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Editorial – Coronavirus disease 2019 and people living with HIV: clinical considerations

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Coronavirus disease (COVID)-19 pandemic temporarily overshadowed other health problems. However, it revealed the extreme fragility of our health system in protecting those who had the highest risk during the pandemic[1,2]. Elders, people residing in long-term healthcare facilities and nursing homes and people affected by other chronic diseases were the categories most at risk during this pandemic[3].

A particular subset of people affected by chronic diseases are people living with HIV (PLWH). PLWH are at risk for a high number of comorbidities, such as cancers, chronic inflammatory disorders, chronic kidney failure[4-12]. Therefore, at the beginning of the pandemics, a huge concern surrounded this special population.

However, PLWH were not hugely affected by COVID-19. Literature reports only few patients around the world of co-infected individuals, and most of them recovered (Table I). Zhu et al[13] presented an interesting thought about immunocompromised patients, which was at a later time questioned by Joob et al[14] on the basis of the fact that no identified inter-relationship between the two viruses had emerged at the time.

However, a subtle link between the two viruses could be hypothesized. First of all, it has been shown that SARS-CoV-2 is able to infect T-lymphocytes, even though it is not able of active replication inside this type of cells[15]. This fact partially provides an explanation to the severe lymphopenia we see in most of the patients affected by COVID-19. Moreover, it might explain why just a few cases of co-infection have been seen, as the two viruses might compete for the infection of T-lymphocytes.

Secondly, it has been shown that SARS-CoV-2 elicits a T helper (T_H)17 response at a later time since the onset of symptoms, especially in recovering patients[16]. Literature reports that subsets of T_H17 contribute to the establishment and persistence of HIV reservoir during combined antiretroviral therapy (cART)[17]. Therefore, a persistent activity, even at a low level, of T_H17 cells might help fighting a SARS-CoV-2 infection.

Third, the natural history of HIV-infection is characterized by a persistently increased level of interferon (IFN)-γ[18]. SARS-CoV-2 shares a lot of pathogenetic characteristics with SARS-CoV[1]. SARS-CoV has been demonstrated to be able to impair the production of IFN type I and II through its nucleocapsid (N) protein. Similarly, it has been shown that SARS-CoV-2 does not elicit any kind of IFN response[19]. As a result, the persistent inflammatory state with persistently high levels of IFN-γ characterizing HIV infected patients, might contribute to a quicker response to SARS-CoV-2. This hypotheses agree with those presented by other authors[20].

Another interesting point to discuss is the use of antiretroviral drugs (ARVs) for the treatment of COVID-19. Some might discuss that PLWH might have been protected by the use of drugs active on SARS-CoV-2. However, Riva et al[21] and Gervasoni et al[22] showed that their patients were not protected by the use of particular ARVs, such as darunavir (DRV). Moreover, in agreement with Härter et al[23]

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Table I. Cases of SARS-CoV-2 – HIV co-infection reported in literature (up-to-date 14 May 2020).

Reference	#Of patients	Age (years)	Sex	Symptoms	HIV-RNA (cps/mL)	CD4+ (cells/μL)	Treatment	Outcome
Riva et al[21]	3	62	M	Dry cough Fever Respiratory failure	< 20	441	DRV/c switched to LPV/r	---
		63	M	Fever	< 20	743	DRV/c switched to LPV/r	Recovery
		57	F	Fever Cough	---	---	DRV/c	Recovery
Zhu et al[13]	1	61	M	Fever Dry cough Dyspnea	---	266	LPV/r	Recovery
Gervasoni et al[22]	47	51 ± 11 (28 proven, 19 probable)	M (76%)	Fever F (24%) Respiratory failure	< 20 Cough 72 (1 case) 134 (1 case)	> 350 52 (1 case)	Various treatment	45 recovery 2 death
Härter et al[23]	33	44	M	Mild	< 50	754	Various treatment	Recovery
		33	F	Mild	< 50	619		Recovery
		38	M	Mild	< 50	1187		Recovery
		53	M	Mild	< 50	810		Recovery
		60	M	Mild	< 50	892		Recovery
		51	M	Mild	< 50	402		Recovery
		42	M	Mild	< 50	1087		Recovery
		65	M	Mild	< 50	1122		Recovery
		82	M	Critical	920	379		Death
		53	M	Critical	842	285		Recovery
		32	M	Mild	< 50	731		Recovery
		31	M	Mild	< 50	1000		Recovery
		37	M	Mild	< 50	946		Recovery
		37	F	Severe	< 50	402		Recovery
		36	M	Critical	< 50	718		Recovery
		68	M	Severe	< 50	499		Recovery
		42	M	Critical	< 50	613		Recovery
		35	M	Mild	< 50	538		Recovery
		55	M	Mild	< 50	780		Recovery
		55	M	Critical	< 50	69		Death

