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CLINICAL CHARACTERISTICS AND OUTCOMES OF COVID-19 IN PEOPLE LIVING WITH HIV IN BELGIUM: A MULTICENTER, RETROSPECTIVE COHORT

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KEYWORDS : Belgium, clinical characteristics, COVID-19, outcomes, people living with HIV

ABSTRACT

The aim of this study was to describe the clinical characteristics and outcomes of coronavirus disease 2019 (COVID-19) among people living with HIV (PLWH) in Belgium. We performed a retrospective multicenter cohort analysis of PLWH with either laboratory-confirmed, radiologically diagnosed, or clinically suspected COVID-19 between February 15, 2020 and May 31, 2020. The primary endpoint was outcome of COVID-19. Secondary endpoints included rate of hospitalization and length of hospital stay and rate of Intensive Care Unit (ICU) admission and mechanical ventilation. One hundred and one patients were included in this study. Patients were categorized as having either laboratory-confirmed (*n* = 65), radiologically-diagnosed (*n* = 3), or clinically suspected COVID-19 (n = 33). The median age was 51.3 years (interquartile range [IQR] 41.3-57.3) and 44% were female. Ninety-four percent of patients were virologically suppressed and 67% had a $CD4^+$ cell count more than or equal to 500 cells/µl. Overall, 46% of patients required hospitalization and the median length of hospital stay was 6 days (IQR 3-15). Age more than or equal to 50 years, Black Sub-Saharan African patients, and being on an integrase strand transfer inhibitor-based regimen were associated with being hospitalized. ICU admission and mechanical ventilation was required for 15% and 10% of all patients respectively. Overall, 9% of patients died while 78 (77%) patients made a full recovery. HIV patients with COVID-19 experienced a high degree of hospitalization despite having elevated $CD4^+$ cell counts and a high rate of virologic suppression. Matched case-control studies are warranted to measure the impact that HIV may have on patients with COVID-19.

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1. Introduction

In December 2019, an outbreak of coronavirus disease 2019 (COVID-19) caused by the novel coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) began in Wuhan, China. As the number of cases continued to increase at an alarming rate worldwide, the World Health Organization declared COVID-19 a pandemic on March 11, 2020.[1] With an estimated 37.9 million people living with HIV (PLWH) worldwide,[2] it would be expected that a significant number of these patients will experience COVID-19. Characteristics such as older age, hypertension, and diabetes mellitus have been identified as risk factors for more severe infection and worse prognosis,[3,4] however there is limited evidence regarding the impact of HIV infection on the severity and mortality related to COVID-19. The presumption is that HIV would have a deleterious effect due to immune deficiency, however, this may also be paradoxically protective. As of June 26, 2020, the time of analysis for this study, Belgium had been one of the more affected countries with 61,106 confirmed COVID-19 cases and 9726 deaths.[5] We describe here the clinical characteristics and outcomes of COVID-19 among PLWH in Belgium.

2. Methods

2.1 STUDY DESIGN

This is a retrospective, observational, multicenter cohort study. Data were anonymously extracted, using a standardized data collection form, from the electronic health records of 10 HIV reference centers (HRCs) in Belgium, which work in concert as members of the Belgian Research on AIDS and HIV Consortium (BREACH). This study was done in accordance with local legislation and informed consent was waived. The inclusion criteria were as follows: male or female patients aged 18 years or above with confirmed HIV-1 infection having one of the following COVID-19 case definitions, defined according to Belgian national guidelines,[6] between February 15, 2020 and May 31, 2020: (i) laboratory-confirmed COVID-19 defined as having ei-ther a positive SARS-CoV-2 antigen (Ag) or qualitative real-time polymerase chain reaction (RT-PCR) assay on any type of respiratory sample or as having a positive SARS-CoV-2 serologic test in blood; or (ii) radiologically diagnosed COVID-19 defined as the combination of upper and/or lower respiratory symptoms compatible with COVID- 19 and typical findings on chest computed tomography (CT) scan in the absence of laboratory confirmation; or (iii) clinically suspected COVID-19 defined as upper and/or lower respiratory symptoms compatible with COVID-19 in the absence of laboratory and radiological confirmation. Data collected included (a) patient-related characteristics such as age, gender, ethnicity, height and weight, tobacco use, and co-morbidities; (b) HIV-related characteristics such as mode of HIV acquisition, $CD4^+$ cell count nadir, HIV treatment status at the time of the COVID-19 episode defined as naïve (never been treated) or experienced (currently being treated or has been

previously treated), $CD4^+$ cell count and HIV-1 viral load (VL) closest to the date of COVID-19 diagnosis, current combined antiretroviral therapy (cART) regimen being taken, and the rate of and

