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The vast majority of SARS-CoV-2 infections were asymptomatic in a clinic-based cohort of people with and without HIV in four African countries

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Abstract

Background Persons living with HIV (PLWH) were prioritized for SARS-CoV-2 vaccination in sub-Saharan Africa, however, SARS-CoV-2 infection and COVID-19 symptomatology have not been well characterized among PLWH. We described SARS-CoV-2 infection prevalence and symptomatology, and examined factors associated with nasal swab RT-PCR positivity in Kenya, Uganda, Tanzania, and Nigeria.

Methods The ongoing African Cohort Study (AFRICOS) follows PLWH and people living without HIV (PLWoH) in four African countries. All participants undergo clinical assessment and socio-behavioral questionnaire administration at enrollment and each six-monthly visits, with CD4 count and viral load collected for PLWH. Optional nasal swabs were collected for SARS-CoV-2 rapid RT-PCR testing at visits after 19 July 2022. Participants were asked if they had experienced COVID-19 symptoms. We used the Agresti-Coull method to estimate the prevalence of SARS-CoV-2 infection at each participant's first nasal swab collection. Adjusted prevalence ratios (aPRs) and 95% confidence intervals (CIs) for factors potentially associated with SARS-CoV-2 infection were estimated using multivariable robust Poisson regression.

Results Between 19 July 2022 and 1 March 2024, 1,187 participants underwent nasal swab collection with a valid SARS-CoV-2 RT-PCR result; 1,032 (86.9%) were PLWH and 155 (13.1%) were PLWoH. A majority were female (57.2%), and the median age was 44.6 (interquartile range 34.4–52.2) years. Prevalence at first nasal swab of SARS-CoV-2 was 6.8% (95%CI 5.5%-8.4%). Most participants with positive SARS-CoV-2 RT-PCR were asymptomatic (97.5%). SARS-CoV-2 was marginally more common among PLWoH as compared to PLWH (10.3% vs. 6.3%; $p=0.093$). In the multivariable model, SARS-CoV-2 was significantly more common among participants who received at least one dose of a COVID-19 vaccine as compared to participants who received no doses (aPR 1.66; 95%CI 1.05–2.62; $p=0.031$)

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and during the omicron wave as compared to non-wave periods (aPR 2.15; 95%CI 1.42–3.25; $p < 0.001$). Among PLWH, CD4 and viral load were not associated with SARS-CoV-2 prevalence.

Conclusion The vast majority of people with positive SARS-CoV-2 RT-PCR were asymptomatic. Universal screening may be needed to fully understand the epidemiology of SARS-CoV-2 and future outbreaks of similar respiratory viruses, capture early infection, and plan for intervention.

Keywords AFRICOS, HIV, SARS-CoV-2, Omicron, RT-PCR

Background

SARS-CoV-2 is a particularly virulent coronavirus that, since emerging in 2019, quickly spread across Africa and the world [1]. Throughout the emerging pandemic, there was concern that the African continent would be particularly vulnerable to poor outcomes due to fragile healthcare infrastructure, limited access to diagnostics, socioeconomic barriers to public health outbreak mitigation strategies, and high prevalence of comorbid conditions such as HIV [2–4]. By September 2021, when the delta variant was making its global spread, most countries in sub-Saharan Africa (SSA) had not met population level targets for vaccination. Although SSA makes up approximately 14% of the world's population, SSA only received 2% of the world's COVID-19 vaccines, so distribution of the limited available vaccines was targeted toward people with the highest potential vulnerability to poor outcomes from SARS-CoV-2 infection [5]. A study done in South Africa after the third wave of COVID-19 and before emergence of the omicron variant showed ≥ 60% SARS CoV-2 seroprevalence, indicating substantial natural infection [6].

People living with HIV (PLWH) suffer a higher burden of comorbidities that could contribute to adverse outcomes from SARS-CoV-2 infection, as compared to people living without HIV (PLWoH) [7]. While a review of studies from SSA did not find an association between HIV status and vulnerability to COVID-19 [8], PLWH are at heightened risk for developing severe COVID-19 [9, 10]. A study in South Africa showed higher risk of in-hospital COVID-19 mortality among PLWH as compared to PLWoH, including greater differences in case fatality rates between PLWH and PLWoH during the Omicron BA.1/BA.2 and Omicron BA.4/BA.5 waves than during earlier waves [11]. A multicenter study done among PLWH with positive SARS-CoV-2 infection showed that older patients with low CD4 counts and at least one comorbidity had higher risk of severe COVID-19 [12].

In a cohort of PLWH and PLWoH in four African countries, we described SARS-CoV-2 prevalence and symptomatology and examined associations with sociodemographic and clinical characteristics. The results from this study may help with understanding the epidemiology of SARS-CoV-2 infections in Africa and inform responses to future respiratory virus outbreaks.

