



ORIGINAL RESEARCH

Qualitative assessment of anti-SARS-CoV-2 spike protein immunogenicity (QUASI) after COVID-19 vaccination in older people living with HIV

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Abstract

Objectives: Effective and safe COVID-19 vaccines have been developed and have resulted in decreased incidence and severity of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and can decrease secondary transmission. However, there are concerns about dampened immune responses to COVID-19 vaccination among immunocompromised patients, including people living with HIV (PLWH), which may blunt the vaccine's efficacy and durability of protection. This study aimed to assess the qualitative SARS-CoV-2 vaccine immunogenicity among PLWH after vaccination.

Methods: We conducted targeted COVID-19 vaccination (all received BNT162b2 vaccine) of PLWH (aged ≥ 55 years per state guidelines) at Yale New Haven Health System and established a longitudinal survey to assess their qualitative antibody responses at 3 weeks after the first vaccination (and prior to receipt of the second dose of the COVID-19 vaccine) (visit 1) and at 2–3 weeks after the second vaccination (visit 2) but excluded patients with prior COVID-19 infection. Our goal was to assess vaccine-induced immunity in the population we studied. Qualitative immunogenicity testing was performed using Healgen COVID-19 anti-Spike IgG/IgM rapid testing. Poisson regression with robust standard errors was used to determine factors associated with a positive IgG response.

Results: At visit 1, 45 of 78 subjects (57.7%) tested positive for SARS-CoV-2 anti-Spike IgG after the first dose of COVID-19 vaccine. Thirty-nine subjects returned for visit 2. Of these, 38 had positive IgG (97.5%), including 20 of 21 subjects (95.2%) with an initial negative anti-Spike IgG. Our bivariate analysis suggested that participants on an antiretroviral regimen containing integrase strand transfer inhibitors [relative risk (RR) = 1.81, 95% confidence interval (CI): 0.92–3.56, $p = 0.085$] were more likely to seroconvert after the first dose of the COVID-19 vaccine, while those with a CD4 count < 500 cells/ μL (RR = 0.59,

95% CI: 0.33–1.05, $p = 0.071$), and those diagnosed with cancer or another immunosuppressive condition (RR = 0.49, 95% CI: 0.18–1.28, $p = 0.15$) may have been less likely to seroconvert after the first dose of the COVID-19 vaccine. The direction of these associations was similar in the multivariate model, although none of these findings reached statistical significance (RR_{integrase inhibitor} = 1.71, 95% CI: 0.90–3.25, $p = 0.10$; RR_{CD4 count} = 0.68, 95% CI: 0.39–1.19, $p = 0.18$; RR_{cancer or another immunosuppressive condition} = 0.50, 95% CI: 0.19–1.33, $p = 0.16$). With regard to immunogenicity, we were able to record very high rates of new seroconversion following the second dose of the COVID-19 vaccine.

Conclusions: Our study suggests that completing a two-dose series of BNT162b2 vaccine is critical for PLWH given suboptimal seroconversion rates after the first dose and subsequent improved seroconversion rates after the second dose.

KEYWORDS

COVID-19, HIV, immunogenicity, SARS-CoV-2, vaccination

INTRODUCTION

The COVID-19 pandemic has spurred the rapid development of safe and highly effective vaccines to prevent infection with and transmission of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus [1,2]. The observed high vaccine efficacy in Phase 3 COVID-19 vaccine trials are a direct result of robust adaptive immune responses generated following vaccination as were observed in the preceding Phase 1/2 trials [3]. However, in the initial phase of early vaccine clinical trials, limited immunogenicity data regarding immunocompromised individuals who may have impaired immune response after vaccination were included in the first wave of vaccine trials. Since then, increasing data regarding COVID-19 vaccination amongst people living with HIV (PLWH) have emerged [4-6].