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reasons for HIV treatment interruption or modification during the COVID-19 episode; and (c) COVID-19-related characteristics such as a description of the symptoms experienced, chest CT scan and SARS- CoV-2 test results, hospitalization and Intensive Care Unit (ICU) admission, and types of treatment(s) received for COVID-19.

The primary endpoint was to evaluate the outcome of COVID-19 in PLWH categorized as either fully recovered, recovery ongoing, or death. Secondary endpoints included the rate of hospitalization and length of hospital stay and the rate of ICU admission and mechanical ventilation.

2.2 STATISTICAL ANALYSIS

Descriptive statistics on demographics were used to describe the overall study population in addition to three subsets of patients; laboratory-confirmed, radiologically diagnosed, and clinically suspected patients with COVID-19. Continuous variables were reported as median and interquartile range (IQR). Categorical values were conveyed as the number of available (and not available) data and as percentages. Analysis of both primary and secondary endpoints was performed on the overall study population in addition to the three subsets of patients. Univariable and multivariable logistic regression analyses were performed to examine for associations between baseline variables and the endpoint of hospitalization. Variables found to be significant ($p < .05$) in the univariable analyses were considered as potential predictive factors and were included in the multivariable logistic regression analysis. All statistical analyses were conducted using Statistical Analysis System (SAS®) software v9.4 (SAS® Institute, Inc.).

3. Results

Of the roughly 16,000 HIV patients that are regularly followed in the 10 participating HRCs, 101 were found to have either confirmed or suspected COVID-19 during the inclusion period. These patients were categorized as having either laboratory-confirmed (n = 65), radiologically diagnosed (n = 3), or clinically suspected COVID-19 (n = 33). Patient-related and HIV-related characteristics are summarized in Tables 1 and 2, respectively. The median age was 51.3 years (IQR 41.3-57.3) and a significant proportion of patients were female (44%). The two most common ethnicities were Black SubSaharan African (55%; identified according to the United Nations Statistics Division classification)[8] and Caucasian (39%). The median body mass index (BMI) was 28.1 kg/m2 (IQR 24.3-31.1). The most common comorbidities were hypertension (34%), diabetes mellitus (13%), and dyslipidemia (13%), and 25% of participants had more than or equal to 2 comorbidities. Acquisition of HIV-1 was predominantly through sexual exposure (85%). At the time of COVID-19 diagnosis, 97% of the study cohort was treatment-experienced, 94% had an HIV-1 VL less than 50 copies/ml, and 67% had a $CD4^+$ cell count more than or equal to 500 cells/µl. The most commonly prescribed type of cART regimen (48%) was that of an integrase strand transfer inhibitor (INSTI) with two nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) with the most frequent amongst those being dolutegravir/abacavir/lamivudine (DTG/ABC/3TC; 22%). No patients were taking

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ritonavir-boosted lopinavir (LPV/r) as part of their cART regimen at the time of COVID-19 diagnosis. Eight patients had their cART regimen interrupted/modified as a result of their COVID-19 episode and the most common causes were drug-drug interactions (n = 3) and renal failure (n = 2).

