Clinical features and outcomes of HIV patients with coronavirus disease 2019

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Abstract

Little is known about the clinical outcomes of HIV patients infected with SARS-CoV-2. We describe 47 patients referred to our hospital between 21 February and 16 April 2020 with proven/probable COVID-19, 45 (96%) of whom fully recovered and two died.

INTRODUCTION

As of April 20, the pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection had affected 2.5 million people all over the world, and led to more than 165,000 deaths (update available at https://coronavirus.jhu.edu/map.html). Initial information from China and evidence accumulated over recent weeks has allowed the identification of some of the risk factors associated with a negative prognosis, includingaging, male gender, hypertension, diabetes mellitus, and cardiovascular, lung and/or kidney diseases.[1-4]

However, little is known about the impact of HIV infection on the clinical outcomes of patients infected with SARS-CoV-2 because, to the best of our knowledge, only case reports or small case series have so far been published.[5-7] Treated people living with HIV who have a normal CD4 T cell count and suppressed viral load may not be at increased risk of serious illness, but many also have other conditions that increase their overall risk: almost half of HIV patients are males, aged >50 years, and affected by chronic cardiovascular and lung diseases.

The aim of this retrospective study was to describe the clinical characteristics and outcomes of HIV-infected patients with a probable/proven diagnosis of SARS-CoV-2 infection who have been regularly followed up by our hospital.

METHODS

We searched our database for HIV patients diagnosed as having probable or proven SARS-CoV-2 infection between 21 February and 20 April 2020. A diagnosis of probable SARS-CoV-2 infection was based on the presence of fever and respiratory symptoms (cough and dyspnea), epidemiological risk factors such as relatives or close colleagues with a proven diagnosis of COVID-19, and/or a chest X-ray or CT diagnosis of interstitial pneumonia; proven SARS-CoV-2 infection required a throat swab positive for viral nucleic acid. We also recorded their main demographic data, pharmacological treatments and clinical outcomes.

The overall population frequency data were stratified by gender and expressed as absolute numbers: the other measures are expressed as mean values ± standard deviation.

This retrospective study was conducted using data collected for clinical purposes, all of which had been previously made anonymous in accordance with the requirements of the Italian Personal Data Protection Code (Legislative Decree No. 196/2003) and the general authorisations issued by the Italian Data Protection Authority. Ethics committee approval was unnecessary because Italian law states it is only required for prospective clinical trials of medical products for clinical use (Arts. 6 and 9 of Legislative Decree No. 211/2003). All of the patients gave their informed consent to the medical procedures used for routine treatment purposes.

RESULTS

The database of our Department of Infectious Diseases included nearly 6,000 HIV-positive patients (74% males; mean age 52±12 years); 90% had <20 copies/mL of HIV viral load and 76% had a CD4 cell count of >500 cells/mm^3 (3% had <200 cells/mm^3). During the observation period, 47 HIV patients with proven or probable SARS-CoV-2 infection were identified. They were mainly males (76%) and had a mean age of 51±11 years. As shown in Table 1, most of the patients showed suppressed HIV viremia and acceptable immune reconstitution (CD4 cell count >350 cells/mm^3); three (all males) had detectable HIV viral loads of 52, 72 and 134 copies/mL. Nearly 64% had at least one co-morbidity (82% of the males and 58% of the females), mainly dyslipidemia (32%), arterial hypertension (30%) and hepatitis B or hepatitis C co-infections (11%). Approximately 80% of the identified patients were receiving integrase inhibitor-based antiretroviral treatment and 11% a protease inhibitor-based regimen (11%); 42% were receiving a tenofovir-based regimen (Table 2).

