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High seroprevalence of SARS-CoV-2 but low infection fatality ratio eight months after introduction in Nairobi, Kenya

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ABSTRACT

Background: The lower than expected COVID-19 morbidity and mortality in Africa has been attributed to multiple factors, including weak surveillance. This study estimated the burden of SARS-CoV-2 infections eight months into the epidemic in Nairobi, Kenya.

Methods: A population-based, cross-sectional survey was conducted using multi-stage random sampling to select households within Nairobi in November 2020. Sera from consenting household members were tested for antibodies to SARS-CoV-2. Seroprevalence was estimated after adjusting for population structure and test performance. Infection fatality ratios (IFRs) were calculated by comparing study estimates with reported cases and deaths.

Results: Among 1,164 individuals, the adjusted seroprevalence was 34.7% (95% CI 31.8-37.6). Half of the enrolled households had at least one positive participant. Seropositivity increased in more densely populated areas (spearman's r=0.63; p=0.009). Individuals aged 20-59 years had at least two-fold higher seropositivity than those aged 0-9 years. The IFR was 40 per 100,000 infections, with individuals ≥60 years old having higher IFRs.

Conclusion: Over one-third of Nairobi residents had been exposed to SARS-CoV-2 by November 2020, indicating extensive transmission. However, the IFR was >10-fold lower than that reported in Europe and the USA, supporting the perceived lower morbidity and mortality in sub-Saharan Africa.

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INTRODUCTION

Sixteen months after the emergence of the coronavirus disease of 2019 (COVID-19), severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection had been confirmed in almost 140 million people globally and led to >2.9 million deaths (WHO, 2021a). In April 2020, the World Bank expressed concern that high virus transmission posed the greatest risk in densely populated urban areas, especially those with poor infrastructure and service delivery systems (The World Bank, 2020). In Africa, the urban population stood at 588 million people in 2020, with 50% of this population living in informal settlements, while 70% of the population were self-employed or working in unregulated sectors, making them vulnerable to income losses and less able to adhere to COVID-19 restrictions and lockdowns (United Nations et al., 2019). These workers use overcrowded public transport systems and marketplaces, which make social distancing almost impossible (Mitlin, 2020; UNHABITAT, 2020). Yet, despite these challenges, countries within sub-Saharan Africa have consistently reported lower COVID-19 cases and deaths throughout the pandemic when compared with other continents. Public health experts have advanced many hypotheses to explain this outcome, ranging from poor surveillance, suboptimal testing and underreporting, to younger populations, warmer and humid weather, and prior exposure to other cross-reacting coronaviruses (Njenga et al., 2020; Diop et al., 2020; Tso et al., 2021; WHO, 2020a). To address the challenge of underreporting, the World Health Organization (WHO) recommended population-based seroprevalence studies to determine the proportion of the population that had been infected over time, and estimate important parameters such as the proportion of asymptomatic infections, infection fatality ratios, and progression towards herd immunity (WHO, 2020b).

Several COVID-19 seroprevalence studies carried out thus far in different locations have revealed varying levels of underreporting, even in countries with mass testing programs for acute infections (Lai et al., 2020; Poustchi et al., 2020; Rostami et al., 2020). Four to nine months into the pandemic, studies in multiple states in the USA and Iran found SARS-CoV-2 seroprevalence to be between 7-23%, and suggested that acute infection testing, which was largely limited to symptomatic persons, initially underestimated total infections by >10-fold (Brown and Walensky, 2020; Poustchi et al., 2020).

The first case of COVID-19 in Kenya was reported on March 13, 2020. By the end of May 2021, the country had reported almost 171,000 cases and 3,167 deaths (case fatality rate = 1.9%) with peaks in July 2020, November 2020, and March 2021 (MOH Surveillance Report No. 439, 2021). By mid-April 2020, community transmission of SARS-CoV-2 was evident in Kenya, which necessitated the closure of schools and social amenities, and cessation of movement in and out of the capital city Nairobi (Ministry of Health, Kenya, 2020). Nairobi (population 4.4. million) is one of the largest cities in East Africa and among the 10 largest cities on the continent (Kenya National Bureau of Statistics, 2019a; The World Bank, 2019). By November 2020, eight months into the pandemic, Nairobi remained a hotspot for SARS-CoV-2 transmission, accounting for 46% of cases and 36% of deaths reported in Kenya (MOH Surveillance Report No. 439, 2021).