COVID-19-related characteristics and outcomes are presented in Table 3. Fever (59%), cough (58%), and fatigue (58%) were the most common presenting symptoms among all patients. Anosmia/ageusia occurred in 32% of patients. Chest CT scan was performed in 35% of

patients overall and bilateral infiltrates were present in 28/35 (80%) patients (two patients had a normal CT scan). Overall, 68 (67%) patients underwent SARS-CoV-2 testing and nasopharyngeal swab was the most common type of sample used (63/68; 93%). Of the 65 patients that had laboratory-confirmed COVID-19, 57 (88%) had a positive SARS-CoV-2 PCR on nasopharyngeal swab, 3 (5%) had a positive SARS-CoV-2 Ag on nasopharyngeal swab, and 3 (5%) had a positive SARS-CoV-2 PCR on bronchoalveolar lavage. In addition to supportive care, 36/101 patients received at least one type of off-label treatment for COVID-19 with 35/ 36 (97.2%) patients receiving hydroxychloroquine. The hospitalization rates for laboratory-confirmed, radiologically diagnosed, and clinically suspected patients with COVID-19 was 63%, 100%, and 6%, respectively. The overall median length of hospital stay was 6 days (IQR 3-15). Multivariable logistic regression analysis revealed that age more than or equal to 50 years (odds ratio [OR] 7.46; 95% confidence interval [CI] 1.94-28.78, p = .004), Black Sub-Saharan African patients (OR 5.89; 95% CI 1.39-25.05, p = .016), and being on an INSTI-based cART regimen (OR 6.72; 95% CI 1.83-24.66, p = .004) were associated with being hospitalized (Table 4). The same variables were observed to be significantly associated with being hospitalized when a similar multivariable analysis was performed on laboratory-confirmed patients only (n = 65; data not shown). ICU admission and mechanical ventilation was required for 15% and 10% of all patients respectively. Overall, 9% of patients died while 78 (77%) patients made a full recovery.

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Table 1. *Baseline characteristics of the study population*

	Laboratory-confirmed COVID-19 N = 65	Radiologically-diagnosed COVID-19 N = 3	Clinically suspected COVID-19 N = 33	Total N = 101
Age, years				
Median (IQR)	51.8 (43.4–59.5)	44.9 (33.4–57.0)	49.1 (40.1–56.6)	51.3 (41.3–57.3)
Gender, *n* (%)				
Male	32 (49)	0 (0)	25 (76)	57 (56)
Female	33 (51)	3 (100)	8 (24)	44 (44)
Ethnicity, *n* (%)				
Caucasian	18 (28)	0 (0)	21 (64)	39 (39)
Black Sub-Saharan African	42 (65)	3 (100)	11 (33)	56 (55)
North African	4 (6)	0 (0)	0 (0)	4 (4)
Other	1 (1)	0 (0)	1 (3)	2 (2)
BMI				
Median (IQR)	29.3 (24.1–34.4)	30.4 (30.4–30.4)	26.3 (24.2–29.8)	28.1 (24.3–31.1)
Smoker, *n* (%)				
Yes	5 (8)	0 (0)	9 (27)	14 (14)
No	47 (72)	3 (100)	16 (49)	66 (65)
Ex-smoker	9 (14)	0 (0)	8 (24)	17 (17)
Data not available	4 (6)	0 (0)	0 (0)	4 (4)
Co-morbidities, *n* (%)				
Hypertension	26 (40)	1 (33)	7 (21)	34 (34)
Diabetes mellitus	10 (15)	0 (0)	3 (9)	13 (13)
Dyslipidemia	9 (14)	1 (33)	3 (9)	13 (13)
Asthma/COPD	5 (8)	0 (0)	1 (3)	6 (6)
Chronic renal disease	5 (8)	1 (33)	0 (0)	6 (6)
Cerebrovascular disease	2 (3)	0 (0)	0 (0)	2 (2)
No comorbidities	30 (46)	1 (33)	25 (76)	56 (55)
1 Comorbidity	14 (22)	1 (33)	5 (15)	20 (20)
≥2 Comorbidities	21 (32)	1 (33)	3 (9)	25 (25)

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; IQR, interquartile range.

