Characteristics, Comorbidities, and Outcomes in a Multicenter Registry of Patients with HIV and Coronavirus Disease-19

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**Key points**

Severe clinical outcomes occurred commonly in PWH and Coronavirus-disease-19 (COVID-19). Age, chronic lung disease, hypertension, and lower CD4 counts were associated with decreased survival rates. We did not find an association between HIV viremia, antiretroviral regimen, and severe COVID-19.
Abstract:

Background:

People with HIV (PWH) may have numerous risk factors for acquiring Coronavirus disease-19 (COVID-19) and developing severe outcomes, but current data are conflicting.

Methods:

Healthcare providers enrolled consecutively by non-random sampling PWH with lab-confirmed COVID-19, diagnosed at their facilities between April 1st and July 1st, 2020. De-identified data were entered into an electronic Research Electronic Data Capture (REDCap). The primary endpoint was severe outcome, defined as a composite endpoint of intensive care unit (ICU) admission, mechanical ventilation, or death. The secondary outcome was the need for hospitalization.

Results:

286 patients were included; the mean age was 51.4 years (SD, 14.4), 25.9% were female, and 75.4% were African-American or Hispanic. Most patients (94.3%) were on antiretroviral therapy (ART), 88.7% had HIV virologic suppression, and 80.8% had comorbidities. Within 30 days of positive SARS-CoV-2 testing, 164 (57.3%) patients were hospitalized, and 47 (16.5%) required ICU admission. Mortality rates were 9.4% (27/286) overall, 16.5% (27/164) among those hospitalized, and 51.5% (24/47) among those admitted to an ICU. The primary composite endpoint occurred in 17.5% (50/286) of all patients and 30.5% (50/164) of hospitalized patients. Older age, chronic lung disease, and hypertension were associated with severe outcomes. A lower CD4 count (<200 cells/mm³) was associated with the primary and secondary endpoints. There was no association between the antiretroviral regimen or lack of viral suppression and predefined outcomes.
Conclusion:

Severe clinical outcomes occurred commonly in PWH and COVID-19. The risk for poor outcomes was higher in those with comorbidities and lower CD4 cell counts, despite HIV viral suppression.

Keywords

HIV; COVID-19; SARS-CoV-2; AIDS
Introduction

Patients with severe Coronavirus disease-19 (COVID-19) requiring hospital admission are more likely to be older, male, and have underlying comorbidities.\(^1\)\(^-\)\(^3\) Additionally, immunocompromising conditions such as malignancy and solid organ transplantation may increase patients' risk for severe COVID-19 and death.\(^4\)\(^-\)\(^8\) Data are conflicting whether people with HIV (PWH) are also at increased risk.

PWH may have numerous factors that could increase their risk of exposure to and acquisition of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). First, PWH are aging and have high rates of smoking, chronic cardiovascular and lung disease, and obesity.\(^9\) In addition, racial and ethnic minorities are disproportionately affected by HIV disease and COVID-19. Ongoing research aims to determine the impact of structural racism in COVID-19 outcomes. While the causes of health disparities are multifaceted, lack of access to healthcare, differences in socioeconomic, and prevalence of chronic diseases are potential contributors.\(^10\),\(^11\)

Several case series have described clinical characteristics of PWH and COVID-19. Many have been either limited to single-center studies, hospitalized patients, or included patients with suspected but not confirmed COVID-19. Most were also limited by small numbers of patients or lacked important HIV-specific variables such as CD4 cell counts, antiretroviral therapy (ART), and plasma HIV viral load.\(^12\)\(^-\)\(^15\) Some of these studies reported that PWH with COVID-19 had similar clinical characteristics and comparable risk of severe disease to the general population.\(^16\)\(^-\)\(^21\) However, other studies found higher rates of SARS-CoV-2 infection and worse outcomes among PWH.\(^22\)\(^-\)\(^24\)

Because current data are conflicting and limited, further investigation in HIV and COVID-19 is warranted. We aim to describe the clinical characteristics and outcomes of COVID-19 in PWH and to characterize PWH at the highest risk for severe COVID-19-associated outcomes through an extensive multicenter registry.
Methods

The COVID-19 in PWH Registry was sponsored by the University of Missouri, Columbia. The study was reviewed by the University of Missouri Institutional Review Board and considered to be exempt. Anonymized patient data were collected without the need for informed consent.

Study design

This multicenter registry was for PWH and COVID-19, who received care between April 1st and July 1st, 2020. The study was listed on ClinicalTrials.gov (NCT04333953) and the Infectious Diseases Society of America (IDSA) website and was open to enrollment in the US and internationally. The registry was promoted in the IDSA and HIV Medical Association discussion forums, and invitation emails were sent to Infectious Disease departments and HIV clinics across the US.