Additionally, emerging evidence has shown that certain immunocompromised groups, such as transplant recipients, exhibit poor immunogenicity to an initial dose of SARS-CoV-2 vaccines [7,8], with seroconversion rates of just 17% in one study [7]. Similar reports have emerged about patients with multiple myeloma after first vaccination with BNT162b2 and ChAdOx1 nCoV-19 vaccines [9]. These observations are not unexpected and are anticipated in other immunocompromised groups. The objective of our study was to assess the qualitative SARS-CoV-2 immunogenicity of PLWH after COVID-19 vaccination and its durability. We hypothesized that PLWH will have decreased immunoglobulin G (IgG) seroconversion rates following COVID-19 vaccination, particularly the first dose, compared with patients in the registration clinical trials – thus, we hypothesized that

this decreased IgG seroconversion would prompt the need for second-dose vaccination.

METHODS

Study design, participants and data sources

Following expanded eligibility for COVID-19 vaccination in Connecticut to individuals aged 55 years and older, and prioritizing individuals with significant medical comorbidities, we conducted targeted COVID-19 vaccination of PLWH who were receiving care at any of two HIV clinics of the Yale New Haven Health System (YNHHS). Coincident with planning the vaccination event, we established a longitudinal survey to assess qualitative SARS-CoV-2 immune responses using point-of-care tests under the US Food and Drug Administration (FDA) Emergency Use Authorization (EUA) over a 6-month period post-vaccination among the PLWH receiving any type of COVID-19 vaccine under the US FDA EUA. At the time of study enrolment, only the BNT162b2 vaccine was being offered to these individuals. Inclusion criteria were having laboratory-confirmed HIV diagnoses, receiving care at YNHHS (allowing access to their medical histories and laboratory tests), ability to provide informed consent and willingness to participate in the study for the intended duration of follow-up. We excluded patients who participated in COVID-19 vaccine trials, those who had prior laboratory-confirmed COVID-19 diagnosis, and those with invalid SARS-CoV-2 antibody test results.

Individuals identified as PLWH were recruited from a prepopulated hospital vaccination schedule, ahead of

their scheduled date, through phone calls by study investigators and were scheduled for research study visits. Three visits were planned: visit 1 was conducted 3 weeks after the first dose of their vaccine and coincident with patients presenting for their second vaccination (before receiving the vaccine); visit 2 was conducted 2 weeks (+1 week window) after receipt of the second vaccination; visit 3 was planned for 6 months (± 2 week window) after the initial vaccination. A research site was established at the vaccination centre for visit 1 for patient convenience, while visits 2 and 3 were conducted at the YNHHS HIV clinic. Only subjects who participated in visit 1 were again contacted via telephone call by research staff to participate in visit 2. In this ongoing study, all patients who participated in visits 1 and/or 2 and had a positive SARS-CoV-2 IgG test will be approached for participation in visit 3 in the future. We would exclude patients who received a third or booster dose of vaccine or who are confirmed to have acquired COVID-19 in between visits 2 and 3.

SARS-CoV-2 vaccine immunogenicity testing

We performed qualitative SARS-CoV-2 vaccine immunogenicity testing utilizing a point-of-care test, Healgen (Houston, TX, USA) COVID-19 anti-Spike IgG/IgM Rapid Test Cassette, a platform that is under EUA by the US FDA [96.7% sensitivity (IgG), 97.5% specificity (IgM/IgG)] utilizing whole blood specimens and conducted per test specifications. This Healgen lateral flow assay point-of-care test produces a binary result (positive or negative) for SARS-CoV-2 anti-spike antibody for both IgG and IgM. Its ability to serve as an accurate point-of-care serology test for COVID-19 has been substantiated [10]. It has been tested predominantly among healthcare workers in a real-world clinical setting, and when compared with a CLIA laboratory-based serum immunoassay antibody test, it demonstrated 93.2% sensitivity and 94.9% specificity in one study [10]. The qualitative antibody lateral flow immunoassay test was selected due to ease of performance in our study, which was being carried out in the context of vaccination implementation in a care and community-based and/or clinic setting (and not a specific research site), amidst the ongoing pandemic. Qualitative lateral flow antibody immunoassays have been compared with a quantitative SARS-CoV-2 antibody assay (Euroimmun, Lübeck, Germany) with percentages of 81–91.5% overall [11].