Methods

Study design and setting

The African Cohort Study (AFRICOS) is an ongoing observational cohort that began enrolling PLWH and PLWoH in a 5:1 ratio in January 2013. It enrolls at 12 clinics across five programs supported by the United States President's Emergency Plan for AIDS Relief (PEPFAR) in Kayunga, Uganda; South Rift Valley, Kenya; Kisumu West, Kenya; Mbeya, Tanzania; and Lagos and Abuja, Nigeria [13]. The primary objective of the study is to longitudinally assess the impact of clinical practices, biological factors, and socio-behavioral issues on HIV acquisition and disease progression in an African context. PLWoH are recruited from serodifferent couples or via HIV testing encounters within participating clinics. PLWH are recruited from clinic clients and newly diagnosed individuals from HIV testing clinics. A small subset of participants is recruited from previous studies in the clinic. Current clinic clients aged 15 years and older who consent to data and specimen collection are eligible for study inclusion. At enrollment and every 6 months thereafter, participants complete questionnaires, undergo medical history-taking and physical examination, and provide biological specimens for laboratory testing.

Data collection and measures

At each study visit, demographic characteristics, including age, sex, program site, education status, marital status, and employment status, were collected using questionnaires. Body mass index (BMI) was calculated using participant weight and height and classified as underweight (< 18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), or overweight/obese (≥ 25.0 kg/m^2). Hyperglycemia was defined as a fasting glucose > 99 mg/dL, non-fasting glucose > 199 mg/dL. Hypercholesterolemia was defined as a total fasting cholesterol > 199 mg/dl. Elevated blood pressure was defined as systolic blood pressure > 139 mmHg and/or diastolic blood pressure > 89 mmHg with abnormal blood pressure repeated for confirmation during the same study visit. HIV-1 RNA (viral load) was quantified via PCR-based platforms used for routine clinical care

at participating sites, as previously described [14]. Viral suppression was defined as HIV-1 RNA < 1000 copies/mL for participants living with HIV.

Nasal swab collection was offered to participants as an optional procedure beginning on 19 July 2022. Nasal swabs were offered at every visit and tested for SARS-CoV-2 using Cepheid Xpert Xpress CoV-2 (catalog number: XPRSARS-COV2-10) rapid, real-time RT-PCR testing. At each visit, participants were asked if they had experienced COVID-19 symptoms. Solicited symptoms included fever, cough, shortness of breath, joint aches, muscle aches, diarrhea, nausea, vomiting, loss of taste, and loss of smell. The case definition for symptomatic COVID-19 required fever plus one or more additional symptom(s), which is similar to both the WHO and US CDC case definitions [15, 16]. Participants were also asked if they had been tested for COVID-19 since the last study visit. COVID-19 vaccination history was extracted from medical records. Vaccines that were available during the COVID-19 pandemic included those manufactured by AstraZeneca, Pfizer, Moderna, Janssen (Johnson & Johnson), and Sinopharm.

Because the SARS-CoV-2 omicron variant was associated with rapid global spread of the virus, the omicron wave was analyzed as an independent predictor of SARS-CoV-2 PCR positivity. For these analyses, the omicron wave was defined by swab collection between 31 October 2022 and 2 January 2023. The start of the wave was determined by two consecutive seven-day periods with > 20% increase in cases in the Africa WHO region; the start date was the beginning of the first seven-day period. The end of the wave was determined by two consecutive seven-day periods with number of cases below the number of cases at the beginning of the wave or two consecutive seven-day periods with < 10% absolute weekly change in number of cases, whichever occurred first.

Statistical analyses

These analyses included PLWH and PLWoH in AFRICOS who had a nasal swab collected and tested with a valid SARS-CoV-2 RT-PCR test result between 19 July 2022 and 1 March 2024. For participants who had multiple nasal swabs collected, only the first result was included. Descriptive statistics were calculated for all clinical and sociodemographic variables of interest, stratified by SARS-CoV-2 infection status. Analyses of time-varying variables used data from the visit at which the nasal swab was collected. Comparisons of categorical variables were performed using Chi-squared tests of independence and comparisons of continuous variables were performed using Wilcoxon rank sum tests. The prevalence of SARS-CoV-2 at first nasal swab during the period between 19 July 2022 and 1 March 2024 was estimated using the Agresti-Coull method, both among the entire analysis population and stratified by HIV status.

Prevalence ratios (PRs) and 95% confidence intervals (CIs) were estimated using robust Poisson regression. Missingness in the covariates was addressed by using a complete-case analysis. Purposeful variable selection was used to select the set of independent variables in the final multivariable model by first including those with a $p < 0.25$ from the unadjusted models in the adjusted model. Variables were then retained in the model based on whether they were significant at the $p < 0.05$ level or if other coefficient estimates changed by more than 20% when the variable was removed from the model. Finally, the independent variables not selected from the univariable models were added one at a time to the model to determine if they became significant ($p < 0.15$) in the presence of other covariates, and the second step was then repeated for these variables [17]. All data were analyzed using R, version 4.3.2 [18].

