SARS-CoV-2 immunity and HIV infection: total recall?

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At the beginning of the COVID-19 pandemic, there was great uncertainty regarding the potential impact of SARS-CoV-2 infection among people living with HIV, with very limited experience with other severe coronavirus infections in terms of susceptibility and severity of infection.[1] People with HIV, especially those with advanced disease, have an increased risk of severe complications resulting from infection with respiratory viruses such as influenza.[2] Influenza immunisation is recommended for people with HIV, even though immunogenicity is considered lower than in the general population.[3]

In *The Lancet HIV*, Matthew Spinelli and colleagues report several observations in a matched case-control study of people with (n=955) and without (n=1062) HIV infection followed up in the same centre in San Francisco (CA, USA).[4] The cohort of people with HIV had a median age of 54 years (IQR 46–63) with good access to antiretroviral therapy (88% with a viral load of ≤200 copies per mL) and a median CD4 count of 452 cells (249–656) per µL. When they compared the seroprevalence of SARS-CoV-2 in both age-matched and date of collection-matched samples of the two groups, a 50% lower risk of SARS-CoV-2 seropositivity was found among people with HIV than among those without HIV. In the subgroup of patients with evidence of past SARS-CoV-2 infection, the authors retrospectively reviewed the medical files to identify cases of severe COVID-19, defined by evidence of lower respiratory tract involvement. People with HIV had an increased risk of severe disease, independently of age and sex. Notably, of five people with HIV who had severe COVID-19, three had CD4 counts of less than 200 cells per µL. Finally, after adjustment for age and sex, both total SARS-CoV-2 IgG and IgG pseudovirus neutralising antibodies were significantly lower in people with HIV than in those without (42% *vs* 53%). Adjustment for time since PCR-confirmed infection yielded similar results.

Spinelli and colleagues hypothesise that the lower seroprevalence in people with HIV could be related to behavioural factors (ie, an increased tendency of people with HIV to respect physical distancing measures and mask wearing), facilitated by support from local and federal authorities. The interpretation of this finding is limited by potentially unidentified behaviour-related confounders linked to distinct characteristics of the patients and different testing access. However, this result supports previous studies in non-US settings that also showed no increased risk of infection in people with HIV.[5,6] The study by Spinelli and colleagues indicates that people with HIV can be reassured that they are not at increased risk of getting infected when appropriate preventive measures are taken.

The low numbers of severe cases of COVID-19 (seven in the whole cohort) does not allow conclusions regarding risk of severe disease in people with HIV. Although large studies have reported an increased risk of severe disease in people with HIV, the respective contribution of ethnicity, social status, and comorbidities to this increased risk remains to be solved.[7]

An important and original finding of the study by Spinelli and colleagues is the lower total SARS-CoV-2-specific IgG and pseudovirus neutralising antibody concentrations found after natural infection. To our knowledge, very limited data exist on immunity after natural respiratory viral infection in people with HIV. This observation was made possible because of the recent emergence of SARS-CoV-2 in the human population as compared with seasonal influenza infection that repeatedly infects people after birth. Post-infection neutralising antibodies against SARS-CoV-2 are associated with prevention against reinfection for at least 7 months in healthy adults.[8] The findings by Spinelli and colleagues are based on a small number of participants and, unfortunately, with no prospective follow-up. No definite correlate of protection has been identified yet; however, with lower neutralising antibody titres after natural infection, people with HIV might theoretically be at higher risk of reinfection.

These findings recall to us the well characterised dysfunctional vaccine responses observed in people with HIV. Lower seroconversion rates are usually reported and antigen-specific antibody responses have shorter half-life after immunisation in this population.[9] Decreased antibody and memory B-cell responses following influenza vaccination are related to persistent immune activation on antiretroviral therapy.[10] People with HIV, even those on antiretroviral therapy with controlled viral load, might thus be at risk of lower response to COVID-19 immunisation. Large prospective studies assessing the

magnitude and the durability of COVID-19 vaccine-induced antibody response in people with HIV are required. If the latter report suboptimal immune response to COVID-19 vaccines, people with HIV (or particular subgroups of people with HIV) could benefit from distinct immunisation strategies with improved immunogenicity, such as an adapted vaccine schedule (additional doses and heterologous revaccination) or use of specific vaccine platform, as with influenza vaccination.[3]

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