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SARS-CoV-2 Antibody Prevalence in People with and without HIV in Rural Western Kenya, January to March 2020

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ABSTRACT

Among 582 participants in Western Kenya who were retrospectively tested from January through March 2020, 19 (3.3%) had detectable SARS-CoV-2 antibodies. The prevalence of detectable SARS-CoV-2 antibodies was similar between participants with and without HIV (3.1% vs. 4.0%, p=0.68). One participant reported a cough in the preceding week but others denied symptoms. These may represent cross-reactivity or asymptomatic infections that predated the first reported COVID-19 cases in Kenya.

Key Words: Africa South of the Sahara; Acquired Immunodeficiency Syndrome; Public Health Surveillance; COVID-19 Testing; Serologic Tests; Asymptomatic Infections

The global pandemic of coronavirus disease-19 (COVID-19), caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), has overwhelmed national health systems in many countries. While the African continent was predicted to be particularly vulnerable, African populations appear to have thus far evaded widespread morbidity and mortality due to COVID-19[1]. Kenya's first identified COVID-19 case was a 27-year-old woman who traveled from the United States to Nairobi. Her diagnosis on 12 March 2020 immediately prompted nationwide mitigation efforts. Still, the infection spread from her to other airline passengers and, within two weeks, COVID-19 infections had been confirmed in five counties including and surrounding Nairobi and Mombasa[2]. This timeline for geographic spread suggested that the local outbreak emanated from arriving travelers at two major ports of entry. However, data from other countries suggest that SARS-CoV-2 was circulating weeks or months before initial cases were detected[3-5]. We retrospectively tested stored serum specimens from people with and without HIV in Western Kenya for evidence of potential SARS-CoV-2 circulation or cross-reactivity before the first Kenyan case was reported in March 2020.

The ongoing African Cohort Study (AFRICOS) enrolls adults with and without HIV in an approximately 5:1 ratio in four countries[6]. Seven hospital-based clinics in Kisumu and Kericho, Kenya, provided samples for these analyses. Cohort procedures include six-monthly medical history-taking, physical examination, and laboratory assessments that include CD4 count and HIV RNA quantification for people living with HIV (PLWH)[7]. At each visit, participants are asked about symptoms in the preceding week. Medical records and laboratory studies are reviewed to identify comorbidities, including some potentially associated with adverse COVID-19 outcomes[6].

Because of the emerging COVID-19 outbreak, AFRICOS study visits were paused on 19 March 2020[8]. For these analyses, stored serum from 1 January 2020 through 19 March 2020 was retrospectively tested using the Platelia SARS-CoV-2 Total Ab assay (Bio-Rad Laboratories, Hercules, CA, USA) to qualitatively detect anti-SARS-CoV-2 nucleocapsid IgM, IgA and/or IgG. Samples with signal-to-cutoff ratio (S/CO) ≥0.8 on initial testing were

retested in duplicate; one or two retest results with S/CO ≥1.0 was considered positive. For each participant with detectable antibodies, stored serum from the preceding study visit (as early as June 2019) was also tested.

A total of 582 participants underwent retrospective testing, including 508 (87.3%) PLWH and 327 (56.2%) females. Participants had a median age of 43.3 (interquartile range 35.7-51.6) years. Nineteen (3.3%) had detectable SARS-CoV-2 antibodies (Table 1), including seven who also had a positive test at their preceding visit and 12 who did not (Supplemental Figure, http://links.lww.com/QAD/C264). The prevalence of detectable SARS-CoV-2 antibodies was similar between participants with and without HIV (3.1% vs. 4.0%, p=0.68).

Our sites in rural Western Kenya are far removed from the urban centers of Nairobi and Mombasa where SARS-CoV-2 was believed to have been introduced into Kenya. However, these sites are near substantial infrastructure development projects such as highway construction backed by Chinese government and commercial entities. Some of the earliest known cases of COVID-19 in Africa were imported by manufacturing workers who traveled from China to Egypt[9] and it is possible that SARS-CoV-2 could have reached the otherwise remote region of our study similarly via construction workers. Expectedly, the seroprevalence estimates in this study were lower than those reported from African settings later in the pandemic, including a 4.3% seroprevalence among Kenyan blood donors in June 2020 that increased to 9.1% by September 2020[10].

However, it is likely that some or all of the positive assays in our study were due to cross-reactivity from pre-existing antibodies or causes other than SARS-CoV-2, particularly among participants who were serofast from previous visits that substantially pre-dated the emerging COVID-19 pandemic. While small studies showed no cross-reactivity between the Platelia assay and common alpha or beta coronaviruses (package insert, Bio-Rad Laboratories 16008597, 2020/06), variations in assay performance based on target antigen and study population limit the ability to compare data across studies and to assert that all positive assays in our study represented true SARS-CoV-2 infections[11]. Recent work has suggested that serologic cross-reactivity is significantly more common in samples from Africa than other settings, documenting pre-pandemic cross-reactive antibodies to the SARS-CoV-2 nucleocapsid protein among approximately 1 out of 6 samples tested in Tanzania[12].