This population-based seroprevalence study was conducted in Nairobi city and its suburbs (Nairobi City County) in November 2020 to determine the level of exposure to the virus and estimate the magnitude of underreporting from government reports. By the time of the study, few population-based seroprevalence studies had been conducted in Africa (Mulenga et al., 2021). Most published serosurveys from the continent were from non-representative samples such as healthcare workers and/or patients attending healthcare facilities, or excluded children and the elderly (Abdelmoniem et al., 2021; Chibwana et al., 2020; Galanis et al., 2021; Halatoko et al., 2020; Kammon et al., 2020; Kassem et al., 2020; Kempen et al., 2020; Uyoga et al., 2021).

METHODS

Study design and eligibility

A WHO unity protocol-aligned, population-based, cross-sectional survey, using multi-stage random sampling of households across the 17 administrative sub-counties within Nairobi City County, was conducted from November 2 to 23, 2020 (WHO, 2020c). Consenting residents, irrespective of age, in selected households, who had lived in the city for at least six months preceding the survey were enrolled. Persons with reported or documented contraindications to venipuncture were excluded.

Sample size and survey procedures

The following were assumed: a seroprevalence of 5-8% (Uyoga et al., 2021), relative precision of 30%, and a design effect of 1.5 to obtain a sample size of 1,216 participants. Estimating an average of three enrolled participants per household, the study planned to enroll 406 households at identified geospatial coordinates (geocodes) but 50% more geocodes were sampled to cater for replacement households. Household selection was conducted using multi-stage random sampling. First, half of the wards in each of the 17 sub-counties were randomly selected, and then the number of households allocated to each ward was determined in proportion to its population size in the national census report (Kenya National Bureau of Statistics, 2019a). Subsequently, random geospatial coordinates (geocodes) were generated using QGIS Version 2.18.15 within each ward, corresponding to the number of allocated households (QGIS Development Team, 2009). Uninhabited areas such as the central business district, game parks, industrial parks, and restricted government compounds/institutions were excluded before generation of geocodes.

Trained study teams, which included a nurse/clinician, a laboratory technologist, and a community health volunteer, used handheld global positioning system (GPS) devices to locate households closest to the geocodes. If no one was present within the household, a revisit within 72 hours occurred before replacing the household with the next geocode within the ward (from the list of replacement geocodes). A household geocode was also replaced if the head of household declined participation of the household and there was no other consenting household near the geocode. In households where a consenting adult was present, all eligible individuals were enrolled upon providing written consent (for adults) and parental permission and assent (for minors aged ≥12 years). Revisits to enroll household members who were not present during the first visit were scheduled within seven days.

Data and sample collection

Data were electronically collected using tablets on the REDCap© platform. Apart from the number of household residents, individual data on social and demographic characteristics, medical history, presence of chronic disease, and current (time of visit), recent (last 14 days), and past (last 12 months) symptoms of respiratory illness were also collected. Respiratory illness was defined as at least two of these symptoms: cough, running nose, sore throat, shortness of breath, chills, and fever. Chronic disease was defined as a self-reported past diagnosis of hypertension, asthma, diabetes, heart disease, stroke, liver disease, kidney disease, cancer, or tuberculosis. Venous blood samples were collected from each participant, transported in a cool box to Kenya Medical Research Insti-

tute (KEMRI) laboratory in Nairobi, and sera were stored at –80 °C before testing.

Detection of SARS-CoV-2 antibodies

Detection of total IgM and IgG antibodies was carried out using the Wantai SARS-CoV-2 two-step antigen sandwich enzyme immunoassay (EIA) kit that uses polystyrene microwell strips coated with recombinant SARS-CoV-2 antigen (Wantai Biological Pharmacy Enterprise Ltd, Beijing, China). The test has high sensitivity and specificity for anti-SARS-CoV-2 total antibodies and good correlation between detection of IgG antibodies and neutralizing antibody titers when compared with other EIA tests (GeurtsvanKessel et al., 2020; Nilsson et al., 2021; Weidner et al., 2020).