The research staff performed venepuncture to obtain about 1 mL of peripheral venous blood sample per participant (this was increased to 3 mL of blood for visit 2 as we later amended the study to allow us to accrue a specimen repository for future research). For the point-of-care test,

a dropper was utilized to add one drop of whole blood to the appropriate well in the test cassette, which is a lateral flow assay, and subsequently one to two drops of buffer provided in the test package were added to the separate designated well as per the package insert instructions. Although the test reports SARS-CoV-2 anti-Spike IgG and IgM results as early as 2 min, the results were uniformly interpreted at 15 min as per the package insert guidelines by research staff, who interpreted and documented these SARS-CoV-2 immunogenicity results onto paper files. Where test results were difficult to interpret by a single member of the research staff, one to two additional research staff adjudicated the result.

Data collection

Medical record review (Epic electronic medical record; Epic Systems Corporation, Verona, Wisconsin, USA) was conducted to obtain patient demographics (age, sex, race/ethnicity), body mass index, medical history including prior COVID-19 diagnosis, medical comorbidities [cancer (i.e. active cancer or actively receiving chemotherapy) or other immunosuppressive condition (i.e. transplant recipient, chronic use of immunosuppressant medication), diabetes mellitus, cardiovascular disease (i.e. coronary artery disease, myocardial infarction, stroke and peripheral vascular disease), lung disease (i.e. chronic obstructive pulmonary disease, asthma, interstitial lung disease), advanced liver disease, chronic kidney disease of any stage], self-reported substance use, years since HIV diagnosis, HIV antiretroviral therapy (ART) regimen and other laboratory data, such as most recent CD4 count and HIV viral load. Results of immunogenicity testing (Table 1) were entered into each patients' unique study folders and all data obtained were subsequently transferred to a deidentified Microsoft Excel (v.16.39) database.

Statistical analysis

Descriptive statistics were utilized to report patient demographics and clinical characteristics stratified by presence or absence of anti-Spike IgG response. Bivariate and multivariate analyses estimating the association between predictor variables and having a positive IgG response after the first dose were performed using Poisson regression with robust standard errors, given Poisson regression is usually used to estimate incidence rate ratios and the modified version (with robust standard errors) allows us to estimate relative risk ratios [12]. The final multivariate model included predictors with a p -value < 0.2 in the bivariate analyses. All analyses used two-sided tests with

TABLE 1 Characteristics of study population and estimated association with mounting an antibody response after SARS-CoV-2 mRNA vaccine (*n* = 78)

	IgG test positivity		Bivariate analyses		Multivariate model ^a	
	Negative (<i>n</i> = 33)	Positive (<i>n</i> = 45)	RR (95% CI)	<i>p</i> -value	RR (95% CI)	<i>p</i> -value
Age (years) [<i>n</i> (%)]						
< 65	28 (85)	36 (80)	Ref	0.56	—	—
≥ 65	5 (15)	9 (20)	1.14 (0.73–1.79)		—	—
Sex [<i>n</i> (%)]						
Male	21 (64)	30 (67)	Ref	—	—	—
Female	12 (36)	15 (33)	0.94 (0.63–1.42)	0.79	—	—
Race/ethnicity [<i>n</i> (%)]						
White, non-Hispanic	13 (39)	18 (40)	Ref	—	—	—
White, Hispanic	3 (9)	2 (4)	0.69 (0.22–2.11)	0.52	—	—
Black, non-Hispanic	17 (52)	25 (56)	1.03 (0.69–1.52)	0.90	—	—
BMI (kg/m ²) categories [<i>n</i> (%)]						
Normal (BMI < 25)	6 (18)	12 (27)	Ref	—	—	—
Overweight (25 ≤ BMI < 30)	13 (39)	14 (31)	0.78 (0.48–1.27)	0.31	—	—
Obese (BMI ≥ 30)	14 (42)	19 (42)	0.86 (0.56–1.33)	0.51	—	—
Self-reported substance use [<i>n</i> (%)] ^b						
Tobacco	17 (52)	18 (40)	0.82 (0.55–1.22)	0.33	—	—
Alcohol	7 (21)	10 (22)	1.03 (0.65–1.62)	0.92	—	—
Other	9 (27)	12 (27)	0.99 (0.64–1.52)	0.95	—	—
Time since HIV diagnosis (years) [median (IQR)]	10 (7–23)	9 (7–24)	0.99 (0.98–1.01)	0.59	—	—
HIV ART regimen [<i>n</i> (%)] ^b						
Integrase Inhibitor	22 (67)	39 (87)	1.81 (0.92–3.56)	0.085	1.71 (0.90, 3.25)	0.10
NNRTI	12 (36)	10 (22)	0.73 (0.44–1.20)	0.22	—	—
Protease Inhibitor	4 (12)	6 (13)	1.05 (0.60–.81)	0.87	—	—
CD4 count (cells/μL) categories [<i>n</i> (%)]						
< 500	13 (39)	8 (18)	0.59 (0.33–1.05)	0.071	0.68 (0.39, 1.19)	0.18
≥ 500	20 (61)	37 (82)	Ref	--	Ref	--
Detectable viral load [<i>n</i> (%)]						
No	28 (85)	37 (82)	Ref	—	—	—
Yes	5 (15)	8 (18)	1.08 (0.67–1.75)	0.75	—	—
Comorbidities [<i>n</i> (%)] ^b						
Cancer or other immunosuppressive condition	7 (21)	3 (7)	0.49 (0.18–1.28)	0.15	0.50 (0.19, 1.33)	0.16
Diabetes	10 (30)	10 (22)	0.83 (0.51–1.35)	0.45	—	—
Cardiovascular disease	13 (39)	16 (36)	0.93 (0.62–1.40)	0.73	—	—
Lung disease	9 (27)	17 (38)	1.21 (0.83–1.77)	0.32	—	—
Advanced liver disease	5 (15)	7 (16)	1.01 (0.60–1.71)	0.96	—	—
Chronic kidney disease	4 (12)	5 (11)	0.96 (0.51–1.78)	0.89	—	—

