

Factors associated with hospital admission for COVID-19 in HIV patients.

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Abstract

This study reports on hospital admission and outcomes of 69 HIV-infected subjects who were diagnosed with SARS-CoV-2 infection between February and May 2020, in a network of Italian centers. Patients' characteristics and median days between symptoms and diagnosis were similar by hospital admission, whereas admitted patients were had lower nadir CD4 cells and current lymphocytes count. These values were also correlated to worse COVID-19 outcome. Antiretroviral drugs did not seem associated with disease severity.

Keywords: SARS-CoV-2; COVID-19; HIV; hospital admission

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As of May 2020, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has affected more than four million people on five continents, and more than 200,000 in Italy. Prognosis for Coronavirus disease 2019 (COVID-19) seemed worse for older people and those with comorbidities (hypertension, diabetes, cardiovascular diseases, lung diseases) [1]. Several clinical features, such as reactive C protein, lymphocyte count and lactic dehydrogenase levels, were suggested as predictors of adverse outcome in the general population [1].

Regarding people living with HIV (PLWHIV), the emergence of COVID-19 created another health burden for a group that may already be at heightened risk for other comorbidities [2], because maintaining adequate standard of HIV care may be hard during this pandemic [3]. Besides these potential extra burdens, few information is available on COVID-19 severity and prognosis in patients with HIV coinfection [4,5]. In Italy, a recent paper reported on 47 patients with HIV and SARS-CoV-2 coinfection [6], suggesting a low death toll (about 4%) as compared to the HIV-negative patients in the same hospital (about 17%).

Here we describe a multi-center experience of COVID-19 in patients infected with HIV-1 in Italy and diagnosed with SARS-CoV-2 infection, observed in a network of Infectious Diseases Departments participating in the CISAI (Coordinamento Italiano per lo Studio dell'Infezione da HIV e Allergie) Study Group [7].

The purpose of this study was to describe the epidemiological and clinical features, as well as the outcomes of 69 HIV patients with confirmed SARS-CoV-2. We explored predictive factors for hospital admissions of subjects with more severe disease.

We collected information about SARS-CoV-2 infection and COVID-19 diagnosis among HIV patients, using a standard collection form, reporting information on patients' and HIV infection characteristics and history, antiretroviral treatment (ART) at SARS-CoV-2 infection diagnosis, hospital admission and COVID-19 clinical outcome. When diagnosed with SARS-

CoV-2 infection, patients signed the consent to the use of their anonymized information for clinical studies.

Twenty-three Infectious Diseases Clinics participated in this survey and 14 collected data of patients with COVID-19. Nine of them did not recorded any symptomatic infections, with or without subsequent hospitalization, among their HIV patients, mainly in the Southern and Central Italy. Almost all COVID-19 cases needing hospital admission were found in Northern Italy, the most hardly hit area in the country.

Among about 22,000 individuals referring to the centers of our network, 69 were diagnosed with SARS-CoV-2 infection and 38 were admitted to hospital due to moderate to severe COVID-19 (3 of them because their housing situation prevented isolation) between February, 21 and May, 12. A diagnosis of SARS-CoV-2 infection was based on a throat swab positive for viral nucleic acid in all patients, irrespectively of their needing of hospital admission. Hospitalized PLWHIV were slightly older, with CDC stage C more frequently B and C than A, lower nadir CD4 count and last lymphocytes count. Using proc logistic to evaluate the risk of requiring hospitalization for COVID-19, we found that the sex- and age-adjusted odds ratio (aOR) for nadir CD4 cells was 0.83 (by 50 cells/mm³, 95% confidence interval (CI) 0.72-0.96) and 0.87 for lymphocytes count (by 100 cells/mm³, 95% CI 0.78-0.97).

In the non-hospitalized group, one patient in an assisted-living facility died, as well as 6 in the hospitalized group. Four patients were still admitted at the time of this analysis and 28 had been discharged.

Among 34 with known outcome, 31 were treated with hydroxychloroquine (with azithromycin in 10 patients), 12 with PI (added to non-PI-including ART in 11), 9 took heparin, 5 steroids, 2 tocilizumab and 6 other antimicrobials. Among those who were admitted to hospital, lower median lymphocyte count was associated with death (700 versus 1530 p=0.033). The median hospital stay length was 12 days (range 1-33).