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Table 2. *HIV-related characteristics of the study population*

	Laboratory-confirmed COVID-19 N = 65	Radiologically-diagnosed COVID-19 N = 3	Clinically suspected COVID-19 N = 33	Total N = 101
Mode of HIV acquisition, *n* (%)				
Heterosexual	43 (66)	2 (67)	11 (33)	56 (55)
MSM	13 (20)	0 (0)	17 (52)	30 (30)
Other/unknown	9 (14)	1 (33)	5 (15)	15 (15)
Nadir $CD4^+$ cell count (cells/μL), *n* (%)				
≥500	4 (6)	0 (0)	7 (21)	11 (11)
200–499	28 (43)	0 (0)	17 (52)	45 (44)
<200	27 (42)	2 (67)	8 (24)	37 (37)
Data not available	6 (9)	1 (33)	1 (3)	8 (8)
cART status at the time of COVID-19 diagnosis, *n* (%)				
Naive	3 (5)	0 (0)	0 (0)	3 (3)
On treatment	62 (95)	3 (100)	33 (100)	98 (97)
Type of CART being taken at the time of COVID-19 diagnosis[a], *n* (%)				
2 NRTI + 1 INSTI	30 (46)	3 (100)	16 (49)	49 (48)
2 NRTI + 1 PI	9 (14)	0 (0)	3 (9)	12 (12)
2 NRTI + 1 NNRTI	13 (20)	0 (0)	9 (27)	22 (22)
1 NRTI + 1 INSTI	2 (3)	0 (0)	4 (12)	6 (6)
1 NNRTI + 1 INSTI	4 (6)	0 (0)	0 (0)	4 (4)
1 PI + 1 INSTI	2 (3)	0 (0)	0 (0)	2 (2)
PI monotherapy	2 (3)	0 (0)	0 (0)	2 (2)
Other	0 (0)	0 (0)	1 (3)	1 (1)
HIV-1 viral load (copies/mL), *n* (%) < 50 ≥ 50				
	61 (94)	2 (67)	32 (97)	95 (94)
	4 (6)	1 (33)	1 (3)	6 (6)
$CD4^+$ cell count (cells/μl), *n* (%)				
≥500	39 (60)	1 (33)	28 (85)	68 (67)
200–499	21 (32)	1 (33)	4 (12)	26 (26)
<200	3 (5)	0 (0)	1 (3)	4 (4)
Data not available	2 (3)	1 (33)	0 (0)	3 (3)
Modification of cART during the COVID-19 episode[a], *n* (%)				
Yes	8 (12)	0 (0)	0 (0)	8 (8)
No	51 (79)	3 (100)	33 (100)	87 (86)
Data not available	3 (5)	0 (0)	0 (0)	3 (3)

Abbreviations: cART, combined antiretroviral therapy; COVID-19, coronavirus disease 2019; INSTI, integrase strand transfer inhibitor; MSM, men who have sex with men; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor; PI, protease inhibitor.
[a]Three patients were treatment naïve.

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4. Discussion

Amid this pandemic, it remains unclear whether PLWH are at a higher risk of experiencing increased morbidity and mortality as a result of COVID-19. Evaluating the experience of previous coronavirus epidemics and other respiratory virus infections in this population provides conflicting evidence. In studies of Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) patients, HIV was not reported to be a risk factor.[8,9] In contrast, PLWH were observed to have more severe influenza virus infections with an increased risk of hospitalization and death as a result.[10,11] The aim of this study was to address some of the unknowns related to COVID-19 in PLWH.

We included three categories of COVID-19 patients; laboratory- confirmed, radiologically diagnosed, and clinically suspected because

first, these were the COVID-19 case definitions used in Belgium,6 second, the influenza season was concluding in Belgium by the time the inclusion period for this study began,[12] and given the low threshold of suspicion for COVID-19 during this pandemic, the presence of upper and/or lower respiratory symptoms compatible with COVID-19 was deemed sufficient to be considered clinically suspect, and lastly, these three categories of patients accurately reflect both our inpatient and outpatient experience during the peak of the COVID-19 pandemic in Belgium. Although our cohort of 101 patients shared certain similarities with the overall Belgian HIV population (median age of cohort 51.3 years vs. 49.6 years for the overall HIV population and rate of virologic suppression of cohort 94% vs. 97% for the overall HIV population),[13] some differences were observed: women accounted for 44% of our cohort (vs. 35% in the Belgian HIV population) and Black Sub-Saharan African patients represented 55% of the cohort (vs. 35% in the Belgian HIV population). These observations tend to indicate that amongst PLWH, women and Black Sub-Saharan African patients may be at higher risk for acquiring COVID-19. Of course, the drastic difference in number between our cohort (n = 101) and the overall Belgian HIV population (n≈16 000) precludes us from forming a definitive conclusion.