Participants with detectable SARS-CoV-2 antibody were almost universally asymptomatic, despite some having risk factors for adverse outcomes of infection. Importantly, our study predominantly enrolls PLWH and, accordingly, most cases of detectable SARS-CoV-2 antibodies were observed amongst PLWH. The absence of any severe clinical cases of COVID-19 among these individuals is consistent with a growing body of literature that well-controlled HIV is not a risk factor for adverse outcomes of SARS-CoV-2 infection[13]. If participants in our study did have asymptomatic infection, then such cases could have contributed to early undetected spread of the pandemic in Kenya. If such participants had pre-existing cross-reactive antibodies, then partial immunity to SARS-CoV-2

could potentially explain the lower than predicted morbidity and mortality due to COVID-19 in Africa.

In conclusion, we present serologic data indicating either cross-reactivity or asymptomatic infections that predated the first reported COVID-19 cases in Kenya. Further research is needed to distinguish the two possible explanations for detectable SARS-CoV-2 antibodies in our study. This finding improves our understanding of early COVID-19 epidemiology and may help to predict its future course in Africa, thereby informing resource allocation and COVID-19 response policy.

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Ethical Assurance

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; and Nigerian Ministry of Defence, Abuja, Nigeria. All participants provided written informed consent prior to enrollment.

Conflicts of Interest

The authors declare no relevant conflicts of interest.

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Table 1. Characteristics of participants with detectable SARS-CoV-2 antibodies prior to COVID-related pause of African Cohort Study (AFRICOS) visits in rural Western Kenya

ID	Date	Age (years)	Sex	HIV status	CD4 (cells/mm^3)	HIV RNA (copies/mL)	BMI	Symptoms*	Comorbid conditions†	Comparison to prior visit
1	Jan 2020	46	M	No HIV	-	-	20.8	None	None	Serofast
2	Jan 2020	66	M	With HIV	548	Undetectable	18.0	Cough	None	Seroconverted
3	Jan 2020	47	F	With HIV	490	Undetectable	18.6	None	None	Serofast
4	Jan 2020	50	M	With HIV	458	Missing	19.7	None	None	Seroconverted
5	Jan 2020	69	M	With HIV	418	Undetectable	22.6	None	Elevated blood pressure	Serofast
6	Jan 2020	50	M	With HIV	194	Undetectable	26.0	None	None	Seroconverted
7	Jan 2020	55	F	No HIV	-	-	28.1	None	None	Seroconverted
8	Feb 2020	30	F	No HIV	-	-	28.3	None	None	Seroconverted
9	Feb 2020	44	F	With HIV	655	123	23.1	None	None	Serofast
10	Feb 2020	49	F	With HIV	713	Undetectable	23.9	None	None	Seroconverted

11	Feb 2020	26	F	With HIV	1044	Undetectable	33.0	None	None	Seroconverted
12	Feb 2020	34	F	With HIV	491	Undetectable	22.6	None	None	Seroconverted
13	Feb 2020	55	F	With HIV	755	<40	27.0	None	None	Serofast
14	Feb 2020	56	F	With HIV	316	Undetectable	21.5	None	Hyperglycemia	Seroconverted
15	Feb 2020	51	F	With HIV	563	Undetectable	23.7	None	Elevated blood pressure, liver disease	Seroconverted
16	Mar 2020	50	F	With HIV	557	Undetectable	30.4	None	None	Serofast
17	Mar 2020	47	F	With HIV	341	<40	27.5	None	None	Seroconverted
18	Mar 2020	49	M	With HIV	370	Undetectable	24.5	None	None	Serofast
19	Mar 2020	41	F	With HIV	833	Undetectable	30.1	None	Elevated blood pressure	Seroconverted

Stored serum samples collected from 1 January 2020 through 19 March 2020 from participants at seven sites in Kenya were tested retrospectively using the Platelia SARS-CoV-2 Total Ab assay to detect anti-SARS-CoV-2 IgM, IgA and/or IgG. Of 582 participants tested, 19 had detectable antibodies against SARS-CoV-2, with participant and testing characteristics summarized above. For each participant with detectable antibodies, serologic testing was also performed on stored serum from the immediately preceding study visit to evaluate for interval seroconversion, with a negative or equivocal prior test interpreted as "seroconverted" (12 participants) and a positive prior test interpreted as "serofast" (7 participants; see Figure).

* Solicited symptoms at each visit included any of the following in the preceding week: fever, cough, shortness of breath, arthralgias, myalgias, nausea, vomiting, diarrhea.

† Comorbid conditions included any of the following: cancer, renal insufficiency, respiratory disease, heart conditions, sickle cell disease, hyperglycemia, asthma, elevated blood pressure, neurologic conditions, immunocompromised state, pregnancy, tobacco smoking.