Patients aged 18 years and older with a known diagnosis of HIV and laboratory-confirmed COVID-19 in both inpatient and outpatient settings were eligible for study inclusion.

Healthcare providers collected study data by chart review of PWH and COVID-19 diagnosed at their facilities and entered anonymous information into a secure electronic Research Electronic Data Capture (REDCap). Patients were enrolled consecutively by non-random sampling. Study variables included patient demographics, HIV-associated variables, underlying medical problems, COVID-19 clinical presentation as reported by patients, laboratory values, treatment, and clinical outcomes.

Providers certified that the information submitted was accurate to the best of their knowledge. Two reviewers cross-validated the data for duplicity by age, gender, race, location, and HIV-1 RNA (viral load).
Study definitions

Laboratory-confirmed COVID-19 was defined as positive reverse-transcriptase–polymerase-chain-reaction (RT-PCR) in respiratory samples or serum SARS-CoV-2 specific IgG/IgM.

The US geographical region of residence was based on the CDC’s National HIV Surveillance System region distribution.27

Chronic lung disease included asthma and COPD. Cardiovascular disease included coronary artery disease and congestive heart failure. Chronic liver disease included cirrhosis, chronic hepatitis B, and chronic untreated hepatitis C. Active malignancy excluded non-melanoma skin cancer. We defined obesity as body mass index (BMI) of ≥ 30.28 We defined virologic suppression as HIV-1 RNA (viral load) < 200 copies/mL.29 We collected the most recent HIV viral load measured before or at the time of COVID-19 presentation. ART categorizations were mutually exclusive.

Study outcomes

The primary endpoint was severe clinical outcome, defined as a composite endpoint of ICU admission, use of mechanical ventilation, or death.1 Outcomes for survival analyses were time from positive SARS-CoV-2 test to ICU admission and death. The secondary outcome of interest was hospitalization.

Statistical analysis

We used descriptive statistics to summarize patient data. For categorical variables, we used frequency and calculated proportions using the number of patients with data available as the denominator. For continuous variables, we used the mean with standard deviation (SD) or the median with interquartile range (IQR).

We analyzed the association between baseline variables with the defined outcomes by univariate analysis using the Chi-square test, Fisher's exact test, or t-tests as indicated. A multivariable logistic regression model was used to assess the association between each outcome of interest, severe outcome
and hospitalization, and independent variables. To obtain the parsimonious model for each multivariable analysis, we identified the significant independent variables using the backward selection method. Variables with a p-value ≤ 0.2 were included in the model in addition to clinically relevant variables. To adjust for within-region differences, we fitted a generalized estimating equation (GEE) logistic regression model, assuming an exchangeable correlation structure and regions as clusters, for each outcome.

To test whether there was a differential effect of CD4 count on ICU- free survival and overall survival, we used the Kaplan-Meier method to analyze survival outcomes and Log-rank statistics to compare the survival distribution of the CD4 groups (< 200, 200 - 500, > 500 cells/mm³) with respect to time from positive SARS-CoV-2 test to ICU admission and death.

In a post-hoc sub-analysis, we included patients from the US to examine the clinical presentation and study outcomes, excluding international locations.

User-defined missing values were treated as missing and not imputed. All tests were two-sided, with a level of significance defined as ≤ 0.05. SAS ® software was used for statistical analysis of data.

**Results**

Between April 1\textsuperscript{st} and July 1\textsuperscript{st}, 2020, we identified 286 unique PWH and laboratory-confirmed COVID-19. Thirty-six institutions from 21 States and three international locations contributed to the data; five duplicate cases were removed.

**Demographics and baseline characteristics**

The mean age was 51.4 years (SD, 14.4); 74 (25.9%) patients were female, 133 (47.5%) were African American, and 78 (27.9%) were Hispanic. The greatest percentage of patients in the US was from the South (47.0%), followed by the Northeast (35.4%), Midwest (5.3%), and West (4.9%); 7.4% were from international locations. Most patients (77.9%; 180/231) had HIV for more than five years, achieved virologic suppression (88.7%; 235/265), and were on ART at the time of COVID-19 diagnosis (94.3%; 263/279). The mean CD4 count was 531 cells/mm³ (SD, 340). The most common
ART regimen was an integrase inhibitor with two nucleoside reverse transcriptase inhibitors (61.3%; 171/279). Hypertension (46.5%), obesity (32.3%), and diabetes (21.3%) were the most common underlying medical problems. When stratified by hospitalization status, older age, lower CD4 counts, number of years living with HIV, not being on ART or virally suppressed, and high comorbidity burden were associated with higher hospitalization rates (Table 1).