Results

Between January 2013 and March 2024, 4,137 participants were enrolled, including 2,567 who had at least one visit after nasal swab collection began on 19 July 2022. Of these participants, 1,187 underwent at least one optional nasal swab collection with a valid result returned; these participants were included in further analyses.

Descriptive statistics stratified by SARS-CoV-2 infection status are presented in Table 1, and demographic characteristics and COVID-19 vaccination status stratified by HIV status are presented in Table 2. Among our analysis population, 1,032 (86.9%) were PLWH and 155 (13.1%) were PLWoH. A slight majority were female (57.2%), and the median age was 44.6 (interquartile range: 34.4- 52.2) years. A higher proportion of PLWoH than PLWH had their first nasal swab collected during the BQ.1/BQ1.1 Omicron wave (36.1% vs 26.3%, $p = 0.010$) and were experiencing symptoms at the time of their first nasal swab (1.9% vs 0.4%, $p = 0.041$).

Among the entire analysis population, the prevalence of SARS-CoV-2 infection at first nasal swab during the period between 19 July 2022 and 1 March 2024 was estimated to be 6.8% (95% CI: 5.5%−8.4%). Among PLWH, the prevalence was estimated to be 6.3% (95% CI: 5.0%−8.0%) and among PLWoH, the prevalence was estimated to be 10.3% (95% CI: 6.4%−16.2%; $p = 0.093$). The unadjusted prevalence ratio for SARS-CoV-2 comparing PLWoH vs. PLWH was 1.64 (95% CI: 0.97–2.75, $p = 0.063$). Most participants with positive SARS-CoV-2 PCR were asymptomatic (97.5%). The only participant with a positive nasal swab who was symptomatic

Table 1 Demographic, clinical, and COVID-19 characteristics, stratified by SARS-CoV-2 infection status

	Total (*N* = 1187) (n, col%)	SARS-CoV-2 negative (*N* = 1106) (n, row%)	SARS-CoV-2 positive (*N* = 81) (n, row%)	*p*-value
HIV status				0.093
PLWH	1032 (86.9%)	967 (93.7%)	65 (6.3%)	
PLWoH	155 (13.1%)	139 (89.7%)	16 (10.3%)	
Sex				0.510
Male	508 (42.8%)	470 (92.5%)	38 (7.5%)	
Female	679 (57.2%)	636 (93.7%)	43 (6.3%)	
Age (years)				0.339
< 30	253 (21.3%)	239 (94.5%)	14 (5.5%)	
30–39	177 (14.9%)	165 (93.2%)	12 (6.8%)	
40–49	393 (33.1%)	359 (91.3%)	34 (8.7%)	
50 +	364 (30.7%)	343 (94.2%)	21 (5.8%)	
Site				**0.007**
Kayunga, Uganda	86 (7.2%)	77 (89.5%)	9 (10.5%)	
South Rift Valley, Kenya	877 (73.9%)	808 (92.1%)	69 (7.9%)	
Kisumu West, Kenya	30 (2.5%)	30 (100.0%)	0 (0.0%)	
Mbeya, Tanzania	166 (14.0%)	164 (98.8%)	2 (1.2%)	
Abuja & Lagos Nigeria	28 (2.4%)	27 (96.4%)	1 (3.6%)	
Education				0.509
None or some primary	291 (24.5%)	267 (91.8%)	24 (8.2%)	
Primary or some secondary	498 (42.0%)	465 (93.4%)	33 (6.6%)	
Secondary and above	398 (33.5%)	374 (94.0%)	24 (6.0%)	
Employment Status				0.706
Not currently employed	907 (76.4%)	847 (93.4%)	60 (6.6%)	
Currently employed	280 (23.6%)	259 (92.5%)	21 (7.5%)	
Marital Status				0.261
Unmarried/single	599 (50.5%)	553 (92.3%)	46 (7.7%)	
Married	580 (48.9%)	546 (94.1%)	34 (5.9%)	
Missing	8 (0.7%)	7 (87.5%)	1 (12.5%)	
Hyperglycemia				0.720
No	1031 (86.9%)	959 (93.0%)	72 (7.0%)	
Yes	108 (9.1%)	102 (94.4%)	6 (5.6%)	
Missing	48 (4.0%)	45 (93.8%)	3 (6.2%)	
Hypercholesterolemia				0.366
No	961 (81.0%)	899 (93.5%)	62 (6.5%)	
Yes	173 (14.6%)	158 (91.3%)	15 (8.7%)	
Missing	53 (4.5%)	49 (92.5%)	4 (7.5%)	
Body mass index				0.196
Underweight (< 18.5 kg/m^2)	104 (8.8%)	101 (97.1%)	3 (2.9%)	
Normal (18.5–24.9 kg/m^2)	641 (54.0%)	592 (92.4%)	49 (7.6%)	
Overweight/Obese (≥ 25.0 kg/m^2)	441 (37.2%)	412 (93.4%)	29 (6.6%)	
Missing	1 (0.1%)	1 (100.0%)	0 (0.0%)	
Elevated blood pressure				0.218
No	1006 (84.8%)	933 (92.7%)	73 (7.3%)	
Yes	181 (15.2%)	173 (95.6%)	8 (4.4%)	
Received COVID-19 vaccine				**< 0.001**
No doses	628 (52.9%)	600 (95.5%)	28 (4.5%)	
One or more doses	559 (47.1%)	506 (90.5%)	53 (9.5%)	