Enzyme immunoassay test validation

To validate the Wantai enzyme immunoassay test kit, it was investigated whether there was cross-reactivity with antibodies to other commonly detected pathogens in patients with acute febrile illness (AFI) in sub-Saharan Africa, including malaria, as suggested in other studies (Huibin Lv et al., 2020; Njenga et al., 2020). This was conducted using blinded sera previously collected from 146 patients as follows:

i 37 patients with AFI, whose sera were collected before August 2019 (KEMRI protocol approval # 2980).
ii 20 febrile patients positive for malaria, whose sera were collected before August 2019 (KEMRI protocol approval # 2980).
iii 89 real-time reverse transcription-polymerase chain reaction (rRT-PCR)-confirmed SARS-CoV-2 patients, hospitalized in various health facilities (Kenyatta National Hospital – University of Nairobi research protocol approval #P223/03/2020).

Following a series of optimization runs in the laboratory using true positives and negatives, it was determined that 10 washes after addition of sera as opposed to five washes, as recommended in the manufacturer's instructions, were required. This was done to eliminate high background cross-reactivity detected with five washes.

All sera collected before August 2019 from malaria-positive and -negative patients with AFI were negative for SARS-CoV-2 antibodies. In contrast, 79.8% (71/89) of the PCR-confirmed COVID-19 patients tested positive for SARS-CoV-2 antibodies. The sera tested from COVID-19 patients were collected at varying time points after rRT-PCR confirmation of SARS-CoV-2 infection, hence the possibility that some of the seronegative patients were sampled during the pre-antibody phase of infection or that the antibodies had waned if sampling was done long after the primary infection. The date of the first known positive COVID-19 test before admission/isolation was available for seven of the 18 patients whose sera tested negative for SARS-CoV-2 antibodies. For these seven patients, sera were collected a median of 6 days (range 3-51 days) after the first recorded rRT-PCR confirmation.

Estimating seroprevalence

The SARS-CoV-2 seroprevalence was determined in three steps. First, respondent characteristics were summarised by antibody positivity using counts and proportions and using median and interquartile ranges (IQR) for continuous variables. Second, the seroprevalence was weighted through post-stratification by raking on sex and age group to the population structure of Nairobi. The age groups applied were 0-9 years, 10-19 years, 20-29 years, 30-39 years, 40-49 years, 50-59 years, and ≥60 years. Finally, the weighted seroprevalence was adjusted for test characteristics as provided by the manufacturer (sensitivity 94.4% and specificity 100%) (Wantai Biological, 2020). The point estimates and 95% confidence interval for the unweighted, weighted and test-adjusted seroprevalence estimates were reported. Household seroprevalence was defined as the proportion of households with at least one seropositive member.

The adjusted sub-county seroprevalence was compared to its population density (average number of persons per kilometer^2) using Spearman's correlation, and the coefficient values were reported. Mixed-effects multivariable logistic regression, accounting for survey weights and clustering at household level, was conducted to determine the association between seropositivity and sex, age category, and history of respiratory illness. Adjusted odds ratio and 95% confidence intervals were reported and two-sided p-values <0.05 were considered significant. All data cleaning and analyses were performed using R statistical software.

Determining level of underestimation and infection fatality ratio in Kenya

Underestimation of infections was defined as the extent to which SARS-CoV-2 infections within the Nairobi population (both symptomatic and asymptomatic) were detected by the Kenya national testing and surveillance system (Gibbons et al., 2014). Using the adjusted age-specific seroprevalence from this study, the number of infections in Nairobi as of 23 November 2020 was calculated in each age group and 95% confidence intervals provided. This was compared with the cumulative number of positive cases in Nairobi reported by the Kenya Ministry of Health (MoH) by the end of November 2020, to obtain age-specific underestimation levels. Age-specific multiplication factors were expressed as 'n'-fold (i.e., the value by which reported cases would be amplified to obtain the true number of infections).

Infection fatality ratio (IFR) was defined as the probability of death following infection. IFR was calculated by dividing the age-specific number of reported COVID-19 deaths (by the end of December 2020) by the age-specific number of infections calculated from this study, and expressed as the number of deaths per 100,000 infections. This approach assumed a maximal lag of 6 weeks between infection and death (Gibbons et al., 2014) and that a significant proportion of COVID-19-related deaths were captured by the Kenya MOH surveillance system, in large part because of heightened awareness of the pandemic, reporting requirements by the WHO, and better capacity to detect severe illnesses and deaths within the capital city.