Table continued

Table I *(Continued)*. Cases of SARS-CoV-2 – HIV co-infection reported in literature (up-to-date 14 May 2020).

Reference	#Of patients	Age (years)	Sex	Symptoms	HIV-RNA (cps/mL)	CD4+ (cells/μL)	Treatment	Outcome
		58	M	Mild	< 50	573		Recovery
		30	M	Mild	< 50	608		Recovery
		26	M	Mild	---	---		Recovery
		59	M	Critical	< 50	718		Death
		31	M	Mild	< 50	647		Recovery
		62	M	Mild	< 50	692		Recovery
		53	M	Mild	< 50	717		Recovery
		54	M	Mild	< 50	437		Recovery
		70	M	Mild	< 50	336		Recovery
		48	M	Mild	< 50	1715		Recovery
		35	M	Mild	< 50	490		Recovery
		45	F	Mild	< 50	234		Recovery
		66	M	Mild	< 50	1250		Recovery
Blanco et al[24]	5	40	T	Fever Cough Malaise Headache	4 cases TND 1 case ART naïve and very late presenter	4 cases > 450 1 case ART naïve and very late presenter	Various treatments	Recovery
		49	M	Fever Cough				Recovery
		29	M	Fever Cough Malaise Headache Dyspnea				Recovery
		40	M	Fever Cough Malaise Headache Dyspnea				Recovery
		31	T	Fever Cough Dyspnea				Recovery

Table continued

Table I *(Continued)*. Cases of SARS-CoV-2 – HIV co-infection reported in literature (up-to-date 14 May 2020).

Reference	#Of patients	Age (years)	Sex	Symptoms	HIV-RNA (cps/mL)	CD4+ (cells/μL)	Treatment	Outcome
Haddad et al[26]	1	41	M	Fever Dry cough Encephalopathy	TND	604	DTG/3TC	Recovery
Chen et al[25]	1	24	M	Fever Dry cough	---	---	EFV/3TC/TDF plus LPV/r	Recovery
Aydin et al[27]	4	34	M	Fever Dry cough Dyspnea	434.782	3	LPV/r plus FTC/TDF	Recovered
		44	M	Fever Dry cough Dyspnea	TND	1385	DTG + FTC/TDF	Death
		35	M	Dry cough Malaïse Diarrhea	---	448	EVG/c/FTC/TAF	Recovery
		36	M	Fever Dry cough	TND	396	EVG/c/FTC/TAF	Recovery
Wang et al[28]	1	37	M	Fever Dry cough Chest pain	---	34	Naïve to treatment	---

Abbreviations: cps = copies; M = male; F = female; T = transgender; TND = target not detected (if the lower limit of detection was not clarified); DRV/c = darunavir/cobicistat; LPV/r = lopinavir/ritonavir; DTG = dolutegravir; 3TC = lamivudine; FTC = emtricitabine; TDF = tenofovir disoproxil fumarate; EVG = elvitegravir; TAF = tenofovir alafenamide fumarate.

and Blanco et al[24] they showed that no particular regimen had a protective role against the infection or a negative outcome, even though tenofovir has been shown to be effective on SARS-CoV-2 RNA-dependent-RNA-polymerase (RdRp)[25].

Despite being a low number of cases, they show that co-infection is possible, and it is the most probable for those PLWH with a viral and immunological control. On the other hand, the cases reported in literature show that COVID-19 might not be as dangerous for PLWH that does not have any comorbidity.

However, the number of patients reported until now and those that will be presented in future will be not able to provide sufficient information about the dimension of the problem. Therefore, it is desirable to determine the seroprevalence of SARS-CoV-2 in PLWH to ascertain the real dangerousness of COVID-19 for HIV-infected individuals.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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