Factors Associated With Coronavirus Disease 2019 Morbidity in a Cohort of People Living With Human Immunodeficiency Virus

To the Editors:

As coronavirus disease-2019 (COVID-19) cases surpass 25 million in the United States, increasing amounts of data on the effects of the causative virus, severe acute respiratory syndrome coronavirus (SARS-CoV-2), on people living with HIV (PLWH) have become available. Early case series and observational studies suggest that factors associated with COVID-19 morbidity and mortality rates in PLWH are similar to those described for non-PLWH. Other studies have described high rate of comorbid illnesses, smoking history, and older age among PLWH who required hospitalization for moderate or severe COVID-19. Still, clinical data on predictors for severe COVID-19 infection in PLWH remain limited. In this observational study, we describe the epidemiology of COVID-19 in a cohort of ethnically diverse PLWH who receive care at a large outpatient center and identify individual characteristics associated with the need for hospitalization.

The Ruth M. Rothstein CORE Center in Chicago is the largest public provider of HIV care in Chicago. As part of the Cook County Health system, it caters mostly to a low-income, racial, and ethnic minority population. From the CORE database, we identified all PLWH aged 18 years or older who tested positive for SARS-CoV-2 through polymerase chain reaction assay from a nasopharyngeal specimen from March 1, 2020, through July 31, 2020. From the electronic medical record, we collected detailed demographic, clinical, laboratory, radiological, and outcome data associated with the diagnosis of SARS-CoV-2 infection in PLWH using a standard data collection form. Patients were also included in the data set if they self-reported a diagnosis of SARS-CoV-2 infection at outside institutions. Individuals with confirmed or self-reported SARS-CoV-2 infection were categorized based on documentation of hospitalization due to COVID-19 in the 30 days after laboratory diagnosis of infection.

Comparisons between participant categories were conducted using t test for continuous variables and the χ² test for categorical variables. To evaluate the effect of individual characteristics on likelihood of hospitalization, we conducted univariate logistic regression analyses. Variables that were found to be significantly associated with the outcome were then incorporated in a multivariable model. All tests were conducted using Stata software (v14.2).

Of 5794 PLWH followed up at the CORE Center in 2019–2020, we identified 100 PLWH with either documented (85%) or self-reported (15%) infection by SARS-CoV-2 during the studied period, resulting in an infection rate of 1.7%. Most of the cases (76%) occurred during the months of April and May 2020, at the height of the first wave of COVID-19 in Illinois. The median age of patients was 50 years; most were men (76%) and self-identified as Hispanic (52%). Fifty-one patients reported at least one comorbid illness, with hypertension and type 2 diabetes being the most prevalent (30% and 26%, respectively). Most of the patients had a documented body mass index (BMI) above 30 (44%) and reported ongoing or past smoking (42%). Ninety-six individuals were on antiretroviral therapy at the time of diagnosis, and 89 (93%) had a suppressed HIV viral load (<40 copies/mL). The median CD4 T-cell count was 555 cells/μL.

Thirty-four percentage of our patients were hospitalized because of COVID-19, of whom 27 (79%) were admitted to our health care system. Compared with nonhospitalized patients, hospitalized PLWH were likely to be older and non-Hispanic Black. Hospitalized PLWH were also more likely to have documented fever and respiratory symptoms at the time of diagnosis than nonhospitalized patients. Nonhospitalized individuals were more likely to have received a tenofovir-containing antiretroviral regimen (tenofovir disoproxil fumarate or tenofovir alafenamide) when compared with hospitalized patients. No differences were observed in rates of comorbid illnesses, smoking history, and HIV treatment metrics (viral load suppression and CD4 T-cell count) between groups (Table 1).