Ethics statement

This study was reviewed and approved by the Kenya Medical Research Institute Scientific and Ethical Review Committee (number SSC 4098), National Commission for Science Technology and Innovation (number 827570), U.S. CDC (number CGH-ET-4/12/21-f3b82), and a reliance approval was provided by Washington State University Institutional Review Board based on in-country ethical reviews as provided for in the Code of Federal Regulations (45 C.F.R part 46 and 21 C.F.R. part 56). Administrative approval was provided by the Kenya MoH and Nairobi City County administration. All participants provided written consent or assent before enrollment.

RESULTS

Household and individual characteristics

Of 670 households that were approached, 528 (78.7%), consisting of 1,787 individuals, agreed to participate in the survey. Of

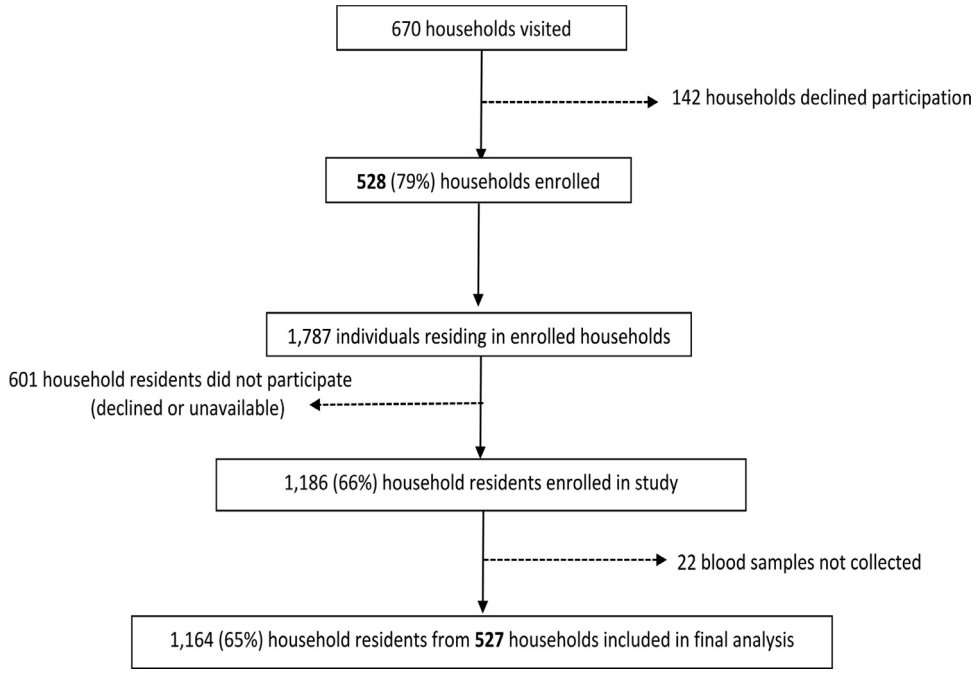

Figure 1. Study enrolment flow chart for the SARS-CoV-2 antibody prevalence survey in Nairobi City County, November 2020

these 1,787 individuals, 1,186 (66.4%) consented and were enrolled, while the rest either declined participation or were unavailable during the visits. The results presented here are based on 1,164 individuals residing in 527 households whose sera were tested for SARS-CoV-2 antibodies (Figure 1).

The median age of the participants was 26 years (IQR 14-37), with the majority (55%) aged between 20-49 years, and 64.4% were female. Seventeen (1.5%) participants were healthcare workers (Table 1). Chronic illnesses were reported by 96 (8.2%) participants, including hypertension [45/96 (46.9%)], asthma [40/96 (41.7%)], diabetes [14/96 (14.6%)], cancer [3/96 (3.1%)], and tuberculosis [3/96 (3.1%)]. Of those with chronic illness, 45% were aged ≥60 years, 29.5% were 50-59 years, and 1.7% were <20 years. One-third of respondents reported a history of respiratory illness sometime during the year 2020 (Table 1).

SARS-CoV-2 seroprevalence

The crude unweighted seroprevalence was 33.0% (95% CI 30.4–35.7), that weighted for sex and age was 32.7% (95% CI 30.0–35.5), and the adjusted seroprevalence weighted for sex and age and corrected for test characteristics was 34.7% (95% CI 31.8–37.6) (Table 2). Participants aged 20-59 years had a seroprevalence of between 38.6% and 43.3%, which was approximately two-fold higher than those aged 0-9 years (19.5%) (Table 2). Participants aged ≥60 years had a slightly higher seroprevalence (23.5% [95% CI 10•3–43•2]) compared with those aged 0-9 years, although the difference was not statistically significant. There were no significant differences in seroprevalence by sex. Working adult participants (including employed, self-employed, unskilled laborers, and healthcare workers) had a higher seroprevalence (41.7%, 95% CI 36.9-46.5) when compared with unemployed adults (35.4%, 95% CI 28.6-42.4).