Abbreviations: ART, antiretroviral therapy; BMI, body mass index; IQR, interquartile range; NNRTI, nonnucleotide/nonnucleoside reverse transcriptase inhibitor; RR, relative risk.

^a Final multivariate model included covariates which had a *p*-value < 0.2 in the bivariate analyses. Percentages may not sum to 100% due to rounding.

^b Total column values for self-reported substance use, HIV ART regimens, and comorbidities may not sum to total as categories are not mutually exclusive of each other (e.g. participants could have reported both tobacco and alcohol use and/or participants may have received NNRTIs and protease inhibitors). Relative risk ratios estimated for these sub-categories compare the binary versions of risk factor (e.g. ratio of mounting antibody response between tobacco users vs. non-users).

$\alpha = 0.05$. Analyses were performed using Stata v.16.1 (StataCorp, College Station, TX, USA). Given that all but one subject did not seroconvert after the two doses, predictors of seroconversion after the second dose were not assessed.

Ethical approval

This study received Human Investigations Committee approval from Yale. Participation was allowed only after informed consent was provided without coercion of any form. Small stipends were provided to each participant during each visit.

RESULTS

Between 28 March 2021 and 2 April 2021, 176 PLWH received the COVID-19 vaccine at the YNHHS vaccination site. Of these, 94 individuals consented to participate in our study. We analysed data on 78 subjects at visit 1, excluding 12 individuals who had prior laboratory-confirmed COVID-19 diagnoses, and four subjects whose test results were invalid (Figure 1). In this paper, we present data following the first two study visits.

Of those eligible for data analysis ($n = 78$ individuals), 82.1% were aged < 65 years, 34.6% were female, and

53.8% and 6.4% were identified as non-Hispanic blacks and Hispanic whites, respectively (Table 1). At visit 1, the median age of subjects analysed was 61 years of age. A total of 64 subjects were between the ages of 55 and 64 years, and a total of 14 subjects were aged 65–80 years. Of note, patients from a younger population were not included in the study, given state guidelines had only approved COVID-19 vaccination for those aged ≥ 55 years at the time of our research study. Furthermore, 42.3% of participants were obese ($\text{BMI} \geq 30 \text{ kg/m}^2$). Regarding HIV status, median duration of HIV diagnoses was 9–10 years, all were receiving ART with the majority being on an integrase strand transfer inhibitor (INSTI)-based or INSTI-containing regimen (78.2%); 73.1% had a CD4 count ≥ 500 cells/ μL and 83.3% had undetectable HIV viral load. The most common medical comorbidities among participants were cardiovascular disease (37.1%), lung disease (33.3%) and diabetes mellitus (25.6%). Notably, 12.8% also had cancer or other immunocompromising conditions.