In the multivariable logistic regression model, the likelihood of hospitalization was associated with increasing age [odds ratio (OR) 1.10, 95% confidence interval (CI) 1.02 to 1.10] and a BMI >40 (OR 9.57, 95% CI: 1.43 to 63.72). We also found a protective effect of tenofovir-containing regimens on odds of hospitalization (OR 0.11, 95% CI: 0.02 to 0.68). There was a trend toward higher odds of hospitalization among non-Hispanic Blacks but did not reach statistical significance (OR 2.62, 95% CI: 0.99 to 6.82). There was no association between likelihood of hospitalization and use of protease inhibitors, nonnucleoside analogs, or integrase inhibitors.

Of the 34 coinfected PLWH who required hospitalization, COVID-19 treatment was known for 27 individuals. Eight (30%) hospitalized patients received hydroxychloroquine under Emergency Use Authorization. Five (19%) patients received tocilizumab (off-label), 7 (26%) patients received remdesivir (initially under investigational protocol, later under Emergency Use Authorization), and one patient received convalescent plasma (under investigational protocol). None of the patients in the cohort received dexamethasone, which was included in the...
treatment guidelines in July 2020. Most of the hospitalized patients (22, 81%) required supplemental oxygen during hospitalization, only 3 (11%) required noninvasive ventilation, and one (3%) required mechanical ventilation. Three patients died during hospitalization.

In summary, we observed 1.7% of rate of infection, which is comparable with rates reported in other series.7 Our hospitalization rate of 34% is comparable with some reports8 but lower than others.7,9 Similar to other case series of SARS-CoV-2–coinfected PLWH,4,8,10 most of our patients had undetectable viral loads and evidence of immune recovery, as measured by CD4+ T-cell counts at the time of SARS-CoV-2 infection. In our cohort, only age and high BMI seemed to mediate an increase in COVID-19 morbidity in PLWH. Both factors have been described in association with poorer outcomes including hospitalization in both PLWH and non-PLWH.6,9 Importantly, we detected a protective effect of tenofovir on COVID-19–related morbidity and mortality has been described in some cohorts9,12 but not in others.7 The in vitro antiviral activity of the tenofovir prodrug on SARS-CoV-2 replication13 has been postulated as a potential pathway for protection against

### TABLE 1. Comparison of Demographic and Clinical Characteristics Between Coinfected PLWH/COVID-19 According to Hospitalization

|                      | PLWH Not Hospitalized | PLWH Hospitalized | P     |
|----------------------|-----------------------|-------------------|-------|
| **Age, yrs, mean (SD)** | 47 (1.5)              | 53 (2)            | 0.01  |
| **Female sex**       | 15 (22)               | 9 (27)            | 0.70  |
| **Race/ethnicity**   |                       |                   | 0.02  |
| Hispanic             | 40 (60)               | 12 (35)           |       |
| Non-Hispanic Black   | 25 (38)               | 19 (56)           |       |
| Non-Hispanic White   | 1 (2)                 | 3 (9)             |       |
| **Comorbidities**    |                       |                   |       |
| Type 2 diabetes      | 15 (22)               | 11 (33)           | 0.30  |
| Hypertension         | 16 (24)               | 14 (41)           | 0.08  |
| Coronary artery disease | 4 (6)               | 3 (9)             | 0.61  |
| Chronic kidney disease | 2 (3)              | 3 (9)             | 0.21  |
| Chronic lung disease | 6 (9)                 | 7 (21)            | 0.11  |
| **BMI categories**   |                       |                   | 0.10  |
| <30                  | 39 (59)               | 17 (50)           |       |
| 30–39.9              | 25 (38)               | 12 (35)           |       |
| >40                  | 2 (3)                 | 5 (15)            |       |
| **Ongoing or past smoking** | 24 (36)       | 18 (53)           | 0.11  |
| **HIV VL <40**       | 58 (88)               | 31 (91)           | 0.62  |
| **CD4+ T-cell count** |                     |                   |       |
| ≥200 cells/µL        | 58 (88)               | 28 (82)           | 0.45  |
| **Antiretroviral regimens** |               |                   |       |
| NRTI                 | 65 (98)               | 31 (92)           | 0.07  |
| PI                   | 9 (14)                | 5 (15)            | 0.88  |
| INSTI                | 58 (88)               | 32 (94)           | 0.33  |
| NNRTI                | 7 (11)                | 5 (15)            | 0.55  |
| Contains TAF/TDF*    | 63 (95)               | 23 (68)           | <0.01 |
| **Symptoms at the time of diagnosis†** | | | |
| Fever                | 30 (52)               | 24 (77)           | 0.01  |
| Cough                | 36 (63)               | 26 (84)           | 0.04  |
| Shortness of breath  | 8 (14)                | 24 (73)           | 0.00  |
| Diarrhea             | 6 (13)                | 6 (22)            | 0.27  |
| Anosmia              | 7 (16)                | 3 (12)            | 0.64  |
| Abnormal CXR at the time of diagnosis‡ | 2 (50)               | 28 (97)           | <0.01 |