Table 1 (continued)

	Total (*N* = 1187) (n, col%)	SARS-CoV-2 negative (*N* = 1106) (n, row%)	SARS-CoV-2 positive (*N* = 81) (n, row%)	*p*-value
Vaccine type (most recent dose)				0.202
AstraZeneca	291 (24.5%)	266 (91.4%)	25 (8.6%)	
Pfizer	71 (6.0%)	62 (87.3%)	9 (12.7%)	
Moderna	26 (2.2%)	25 (96.2%)	1 (3.8%)	
Johnson & Johnson	169 (14.2%)	152 (89.9%)	17 (10.1%)	
Sinopharm	2 (0.2%)	1 (50.0%)	1 (50.0%)	
N/A, did not receive vaccine	628 (52.9%)	600 (95.5%)	28 (4.5%)	
COVID-19 wave at visit date				**< 0.001**
BQ.1/BQ1.1 Omicron Wave (10/31/22—1/2/23)	327 (27.5%)	287 (87.8%)	40 (12.2%)	
Non-wave	860 (72.5%)	819 (95.2%)	41 (4.8%)	
Experiencing COVID-19 symptoms[a]				0.969
No	1174 (98.9%)	1095 (93.3%)	79 (6.7%)	
Yes	7 (0.6%)	6 (85.7%)	1 (14.3%)	
Missing	6 (0.5%)	5 (83.3%)	1 (16.7%)	
Among PLWH(*N* = 1032):				
CD4 count (cells/mm^3)				0.255
< 200	60 (5.8%)	53 (88.3%)	7 (11.7%)	
200–349	109 (10.6%)	104 (95.4%)	5 (4.6%)	
350–499	221 (21.4%)	205 (92.8%)	16 (7.2%)	
≥ 500	622 (60.3%)	586 (94.2%)	36 (5.8%)	
Missing	20 (1.9%)	19 (95.0%)	1 (5.0%)	
Viral suppression (copies/mL)				> 0.999
≥ 1000	59 (5.7%)	55 (93.2%)	4 (6.8%)	
< 1000	956 (92.6%)	896 (93.7%)	60 (6.3%)	
Missing	17 (1.6%)	16 (94.1%)	1 (5.9%)	

PLWH People living with HIV, *PLWoH* People living without HIV

[a] Fever plus one of the following: cough, shortness of breath, joint aches, muscle aches, diarrhea, nausea, vomiting, loss of taste, or loss of smell

reported fever, chills, loss of taste or smell, body aches, malaise/fatigue, and headache.

The prevalence of SARS-CoV-2 varied by study site; in Kayunga, Uganda, 9/86 (10.5%) tested positive for SARS-CoV-2; 69/877 (7.9%) in South Rift Valley, Kenya; 1/28 (3.6%) in Abuja and Lagos, Nigeria; 2/166 (1.2%) in Mbeya, Tanzania; and 9/30 (30.0%) in Kisumu West, Kenya ($p = 0.007$). Fifty-four of 571 (9.5%) participants who received one or more doses of COVID-19 vaccination had a positive SARS-CoV-2 test result, compared to 27/616 (4.4%) who didn't receive any doses of COVID-19 vaccine ($p < 0.001$). There was no significant difference in COVID-19 vaccination status by HIV status; 484/1032 (46.9%) PLWH had received at least one dose of a COVID-19 vaccine, and 75/155 (48.4%) PLWoH had received at least one dose ($p = 0.729$). A greater proportion of participants who had a nasal swab collected during a COVID-19 wave had a positive test result (40/327, 12.2%) compared to participants who had nasal swab collected during a non-wave period (41/860, 4.8%; $p < 0.001$). Among PLWH, there were no significant differences in SARS-CoV-2 infection status by CD4 category or viral suppression status.