The overall hospitalization rate for our cohort was 46%. The hospitalization rate for PLWH described in the literature ranges between 27.7% and 42.4%.[14,15] The ICU admission rate and the rate of mechanical ventilation in our cohort was 15% and 10%, respectively. Various studies have reported an ICU admission rate ranging between 7.1% and 18.2%[15-17] and a rate of mechanical ventilation ranging between 4.3% and 55.6%.[14-19] In terms of recovery, 77% of patients in our cohort experienced a full recovery while 9% died. Mortality rates among PLWH coinfected with SARS-CoV-2 have been reported to be as low as 4% increasing up to 78%.[14,16-20] This wide ranging variation in the aforementioned results may be explained by the heterogeneous composition of the patient populations, varying sample sizes among the

cohorts, time of follow-up, baseline $CD4^+$ cell counts, and HIV VLs, and variations in the reporting of COVID-19 cases and deaths in each respective country/region. Exploring further for the presence of any patient-related or HIV-related factors within our cohort that may be associated with worse outcomes, we found that Black Sub-Saharan African patients and those above the age of 50 had a significantly higher risk of being hospitalized, findings which have been previously reported.[19,20] In

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contrast to previous reports, however, being an active smoker and having hypertension or diabetes mellitus were not found to be significant risk factors for hospitalization.[3,4] Potential factors that may explain the discrepancy between our findings and those of other studies include differences in age and overall prevalence of comorbidities as well as the small sample size of our cohort. There is a debate whether antiretrovirals play a role in preventing or treating COVID-19. Indeed, there have been reports that have suggested that certain antiretroviral (ARV) agents such as LPV/r, tenofovir prodrugs, or INSTIs may have a protective effect against COVID-19.[21-23] Our results showed no specific type of ARV to be protective against hospitalization. Interestingly however, we did find that being on an INSTIbased cART regimen was significantly associated with being hospitalized. However, given the observational design of our study, the small sample size of the analysis, and the significant therapeutic benefits that INSTIs may provide to these patients, this finding should not be used as the basis for the formulation of a generalized conclusion against the use of INSTIs in PLWH coinfected with SARS-CoV-2 but rather should warrant further study in the future.

For the purposes of making comparisons to the general population in Belgium, we were limited to using the data from laboratory- confirmed COVID-19 patients in our cohort as national data for radiologically diagnosed and clinically suspected cases were not available.[5] The COVID-19 hospitalization rate for laboratory- confirmed patients in our cohort was 63% (41/65 patients) as compared with 29% (17 707 hospitalizations out of 61,106 confirmed cases) in the Belgian general population at the time of analysis.[5] Of the hospitalized confirmed cases in our cohort, 50% were male (compared with 53% in the general population), 67% were more than or equal to 50 years old (compared with 69% being older than 60 years in the general population), 46% had hypertension (compared with 40% in the general population), 22% had diabetes mellitus (compared with 21% in the general population), and 11% had a chronic pulmonary condition (compared with 15% in the general population). At face value, the aforementioned results would suggest that PLWH diagnosed with COVID-19 are hospitalized at a higher rate when compared to the general population. There have been previous reports that have indicated there may be substantial morbidity associated with COVID-19 in PLWH, even amongst those with higher $CD4^+$ cell counts and on suppressive cART.[16,17,19,20,24] In our cohort, 94% of laboratory-confirmed COVID-19 patients had an HIV-1 VL less than 50 copies/ml and 67% had a $CD4^+$ cell count of more than or equal to 500 cells⁄μl. A possible explanation for such an increased rate of complication in PLWH may be the fact that the host response to SARS-CoV-2 requires lymphocytes and HIV-related lymphopenia may promote the progression of disease.[19] However, perhaps this striking difference in hospitalization rates between our cohort and the general population can be explained by a form of "hospitalization bias" whereby physicians may perceive PLWH as more fragile or at risk of complication and choose to admit these patients out of an abundance of caution resulting in a higher rate of hospitalization. Data concerning the onset and duration of symptoms along with the vital signs, laboratory results, and socioeconomic status of patients upon admission to the hospital was incomplete, preventing us from providing further insight on this matter. Moreover, the case fatality rate among laboratory-confirmed COVID-19 patients in our cohort was 14% (9/65 patients), which was slightly lower than the general population in Belgium (16%), where 9726 patients out of 61,106 confirmed COVID-19 cases died.[5] Indeed, there have been reports that PLWH coinfected with SARS-CoV-2 are not at