**SARS-CoV-2 diagnosis and clinical presentation**

A SARS-CoV-2 RT-PCR test was used to diagnose all but one patient, who was diagnosed based on serologic testing. The most frequently reported symptoms within 72 hours of diagnostic testing were cough (76.2%; 205/269), fever (70.7%; 198/280), and fatigue (66.0%; 140/212). PWH hospitalized with COVID-19 were significantly more likely to have fever, fatigue, dyspnea, gastrointestinal symptoms, and altered mental status. Whereas, PWH who were not hospitalized were more likely to have upper respiratory symptoms such as sore throat and nasal congestion, and headache. At presentation, all patients with a peripheral oxygen saturation of < 94% on room air (30.6%; 72/235) and a Quick Sequential Organ Failure Assessment (q-SOFA) score of ≥ 2 (8.3%; 17/206) were hospitalized. A chest X-ray was obtained in 194 (67.8%) patients, of whom 77.8% had abnormal findings, and a computerized tomography (CT) scan was performed for 44 (15.4%) patients of whom 86.4% had abnormal findings. Patients who were hospitalized were more likely to have imaging done and to have abnormal findings (Table 2).

**Treatment and clinical course**

Within 30 days of positive SARS-CoV-2 testing, 164 (57.3%) patients were hospitalized. Among hospitalized PWH, potential SARS-CoV-2 targeted treatments, excluding placebo-controlled clinical trials, were given to 99 (60.4%) patients, the most common medication being hydroxychloroquine (40.9%) (Table 3).

Forty-seven (28.7%) patients required ICU admission, with a median time of 2.0 days (IQR 0.0 – 9.0) from time of testing, 35 (21.3%) patients required vasopressors, 37 (22.6%) required invasive mechanical ventilation, and 27 (16.5%) died with a median time of 16 days (IQR 8 – 24) from time of
testing. When stratified by age groups (<40, 40 – 60, >60 yrs.), the relative risk for all poor outcomes was more than one for older age groups compared to less than 40. Patients who are older than 60 were significantly more likely to require respiratory support, develop acute kidney injury, and die, compared to patients who were less than 40 years old (Table 3).

**Study outcomes**

Multivariable analysis identified higher age, lower CD4 counts, chronic kidney disease, and chronic lung disease as independent predictors of hospitalization. PHW with three or more comorbidities, compared to having only HIV disease, were also more likely to be hospitalized. (Table 4).

A severe clinical outcome occurred in 17.5% (50/286) of all patients and 30.5% (50/164) of hospitalized patients. In univariate analyses, there were statistically significant associations with severe outcome among older age (59.3 vs. 49.7 years; p<0.01), lower CD4 count (< 200 cells/mm$^3$) (25.5 vs. 13.1%; p=0.02), hypertension (72.0 vs. 41.1%; p<0.01), diabetes (32.0 vs. 19.1%; p=0.04), chronic lung disease (32.0 vs. 14.0%; p<0.01), and CKD (30.0 vs. 14.0%; p<0.01). In a multivariable analysis, older age, lower CD4 count, chronic lung disease, hypertension, and high comorbidity burden were significantly associated with severe outcomes (Table 4).

**Survival Analysis of time from test to ICU admission and death**

Based on 47 patients admitted to an ICU and 27 deceased patients, CD4 cell count had a significant effect on survival. The pairwise comparison showed a significant difference between the CD4 count < 200 and CD4 count > 500 cells/mm$^3$ for both ICU-free survival (p=0.04) and overall survival (p=0.05) (Figure 1).

In post-hoc analysis, we included PWH diagnosed with COVID-19 from the US (n=265) and excluded those from international locations (n=21). There were no significant differences in presentation and predictors of outcomes, except for hypertension. Hypertension was not significantly associated with severe outcome, after adjusting for other variables. Analysis presented in supplementary material (Tables 1 - 4 S.).
Discussion

In this multicenter analysis, severe clinical outcomes occurred commonly in PWH and COVID-19. As reported in multiple other studies in people without HIV, we found that age, chronic lung disease, and comorbidity burden were associated with increased rates of severe outcomes. In addition, among HIV-specific factors, we found that a lower CD4 count (< 200 cells/mm3) was associated with poor outcomes, including higher hospitalization rates, lower ICU-free survival, and overall survival. Our study is the first to characterize outcomes in a large number of geographically diverse PWH with laboratory-confirmed COVID-19.

The clinical and radiologic presentations of the PWH in our study were similar to those reported in other studies of patients with COVID-19, with or without HIV co-infection.1,17,22,30

Our study confirms the unequal racial and gender distribution of PWH and COVID-19. It mirrors the demographics of PWH in the US with a higher proportion of men, African American, and Hispanic patients.31 However, we did not find that race and gender were associated with worse outcomes in this cohort. Our findings demonstrate a high prevalence of comorbidities among PWH and COVID-19. Consistent with other studies,22,32 we found that underlying comorbidities constitute a significant risk factor for hospitalization and poor outcomes in PWH.