Since the start of this pandemic, HIV patients' management was an issue, and evidence regarding coinfection with SARS-CoV-2 was episodic and forcibly limited. Two case series do not support the case for higher risk of death in PLWHIV than in the general population: in a multicentric study on hospitalized subjects in 12 German centers, 3 patients out of 33 died (9%) [8], whereas 2 deaths out of 13 (15%) patients needing hospital admission were observed in an Italian study [6], for an overall death rate of 4% (2/47). In our study, 10% of the whole sample and 16% of hospitalized patients died over the study period.

Due to the different testing strategies performed in the centers of our network, we cannot infer the proportion of subjects who experienced moderate to severe COVID-19, or even death, in the general population of PLWHIV. However, we could compare the characteristics of those who did or did not need hospital admission.

First, the lowest level of CD4 cells count was significantly associated with hospital admission, irrespectively of the CD4 cells count at last visit before diagnosis. This suggests that, as well as for other conditions such as non-AIDS events, a low number of nadir CD4 cells seems to be a strong factor associated with the development of severe cases of COVID-19 [9].

Second, despite almost all patients were treated with hydroxychloroquine and/or other agents suggested for COVID-19 treatment, the outcomes were not significantly better than in previous case-series [6,8], where a not negligible part of subjects did not receive these treatments.

Last, PLWHIV included in this study were on antiretroviral treatments. Although the sample size is too small to draw any significant conclusions, we did not observe differences between need for hospital admission according to class of ART drugs.

Conflict of interest

There are no conflicts of interest.

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Table. Characteristics of 69 HIV-infected patients diagnosed with COVID-19, according to hospital admission.

Patient's characteristics	No hospital admission		Hospital admission		P [§]
	N*=31	%*	N*=38	%*	
Male sex	20	64.5	30	79	18
Age at hospital admission, years (median, IQR)	52	45-58	55	50-62	0.047
Caucasian ethnicity	28	90.3	31	81.6	0.49
Risk factor for HIV acquisition					
MSM	12	38.7	14	36.8	0.69
Heterosexual	6	19.4	10	26.3	
IDU	13	41.9	13	34.2	
Other	0	0	1	2.6	
CDC stage					
A	19	61.3	12	32.4	0.022
B	5	16.1	9	24.3	
C	7	22.6	16	43.2	
Nadir CD4 T, cells/mm ³ (median, IQR)	399	220-548	167	57-363	0.002
HIV infection duration, years (median, IQR)	11	6-20	16	7-20	0.28
ART duration, years (median, IQR)	7	4-16	11	6-18	0.26
At last control					
HIV-RNA <50 copies/mm ³	25	80.6	36	94.7	0.13
CD4, cells/mm ³ (median, IQR)	602	517-788	578	382-764	0.34
CD8, cells/mm ³ (median, IQR)	688	655-855	709	511-813	0.75
CD4/CD8 ratio (median, IQR)	0.84	0.71-1.09	0.86	0.69-1.06	0.95

Leucocytes, cells/mm ³ (median, IQR)	5190	4850-6110	5210	3800-6250	0.60
Lymphocytes, cells/mm ³ (median, IQR)	1927	1420-2160	1360	885-1810	0.002
ART at SARS-CoV-2 diagnosis					
PI based	9	29.0	8	21.1	0.44
NNRTI based	11	35.5	12	31.6	0.73
INSTI-based	12	38.7	20	52.6	0.25
Tenofovir-containing	21	67.7	20	52.6	0.20
Comorbidities					
Hypertension	11	35.5	20	52.6	0.15
Diabetes	3	9.7	7	18.4	0.49
Cardiovascular diseases	3	9.7	6	15.8	0.50
Other	13	41.9	19	50.0	0.50
Days from symptoms to diagnosis (median, IQR)	5	4-6	6.5	3-7	0.21
Pneumonia	2	6.4	30	79.0	<0.0001
Outcome					
Death	1	3.3	6	15.8	
Recovery	30	96.7	28	73.7	N.A.
Still in hospital	-	-	4	10.5	

* if not otherwise specified; § P refers to Pearson or Fisher exact or Mantel-Haenszel chi-square test, as appropriate, for frequencies, and to Mann-Whitney test for continuous variables.

IQR: interquartile range; MSM: males having sex with males; IDU: intravenous drug use; ART: antiretroviral therapy; PI: protease inhibitors; NNRTI: non-nucleoside reverse transcriptase inhibitors; INSTI: integrase strand transferase inhibitors