Table 3 shows the results of the univariable robust Poisson regression models as well as the final adjusted model. Independent variables that were candidates to be included in the adjusted model included HIV status, sex, age category, country, education level, employment status, BMI category, SARS-CoV-2 vaccination status, and COVID-19 wave. Study site was collapsed to become a country variable due to one of the Kenyan sites having no positive nasal swabs.

After conducting purposeful variable selection, country, COVID-19 vaccination status, and COVID-19 wave

Table 2 Demographic and clinical characteristics and COVID-19 vaccination status, stratified by HIV status

	PLWH (*N* = 1032) (n, col%)	PLWoH (*N* = 155) (n, col%)	*p*-value
Sex			0.523
Male	438 (42.4%)	70 (45.2%)	
Female	594 (57.6%)	85 (54.8%)	
Age (years)			0.130
< 30	214 (20.7%)	39 (25.2%)	
30–39	149 (14.4%)	28 (18.1%)	
40–49	341 (33.0%)	52 (33.5%)	
50 +	328 (31.8%)	36 (23.2%)	
Site			0.247
Kayunga, Uganda	69 (6.7%)	17 (11.0%)	
South Rift Valley, Kenya	765 (74.1%)	112 (72.3%)	
Kisumu West, Kenya	28 (2.7%)	2 (1.3%)	
Mbeya, Tanzania	144 (14.0%)	22 (14.2%)	
Abuja & Lagos Nigeria	26 (2.5%)	2 (1.3%)	
Education			0.923
None or some primary	255 (24.7%)	36 (23.2%)	
Primary or some secondary	432 (41.9%)	66 (42.6%)	
Secondary and above	345 (33.4%)	53 (34.2%)	
Employment Status			0.131
Not currently employed	796 (77.1%)	111 (71.6%)	
Currently employed	236 (22.9%)	44 (28.4%)	
Marital Status			**0.013**
Unmarried/single	536 (51.9%)	63 (40.6%)	
Married	488 (47.3%)	92 (59.4%)	
Missing	8 (0.8%)	0 (0.0%)	
Hyperglycemia			0.420
No	897 (86.9%)	134 (86.5%)	
Yes	96 (9.3%)	12 (7.7%)	
Missing	39 (3.8%)	9 (5.8%)	
Hypercholesterolemia			**0.002**
No	851 (82.5%)	110 (71.0%)	
Yes	137 (13.3%)	36 (23.2%)	
Missing	44 (4.3%)	9 (5.8%)	
Body mass index			0.061
Underweight (< 18.5 kg/m^2)	95 (9.2%)	9 (5.8%)	
Normal (18.5–24.9 kg/m^2)	567 (54.9%)	74 (47.7%)	
Overweight/Obese (≥ 25.0 kg/m^2)	369 (35.8%)	72 (46.5%)	
Missing	1 (0.1%)	0 (0.0%)	
Elevated blood pressure			0.420
No	878 (85.1%)	128 (82.6%)	
Yes	154 (14.9%)	27 (17.4%)	
Received COVID-19 vaccine			0.729
No doses	548 (53.1%)	80 (51.6%)	
One or more doses	484 (46.9%)	75 (48.4%)	
Vaccine type (most recent dose)			0.594
AstraZeneca	258 (25.0%)	33 (21.3%)	
Pfizer	58 (5.6%)	13 (8.4%)	
Moderna	23 (2.2%)	3 (1.9%)	
Johnson & Johnson	143 (13.9%)	26 (16.8%)	
Sinopharm	2 (0.2%)	0 (0.0%)	
N/A, did not receive vaccine	548 (53.1%)	80 (51.6%)	
COVID-19 wave at visit date			**0.010**
BQ.1/BQ1.1 Omicron Wave (10/31/22—1/2/23)	271 (26.3%)	56 (36.1%)	
Non-wave	761 (73.7%)	99 (63.9%)	
Experiencing COVID-19 symptoms[a]			**0.041**
No	1022 (99.0%)	152 (98.1%)	
Yes	4 (0.4%)	3 (1.9%)	
Missing	6 (0.6%)	0 (0.0%)	

PLWH People living with HIV, *PLWoH* People living without HIV

[a] Fever plus one of the following: cough, shortness of breath, joint aches, muscle aches, diarrhea, nausea, vomiting, loss of taste, or loss of smell

were included in the final model. In the final model, factors associated with a higher likelihood of a positive nasal swab were having received at least one dose of a COVID-19 vaccine and the nasal swab being collected during the BQ.1/BQ1.1 Omicron wave (10/31/22—1/2/23). Participants who had received at least one dose of a COVID-19 vaccine had a 66% higher prevalence of SARS-CoV-2 than participants who had received no doses (aPR 1.66; 95%CI 1.05–2.62; $p = 0.031$). Participants whose nasal swabs were collected during the BQ.1/BQ1.1 Omicron wave had a 115% higher prevalence of SARS-CoV-2 than participants whose swabs were collected during a non-wave period (aPR 2.15; 95%CI 1.42–3.25; $p < 0.001$).