Available data indicate considerable variability in mortality rates, ICU admission rates and need for invasive mechanical ventilation among PWH diagnosed with COVID-19.16, 18-20, 22 Based on our analyses, rates of ICU admission, mechanical ventilation use, and death among PWH and COVID-19 were consistent with the general US data.30

We did not identify HIV viremia (a proxy for not taking ART) as a risk factor for severe COVID-19, but the proportion of study participants with HIV viremia was small and more than 90% of our study enrollees were receiving ART. Hence our ability to compare the outcomes between those with and without HIV control was limited.
It has been postulated that patients with advanced HIV, low CD4 counts, and severe immunosuppression cannot mount the robust inflammatory response responsible for COVID-19-associated complications.\textsuperscript{15, 16, 18, 21} Our study does not support this hypothesis for those who are virologically suppressed but have low CD4 cell counts. Although we did not collect information about nadir CD4 cell count or duration of ART, this population (low CD4 but virally suppressed) usually has a history of severe immunosuppression, recent ART initiation, or both. Our findings show a significant association between low CD4 counts and poor outcomes contrasting recently published cases series. The study by Karmen-Tuohy et al. showed that 6 patients out of 19 had CD4 < 200 cells/mm\textsuperscript{3} and the CD4 count was not associated with mortality in HIV-positive patients.\textsuperscript{19} Whereas, the study from Collins et al. from GA, had 20 PWH and COVID-19 and showed that all three PWH and COVID-19 who died had CD4 > 200 cells/mm\textsuperscript{3}.\textsuperscript{21} In our study, there were deaths among PWH with CD4 > 200 cells/mm\textsuperscript{3}, but possibly our larger sample size was able to detect a difference between PWH with CD4 counts < 200, 200 - 500, and > 500 cells/mm\textsuperscript{3}.

A recent study from Spain suggested that PWH receiving tenofovir disoproxil fumarate (TDF) in combination with emtricitabine as part of their ART regimen have a lower risk for SARS-CoV-2 acquisition and related hospitalizations than those on other ART regimens.\textsuperscript{34} Although the data we gathered were not specific to address the differences between those on TDF and other nucleoside reverse transcriptase inhibitors, in our study, we did not find an association between the class of ART or the use of darunavir-containing regimens and predefined outcomes.

This study has several limitations. First, this study cannot comment on the prevalence of SARS-CoV-2 infection among PWH. Second, COVID-19 testing, treatment, and hospitalization were all done at the discretion of individual healthcare providers and may have varied widely between sites as well as between different time points during the pandemic, reflective of local test availability and policies. There may also be selection bias, as contributors entered cases voluntarily and may not have entered every case from their institutions or clinics. However, 17 out of 36 institutions (accounting for 246 patients out of 286), have included systematically all HIV patients with COVID identified through the search performed in their corresponding centers during the study period. We could not control for
COVID-19 therapies because we did not collect data on steroid use and clinical trial participation, as well as the small number of patients in each treatment group. We also did not collect data on social determinants of health, which may have impacted the clinical course of COVID-19. Future studies should assess whether specific socioeconomic factors impart a greater risk related to COVID-19 for PWH. Finally, death is counted as all-cause mortality; we did not verify the exact cause of death. Despite these limitations, evaluating outcomes for PWH with COVID-19 who were hospitalized or non-hospitalized from multiple sites and settings (community hospitals, clinics, and large academic centers) make these results more generalizable.

In conclusion, our study adds to existing reports of the clinical characteristics of COVID-19 among PWH. The strengths of this analysis include a relatively large sample size and a population broadly representative of the PWH in the United States. Although we did not have a comparison group, our results suggest comparable outcomes and non-HIV risk factors for severe disease observed in people without HIV. Among HIV-related factors, our observation that those with lower CD4 cell counts are at higher risk for poor outcomes despite viral suppression suggests that people with a history of advanced HIV-related immunosuppression or relatively recent ART initiation may warrant closer observation and monitoring. The results of the study can also help prioritize interventions in PWH in areas with an ongoing high incidence of SARS-CoV-2 infection to mitigate the impact of COVID-19.
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As principal investigator, Dr. Dandachi had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

*Study concept and design*: Dandachi, Geiger

*Acquisition of data*: All authors

*Analysis and interpretation of data*: All authors.

*Drafting of the manuscript*: Dandachi, Geiger, Chow

*Critical revision of the manuscript for important intellectual content*: All authors.