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greater risk of experiencing complications.[14,15,18,25] The hypothesis put forth explaining this is that there is a paradoxical prevention from the cytokine storm seen in COVID-19 due to a combination of the absence of T cell activation and HIV-related lymphopenia.[26]

Our study has some limitations. The small sample size prevents us from generalizing our results. Comparison with patients without HIV was not done for this study. Lastly, it is to be noted that the number of laboratory-confirmed cases in our cohort, as in the general population in Belgium, is probably underestimated given that early in the pandemic national recommendations placed restrictions on confirmatory testing of cases.

In conclusion, the results of this analysis suggest that HIV patients with COVID-19 are at a greater risk of hospitalization, when compared to the general population, but have a similar mortality rate. Matched case-control studies are warranted therefore to precisely measure the impact of HIV on the clinical course of COVID-19. Furthermore, PLWH should be included in future investigational trials that will evaluate the potential of treatments against COVID-19.

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***Table 3**. COVID-19-related characteristics and outcomes of the study population*

	Laboratory-confirmed COVID-19 N = 65	Radiologically diagnosed COVID-19 N = 3	Clinically suspected COVID-19 N = 33	Total N = 101
Clinical characteristics, *n* (%)				
Dyspnea	40 (62)	1 (33)	13 (39)	54 (54)
Confusion	7 (11)	0 (0)	4 (12)	11 (11)
Cough	38 (59)	3 (100)	18 (55)	59 (58)
Fever	42 (65)	2 (67)	16 (49)	60 (59)
Anosmia/agueusia	15 (23)	0 (0)	17 (52)	32 (32)
Myalgia	20 (31)	2 (67)	22 (67)	44 (44)
Conjunctivitis	0 (0)	0 (0)	3 (9)	3 (3)
Sore throat	11 (17)	0 (0)	9 (27)	20 (20)
Headache	22 (34)	0 (0)	12 (36)	34 (34)
Diarrhea	10 (15)	2 (67)	9 (27)	21 (21)
Rash	2 (3)	0 (0)	2 (6)	4 (4)
Fatigue	30 (46)	1 (33)	28 (85)	59 (58)
Rhinitis	9 (14)	1 (33)	17 (52)	27 (27)
Asymptomatic	5 (8)	0 (0)	0 (0)	5 (5)
Hospitalization, *n* (%)				
Yes	41 (63)	3 (100)	2 (6)	46 (46)
No	24 (37)	0 (0)	31 (94)	55 (54)
Length of hospital stay (days)				
Median (IQR)	7 (4–15)	3 (3 –24)	1.5 (1–2)	6 (3–15)
Hospitalization in ICU, *n* (%)				
Yes	15 (23)	0 (0)	0 (0)	15 (15)
No	50 (77)	3 (100)	33 (100)	86 (85)
COVID-19 treatment, *n* (%)				
No treatment received	32 (49)	0 (0)	33 (100)	65 (64)
Received 1 type of treatment	24 (37)	3 (100)	0 (0)	27 (27)
Received ≥ 2 types of treatment	9 (14)	0 (0)	0 (0)	9 (9)
Hydroxychloroquine	32 (49)	3 (100)	0 (0)	35 (35)
Azithromycin	4 (6)	0 (0)	0 (0)	4 (4)
Corticosteroids	4 (6)	0 (0)	0 (0)	4 (4)
Lopinavir/ritonavir	1 (2)	0 (0)	0 (0)	1 (1)
Outcome, *n* (%)				
Fully recovered	45 (69)	2 (67)	31 (94)	78 (77)
Recovery ongoing	10 (15)	1 (33)	2 (6)	13 (13)
Death	9 (14)	0 (0)	0 (0)	9 (9)
Unknown	1 (2)	0 (0)	0 (0)	1 (1)

Abbreviations: COVID-19, coronavirus disease 2019; ICU, intensive care unit; IQR, interquartile range.