*Among the 86 individuals receiving tenofovir-based regimen, 6 individuals received TDF (5 not hospitalized and 1 hospitalized) and 81 received TAF (58 not hospitalized and 22 hospitalized).
†Percentages calculated based on the total number of individuals who had reported the listed symptoms: fever = 89, cough = 88, anosmia = 71, diarrhea = 75, and shortness of breath = 90.
‡Percentages calculated based on the total number of individuals with documented chest radiographs (n = 33).

CXR, chest radiography; INSTI, integrase strand transfer inhibitor; NNRTI, nonnucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate.
SARS-CoV-2 infection and/or severe disease, but the conflicting results from the abovementioned cohorts and negative results in non-PLWH\textsuperscript{14} suggest that our findings should be interpreted with caution. In addition, we did not find any difference in odds of hospitalization according to HIV treatment metrics [undetectable HIV viral load and low (<200 cells/\mu L) CD4\textsuperscript{+} T-cell counts]. The lack of association between severity of COVID-19 and measures of HIV control is compatible with findings of other PLWH cohorts,\textsuperscript{4,7} with the caveat that most cohorts included very few individuals with uncontrolled HIV disease. Indeed, a study from the largest cohort of coinfected PLWH to date\textsuperscript{12} showed an association between COVID-19–related death and low CD4\textsuperscript{+} T-cell counts in hospitalized coinfected PLWH, suggesting that persistent immunosuppression may remain a risk factor in this population.

Our study has a few limitations. First, it is possible that the rate of infection and hospitalization in our patients is underestimated. Despite extensive engagement with CORE Center attendees during the pandemic, some patients may have sought care elsewhere. However, providers and support staff in our clinic increased outreach efforts during the COVID-19 pandemic, with emphasis on documentation of SARS-CoV-2 testing outside of our health care system. Second, because our cohort size was small, we may have lacked power to detect the influence of other factors such as race, ethnicity, and presence of comorbid illnesses, which mediate COVID-19 morbidity in non-PLWH.\textsuperscript{5,10}

Across the United States, both HIV disease and COVID-19 have disproportionately affected low-income communities of race. Our findings corroborate that age and high BMI mediate higher COVID-19 morbidity in PLWH similar to what has been described for non-PLWH. We also identified a protective effect of tenofovir-containing regimens on likelihood of hospitalization, which merits further study and corroboration in larger series. Several questions regarding the risk of COVID-19 recurrence in PLWH and the risk of long-term symptoms described in non-PLWH\textsuperscript{15} remain unanswered. Larger studies and prospective longitudinal follow-up will help clarifying these important issues for PLWH communities, which have been long affected by economic and health disparities and are now standing at the intersection of the old and new pandemics.

Vanessa Sardá, MD, MPH\textsuperscript{a,b}
Christian Gomez, MD\textsuperscript{a}
Jorge Soria, MD\textsuperscript{a}
Juan Sarmiento, MD\textsuperscript{a}
Sheila Badri, MD\textsuperscript{a,b}
Monica Merçon, MD\textsuperscript{a,b}

\textsuperscript{a}Internal Medicine, Cook County Health, Chicago, IL
\textsuperscript{b}Internal Medicine, Rush Medical College, Chicago, IL

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