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Correspondence: I. Zacharioudakis, New York University Grossman School of Medicine, 150 55th St, 3rd floor, Office 339, Brooklyn, New York 11220, USA (Ioannis.Zacharioudakis@nyulangone.org).

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A High Percentage of People With Human Immunodeficiency Virus (HIV) on Antiretroviral Therapy Experience Detectable Low-Level Plasma HIV-1 RNA Following Coronavirus Disease 2019 (COVID-19)

To the Editor—We read with interest the recent article by Geretti et al in which, among adults <60 years of age with acute severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, human immunodeficiency virus (HIV) seropositivity was shown to be significantly associated with 28-day mortality, even when adjusted for age and other potentially important factors [1]. As the authors discuss in detail, these data contrast with a study recently published in *Clinical Infectious Diseases* by Sigel et al of people with HIV (PWH) who were hospitalized for acute SARS-CoV-2; in that study, there were no differences in adverse outcomes compared to a demographically similar HIV-seronegative group [2]. While a number of case series and retrospective studies have also shown no differences in coronavirus disease 2019 (COVID-19) mortality or severity in PWH [3–8], there is emerging evidence for exacerbations of lymphocyte dysfunction and aberrant immune activation in the setting of SARS-CoV-2/HIV coinfection [9]. Furthermore, COVID-19 often leads to increased markers of immune activation, inflammation, and immune dysregulation, regardless of concomitant chronic infections [10]. It is therefore plausible that, in addition to HIV modulating SARS-CoV-2 infection, COVID-19 may have a short- or longer-term impact on HIV disease following acute SARS-CoV-2 infection in PWH on effective antiretroviral therapy (ART). As a result, we sought to identify if SARS-CoV-2/HIV-1 coinfection may lead to an increase in the frequency of detectable, but low-level plasma HIV-1 RNA levels that would not necessarily be detected by clinical viral load assays.

We tested large volumes of plasma for HIV-1 RNA using a highly sensitive single copy assay (SCA) from 12 PWH on ART using a replicate (9×) technology as previously described [11] with polymerase chain reaction–confirmed, convalescent SARS-CoV-2 infection a median of 37 days since onset of COVID-19 symptoms, and from 17 PWH on ART with plasma collection prior to COVID-19 (March 2018–October 2019). Table 1 summarizes participant demographics, ART use, and low-level residual HIV-1 RNA. Whereas 83.3% of PWH had detectable HIV-1 RNA by SCA, only 58.8% of PWH had detectable HIV-1 RNA prior to the COVID-19 pandemic despite similar input plasma volumes. The median HIV-1 RNA level was 1.59 copies/mL in PWH with recent COVID-19 compared

Table 1. Characteristics of People With Human Immunodeficiency Virus on Antiretroviral Therapy With Recent Coronavirus Disease 2019 (COVID-19) and Prior to COVID-19 Including Detectable Low-Level Plasma HIV-1 RNA

Characteristic	PCR$^+$ COVID-19	Pre–COVID-19
No. of patients	12	17
Time from onset of COVID-19 symptoms to initial sampling, days, median (IQR)	37 (29–62)	NA
Hospitalized for COVID-19	2 (16.7)	NA
Median age, y (IQR)	57 (53–64)	63 (57–69)
Male sex	12 (100)	16 (94)
Race		
White	10 (83.3)	14 (82.3)
Black/African American	1 (8.3)	3 (17.6)
Asian/Pacific Islander	1 (8.3)	…
ART		
INSTI use	11 (91.7)	12 (70.6)
NNRTI use	1 (8.3)	3 (17.6)
PI use	2 (16.7)	2 (11.8)
Leronlimab use	0 (0)	2 (11.8)
CD4 count, cells/μL, median (IQR)	658 (540–804)	537 (457–827)
Detectable plasma HIV-1 RNA (SCA positive)[a]	10 (83.3)	10 (58.8)
No detectable plasma HIV-1 RNA (SCA negative)[b]	2 (16.7)	7 (41.2)
Plasma HIV-1 RNA, copies/mL, median (IQR)	1.59 (0.39–6.95)	0.38 (0.0–5.67)

Data are presented as No. (%) unless otherwise indicated.

