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COVID-19 Outcomes in Patients With Uncontrolled HIV-1 Infection

To the Editors:

In December 2019, an interstitial pneumonia caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in Wuhan city, China. This viral disease, which has subsequently been named coronavirus disease 2019 (COVID-19), became in the following weeks a disastrous global pandemic, with more than 12 million confirmed cases and 500,000 deaths worldwide on July 15, 2020.[1–3]

Clinical studies suggest advanced age and chronic comorbidities (mostly hypertension, diabetes mellitus, and obesity) are associated with worse outcomes of SARS-CoV-2 infection, but it is not clear to date if human immune deficiency virus-1 (HIV-1) infection is a risk factor for greater severity and higher mortality of COVID-19.[4,5]

In some cohort studies, HIV-infected persons hospitalized for COVID-19 had similar clinical characteristics and outcomes with other hospitalized cohorts of HIV-uninfected patients, and risk of COVID-19 and severe disease in suppressed HIV-positive people seems to be comparable with the general population.[6–16] Particularly, a recent systematic review suggests that patients with controlled HIV infection (or rather with $CD4^+$ lymphocyte count >200 cells/mm^3 and undetectable viral load) have the same risk of contracting SARS-CoV-2 infection or experiencing more severe COVID-19 in comparison with HIV-uninfected people.[17]

However, very limited evidence is available still today about the clinical course and outcomes of COVID-19 in HIV-positive persons with poor immunological status and detectable HIV RNA. So, we have performed a retrospective analysis of patients with uncontrolled HIV infection and COVID-19 diagnosed in our clinics.

Uncontrolled HIV infection was defined by current $CD4^+$ lymphocyte count <350 cells/mm^3 and HIV RNA ≥ 50 copies/mL. Diagnosis of COVID-19 was made by detection of SARS-CoV-2 RNA in oropharyngeal and/or nasopharyngeal swab specimens by real-time RT-PCR targeting regions in the *N* gene, following the US CDC protocol.

Between March 1, 2020, and June 30, 2020, a total of 31 coinfections with HIV-1 and SARS-CoV-2 were diagnosed at the S.Orsola Hospital in Bologna (Emilia-Romagna region, Italy). Among these cases, 9 patients (29%) had an uncontrolled HIV infection. Characteristics, treatments, and outcomes of these patients are summarized in Table 1.

All patients gave informed consent. Overall, 7 (78%) were men, the median age was 56.2 years (range, 41–73), and all were currently treated with combination antiretroviral therapy (cART). Six subjects had $CD4^+$ lymphocyte count ranging between 200 and 350 cells/mm^3, and 3 subjects had $CD4^+$ lymphocyte count <200 cells/mm^3. Four patients had a previous diagnosis of an AIDS-defining condition: *Pneumocystis jirovecii* pneumonia in 3 cases, and Kaposi's sarcoma in 1 case. Plasma HIV RNA ranged between 66 and 1240 copies/mL, and 7 patients had HIV RNA <200 copies/mL. Current cART included 1boosted protease inhibitor (PI) in 3 cases, 1 integrase strand transfer inhibitor in 4, and 1 nonnucleoside reverse transcriptase inhibitor in 2. Seven patients had one or more comorbidities, and 3 patients had 2 comorbidities.

Clinical diagnosis was represented by upper respiratory tract infection in 7 cases and interstitial pneumonia in 2. At diagnosis, the median duration of symptoms was 3.6 days, and most frequent symptoms were fever >38°C, cough, fatigue, and myalgia. Only 1 subject had an initial respiratory failure with a PaO_2/FiO_2 ratio <300 at arterial blood gas analysis.

Overall, 3 patients (33%) were hospitalized, whereas other 6 subjects had mild symptoms and spent their disease period at home. At diagnosis, 3 patients were receiving a PI-based cART, including darunavir–cobicistat in all cases. A transitional change in cART was made in other 2 patients who were treated with a non-boosted PI-based regimen, because of the potential activity of HIV PIs against the coronavirus protease.[18] So, darunavir/cobicistat replaced rilpivirine in 1 case and efavirenz in 1 case. Regarding other drug treatments, we prescribed hydroxychloroquine in 5 subjects and enoxaparin in 3, whereas tocilizumab and corticosteroids were not used.

A clinical recovery was obtained in all patients, whereas there were no admissions to the ICU and no deaths. The 3 hospitalized patients were discharged after a median of 8.5 days, and the median global duration of symptoms before recovery in all observed patients was 9.2 days. The median duration of positivity for SARS-CoV-2 RNA in oropharyngeal and/or nasopharyngeal swab was 16.2 days, and all patients tested negative at oro and/or nasopharyngeal swab 21 days after the onset of symptoms.