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David Koren reports other from Thera (Advisory Board), other from Janssen (Advisory Board), other from Gilead Sciences (Independent Consulting) and other from Abbvie (Independent Consulting), outside of the submitted work. Jeremy Chow reports grants from Gilead Sciences, outside the submitted work. All other authors have no potential conflicts to disclose.
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TABLE 1: Patient Demographics and Baseline Characteristics, stratified by hospitalization (n=286)

| Variables                        | n (%)   | Non-hospitalized | Hospitalized | p-value |
|----------------------------------|---------|------------------|--------------|---------|
| Mean age, years (N=286)          |         |                  |              | < 0.01  |
|                                  | 51.4 (SD 14.4) | 45.4 (SD 12.7) | 55.8 (SD 14.0) |         |
| Age in years                     |         |                  |              | < 0.01  |
| <40                              | 66 (23.1%) | 42 (34.4%)       | 24 (14.6%)   |         |
| 40-60                            | 146 (51.0%) | 64 (52.5%)       | 82 (50.0%)   |         |
| >60                              | 74 (25.9%) | 16 (13.1%)       | 58 (35.4%)   |         |
| Sex (N=286)                      |         |                  |              | 0.23    |
| Female                           | 74 (25.9%) | 36 (29.5%)       | 38 (23.2%)   |         |
| Male                             | 212 (74.1%) | 86 (70.5%)       | 126 (76.8%)  |         |
| Race / Ethnicity (N=280)         |         |                  |              | 0.89    |
| African American                 | 133 (47.5%) | 59 (49.2%)       | 74 (46.3%)   |         |
| Hispanic                         | 78 (27.9%) | 32 (26.7%)       | 46 (28.8%)   |         |
| White                            | 48 (17.1%) | 19 (15.8%)       | 29 (18.1%)   |         |
| Asian / Other                    | 21 (7.5%) | 10 (8.3%)        | 11 (6.9%)    |         |
| Years with HIV (N=231)           |         |                  |              | < 0.01  |
| < 1 year                         | 14 (6.1%) | 5 (4.6%)         | 9 (7.3%)     |         |
| 1 - 5 years                      | 37 (16.0%) | 26 (24.1%)       | 11 (8.9%)    |         |
| > 5 years                        | 180 (77.9%) | 77 (71.3%)       | 103 (83.7%)  |         |
| CD4 Count (N=268)                |         |                  |              | < 0.01  |
| < 200 cells/mm3                  | 41 (15.3%) | 5 (4.5%)         | 36 (23.1%)   |         |
| 200 – 500 cells/mm3              | 98 (36.6%) | 33 (29.5%)       | 65 (41.7%)   |         |
| > 500 cells/mm3                  | 129 (48.1%) | 74 (66.1%)       | 55 (35.3%)   |         |
| Viral Load suppression a (N=265)  |         |                  |              | 0.02    |
|                                  | 235 (88.7%) | 107 (93.9%)      | 128 (84.8%)  |         |
| Anti-Retroviral Therapy (N=279)  |         |                  |              | 0.04    |
| INI + 2 NRTI                     | 171 (61.3%) | 85 (70.8%)       | 86 (54.1%)   |         |
| NNRTI + 2 NRTI                   | 20 (7.2%) | 8 (6.7%)         | 12 (7.5%)    |         |
| PI + 2 NRTI                      | 20 (7.2%) | 9 (7.5%)         | 11 (6.9%)    |         |
| Dual ART regimen | Other | Not on ART |
|------------------|-------|------------|
|                  | 22 (7.9%) | 7 (5.8%) | 15 (9.4%) |
| Other            | 30 (10.8%) | 8 (6.7%) | 22 (13.8%) |
| Not on ART       | 16 (5.7%) | 3 (2.5%) | 13 (8.2%) |

### Underlying medical problems (N=286)

| Condition                                      | None (N=286) | Other (N=286) | Not on ART (N=286) | p-value |
|------------------------------------------------|---------------|---------------|---------------------|---------|
| Hypertension                                   | 133 (46.5%)   | 43 (35.2%)    | 90 (54.9%)          | < 0.01  |
| Diabetes                                       | 61 (21.3%)    | 19 (15.6%)    | 42 (25.6%)          | 0.04    |
| Chronic lung disease \(^b\)                    | 49 (17.1%)    | 11 (9.0%)     | 38 (23.2%)          | < 0.01  |
| Chronic kidney disease \(^e\)                  | 48 (16.8%)    | 9 (7.4%)      | 39 (23.8%)          | < 0.01  |
| Cardiovascular disease \(^d\)                  | 30 (10.5%)    | 5 (4.1%)      | 25 (15.2%)          | < 0.01  |
| Chronic liver disease \(^e\)                   | 28 (9.8%)     | 10 (8.2%)     | 18 (11.0%)          | 0.43    |
| Active malignancy \(^g\)                       | 13 (4.5%)     | 2 (1.6%)      | 11 (6.7%)           | 0.04    |
| Obesity: BMI ≥ 30 (N=257)                      | 83 (32.3%)    | 37 (34.3%)    | 46 (30.9%)          | 0.57    |