Discussion

Our study found that the vast majority of people with positive SARS-CoV-2 RT-PCR were asymptomatic (97.5%). This is consistent with previously published work, including a systematic review and meta-analysis that revealed that most patients who present asymptomatically remain asymptomatic throughout their disease course, though more than half have imaging abnormalities [19]. A study done in Guinea-Bissau on SARS-CoV seroprevalence among people living with HIV showed that 71.2% of seropositive unvaccinated PLWH reported no symptoms of COVID-19 [20]. This further explains the importance of universal screening during future

Table 3 Exploration of factors potentially associated with a positive SARS-CoV-2 nasal swab ($n=1186$)

	Univariable Models			Multivariable Model		
	Unadjusted PR	**Unadjusted 95% CI**	***P*-value**	**Adjusted PR**	**Adjusted 95% CI**	***P*-value**
HIV status						
PLWH	Reference					
PLWoH	1.64	(0.97,2.75)	0.063			
Sex						
Female	Reference					
Male	1.18	(0.78,1.8)	0.433			
Age (years)						
< 30	Reference					
30–39	1.23	(0.58,2.59)	0.594			
40–49	1.56	(0.86,2.85)	0.146			
50 +	1.05	(0.54,2.02)	0.894			
Country						
Uganda	Reference			Reference		
Kenya	0.73	(0.38,1.41)	0.344	0.72	(0.37,1.40)	0.335
Tanzania	**0.12**	**(0.03,0.52)**	**0.005**	0.21	(0.04,1.03)	0.053
Nigeria	0.34	(0.05,2.58)	0.297	0.40	(0.05,3.10)	0.379
Education						
None or some primary	1.37	(0.8,2.37)	0.255			
Primary or some secondary	1.1	(0.66,1.83)	0.717			
Secondary and above (ref)	Reference					
Employment status						
Not currently employed (ref)	Reference					
Currently employed	1.13	(0.7,1.83)	0.61			
Body mass index						
Underweight	Reference					
Normal	2.65	(0.84,8.35)	0.096			
Overweight/Obese	2.28	(0.71,7.34)	0.167			
COVID-19 wave at visit date						
Non-wave	Reference			Reference		
BQ.1/BQ1.1 Omicron Wave (10/31/22—1/2/23)	**2.56**	**(1.69,3.89)**	**< 0.001**	**2.15**	**(1.42,3.25)**	**< 0.001**
Received COVID-19 vaccine						
No doses	Reference			Reference		
One or more doses	**2.12**	**(1.36,3.31)**	**0.001**	**1.66**	**(1.05,2.62)**	**0.031**

CI Confidence interval, *PLWH* People living with HIV, *PLWoH* People living without HIV, *PR* Prevalence ratio

outbreaks of respiratory diseases in order to fully understand transmission dynamics.

In this study, the overall prevalence of SARS-CoV-2 at first nasal swab was 6.8%. PLWH were slightly less likely to have a positive test result compared to PLWoH (6.3% vs 10.3%). Our study further showed that the BQ.1/BQ1.1 omicron wave was associated with more positive tests. This is in line with documented evidence from different countries during the omicron wave period [21]. A report from the European Union corroborated these findings, having detected more than 50% of SARS-CoV-2 infections due to BQ.1/BQ.1.1 circulating between October 2023 and February 2023 [22].

In the multivariable model, SARS-CoV-2 was significantly more common among participants who received at least one dose of a COVID-19 vaccine as compared to participants who received no doses and during the omicron wave as compared to non-wave periods. Furthermore, there were significant differences in the prevalence of SARS-CoV-2 at first nasal swab by country in the unadjusted model, which aligns with overall differences in numbers of cases with Kenya having more cases per

100,000 than the other three countries as of June 2021 [23]. However, we did not identify any demographic characteristics in the multivariable model that were predictive of SARS-CoV-2 infection. Pre-test probability of an asymptomatic case is therefore hard to predict and hard to use for allocation of limited screening resources. Instead, we might need to screen everyone during surges, if resources allow, or focus on groups with potentially worse outcomes.

Among PLWH in our analysis population, there were no significant differences by SARS-CoV-2 infection status in CD4 category or viral suppression. This lack of apparent differences could be related to the relatively small numbers of people with SARS-CoV-2 infection, a low CD4 count, and an unsuppressed viral load. In general, participants in AFRICOS are ART-experienced with high adherence to clinic visits for their HIV care. Therefore, we might not have had sufficient variability in our analysis population to ascertain associations between immunosuppression and viremia with SARS-CoV-2 infection. Other studies have shown mixed results regarding potential associations between SARS-CoV-2 infection and either CD4 count or viral load [24–26].

