%	81%
Females	53%	21%	19%
Age			
Mean	52	46	49
Median	52	48	51
Race/Ethnicities			
Hispanic	7%	6%	9%
Black	32%	56%	68%
White	39%	34%	16%
Unknown	23%	4%	7%
Deaths (N, %)	5942 (9%)	—	23 (8%)
Hospitalization, %	20%	—	21%
Requiring ventilation, %	3%	—	5%

clinical information, these individuals have not been included in this series.

Our study had some limitations. We had a small sample size and it is unclear if our findings can be applied to a larger number of patients. All patients also received hydroxychloroquine that was consistent with our institution's guidelines during that period before the emergency use authorization being rescinded. However, data remain limited on coinfection with HIV and COVID-19, and it is important to share experiences between health care professionals to enhance our knowledge about COVID-19.

In conclusion, although in our series all patients coinfected with HIV and SARS-CoV-2 were either African American or Hispanic, they experienced a clinical course that was similar to that reported in the literature for individuals not infected with HIV. In this small group of individuals, we did not observe an unexpected increase in disease severity or mortality. It is possible that PLWH are more likely to take precautions to prevent exposure, more likely to seek medical care, or more likely to be tested for COVID-19, which may skew data to earlier and less symptomatic infection. Nevertheless, we have seen no signals yet to suggest that care for patients coinfected with HIV and SARS-CoV-2 should be different from care for patients with COVID-19 who are not infected with HIV.

ACKNOWLEDGMENTS

The authors thank our patients with HIV and our health care colleagues for providing care in our hospital system.

REFERENCES

1. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet.* 2020;395:1054–1062.
2. World Health Organization. *Novel Coronavirus (2019-nCoV) Situation Report - 1: 21 January 2020*. World Healht Organziation; 2020. Available at: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200121-sitrep-1-2019-ncov.pdf. Updated January 20. Accessed 30 March, 2020.
3. GISAID Initiative. *Genomic Epidemiology of hCoV-19*. GISAID Database; 2020. Available at: https://www.gisaid.org/CoV2020. Updated 8 April 2020. Accessed April 8, 2020.
4. World Health Organization. *WHO Director-General's Opening Remarks at the Media Briefing on COVID-19*. World Health Organization; 2020. Available at: https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19—11-march-2020. Updated March 11, 2020. Accessed April 7, 2020.
5. *Coronavirus Web Site*. Available at: https://www.michigan.gov/coronavirus/0,9753,7-406-98163-520743–,00.html. Accessed May 7, 2020.
6. Elfiky AA. Ribavirin, remdesivir, sofosbuvir, galidesivir, and tenofovir against SARS-CoV-2 RNA dependent RNA polymerase (RdRp): a molecular docking study. *Life Sci.* 2020:117592.
7. 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;382:1787–1799.
8. Blanco JL, Ambrosioni J, Garcia F, et al. COVID-19 in patients with HIV: clinical case series. *Lancet HIV.* 2020;7:e314–e316.
9. Härter G, Spinner CD, Roider J, et al. COVID-19 in people living with human immunodeficiency virus: a case series of 33 patients. *Infection.* 2020:1–6. doi:10.1007/s15010-020-01438-z. [epub ahead of print].
10. Vizcarra P, Pérez-Elías MJ, Quereda C, et al. Description of COVID-19 in HIV-infected individuals: a single-centre, prospective cohort. *Lancet HIV.* 2020:30163–30166.
11. Suleyman G, Fadel RA, Malette KM, et al. Clinical characteristics and morbidity associated with coronavirus disease 2019 in a series of patients in metropolitan Detroit. *JAMA Netw Open.* 2020;3:e2012270.
12. Park SJ, Yu KM, Kim YI, et al. Antiviral efficacies of FDA-approved drugs against SARS-CoV-2 infection in ferrets. *mBio.* 2020;11:e01114–e01120.
13. Del Amo J, Polo R, Moreno S, et al. Incidence and severity of COVID-19 in HIV-positive persons receiving antiretroviral therapy: a cohort study. *Ann Intern Med.* 2020. doi:10.7326/M20-3689. [epub ahead of print].
14. Muema DM, Akilimali NA, Ndumnego OC, et al. Association between the cytokine storm, immune cell dynamics, and viral replicative capacity in hyperacute HIV infection. *BMC Med.* 2020;18:81.
15. Melchjorsen J, Risør MW, Søgaard OS, et al. Tenofovir selectively regulates production of inflammatory cytokines and shifts the IL-12/IL-10 balance in human primary cells. *J Acquir Immune Defic Syndr.* 2011;57:265–275.
16. Hladik F, Burgener A, Ballweber L, et al. Mucosal effects of tenofovir 1% gel. *eLife.* 2015;4:e04525.
17. Guan WJ, Liang WH, Zhao Y, et al. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. *Eur Respir J.* 2020;55:2000547.
18. Jones R, Nelson M, Bracchi M, et al. COVID-19 in patients with HIV. *The lancet HIV.* 2020;7:e383.