### Comorbidity burden (N=286)

| Comorbidity burden                                      | None (N=286) | Other (N=286) | Not on ART (N=286) | p-value |
|---------------------------------------------------------|---------------|---------------|---------------------|---------|
| HIV disease with no other known comorbidity             | 41 (14.3%)    | 24 (19.7%)    | 17 (10.4%)          | <0.01  |
| HIV with 1 or 2 comorbidities                          | 168 (58.7%)   | 82 (67.2%)    | 86 (52.4%)          |        |
| HIV with 3 or more comorbidities                       | 77 (26.9%)    | 16 (13.1%)    | 61 (37.2%)          |        |

### Smoking history \(^b\) (N=275)

| Smoking history | None (N=286) | Other (N=286) | Not on ART (N=286) | p-value |
|-----------------|---------------|---------------|---------------------|---------|
| 105 (38.2%)     | 38 (31.9%)    | 67 (42.9%)    | 0.06                |

\(^a\) Virologic suppression defined as HIV RNA < 200 copies/mL.

\(^b\) Chronic lung disease including asthma & COPD

\(^c\) Chronic kidney disease, includes end-stage renal disease

\(^d\) Cardiovascular disease includes coronary artery disease and congestive heart failure

\(^e\) Chronic liver disease includes cirrhosis, chronic hepatitis B, and chronic untreated hepatitis C

\(^f\) Active malignancy, excludes non-melanoma skin cancer

\(^g\) Current or former smokers

**Abbreviations:** ART, antiretroviral therapy; BMI, body mass index; INI, integrase Inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI: protease inhibitor
| Symptoms                                                                 | Non-hospitalized | Hospitalized | p-value  |
|--------------------------------------------------------------------------|------------------|--------------|----------|
| Cough (n=269)                                                            | 87 (73.7%)       | 118 (78.1%)  | 0.40     |
| Fever, chills (n=279)                                                    | 75 (64.1%)       | 123 (75.9%)  | 0.03     |
| Fatigue (n=212)                                                          | 53 (55.2%)       | 87 (75.0%)   | <0.01    |
| Myalgia, Arthralgia (n=229)                                              | 51 (49.5%)       | 77 (61.1%)   | 0.08     |
| Dyspnea (n=267)                                                          | 33 (29.5%)       | 113 (72.9%)  | <0.01    |
| Headache (n=219)                                                         | 40 (40.4%)       | 29 (24.2%)   | 0.01     |
| Sore throat (n=216)                                                      | 35 (34.0%)       | 21 (18.6%)   | 0.01     |
| Nausea, vomiting (n=240)                                                 | 20 (20.6%)       | 47 (32.9%)   | 0.04     |
| Diarrhea (n=245)                                                         | 12 (12.2%)       | 51 (34.7%)   | <0.01    |
| Chest pain (n=242)                                                       | 20 (19.8%)       | 34 (24.1%)   | 0.43     |
| Nasal congestion (n=205)                                                 | 23 (24.7%)       | 14 (12.5%)   | 0.02     |
| Anosmia, ageusia or dysgeusia, reported as other symptoms (n=286)        | 12 (9.8%)        | 11 (6.7%)    | 0.54     |
| Altered mental status (n=272)                                            | 0 (0%)           | 21 (13.4%)   | <0.01    |

**Initial laboratory values, Median (IQR)**

|                          | Non-hospitalized | Hospitalized | p-value  |
|--------------------------|------------------|--------------|----------|
| White blood cell count, $10^9$/L (n=204) | 5.6 (4.2 – 7.0) | 6.4 (4.8 – 8.5) | 0.03     |
| Neutrophil percentage, (n=201) | 57.0 (46.5 – 72.5) | 69.9 (59.7 – 79.0) | <0.01    |
| Lymphocyte count, $10^9$/L (n=201)  | 30.0 (17.7 – 41.9) | 19.0 (12.0 – 28.1) | <0.01    |
| Creatinine, mg/dL (n=201)    | 1.0 (0.8 – 1.3)  | 1.1 (0.9 – 1.5)  | 0.20     |
| Alanine aminotransferase, Units/L (n=195) | 23.0 (17.0 – 37.5) | 27.5 (19.7 – 44.2) | 0.11     |