At visit 1, 45 of 78 subjects (57.7%) had positive SARS-CoV-2 anti-Spike IgG (Table 2). Bivariate or multivariate analyses did not reveal any statistically significant associations with seroconversion after the first dose, although several key relationships were observed. Our bivariate analyses suggested that participants on an INSTI-based antiretroviral regimen may have been associated with a higher rate of seroconversion after the first dose of COVID-19 vaccine

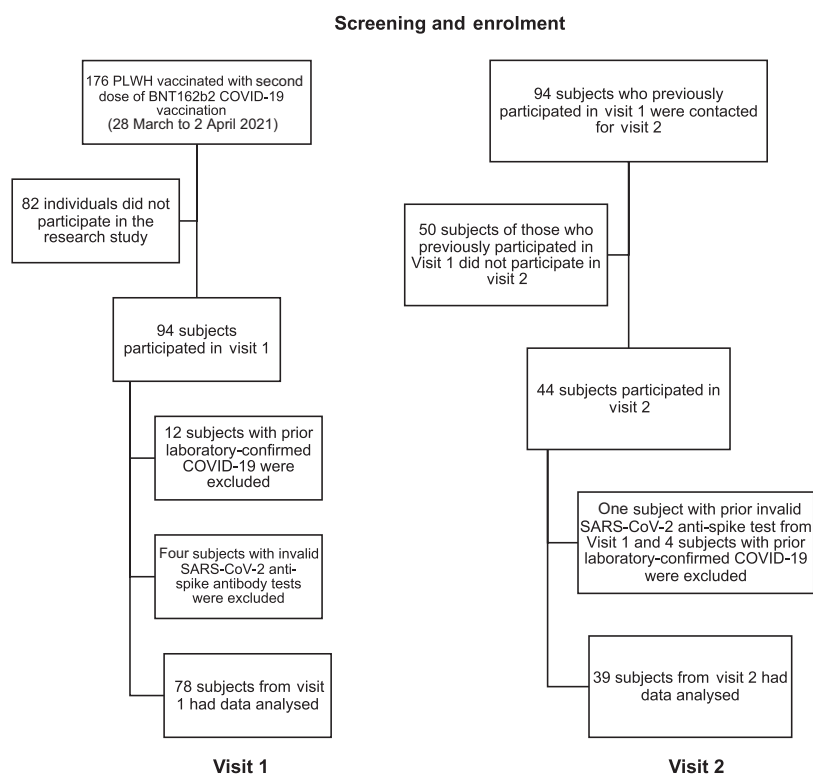


FIGURE 1 Screening and enrolment

TABLE 2 SARS-CoV-2 immunogenicity data summary after COVID-19 vaccination

	No. of subjects with positive SARS-CoV-2 anti-spike IgG	No. of subjects with negative SARS-CoV-2 anti-spike IgG	Percentage with positive SARS-CoV-2 anti-spike IgG (%)
Visit 1 (3 weeks after first dose of COVID-19 vaccine)	45	33	57.7
Visit 2 (2–3 weeks after second dose of COVID-19 vaccine)	39	1	97.5
Subjects who attended visit 2 stratified by visit 1 serostatus			
Positive SARS-CoV-2 anti-spike IgG at visit 1	18	0	100.0
Negative SARS-CoV-2 anti-spike IgG at visit 1	21	1	95.5

(RR = 1.81, 95% CI: 0.92–3.56, $p = 0.085$). The direction of this effect estimate was consistent in the multivariate analysis (RR = 1.71, 95% CI: 0.90–3.25, $p = 0.10$). Our bivariate analyses also suggested that characteristics of CD4 count < 500 cells/ μ L (RR = 0.59, 95% CI: 0.33–1.05, $p = 0.071$) and cancer or other immunosuppressive condition (RR = 0.49, 95% CI: 0.18–1.28, $p = 0.15$) may have been associated with lower rates of seroconversion after the first dose of COVID-19 vaccine. The direction of these findings remained unchanged when included in the multivariate analyses (RR_{CD4 count < 500} = 0.68, 95% CI: 0.39–1.19, $p = 0.18$; RR_{cancer or other immunosuppressive condition} = 0.50, 95% CI: 0.19–1.33, $p = 0.16$).

