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/mm³ 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/mm³ 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 infections 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/mm³, and 3 subjects had CD4+ lymphocyte count <200 cells/mm³. 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 1 boosted protease inhibitor (PI) in 3 cases, 1 integrase strand transfer inhibitor in 4, and 1 non-nucleoside 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 PaO₂/FiO₂ 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 PI 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 al19 was admitted to the ICU and required noninvasive ventilation but responded well to drug therapy and was discharged after 12 days. Guo et al20 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/mm³) who experienced an interstitial pneumonia with a very long disease course (2 months) and delayed immune response was presented by Wang et al.21 Harter et al22 described 4 patients with low CD4+ lymphocyte count: 1 patient with 69 CD4+ lymphocytes/mm³ had severe interstitial pneumonia and died, whereas 3 subjects had mild infections and...
TABLE 1. Demographic Data, Clinical Characteristics, Treatment, and Outcomes of Patients With COVID-19 and Uncontrolled HIV Infection

| Description                                                                 | Patients, n. (%) |
|----------------------------------------------------------------------------|------------------|
| Men                                                                        | 7 (77.8)         |
| White                                                                      | 8 (88.9)         |
| AIDS diagnosis                                                             | 4 (44.4)         |
| 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) |
| Current CD4⁺ lymphocyte count (cells/mm³), median (IQR)                    | 258 (156–343)    |
| Patients with current CD4⁺ lymphocyte count <200 cells/mm³, n. (%)         | 3 (33.3)         |
| Patients with HIV RNA <200 copies/mL, n. (%)                              | 7 (77.8)         |
| Patients with chronic obstructive pulmonary disease, n. (%)               | 1 (11.1)         |
| Diagnosis: Up respiratory tract infection, n. (%)                          | 7 (77.8)         |
| Intersitial pneumonia, n. (%)                                              | 2 (22.2)         |
| Intersitial pneumonia with ARDS, n. (%)                                    | 0                |
| Superimposed bacterial pneumonia                                          | 0                |
| Admision 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                |
| PaO₂/FiO₂ ratio <300, n. (%)                                               | 1 (11.1)         |
| Patients with lymphocyte count <1000 cells per 10⁶/L, n. (%)              | 1 (11.1)         |
| Patients with platelet count <150,000 cells per 10⁶/L, n. (%)             | 1 (11.1)         |
| Hospitalization, n. (%)                                                    | 3 (33.3)         |
| Temperature ≥38°C, n. (%)                                                  | 9 (100)          |
| Cough, n. (%)                                                             | 7 (77.8)         |
| Myalgia, n. (%)                                                           | 3 (33.3)         |
| Fatigue, n. (%)                                                           | 7 (77.8)         |
| Anosmia and/or ageusia, n. (%)                                            | 2 (22.2)         |
| Dyspnea, n. (%)                                                           | 9 (100)          |
| nadir CD4⁺ lymphocyte count (cells/mm³), median (IQR)                     | 129 (44–202)     |
| Duration of symptoms before diagnosis (d), median (IQR)                   | 3.6 (1.8–5.7)    |
| Patients with BMI >30 Kg/m², n. (%)                                        | 1 (11.1)         |
| Patients with HIV RNA, n. (%)                                              | 7 (77.8)         |
| Patients with one or more comorbidities, n. (%)                           | 7 (77.8)         |
| Patients with arteriopathy, n. (%)                                         | 6 (66.7)         |
| Patients with diabetes mellitus, n. (%)                                    | 2 (22.2)         |
| Patients with AIDS diagnosis, n. (%)                                       | 4 (44.4)         |
| Duration of HIV infection (yr), median (IQR)                               | 21.4 (13.6–29.2) |
| Patients with BMI <30 Kg/m², n. (%)                                        | 3 (33.3)         |
| Patients with HIV RNA >200 copies/mL, n. (%)                               | 4 (44.4)         |
| Patients with diabetes mellitus, n. (%)                                    | 7 (77.8)         |
| Patients with BMI >30 Kg/m², n. (%)                                        | 1 (11.1)         |
| 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 arteriopathy, n. (%)                                         | 6 (66.7)         |
| Patients with diabetes mellitus, n. (%)                                    | 2 (22.2)         |
| Patients with BMI >30 Kg/m², n. (%)                                        | 1 (11.1)         |
| Patients with chronic obstructive pulmonary disease, n. (%)               | 1 (11.1)         |

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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