Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Lower probability of persistence of total anti-SARS-CoV-2 antibodies after COVID-19 among people living with HIV

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To the editor,

There is limited and controversial data on the immune response to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection among people living with human immunodeficiency virus (HIV) (PLWH) infection. There are also contradictory findings on the severity of coronavirus disease 2019 (COVID-19) in PLWH, although two recent meta-analyses suggested that PLWH have a higher risk of death from COVID-19 [1,2]. On the contrary, the BNT162b2 mRNA vaccine and the ChAdOx1 nCoV-19 (AZD1222) vaccine are equally immunogenic in PLWH and in individuals without HIV infection after a short follow-up [3,4]. However, no data exist comparing the kinetics of antibodies after SARS-CoV-2 natural infection in PLWH and people without HIV infection. Because of this, we compared the persistence of total antibodies against SARS-CoV-2 after COVID-19 between PLWH and people without HIV infection (controls).

All COVID-19 cases among PLWH diagnosed from March 8, 2020 to March 30, 2021 were identified from a prospective cohort followed at our centre. A parallel group of COVID-19 controls was recruited among consecutive patients who attended as outpatients after admission due to COVID-19 or referral from primary care or the emergency department (March 8, 2020–July 30, 2020), or their infected contacts. The PLWH cohort was followed at least every 6 months. The control group was scheduled for follow-up at 3 and 6 months after COVID-19. COVID-19 severity was assessed for all individuals (Appendix 1). All serum samples collected at each visit were tested for SARS-CoV-2 total serum antibodies (ELECSYS Anti-SARS-CoV-2, Roche Diagnostic International, Rotkreutz, Switzerland). All serum samples collected 6 months after COVID-19 were tested for anti-spike antibody levels (Appendix 1).

The main characteristics of the PLWH and controls are summarized in Table 1. There was a statistically significant difference in median age and sex distribution between PLWH and controls. The severity of COVID-19 and the Charlson index were similar between the groups. After 6 months, the proportion of PLWH with detectable SARS-CoV-2 total serum antibodies was 86% (95% CI, 75%–93%), and the frequency of detectable antibodies for controls was 98% (95% CI, 93%–99.8%; Table 1). The difference in the frequency of detectable antibodies was −12% (95% CI, −6.8% to −18%), which was mainly due to a higher rate of antibody seroreversion among PLWH (Table 1).

The anti-spike antibody titres were significantly lower for PLWH (Table 1). Among PLWH, median (Q1–Q3) nadir CD4 cell counts were 325 cells/mL (range, 153–439 cells/mL) and 278 cells/mL (range, 83–363 cells/mL) for those with and without detectable antibodies, respectively ($p = 0.220$). Other characteristics of PLWH are summarized in Appendix 1. Multivariate analysis showed that HIV infection was independently associated with persistence of anti–SARS-COV-2 total antibodies and with anti-spike antibody levels 6 months after COVID-19 (Appendix 1).

The results of this study show that 6 months after COVID-19, PLWH have a lower probability of showing detectable total serum antibodies against SARS-CoV-2 than people without HIV infection.

There are some issues that could limit our findings. First, the sample size was relatively small. Despite this, differences in antibody response, both qualitative and quantitative, after COVID-19 could be identified. However, the study could be underpowered

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Table 1
Characteristics of PLWH and people without HIV infection with SARS-CoV-2 infection

Characteristic	PLWH ($n = 63$)	Controls ($n = 108$)	p-value
Age (y)[a]	49 (36–55)	56 (42–65)	0.006
Male sex, *n* (%)	55 (87)	41 (38)	<0.001
Charlson index >2, *n* (%)	15 (24)	33 (31)	0.344
COVID-19 pneumonia, *n* (%)	10 (16)	28 (26)	0.127
Severe COVID-19 pneumonia, *n* (%)	4 (6.3)	8 (7.4)	0.794
CD4 cell counts (cells/mL)[a]	717 (535–875)	—	—
Nadir CD4 (cells/mL)[a]	306 (148–425)	—	—
Undetectable HIV RNA, *n* (%)	61 (97)	—	—
Antiretroviral therapy, *n* (%)	63 (100)	—	—
Positive anti-SARS-CoV-2 total antibodies 6 mo after COVID-19, *n* (%)	54 (86)	106 (98)	0.002
Seroreversion, *n* (%)	7 (11)	1 (0.9)	0.004
No response, *n* (%)	2 (3)	1 (0.9)	0.555
Anti-spike IgG antibodies 6 mo after COVID-19 (BAU/mL)[a]	42.7 (16.2–236.5)	231 (63–312)	0.004

COVID-19, coronavirus disease 2019; HIV, human immunodeficiency virus; PLWH, people living with HIV; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
[a] Median (Q1–Q3).

to detect potential differences in nadir CD4 cell counts between PLWH with and without persistence of antibody. Second, we did not assess neutralizing antibodies against SARS-CoV-2. However, anti-spike antibodies and antibodies against the receptor-binding domain showed a strong correlation with neutralizing antibodies in vaccine trials recruiting PLWH [3,4]. Thus, according to those proven correlations, differences in anti-spike antibody titres between PLHW and controls in the present study might reflect differences in neutralization antibody levels. Third, differences in the severity of COVID-19 could underlie the lower rate of positive serology among PLWH 6 months after the episode, because the duration of the IgG response is longer for symptomatic COVID-19 cases due to higher initial concentrations [5]. However, the frequency of variables related to COVID-19 severity was similar between the groups. Fourth, PLWH were statistically younger than controls. However, the difference in median age was 7 years, and a biological impact of this difference is unlikely. In addition, age may not influence the magnitude of antibody responses after accounting for disease severity [5]. Fifth, as expected, there were significantly more men in the group of PLWH. Nevertheless, sex did not influence nucleocapsid IgG antibody levels after COVID-19. The strengths of the study include confirmation of the lower likelihood of antibody persistence after COVID-19 for PLWH after multivariate adjustment and the replication of the finding for anti-spike antibody levels.

The most likely explanation for the finding of a lower persistence of anti-SARS-CoV-2 antibodies after natural infection among PLW is humoral response dysfunction associated with HIV infection. This altered immune response underlies the lower immunogenicity of other vaccines in PLWH. All PLWH in the present study were on antiretroviral therapy, most with suppressed HIV replication and high CD4 cell counts. However, nadir CD4 cell counts were relatively low. Thus, incomplete humoral immune restoration induced by antiretroviral therapy is a possible reason for these study results.

According to these results, PLWH might be more prone to SARS-CoV-2 reinfection. Although response to vaccines against SARS-CoV-2 has been reported to be similar in PLWH and the general population in the short term, data after longer follow-up are required; if plasma antibody kinetics after SARS-CoV-2 vaccination mirrors what happens in natural infection, PLWH may be at risk for breakthrough infection. Booster vaccine doses have been recommended for PLWH. Longer periods of follow-up within vaccine trials including PLWH are needed to make rational decisions on the timing of booster doses.

Transparency declaration

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Author contributions

All authors have made substantial contributions to this work and have approved the final manuscript. Concept and supervision: JM, JAP; acquisition and analysis of data: JM, MFF, ACG, NO, LR, JAP; interpretation of data: JM, LR, JAP; Writing of the original draft: JM, JAP.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cmi.2022.01.028.

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