Abbreviations: ART, antiretroviral therapy; COVID-19, coronavirus disease 2019; HIV-1, human immunodeficiency virus type 1; INSTI, integrase strand transfer inhibitor; IQR, interquartile range; NA, not applicable; NNRTI, nonnucleoside reverse transcriptase inhibitor; PCR, polymerase chain reaction; PI, protease inhibitor; SCA, HIV-1 single copy assay (plasma RNA).

[a]No significant difference between recent COVID-19–positive and COVID-19–negative participants using Fisher exact test ($P = .23$).

[b]No significant difference between recent COVID-19–positive and COVID-19–negative participants using Mann-Whitney test ($P = .36$).

with 0.38 in the pre–COVID-19 group. Four COVID-19–positive participants who all had detectable blips had subsequent testing a median of 75 days after onset of symptoms (interquartile range [IQR], 58–90 days); 3 had persistence of detectable HIV-1 plasma RNA (median, 1.95 [IQR, 0.1–14.53] copies/mL).

Although sample sizes were modest and there were no significant differences between the COVID-19–positive and pre–COVID-19 groups, the above results suggest that lasting perturbations of immune function and systemic inflammation may impact the natural course of HIV infection, potentially months following SARS-CoV-2 infection. Whereas these low-level viremic episodes are unlikely to have direct clinical implications for patients, larger, prospective studies will be needed to fully understand the long-term impact of COVID-19 on HIV dynamics and viral immune responses.

Notes

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Michael J. Peluso,[1] Sonia Bakkour,[2] Michael P. Busch,[2] Steven G. Deeks,[3] and Timothy J. Henrich[4]

[1]Division of Infectious Diseases, University of California, San Francisco, San Francisco, California, USA, [2]Vitalant Research Institute, San Francisco, California, USA, [3]Division of HIV, Infectious Diseases and Global Medicine, University of California, San Francisco, San Francisco, California, USA, and [4]Division of Experimental Medicine, University of California, San Francisco, San Francisco, California, USA

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Correspondence: T. J. Henrich, Division of Experimental Medicine, University of California, San Francisco, 1001 Potrero Ave, Bldg 3, Rm 525A, San Francisco, CA 94706 (timothy.henrich@ucsf.edu).

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Typhoid in US Children: A Need to Understand Prevention Attitudes in South Asian Immigrant Communities

To the Editor—McAteer et al [1] demonstrate rising drug-resistant pediatric typhoid fever (TF) cases in the United States; importantly, they show that cases are predominantly travel-related (81.1%), in those visiting friends and relatives (VFR; 70.9%) in South Asian countries (78.7%). South Asian immigrant communities have long been noted in the United States and internationally as the group at the highest risk of travel-related TF [2, 3]. Indeed, US travelers to India surveyed at airports revealed that <10% of VFRs were deemed TF protected [4]. We agree with McAteer et al [1] that improving typhoid vaccination is critical to the emergence of extensively drug resistant (XDR) TF, yet the barriers remain unclear [5, 6].

To this aim, we report the results of our online survey to assess knowledge and attitudes towards TF preventive behavior and vaccination in US South Asian immigrants. A web-based 25-item survey was distributed (15 May–12 June 2020) among online South Asian diaspora communities. The survey collected information on demographics, TF knowledge, and attitudes related to prevention and vaccination, and was approved by Northwell Health's institutional review board.

We collected 250 responses. Most respondents (75.4%) were first-generation immigrants, male (73.4%), between 18–29 years (68.3%), schooled for >12 years (93.3%), and insured (85.4%; Table 1). Almost all (94.8%) had traveled to South Asia, and most (87.2%) planned to travel again. A quarter (24.8%) had good TF-specific knowledge, and less than half (39.2%) had a desirable attitude towards prevention behavior. In contrast, most (79.5%) indicated they would consider a TF vaccination. Of those not considering it, most (n = 37/48; 77.1%) did not view themselves at risk or viewed the vaccine as unimportant. Other reasons were "my physician did not recommend to me" (n = 16/48; 33.3%), and concerns about cost (n = 10/48; 20.8%), efficacy (n = 7/48; 14.6%), and safety (n = 5/48; 10.4%). More desirable prevention attitudes were noted in females as compared to males (54.8% vs 35.2%, respectively), US-born compared to foreign-born (57.4% vs 33.2%, respectively), and