Of the 78 participants from visit 1, 39 (67.5%) returned for visit 2 (Figure 1). Of these, 38 (97.4%) showed a positive IgG response after the second vaccine dose. Of the 21 subjects with an initial negative IgG at visit 1, 20 (95.2%) had seroconverted after the second dose (Table 2). The only individual with a negative IgG test after the second dose was a solid organ transplant recipient on immunosuppressants (Table 2). Although a substantial proportion of participants from visit 1 did not show up for visit 2, there was little evidence to suggest that this group of individuals differed from those participants who showed up for visit 2 (Table S1).

DISCUSSION

Our study data showed that 3 weeks after the first dose of COVID-19 vaccine, 45 out of 78 (57.7%) participants had positive SARS-CoV-2 anti-Spike IgG test results. This differs remarkably from the 100% anti-Spike IgG seroconversion noted in the Phase 1/2 clinical trial studies of the BNT162b2 vaccine, which includes an overall healthier population and relatively smaller subset of PLWH. Another study has demonstrated that in subjects who received the BNT162b2 vaccine, 143 PLWH

had decreased immune response at 14 days after the initial vaccination dose, compared with the control group [5]. In this study, at 14 days, 51% of PLWH developed antibodies, while 59% of those without HIV developed antibodies [5]. Our results differ from a study of SARS-CoV-2 immunogenicity in PLWH after single dose of mRNA COVID-19 vaccination (50% BNT162b2, 50% mRNA-1273), which demonstrated that all subjects developed antibodies to SARS-CoV-2 Spike receptor binding domain after the initial dose [4]. However, that study also had a small sample size ($n = 12$) and participants were demographically different from our study subjects [all subjects were male; 92% were white; median age = 64 years (range 57–70)] [4]. Antibody responses after single-dose COVID-19 vaccine have been described in immunocompetent hosts [3] as well as immunocompromised solid organ transplant recipients with decreased antibody detection of 31% and 69% after single-dose Pfizer-BioNTech and Moderna mRNA COVID-19 vaccines, respectively [7]. Another study demonstrated decreased memory B-cell and plasma cell responses (including decreased IgG) among dialysis and renal transplant recipients after BNT162b2 vaccination, in comparison with healthy controls with 100% seroconversion; in that study, dialysis patients had 70.5% anti-S1 IgG at 3–4 weeks after vaccination boost and renal transplant recipients did not develop IgG positivity, aside from one with prior infection [8]. Furthermore, a study demonstrated that only 52 of 93 (56%) multiple myeloma patients had detectable SARS-CoV-2 IgG antibodies at 21 days or more after the initial dose of COVID-19 vaccine [9]. For PLWH, HIV infection-driven immune activation and dysregulation may result in impaired B-cell responses that impact vaccine-induced seroconversion rates [13,14]. Impaired vaccine responses have been noted in PLWH (including those virologically suppressed on ART) which is attributed to impaired B-cell and T-follicular helper-cell function and can be

enhanced by the process of ageing [15,16]. Poor antibody responses to vaccines in PLWH may be attributed to HIV infection, leading to dysregulation of T-follicular helper cells [17], as well as an array of B cell-specific defects that have been noted in the setting of HIV infection [18].

Therefore, more attention needs to be paid to these groups of patients who potentially may not experience similar levels of protection from COVID-19 vaccine as their healthy peers. A caveat is that many of these studies did not evaluate T-cell responses which do confer protection against COVID-19 infection [19]. Nonetheless, the almost complete seroconversion noted after the second vaccination suggests that the diminished responsiveness among PLWH can be overcome with subsequent booster vaccinations and should be an option explored not just for those who do not seroconvert after a single dose, but also after the second dose in certain circumstances. It also begs the question as to the use of higher vaccine dosage or additional booster doses for immunocompromised patients, which is a tantalizing question that has yet to be rigorously explored or evaluated. This is particularly important for certain SARS-CoV-2 variants which are less susceptible to vaccine-induced immunity [20]. The one subject who did not seroconvert had multiple overlapping explanations for the absence of an immune response to the vaccine, being both a transplant patient and a PLWH, further adding complexity among patients with multiple immunocompromising conditions.