The clinical course and outcome of COVID-19 among patients with uncontrolled HIV infection are still unknown, and so far, only few cases of COVID-19 in subjects with poor immunological status or AIDS have been described in case series.[17] One patient with AIDS reported by Blanco et al[8] was admitted to the ICU and required noninvasive ventilation but responded well to drug therapy and was discharged after 12 days. Guo et al[19] described 1 patient with AIDS who tested positive for SARS-CoV-2 but had an asymptomatic infection with a normal chest CT scan. A patient with very low $CD4^+$ lymphocyte count (34 cells/mm^3) who experienced an interstitial pneumonia with a very long disease course (2 months) and delayed immune response was presented by Wang et al.[20] Harter et al[10] described 4 patients with low $CD4^+$ lymphocyte count: 1 patient with 69 $CD4^+$ lymphocytes/mm^3 had severe interstitial pneumonia and died, whereas 3 subjects had mild infections and

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TABLE 1. Demographic Data, Clinical Characteristics, Treatment, and Outcomes of Patients With COVID-19 and Uncontrolled HIV Infection

Patients, n.	9
Men, n. (%)	7 (77.8)
White, n. (%)	8 (88.9)
Age (yr), median (IQR)	56.2 (42.2–69.5)
HIV transmission risk category, n. (%):	
IDU	3 (33.3)
MSM	4 (44.4)
Heterosexual	2 (22.2)
Current $CD4^+$ lymphocyte count (cells/mm^3), median (IQR)	258 (156–343)
Nadir $CD4^+$ lymphocyte count (cells/mm^3), median (IQR)	129 (44–202)
Patients with current $CD4^+$ lymphocyte count <200 cells/mm^3, n. (%)	3 (33.3)
Patients with HIV RNA <200 copies/mL, n. (%)	7 (77.8)
Patients with AIDS diagnosis, n. (%)	4 (44.4)
Duration of HIV infection (yr), median (IQR)	21.4 (13.6–29.2)
Patients with one or more comorbidities, n. (%)	7 (77.8)
Patients with arterial hypertension, n. (%)	6 (66.7)
Patients with diabetes mellitus, n. (%)	2 (22.2)
Patients with BMI >30 Kg/m^2, n. (%)	1 (11.1)
Patients with chronic obstructive pulmonary disease, n. (%)	1 (11.1)
Diagnosis:	
Upper respiratory tract infection, n. (%)	7 (77.8)
Interstitial pneumonia, n. (%)	2 (22.2)
Interstitial pneumonia with ARDS, n. (%)	0
Superimposed bacterial pneumonia	0
Duration of symptoms before diagnosis (d), median (IQR)	3.6 (1.8–5.7)
Temperature ≥38°C, n. (%)	9 (100)
Cough, n. (%)	7 (77.8)
Myalgia, n. (%)	7 (77.8)
Fatigue, n. (%)	9 (100)
Anosmia and/or ageusia, n. (%)	3 (33.3)
Dyspnea, n. (%)	2 (22.2)
PaO_2/FiO_2 ratio <300, n. (%)	1 (11.1)
Patients with lymphocyte count <1000 cells per 10^6/L, n. (%)	1 (11.1)
Patients with platelet count <150,000 cells per 10^6/L, n. (%)	1 (11.1)
Hospitalization, n. (%)	3 (33.3)
Admission to an ICU, n. (%)	0
Non-invasive mechanical ventilation, n. (%)	0
Lopinavir/ritonavir, n. (%)	1 (11.1)
Darunavir/ritonavir or darunavir/cobicistat, n. (%)	4 (44.4)
Hydroxychloroquine, n. (%)	5 (55.6)
Azithromycin, n. (%)	3 (33.3)
Enoxaparin, n. (%)	3 (33.3)
Recovery, n. (%)	9 (100)
Death, n. (%)	0
Duration of hospitalization (d), median (IQR)	8.5 (5.9–11.3)
Duration of symptoms (d), median (IQR)	9.2 (5.1–13.4)
Duration of positivity for SARS-CoV-2 RNA in oropharyngeal and/or nasopharyngeal swab specimens (d), median (IQR)	16.2 (7.5–22.1)

ARDS, acute respiratory distress syndrome; BMI, body mass index; ICU, intensive care unit; IQR, interquartile range; IDU, injection drug users; MSM, men who have sex with men.

recovered. So, outcomes of COVID-19 in HIV-infected patients with low $CD4^+$ cell count ranged from asymptomatic infection to severe disease and death, and conclusions cannot be drawn on the severity of COVID-19 in AIDS patients.

In our experience, COVID-19 in patients with uncontrolled HIV infection was frequently associated with chronic comorbidities and had a clinical presentation comparable with that of both patients with controlled HIV infection and HIV-negative population. No patients were admitted to the ICU or required mechanical ventilation, and all subjects recovered after a median of 9 days. Therefore, in our report, uncontrolled HIV infection did not seem to be associated with greater severity and worse outcome of SARS-CoV-2 infection.

Obviously, our study is limited by the retrospective design and the very limited number of patients; so, larger cohort studies are needed to better understand the real effect of HIV infection on COVID-19.

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