Our study identified an unexpected association between vaccination and higher prevalence of COVID-19. This may be due to vaccines being effective at preventing symptomatic COVID-19 [27], as only one participant with a positive nasal swab was symptomatic. During the study period, people at higher risk of SARS-CoV-2 infection were prioritized in the vaccine rollout, so it may be that participants at higher risk of infection were both more likely to be vaccinated and more likely to have a positive nasal swab. This may be related to a type of selection bias in observational studies described elsewhere, in which persons susceptible to COVID-19 are more likely to obtain a vaccination booster [28]. It is also likely that most participants had their most recent vaccine dose more than 6 months before their nasal swab was collected, so protection from the vaccine, which may otherwise have mitigated this higher risk of infection among people prioritized for vaccination, may have waned [29].

Strengths of our study included the inclusion of geographically diverse sites, which allowed for enrollment of participants from different backgrounds, and standardized data collection tools, which consistent and high-quality data collection. However, this study also has some limitations. AFRICOS participants are engaged in care at PEPFAR-supported clinics and have opted to participate in an intensive, long-term observational study; results from this study may not be generalizable to other populations. Within AFRICOS, people who choose to undergo optional nasal swab collection may differ from participants who decline this optional procedure. We observed variation within clinics for participants who chose to undergo optional nasal swab collection, and nasal swab collection was also influenced by logistical and regulatory timelines to implement SARS-CoV-2 testing at each site. Participants with symptoms may also have sought care elsewhere instead of coming for regular study visits. Finally, our analysis population included an insufficient number of PLWoH with a positive nasal swab to stratify the multivariable model by HIV status, so we were unable to assess differences in effects between PLWH and PLWoH.

Conclusion

These study findings characterize sociodemographic and clinical correlates of SARS-COV-2 prevalence and symptomatology among a cohort of PLWH and PLWoH. We demonstrate that the majority of people with positive SARS-CoV-2 PCR were asymptomatic, with no differences by HIV status. Self-report or clinical diagnoses may underestimate the prevalence of SARS-CoV-2 and universal screening may aid early detection and intervention. This may also apply to future outbreaks of similar respiratory viruses.

Abbreviations

AFRICOS	African Cohort Study
PLWH	People Living With HIV
PLWoH	People Living without HIV
CI	Confidence Interval
COVID-19	Coronavirus Disease 2019
HIV	Human Immunodeficiency Virus
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SRV	South Rift Valley
SSA	Sub-Saharan Africa

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Authors' contributions

JAA and NS acquired funding for the study and provided oversight and leadership. RL, RG, HK, JO, VS, JM, ZP, AT, and EB collected primary data and oversaw study operations at the clinical research sites. ID and MI oversaw laboratory evaluations and operations, including testing for SARS-CoV-2. NB, NFD and SF contributed to data analysis. TAC, MLR, APP, ERD, BO, and JH contributed to study oversight, operations, and data analysis. All authors contributed to the writing and/or editing of the report and approved the final version.

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Data availability

The data sets generated and/or analyzed during the current study are not publicly available due to privacy protections but are available from the corresponding author on reasonable request. The Henry M. Jackson Foundation for the Advancement of Military Medicine (HJF) and the Water Reed Army Institute of Research (WRAIR) are committed to safeguarding the privacy of research participants. Distribution of data will require compliance with all applicable regulatory and ethical processes, including the establishment and approval of an appropriate data-sharing agreement. To request a minimal data set, please contact the data coordinating and analysis Centre (DCAC) at PubRequest@hivresearch.org and indicate the RV329 study along with the name of the manuscript.

Declarations

Ethics approval and consent to participate

The African Cohort Study was approved by institutional review boards of the Walter Reed Army Institute of Research Silver Spring, MD, USA; Makerere University School of Public Health, Kampala, Uganda; Kenya Medical Research Institute, Nairobi, Kenya; Tanzania National Institute of Medical Research, Mbeya, Tanzania; Nigerian Ministry of Defence, Abuja, Nigeria; and all collaborating institutions. All participants provided written informed consent prior to any study procedures. All work was conducted in accordance with the Declaration of Helsinki.

Consent for publication

Not Applicable.

Competing interests

The authors declare no competing interests.