Twenty-eight patients (>50%) tested positive for SARS-CoV-2, including one female asymptomatic patient who was tested because she was a healthcare provider; the remainder were not tested mainly because they lived in the high-risk provinces of Bergamo and Brescia (Lombardy) but were isolated at home and cared for by their general practitioners. The COVID-19 diagnosis of the untested patients was based on their clinical symptoms and the presence of risk factors (13% were healthcare providers; 9% had been in close contact with SARS-CoV-2 positive working colleagues and 23% with SARS-CoV-2 positive relatives). Interstitial pneumonia was diagnosed by means of an X-ray in three cases, and ground-glass opacity was identified by means of CT in one.

Thirteen of the 28 SARS-CoV-2 positive patients were hospitalised. Six had severe lung disease (respiratory rate ≥30 breaths/min; resting percutaneous oxygen saturation ≤93% in room air), two of whom required mechanical ventilation: one recovered and was discharged and the other (a 47-year-old overweight man without other co-morbidities) died. Another

patient with cardiovascular disease and a recent diagnosis of lung cancer died during hospitalisation. For comparative purposes, the crude mortality rate of the HIV-negative COVID-19 patients in our hospital (n=502, 67% males, mean age 61±16 years) is currently ~17%.

Forty-five of the patients recovered 14±8 days after symptom onset, with no significant difference between the females and males (11±7 *versus* 14±9 days; p=0.338).

As shown in Table 2, fewer than 50% of the patients were given potential anti-SARS-CoV-2 treatments, specifically hydroxychloroquine (17%), azithromycin (15%), lopinavir/ritonavir (11%); one was treated with tocilizumab and remdesivir, and one with toxicizumab alone.

DISCUSSION

This report describes our experience with HIV-positive patients regularly followed by our hospital (a reference hospital for the management of HIV infection in Italy) who were infected with SARS-CoV-2. As in the general population, the large majority of our patients were males, but their mean age was nearly 10 years lower than that observed in HIV-negative COVID-19 patients.[8-10] This is in line with the recent finding of Blanco *et al*. who described five HIV-infected patients with COVID-19 from Spain who were aged 29-49 years.[5] The difference in age between HIV-positive and HIV-negative patients with COVID-19 may possibly be explained by the general belief that HIV infection can add nearly 10 years to the chronological age.[11,12] This is indirectly supported by the fact that, although they are about 50 years old, the large majority of our patients have at least one co-morbidity, a picture that is more frequently observed in patients aged >60 years in the general population.

The risk of severe disease in our HIV-patients compared favourably with that observed in the general population of COVID-19 patients.[13] Likewise, the risk of death or admission to an intensive care unit was lower than that observed in the HIV-negative patients treated at our hospital and in another cohort of HIV-negative COVID-19 patients of a similar mean age.[14]

It is worth noting that these positive outcomes were achieved even though fewer than 50% of the patients were treated with drugs currently considered to be potential treatments for SARS-CoV-2 infection, and only two received remdesivir or tocilizumab. It could be argued that antiretroviral therapy may have played a role in the positive evolution of COVID-19 in our HIV patients; indeed, lopinavir/ritonavir, darunavir/ritonavir and darunavir/cobicistat were all initially suggested as candidate treatments for SARS-CoV-2 infection.[15] However, we have recently shown that darunavir does not prevent SARS-CoV-2 infection in people living with HIV or protect against worsening respiratory function, at least not at a dose of 800 mg.[16] Furthermore, the findings of this study document favourable outcomes in HIV patients treated mainly with integrase inhibitors (11% protease inhibitors), which apparently indicates that antiretroviral therapy does not play a key role,

although a potentially protective effect of tenofovir cannot be ruled out given its recently reported effect against SARS-CoV-2 RNA-dependent RNA polymerase.[17]

Another possible explanation of the more favourable clinical outcome observed in our HIV-positive patients is that, despite their effective antiretroviral therapy, they still had deficient immune systems (albeit to different degrees) and showed some persistent immune activation: consequently, the evolution of COVID-19 may be milder and not progress to a severe cytokine storm.18 Finally, as all of our HIV-negative patients required hospitalisation, they may have been more susceptible to an unfavourable outcome.

