COVID-19 in patients with HIV: clinical case series

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For the **Johns Hopkins University dashboard of coronavirus cases** see https://www.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6

As of March 24, 2020, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has affected almost 400 000 people in 168 countries on five continents. Older patients (>60 years) and those with comorbidities (eg, hypertension, diabetes, cardiovascular disease, lung disease, and chronic kidney disease) present with more severe infection and worse prognosis.[1] Coronavirus disease 2019 (COVID-19) has been described in only one patient with HIV in Wuhan, China,[2] but case series in patients with HIV are lacking despite 37·9 million people having HIV globally.[3] Here we describe, to our knowledge, the first single-centre experience of COVID-19 in patients infected with HIV-1, including clinical characteristics, antiviral and antiretroviral treatment, and outcomes.

All patients gave informed consent for publishing their clinical data. We used nasopharyngeal swab samples for all diagnoses, amplifying the betacoronavirus *E* gene and the specific SARS-CoV-2 *RdRp* gene by PCR.

On March 9, 2020, 2 weeks into the COVID-19 outbreak in Spain, 543 consecutive patients with SARS-CoV-2 infection had been admitted to hospital at Hospital Clínic Barcelona, Barcelona, Spain. We admitted 62 (12%) into intensive care units and we discharged 208 (38%) with supervised outpatient care. Of all patients, five (0·92%; 95% 0·39–2·14) were HIV positive (table), of whom three were male and two were transgender, and four identified as men who have sex with men (MSM). Two patients had comorbid conditions. Two patients were sex workers.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Demographics and baseline HIV status					
Age (years)	40	49	29	40	31
Gender	Transgender	Male	Male	Male	Transgender
HIV-risk factor and exposure	MSM, gym worker	Bisexual man, health-care worker	MSM, sexual worker participant in ChemSex session 6 days before	MSM, dinner 5 days before with another person who was COVID-19 positive	MSM, sexual worker
Comorbidities*	None	Hypothyroidism	None	Asthma	None
HIV status					
Year of HIV diagnosis	2007	2003	2013	2003	2020
Last CD4 cell count (cells per µL)	616	445	604	1140	13
Last CD4:CD8 ratio	0·8	0·46	1·1	1·2	0·1
HIV viral load at or before admission (copies per mL)	<50	<50	<50	<50	45 500
ART-regimen before admission	Tenofovir alafenamide, emtricitabine, and darunavir-boosted cobicistat	Abacavir, lamivudine, and dolutegravir	Tenofovir alafenamide, emtricitabine, and darunavir-boosted cobicistat	Abacavir, lamivudine; and dolutegravir	No ART: current diagnosis is late presenter
Clinical findings on admission					
Duration of symptoms, days	2	5	2	3	7
Diagnosis	Upper respiratory tract infection	Lower respiratory tract infection	Upper respiratory tract infection	Lower respiratory tract infection	Lower respiratory tract infection
Symptoms and vital signs					
Temperature	Fever (38·7°C)	Fever (39°C)	Fever (39·5°C)	Fever (39·5°C)	Fever (38·5°C)
Symptoms	Cough, malaise, headache	Cough	Cough, malaise, headache, dyspnoea	Cough, malaise, headache, dyspnoea	Cough, dyspnoea
Blood pressure (mm Hg)	140/90	110/70	129/69	115/76	127/56
Respiratory rate (breaths per min)	14	28	16	24	20
Heart rate (beats per min)	90	94	78	103	121
Chest x-ray findings	Normal	Bilateral ground-glass opacities	Normal	Right basal interstitial infiltrate	Right basal pneumonia with pleural effusion
O_2 saturation in ambient air	SpO_2 100%	SpO_2 <90%	SpO_2 97%	SpO2 94%	SpO2 <90%
PaO_2/FiO_2 ratio	ND	182	ND	ND	230
Laboratory results					
White blood cell count (cells per 10^6/L)	7840	29 160	6730	6140	14 670
Lymphocyte (cells per 10^6/L)	2700	1170 (4%)	1500	1600	900

(Table continues on next page)