Despite the relatively small sample size, we found that those with lower CD4 counts and cancer or other immunosuppressive conditions (other than HIV) may be less likely to seroconvert after the first dose of COVID-19 vaccine. Although these findings did not reach statistical significance (possibly in part due to our small sample size), the direction of the effects are not surprising as these are known conditions that may impact immune responsiveness to vaccine antigens [21]. Our data also demonstrated that participants who were on an antiretroviral regimen containing INSTIs were more likely to seroconvert, although the association did not reach statistical significance. These observations merit evaluation in larger cohorts of PLWH to confirm our exploratory findings and analyses.

This study had several limitations. First, our small sample size may have reduced the power of this study to detect statistically significant differences in risk factors for seroconversion, but the differences in immune responses in the two time periods reported remain noteworthy and the directions of our effect estimates are consistent with prior studies that associate immunocompromised conditions with lack of seroconversion [7-9]. Second, 50% of participants were lost to follow-up by visit 2. We attribute this to loss of convenience to study participants, as visit 1 took place at a community-based

vaccination site but visit 2 was relocated to the HIV clinic at our hospital. This required complex logistical planning. Some participants were unable to, or did not want to, come to the clinic because of concern regarding SARS-CoV-2 infection risk or for other reasons, including time constraints, for follow-up or cited scheduling conflicts when approached. However, as 67% of participants in visit 1 who had a negative IgG test returned for follow-up, we were able to record very high rates of new seroconversion (97.5%) that allowed us to assess immunogenicity of the vaccine in that subset following a second dose of vaccine. Furthermore, demographic and immunological characteristics were similar between those who were retained in visit 2, compared with those who did not receive the second dose in the requisite time period; thus, we believe the conclusions that could be drawn from higher subject retention at visit 2 would probably not change the results significantly (Table S1). Third, our cohort consisted of PLWH aged ≥ 55 years and findings from this study may not be generalizable to a younger population. A significant proportion of our study subjects (12.8%) had immunocompromising conditions other than HIV that could have explained relatively lower immunogenicity results after the first vaccination, such that it may not be attributable to their HIV status alone. An additional limitation is that we utilized a qualitative immunoassay that detects SARS-CoV-2 anti-spike antibody, but does not measure neutralizing antibody, and the results cannot distinguish between prior COVID-19 infection and vaccine-induced immunity. We excluded patients with prior history of COVID-19, although without baseline antibody testing, those with asymptomatic infection may have been missed. However, this would have led to an underestimation and not an overestimation of non-seroconversion to the vaccine. Although there was no HIV-negative matched control group, we used robust historical data for comparison. Having a control immunocompetent group at an external site would have been ideal, but the feasibility and practicality of this option were unfortunately limited by resources and the HIV-specific clinic study site. Lastly, further immunogenicity data regarding other types of COVID-19 vaccines included would provide additional information about a broad range of vaccines and vaccine-induced immunity; however, administration of a single type of COVID-19 vaccine has the advantage of demonstrating the immune response to a single vaccine type with less confounding factors. Nevertheless, the findings from our study lend importance to future larger studies to evaluate immunogenicity, including vaccine-related seroconversion rates and durability of immune responses following COVID-19 vaccine among PLWH. Although recognizing these limitations, we present this study because of its relevance in a population with immune dysregulation affected by both current epidemics of HIV and COVID-19 globally and in the expectation that it will stimulate additional study and relevant information in the near future.

In conclusion, our study suggests that the completion of a two-dose series of BNT162b2 is critical for individuals living with HIV, especially those with low CD4 counts or who have other concurrent immunocompromising conditions.

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CONFLICTS OF INTEREST

The authors declare there are no conflicts of interest.

AUTHOR CONTRIBUTIONS

All authors had full access to the study data and are responsible for data integrity and accurate data analysis. Concept and design: OO and LB. Acquisition of data: JJT, LB, OO, LA, SM, BT and LR. Analysis or interpretation of data: all authors. Drafting of the manuscript: JJT, OO. Revision of the manuscript: all authors. Statistical analysis: MER.

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