The main limitation of this retrospective observational study is that it also includes HIV patients with probable but not confirmed COVID-19. However, given the paucity of the data published so far, we believe that our real-life experience can provide useful information concerning the management of HIV-infected patients with SARS-CoV-2 infection that may eventually be used for prospective investigations.

In conclusion, our findings suggest that HIV-positive patients with SARS-CoV-2 infection are not at greater risk of severe disease or death than HIV-negative patients. However, the observed more favourable outcomes need to be confirmed in larger cohort studies.

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Potential conflicts of interest

CG and A.R. have received personal fees from MSD, ViiV, Gilead and Janseen Cilag for services unrelated to this study, and DC has received personal fees from MSD, ViiV, and Janseen Cilag for services unrelated to this study. None of the other authors has any potential conflict of interest.

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Table 1. Characteristics and symptoms of HIV-patients infected with SARS-CoV-2

Clinical features	**Overall**	**Females**	**Males**
Patients, n	47	11 (23%)	36 (77%)
Age, years	51 ± 11	53 ± 12	50 ± 11
CD4 cell count, cells/mm^3	636 ± 290	658 ± 279	630 ± 296
Patients with HIV viral load <20 copies/mL	44 (94%)	11 (100%)	33 (92%)
Patients with at least one comorbidity	30 (64%)	9 (82%)	21 (58%)
Comorbidities per patient, n	2.0 ± 1.0	1.9 ± 0.8	2.0 ± 1.0
Co-morbidities, n			
- dyslipidemia	15	7	8
- hypertension	14	5	9
- hepatitis C or B co-infection	5	1	4
- renal disease	4	0	4
- diabetes mellitus	3	1	2
- epilepsy	2	0	2
- cardiovascular disease	2	1	1
- neoplasms	3	0	3
- gastritis	2	0	2
- organ transplantation	1	0	1
- chronic obstructive pulmonary disease	2	0	1
Symptoms at onset, n			
- fever	41	9	32
- cough	23	7	16
- dyspnea	10	3	7
- diarrhea	7	2	5
- myalgia	4	2	2
- headache	3	2	1
Time from onset to offset, days	14 ± 8	11 ± 7	14 ± 9
Patients with SARS-CoV-2 testing, n	28 (60%)	6 (55%)	22 (61%)
- PCR positive test	26	6	20
- IgG/IgM *Rapid Test*	2	0	2
Patients with risk factors for COVID-19, n	21 (45%)	6 (55%)	15 (42%)
- healthcare providers	6	3	3
- colleagues with COVID-19	4	0	4

- relatives with COVID-19	11	3	8
Hospitalised patients, n	13 (28%)	2 (18%)	11 (31%)
Chest CT-confirmed pneumonia, n	12 (25%)	2 (18%)	10 (28%)
Oxygen demand, n	4	1	3
Mechanical ventilation, n	2	0	2
Deaths, n	2	0	2
Fully recovered, n45 (96%)11 (100%)34 (94%)			

Table 2. Pharmacological treatments of HIV patients infected with SARS-CoV-2

Drugs	**Overall (n=47**	**Females (n=11)**	**Males (n=36)**
COVID-19 therapies			
Paracetamol	25	5	20
Hydroxychloroquine	8	3	5
Azithromycin	7	3	4
Other antibiotics	6	1	5
Lopinavir/ritonavir	5	1	4
Tocilizumab	2	0	2
Remdesivir	1	0	1
Antiretroviral therapies			
TAF/FTC/bictegravir*	10	2	8
ABC/3TC/dolutegravir*	10	1	9
TAF/FTC + INI	6	1	5
Dolutegravir/3TC*	5	0	5
Dolutegravir + boosted PI	5	2	3
TAF/FTC + boosted PI5	23		
Other regimens633			

*Single-tablet regimen; TAF: tenofovir, alafenamide; FTC: emtricitabine; 3TC: lamivudine; PI: protease inhibitor; INI: integrase inhibitor