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
(Continued from previous page)					
Platelets (cells per 10^6/L)	345 000	135 000	124 000	186 000	309 000
LDH (U/L)	ND	316	256	465	1149
C-reactive protein (mg/dL)	ND	30	0·72	0·43	40
D-dimer (ng/mL)	ND	>10 000	400	300	ND
Ferritin (ng/mL)	ND	1020	ND	1044	866
Procalcitonin (ng/mL)	ND	ND	<0·03	ND	ND
Severity of the infection at admission	Mild	Severe	Mild	Moderate	Severe
Treatment and outcomes					
ART†	ART at admission maintained	Tenofovir disoproxil fumarate, and emtricitabine plus lopinavir-boosted ritonavir (on going)	Tenofovir disoproxil fumarate, and emtricitabine plus lopinavir-boosted ritonavir (for 3 days)	Tenofovir disoproxil fumarate, and emtricitabine plus lopinavir-boosted ritonavir (for 14 days)	Tenofovir alafenamide, emtricitabine, and darunavir-boosted cobicistat (on going)
Other antiviral treatments	No	Interferon beta-1b (for 7 days), hydroxychloroquine (for 7 days)	Hydroxychloroquine (for 5 days)	Hydroxychloroquine (for 5 days)	Interferon beta-1b (for 4 days), hydroxychloroquine (for 5 days)
Other antibiotics	No	Meropenem (for 16 days), linezolid (for 14 days)	Azithromycin (for 5 days)	Azithromycin (for 5 days), cefixime (for 5 days)	Azithromycin (for 5 days), ceftaroline fosamil (for 7 days), co-trimoxazole (for 21 days, followed by secondary prophylaxis)
Admitted to an intensive care unit	No	Yes	No	No	Yes
Invasive or non-invasive mechanical ventilation	No	Invasive	No	No	Non-invasive
Corticosteroids or tocilizumab	No	Tocilizumab, 400 mg one single dose (on day 10)	No	Inhaled corticosteroids	Corticosteroids
Length of hospital stay (days)	1	21	3	4	12
Length of home hospitalisation (days)‡	13	..	..	10	..
Outcomes	Cured	Still at hospital	Cured	Cured	Cured
Additional comments	..	Extracorporeal membrane oxygenation since day 13 (on going)	..	..	Concomitant *Pneumocystis jiroveci* and bacterial pneumonia treatment

Lopinavir-boosted ritonavir was given as 400 mg of ritonavir boosted with 100 mg of lopinavir twice a day for 14 days; azithromycin was given as 500 mg once a day, with a loading dose on the first day, and then 250 mg once a day for 4 days; hydroxychloroquine was given as 400 mg twice a day with a loading dose on the first day and then 200 mg twice a day for 4 days, and interferon beta-1b was given as 250 µg (8 million units) every 48 h. MSM=men who have sex with men. ND=Not done. *Hepatitis C virus, hepatitis B virus, chronic obstructive pulmonary disease, asthma, chronic kidney failure, hypertension, cardiovascular disease, diabetes, solid organ transplantation, use of biologics, other types of immunosuppression. †Tenofovir alafenamide, emtricitabine, and darunavir-boosted cobicistat was indicated before the information provided by Janssen on March 18, 2020. ‡Discharged with a supervised home-care programme.

***Table*: Demographics, clinical characteristics at admission, treatment, and outcomes of five patients with HIV and COVID-19**

Four were virologically suppressed: two with protease-inhibitor (darunavir-boosted cobicistat) and two with integrase-inhibitor (dolutegravir)-based antiretroviral therapy (ART). CD4 counts were above 400 cells per µL in all patients apart from patient 5, who was ART naive and a very advanced late presenter. Two patients had upper-respiratory tract infections, and three had viral pneumonia, including two requiring admission to the intensive care unit with invasive (patient 2) and non-invasive (patient 5) mechanical ventilation.

We started all five patients on anti-SARS-CoV-2 treatment on the day of diagnosis. We gave all five patients boosted-protease inhibitor ART. We explained to patients treated with ART that we were making a transitional change in their regimen on the basis of the fact that HIV protease inhibitors might have activity against the coronavirus protease and that once the treatment ended they would return to their usual regimen. Patient 1 with darunavir-boosted cobicistat, and patients 2–4 were adapted to lopinavir-boosted ritonavir. We gave patient 5 darunavir-boosted cobicistat. We left patient 1, who had mild infection, on his normal ART. We gave the other patients hydroxychloroquine (patients 2, 3, 4, and 5) with azithromycin (patients 3, 4, and 5), and interferon beta-1b (patient 2 and 5). No patients were given remdesivir (only available through clinical trials, with restricted access at the time these patients were evaluated).