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***Table 4**. Univariable and multivariable logistic regression analysis of predictors for hospitalization for the overall cohort (n = 101)*

Variable at the time of COVID-19 diagnosis	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*p*	OR (95% CI)	*p*
Age ≥ 50 years	2.67 (1.10–6.56)	**.027**	7.46 (1.94–28.78)	**.004**
Gender	0.62 (0.26–1.47)	.31	–	–
Black Sub-Saharan African ethnicity	2.95 (1.20–7.34)	**.01**	5.89 (1.39–25.05)	**.016**
BMI ≥ 30 kg/m^2	2.56 (0.97–6.84)	**.048**	0.97 (0.26–3.55)	.96
Smoker	0.81 (0.24–2.62)	.79	–	–
Diabetes mellitus	4.81 (1.12–28.68)	**.019**	1.05 (0.13–8.50)	.97
Hypertension	2.71 (1.07–6.97)	**.022**	2.25 (0.55–9.20)	.26
Dyslipidemia	3.10 (0.78–14.69)	.08	–	–
Nadir CD4$^+$ cell count < 200 cells/μl	1.21 (0.43–2.31)	.11	–	–
HIV treatment status	0.59 (0.01–11.72)	1.00	–	–
HIV-1 VL < 50 copies/ml	0.58 (0.05–4.29)	.69	–	–
CD4$^+$ cell count < 500 cells/μl	1.34 (0.52–3.48)	.52	–	–
Having an INSTI-based cART regimen	2.63 (1.07–6.63)	**.026**	6.72 (1.83–24.66)	**.004**
Having a PI-based cART regimen	0.81 (0.24–2.73)	.79	–	–
Having a TAF or TDF-based regimen	0.75 (0.32–1.78)	.56	–	–

Note: The bold values indicate statistically significant results (i.e. p < .05).
Abbreviations: BMI, body mass index; CI, confidence interval; cART, combined antiretroviral therapy; INSTI, integrase strand transfer inhibitor; OR, odds ratio; PI, protease inhibitor; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; VL, viral load.

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References

1. World Health OrganizationWHO Director-General's Opening Remarks at the Media Briefing on COVID-19. Geneva: WHO; 2020. https://www.who.int/dg/speeches/detail/who-director-general-s-openingremarks-at-the-media-briefingon-covid-19-11-march-2020 Accessed June 4, 2020.

2. Joint United Nations Programme on HIV/AIDS. Fact Sheet: World AIDS Day 2019—Global HIV Statistics. Geneva: UNAIDS; 2019. https://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf

3. Guan W, Ni Z, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020;382(18):1708-1720.

4. Onder G, Rezza G, Brusaferro S. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. JAMA. 2020; 323(18):1775-1776.

5. Sciensano. COVID-19–Bulletin Epidémiologique Brussels, Sciensano. 2020. https://covid-19.sciensano.be/fr/covid-19-situationepidemiologique. Accessed June 26, 2020.

6. Sciensano. Définition de Cas, Indications de Demande d'un Test et Déclaration Obligatoire de Cas COVID-19 Brussels, Sciensano. 2020. https://covid-19.sciensano.be/sites/default/files/Covid19/COVID-19_Case%20definition_Testing_FR.pdf. Accessed June 1, 2020.

7. United Nations Statistics Division. Composition of Macro Geographical (Continental) Regions, Geographical Sub-Regions, and Selected Economic Other Groupings. New York: UNSD; 2003. https://unstats.un.org/unsd/mi/africa.htm

8. Peiris J, Chu C, Cheng V, et al. Clinical progression and viral load in a community outbreak of coronavirus-associated SARS pneumonia: a prospective study. Lancet. 2003;361:1767-1772.