**SpO2 on room air**

|                          | Non-hospitalized | Hospitalized | p-value  |
|--------------------------|------------------|--------------|----------|
| SpO2 ≥94% (n=163)        | 78 (100%)        | 85 (54.1%)   | <0.01    |
| SpO2 <94% (n=72)         | 0 (0%)           | 72 (45.9%)   | <0.01    |

**q-SOFA score**

|                          | Non-hospitalized | Hospitalized | p-value  |
|--------------------------|------------------|--------------|----------|

<0.01*
| Value (n) | Count | Percentage |
|----------|-------|------------|
| 0 (n=119) | 63 | 94.0% |
| 1 (n=70) | 4 | 6.0% |
| 2 (n=14) | 0 | 0% |
| 3 (n=3) | 0 | 0% |

**Chest X-Ray obtained (n=194)**

| Value | Count | Percentage |
|-------|-------|------------|
| 0 (n=119) | 35 | 28.7% |
| 1 (n=70) | 159 | 97.0% |

**CXR Findings†**

| Type | Count | Percentage |
|------|-------|------------|
| Normal (n=43) | 20 | 57.1% |
| Multifocal or patchy opacities (n=104) | 11 | 31.4% |
| Interstitial abnormalities (n=39) | 3 | 8.6% |
| Other findings (n=18) | 2 | 5.7% |
| Lobar consolidation (n=9) | 1 | 2.9% |

**Chest CT obtained (n= 44)**

| Value | Count | Percentage |
|-------|-------|------------|
| 0 (n=119) | 35 | 28.7% |
| 1 (n=70) | 159 | 97.0% |

**CT findings†**

| Type | Count | Percentage |
|------|-------|------------|
| Normal (n=6) | 1 | 20% |
| Multifocal patchy or ground-glass opacities (n=29) | 3 | 60.0% |
| Interstitial abnormalities (n=6) | 0 | 0% |
| Lobar consolidation (n=6) | 0 | 0% |

* Using Fisher's exact test

† Findings on CXR and CT chest are not mutually exclusive

**Abbreviations:** CT: computed tomography; peripheral oxygen saturation (SpO2)
TABLE 3: Treatment and clinical course of hospitalized patients with HIV and COVID-19 (n=164)

| Received experimental targeted therapy |   |
|---------------------------------------|--|
|                                       | 99 (60.4%) |
| Hydroxychloroquine | 67 (40.9%) |
| Azithromycin | 36 (22.0%) |
| Interleukin-6 receptor antagonist (tocilizumab or sarilumab) | 14 (8.5%) |
| Remdesivir | 12 (7.3%) |
| Convalescent plasma | 8 (4.9%) |
| Lopinavir/ ritonavir | 6 (3.7%) |

Clinical course among hospitalized patients with HIV and COVID-19, stratified by age

|                          | n (%) | n (%) | RR | RR | p-value |
|--------------------------|-------|-------|----|----|---------|
|                          | < 40 yrs. | 40 – 60 yrs. | > 60 yrs. | |
|                          | (n=24) | (n=82) | (n=58)  | |
| ICU admission            |       |        |      |    |         |
|                          | 47 (28.7%) | 22 (26.8%) | 21 (36.2%) | 2.2 | 0.11    |
|                          | 4 (16.7%) | 14 (17.1%) | 17 (29.3%) | 1.8 | 0.26    |
| Vasopressor use          |       |        |      |    |         |
|                          | 35 (21.3%) | 14 (17.1%) | 17 (29.3%) | 1.8 | 0.26    |
|                          | 4 (16.7%) | 14 (17.1%) | 17 (29.3%) | 1.8 | 0.26    |
| Respiratory support use  |       |        |      |    |         |
|                          | 123 (75.0%) | 63 (76.8%) | 48 (82.8%) | 1.7 | 0.02    |
|                          | 12 (50.0%) | 63 (76.8%) | 48 (82.8%) | 1.7 | 0.02    |
| Highest level of respiratory support |       |        |      |    |         |
| NC or face mask          |       |        |      |    |         |
|                          | 69 (42.1%) | 42 (51.2%) | 20 (34.5%) | 1.2 | 0.65    |
| High-flow NC or NRB      |       |        |      |    |         |
|                          | 17 (10.4%) | 7 (8.5%) | 9 (15.5%) | 3.7 | 0.20    |
| Invvasive mechanical ventilation |       |        |      |    |         |
|                          | 37 (22.6%) | 14 (17.1%) | 19 (32.8%) | 2.0 | 0.17    |
| Acute kidney injury b     |       |        |      |    |         |
|                          | 62 (38.0%) | 26 (32.1%) | 31 (50.0%) | 2.6 | 0.02    |
| Liver injury c           |       |        |      |    |         |
|                          | 46 (28.9%) | 19 (24.1%) | 20 (35.1%) | 1.1 | 0.69    |
| Death                    |       |        |      |    |         |
|                          | 27* (16.5%) | 8 (9.8%) | 2.3 | 18 (31.0%) | 7.4 | 0.04    |
| Severe outcome           |       |        |      |    |         |
|                          | 50 (30.5%) | 22 (16.7%) | 24 (16.7%) | 2.5 | 0.06    |
†RR calculated based on < 40 years age group as a reference