We administered concomitant antibacterials in all three patients who had pneumonia (patients 2, 4, and 5), and corticosteroids in two patients (patients 4 and 5) and tocilizumab in one (patient 2). We have discharged four patients (80%); one remains in hospital in the intensive care unit (patient 2).

For more on **COVID-19 drug interactions** see www.covid19-druginteractions.org

Our preliminary experience highlights several issues. First, patients with HIV accounted for almost 1% of patients with COVID-19 who required admission to hospital in Barcelona. We only observed the infection in people younger than 50 years, who identified as MSM, and who have a COVID-19 clinical pictures resembling the general population. None of these five patients has died, although we admitted two to intensive care, where one remains. More studies of COVID-19 in patients with HIV are needed in the older MSM population, drug users, and heterosexual men and women in middle-income and lower-income settings. Second, two patients who were MSM were sex workers, one reporting participating in a chemsex party 6 days before admission to hospital. During this pandemic, implementing health education programmes is very important to explain that such activities as these could cause clusters of SARS-CoV-2 transmission. Third, we adapted ART in all patients to a regimen based on protease inhibitors: three patients were given lopinavir-boosted ritonavir and two were given darunavir-boosted cobicistat. In the past month, a clinical trial[4] found that lopinavir-boosted ritonavir was ineffective as a monotherapy against severe pneumonia associated with COVID-19 in China. Therefore, investigation of the efficacy of this treatment in patients with COVID-19 in combined therapy in earlier stages of the disease is needed. Additionally, Janssen reported on March 18, 2020, that darunavir was ineffective against SARS-CoV-2 due to low affinity to coronavirus protease. Fourth, we did not give our patients remdesivir, the most active in-vitro and in-vivo antiviral drug against coronavirus to date,[5] and is currently only available through clinical trials or for compassionate use. This drug has no pharmacokinetic interactions with any medication including ART drugs. Finally, in advanced patients (ie, late presenters), we must ensure differential diagnosis and initial antimicrobial treatment to address pulmonary opportunistic infections (eg, Pneumocystis jirovecii, as seen in patient 5) presenting with similar clinical and radiological symptoms. This pandemic is a challenge affecting everyone. By generating information such as we present here, the management and prognosis of patients co-infected with HIV and SARS-CoV-2 might be improved.

See Online for appendix

For the **report from Janssen on darunavir-based treatments for SARS-CoV-2** see https://www.janssen.com/uk/sars-cov-2-treatment

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Is increasing pre-treatment HIV drug resistance a real menace or minor detail?

In a randomised study in Kenya, Chung and colleagues[1] report a lower effect of pretreatment drug resistance (PDR) to non-nucleoside reverse transcriptase inhibitor (NNRTI) on the virological outcomes of antiretroviral therapy (ART) than previously reported. Given the increasing prevalence of NNRTI PDR in many low-income and middle-income countries,[2] this conclusion might lead to complacency in addressing the effect of PDR. In our view, the study findings need to be interpreted in light of the following considerations.

First, several studies have shown a significant effect of any PDR (regardless of the number of mutations) on virological failure for efavirenz-containing ART, which is concerning given that PDR to efavirenz is above 10% in several countries.[3] Moreover, despite the overall lower effect of PDR in the study by Chung and colleagues, the authors also observed that among participants with NNRTI-associated PDR, those receiving protease-inhibitor-based regimens had lower odds of virological failure than did those who received first-line NNRTI-based ART (odds ratio [OR] 0·32; p=0·036), supporting the argument that the use of NNRTIs in patients with NNRTI PDR should be avoided.

Second, the regimen being compared with efavirenz-based ART was based on ritonavir-boosted lopinavir, which yielded a slightly lower suppression rate among participants with no PDR (92·0%) than in those with PDR (93·6%). The