9. Arabi YM, Arifi AA, Balkhy HH, et al. Clinical course and outcomes of critically ill patients with middle east respiratory syndrome coronavirus infection. Ann Intern Med. 2014;160:389-397.

10. Dauby N. Potential impact of COVID-19 in people living with HIV: experience from previous 21st century coronaviruses epidemics. AIDS. 2020;34(8):1255-1256.

11. Cohen C, Moyes J, Tempia S, et al. Severe influenza-associated respiratory infection in high HIV prevalence setting, South Africa, 2009–2011. Emerg Infect Dis. 2013;19:1766-1774.

12. Sciensano. Influenza–Bulletin Epidémiologique Brussels, Sciensano. 2020. https://epidemio.wiv-isp.be/ID/diseases/Pages/Influenza.aspx. Accessed June 1, 2020

13. Sciensano. Epidémiologie du Sida et de l'Infection à VIH en Belgique: situation au 31 Décembre 2018 Brussels, Sciensano. 2019. https://www.sciensano.be/sites/default/files/report_sida_2018_fr_final_28_11.pdf. Accessed June 8, 2020

14. Gervasoni C, Meraviglia P, Riva A, et al. Clinical features and outcomes of HIV patients with coronavirus disease 2019 [published online ahead of print May 14, 2020]. Clin Infect Dis. 2020.

15. Härter G, Spinner CD, Roider J, et al. COVID-19 in people living with human immunodeficiency virus: a case series of 33 patients [published online ahead of print May 11, 2020]. Infection. 2020:1-6.

16. Guo W, Ming F, Feng Y, et al. Patterns of HIV and SARS-CoV-2 coinfection in Wuhan, China. J Int AIDS Soc. 2020;23(7):e25568.

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17. Vizcarra P, Pérez-Elías MJ, Quereda C, et al. Description of COVID-19 in HIV-infected individuals: a single-centre, prospective cohort [published online ahead of print May 28, 2020]. Lancet HIV. 2020; (20):30164-30168.

18. Shalev N, Scherer M, LaSota ED, et al. Clinical characteristics and outcomes in people living with HIV hospitalized for COVID-19 [published online ahead of print May 30, 2020]. Clin Infect Dis. 2020.

19. Suwanwongse K, Shabarek N. Clinical features and outcome of HIV/SARS-CoV-2 coinfected patients in the Bronx, New York city[published online ahead of print May 28, 2020]. J Med Virol. 2020;92:2387-2389. https://doi.org/10.1002/jmv.26077

20. Childs K, Post FA, Norcross C, et al. Hospitalized patients with COVID-19 and HIV: a case series [published online ahead of print May 28, 2020]. Clin Infect Dis. 2020.

21. Choy K, Wong AY, Kaewpreedee P, Sia SF. Remdesivir, lopinavir, emetine, and homoharringtonine inhibit SARS-CoV-2 replication in vitro. Antiviral Res. 2020;178:104786.

22. Elfiky AA. Ribavirin, remdesivir, sofosbuvir, galidesivir, and tenofovir against SARS-CoV-2 RNA dependent RNA polymerase (RdRp): a molecular docking study. Life Sci. 2020;253:117592.

23. 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 [published online ahead of print June 26, 2020]. Ann Intern Med. 2020;173:536-541. https://doi.org/10.7326/M20-3689

24. Ho H-E, Peluso MJ, Margus C, et al. Clinical outcomes and immunologic characteristics of Covid-19 in people with HIV [published online ahead of print June 30, 2020]. J Infect Dis. 2020.

25. Blanco JL, Ambrosioni J, Garcia F, et al. COVID-19 in patients with HIV: clinical case series. Lancet HIV. 2020;7(5):e314-e316.

26. Mascolo S, Romanelli A, Carleo MA, Esposito V, Could HIV. Infection alter the clinical course of SARS-CoV-2 infection? when less is better [published online ahead of print April 15, 2020]. J Med Virol. 2020;92:1777-1778. https://doi.org/10.1002/jmv.25881