a Invasive mechanical ventilation includes 2 patients on extracorporeal membrane oxygenation

b Acute kidney injury, defined as creatinine increase of 0.3 mg/dL above baseline, including 7 patients required new renal replacement therapy

c Liver injury, defined by an increase of over two times from baseline in serum alanine aminotransferase

* Including 2 deaths one after hospital discharge to hospice and one in emergency department

Abbreviations: ICU, intensive care unit; NC: nasal cannula, NRB: non-rebreather mask; yrs.: years
TABLE 4. Multivariable analysis examining the association between hospitalization, severe outcome, and clinical characteristics of patients with HIV and COVID-19 (n=286)

| Outcome                  | Logistic regression analysis | Generalized Estimating Equation (GEE) |
|--------------------------|------------------------------|--------------------------------------|
|                          | Odds ratio (95% CI)          | p-value                              | Odds ratio (95% CI)          | p-value |
| **Hospitalization**      |                              |                                      |                              |         |
| Age, years               | 1.04 (1.01-1.08)             | 0.01                                 | 1.08 (1.04-1.07)             | 0.03    |
| CD4 count                |                              |                                      |                              |         |
| < 200 cells/mm3          | 5.22 (1.28-21.35)            | 0.02                                 | 3.67 (1.64-17.1)             | <0.01   |
| 200 – 500 cells/mm3      | 1.47 (0.7-3.08)              | 0.30                                 | 1.12 (1.1-12.22)             | 0.03    |
| > 500 cells/mm3          | 1.00 (reference)             |                                      |                              |         |
| Chronic kidney disease   | 5.12 (1.60-16.85)            | <0.01                                | 4.08 (1.45 – 11.52)          | <0.01   |
| Chronic lung disease     | 4.54 (1.58-13.01)            | <0.01                                | 4.06 (1.87 – 8.81)           | <0.01   |
| Comorbidity burden       |                              |                                      |                              |         |
| HIV disease with no other known comorbidity | 1.00 (reference) |                    |                              |         |
| HIV with 1 or 2 comorbidities | 1.19 (0.56-2.55)  | 0.65                                | 1.13 (0.49-2.6)              | 0.78    |
| HIV with 3 or more comorbidities | 4.56 (1.81-11.48) | <0.01                              | 3.57 (1.29-9.9)              | 0.01    |
| **Severe outcome**       |                              |                                      |                              |         |
| Age, years               | 1.04 (1.01-1.07)             | 0.02                                 | 1.04 (1.0-1.07)              | 0.02    |
| CD4 count                |                              |                                      |                              |         |
| < 200 cells/mm3          | 3.32 (1.11-9.93)             | 0.03                                 | 2.8 (1.02-7.67)              | 0.05    |
| 200 – 500 cells/mm3      | 1.75 (0.76-4.02)             | 0.19                                 | 1.93 (0.73-5.06)             | 0.18    |
| > 500 cells/mm3          | 1.00 (reference)             |                                      |                              |         |
| Hypertension             | 2.44 (1.01-5.55)             | 0.03                                 | 2.43 (1.2- 4.93)             | 0.01    |
| Chronic lung disease     | 3.65 (1.56-8.56)             | <0.01                                | 3.37 (1.63-6.97)             | <0.01   |
The model for hospitalization outcome is adjusted for age, sex, race/ethnicity, years with HIV, CD4 count, HIV viral load suppression, antiretroviral regimen, hypertension, diabetes, chronic lung disease, chronic kidney disease, cardiovascular disease, active malignancy, and chronic liver disease.

The model for severe outcome is adjusted for age, sex, race/ethnicity, CD4 count, HIV viral load suppression, hypertension, diabetes, chronic lung disease, chronic kidney disease, and chronic liver disease.

The model for the association between hospitalization, severe outcome, and comorbidity burden is adjusted for age, sex, and race/ethnicity.

† Severe outcome, defined as a composite outcome of intensive care admission, invasive mechanical ventilation, or death.
Figure legends

Figure 1A. Overall survival curves by CD4 groups (< 200, 200 - 500, > 500 cells/mm³) (p=0.05). 1B. ICU-free survival curves by CD4 groups (p=0.04).