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References

1. Mandala WL, Liu MKP. SARS-CoV-2 and HIV-1: should HIV-1-infected individuals in Sub-Saharan Africa be considered a priority group for the COVID-19 vaccines? Front Immunol. 2021;12:797117.
2. Paintsil E. COVID-19 threatens health systems in sub-Saharan Africa: the eye of the crocodile. J Clin Invest. 2020;130(6):2741–4.
3. El-Sadr WM, Justman J. Africa in the path of Covid-19. N Engl J Med. 2020;383(3):e11.
4. Gilbert M, et al. Preparedness and vulnerability of African countries against importations of COVID-19: a modelling study. Lancet. 2020;395(10227):871–7.
5. *Fifteen African countries hit 10% COVID-19 vaccination goal*. 2021; Available from: https://www.afro.who.int/news/fifteen-african-countries-hit-10-covid-19-vaccination-goal.Cited 2024 06 September

6. Kleynhans J, et al. SARS-CoV-2 seroprevalence after third wave of infections. South Africa Emerg Infect Dis. 2022;28(5):1055–8.
7. Vizcarra P, et al. Description of COVID-19 in HIV-infected individuals: a single-centre, prospective cohort. Lancet HIV. 2020;7(8):e554–64.
8. Drain PK, Garrett N. SARS-CoV-2 pandemic expanding in sub-Saharan Africa: Considerations for COVID-19 in people living with HIV. EClinicalMedicine. 2020;22: 100342.
9. Karim F, et al. HIV status alters disease severity and immune cell responses in Beta variant SARS-CoV-2 infection wave. Elife. 2021;10:e67397.
10. Tapera T, et al. Intersecting epidemics: COVID-19 and HIV in Sub-Saharan Africa. A systematic review (2020–2022). J Public Health Afr. 2023;14(9):2658.
11. Jassat W, et al. Trends in COVID-19 admissions and deaths among people living with HIV in South Africa: analysis of national surveillance data. Lancet HIV. 2024;11(2):e96–105.
12. Hoffmann C, et al. Immune deficiency is a risk factor for severe COVID-19 in people living with HIV. HIV Med. 2021;22(5):372–8.
13. Ake JA, et al. Noninfectious comorbidity in the African cohort study. Clin Infect Dis. 2019;69(4):639–47.
14. Kibuuka H, et al. Predictors of All-Cause Mortality Among People With Human Immunodeficiency Virus (HIV) in a Prospective Cohort Study in East Africa and Nigeria. Clin Infect Dis. 2022;75(4):657–64.
15. Centers for Disease Control and Prevention. Centers for Disease Control and Prevention Coronavirus disease 2019 (COVID-19). United States: centers for disease control and prevention; 2020. Available from: https://www.cdc.gov/coronavirus/2019-ncov/index.html. Accessed 2025.
16. World Health Organization. WHO COVID-19: case definitions: updated in public health surveillance for COVID-19. 2020.
17. Bursac Z, et al. Purposeful selection of variables in logistic regression. Source Code Biol Med. 2008;3:17.
18. R Core Team. R: A language and environment for statistical computing. Vienna: R Foundation for Statistical Computing; 2023. https://www.R-project.org/.
19. Kronbichler A, et al. Asymptomatic patients as a source of COVID-19 infections: A systematic review and meta-analysis. Int J Infect Dis. 2020;98:180–6.
20. Dutschke A, et al. SARS-CoV-2 seroprevalence among people living with HIV in Guinea-Bissau. Public Health. 2022;209:36–8.
21. Akash S, Islam MR, Dhama K. Emergence BQ.1 and BQ.1.1 as newly identified omicron subvariants: current scenario and future outlook - an update. Ann Med Surg (Lond). 2023;85(4):1329–30.
22. Spread of the SARS-CoV-2 Omicron variant sub-lineage BQ.1 in the EU/EEA. 2022, European Center for Disease Prevention and Control: https://www.ecdc.europa.eu/en/publications-data/spread-sars-cov-2-omicron-variant-sub-lineage-bq1-eueea. p. 7.
23. Obande GA, et al. Current State of COVID-19 Pandemic in Africa: lessons for today and the future. Int J Environ Res Public Health. 2021;18(19):9968.
24. Tang ME, et al. People with HIV have a higher risk of COVID-19 diagnosis but similar outcomes to the general population. HIV Med. 2022;23(10):1069–77.
25. Maggiolo F, Comi L, Arosio M, Valenti D, Guarneri D, Rizzi M, Callegaro A. SARS-CoV-2 infection clinical picture and outcomes in adults living with HIV: a cohort analysis. New Microbiol. 2023;46(1):18–23.
26. Lambarey H, et al. SARS-CoV-2 infection is associated with uncontrolled HIV viral load in non-hospitalized HIV-infected patients from Gugulethu, South Africa. Viruses. 2022;14(6):1222.
27. Ssentongo P, et al. SARS-CoV-2 vaccine effectiveness against infection, symptomatic and severe COVID-19: a systematic review and meta-analysis. BMC Infect Dis. 2022;22(1):439.
28. Monge S, Pastor-Barriuso R, Hernan MA. The imprinting effect of covid-19 vaccines: an expected selection bias in observational studies. BMJ. 2023;381: e074404.
29. Chemaitelly H, Abu-Raddad LJ. Waning effectiveness of COVID-19 vaccines. Lancet. 2022;399(10327):771–3.

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