On univariable analysis, participants reporting chronic diseases had higher seropositivity (39.1%, 95% CI 28.8-50.5%) compared with those without (34.3%, 95% CI 31.3-37.3%), but the difference was not statistically significant. Those reporting a history of respiratory illness during 2020 had a significantly (p=0.043) higher seroprevalence (39.0%, 95% CI 33.6-44.5%) compared with those who did not report a history of respiratory illness (31.8%, 95% CI 28.1-35.5%) (Table 2). The SARS-CoV-2 seroprevalence in 17 sub-counties of Nairobi ranged 13.2-60.4%, with a median of 33.9% (IQR 25.9, 42.2). The seroprevalence was higher in more densely populated sub-counties (Spearman's r=0.63, p=0.009) (Figure 2).

Adjusting for sex, history of respiratory illness, and reported chronic disease, the age groups of 10-19 years, 20-29 years, 30-39 years, 40-49 years, and 50-59 years had a nearly two-fold to three-fold higher odds of seropositivity compared with the 0-9 years age group (Figure 3).

Among enrolled households, 261 (49.5%) had at least one participant who tested positive for SARS-CoV-2 antibodies. Among these households, the median number of seropositive individuals per household was 1.0 (IQR 1.0-2.0; range 1.0-7.0), whereas among 324 households where two or more persons were tested, 130 (40.1%) had more than one seropositive participant.

Underestimation and infection fatality ratio

The adjusted seroprevalence of 34.7% indicated that at least 1.5 million Nairobi residents may have been infected with SARS-CoV-2 since March 2020. These findings indicate the national surveillance system detected 2.4% of all SARS-CoV-2 infections in Nairobi, reflecting an underestimation ratio of 42:1. Older age groups had lower underestimation levels, with a ratio of 17:1 for cases aged 50-59 years and 10:1 for cases aged ≥60 years, when compared to a ratio of 101:1 for cases aged <10 years.

The estimated overall IFR associated with SARS-CoV-2 infections was 40 deaths per 100,000 infections among Nairobi residents but ranged from 1 death per 100,000 infections among those aged 10-19 years to 115 deaths per 100,000 infections among those aged ≥60 years. Those aged ≥60 years had a 28-fold higher IFR than the county average (Table 3).

DISCUSSION

This population-based seroprevalence study of SARS-CoV-2 is among the first to document overall and age-stratified infection levels in a populous African city (Mulenga et al., 2021; Wiens et al., 2021). Eight months after detection of the first case in Kenya, SARS-CoV-2 individual seropositivity in Nairobi was found to be 34.7%, while approximately half of the households had at least one

Table 1
Baseline characteristics of SARS-CoV-2 serosurvey participants in Nairobi city county, November 2020.

Characteristics	Total sample (N=1,164)	Number (%)
Sex	1,164	
Female		750 (64•4%)
Male		414 (35•6%)
Age group in years	1,164	
0-9		179 (15•4%)
10-19		244 (21•0%)
20-29		265 (22•8%)
30-39		241 (20•7%)
40-49		134 (11•5%)
50-59		61 (5•2%)
60+		40 (3•4%)
Subcounty	1,163*	
Embakasi North		105 (9•0%)
Makadara		103 (8•9%)
Embakasi East		98 (8•4%)
Embakasi Central		89 (7•7%)
Kibra		83 (7•1%)
Kasarani		80 (6•9%)
Ruaraka		76 (6•5%)
Dagoretti North		73 (6•3%)
Kamkunji		71 (6•1%)
Mathare		67 (5•8%)
Dagoretti South		61 (5•2%)
Roysambu		59 (5•1%)
Embakasi South		45 (3•9%)
Westlands		44 (3•8%)
Embakasi West		42 (3•6%)
Langata		39 (3•4%)
Starehe		28 (2•4%)
Highest completed education level among adults enrolled	769*	
No formal education		40 (5•2%)
Primary education		247 (32%)
Secondary eduation		268 (35%)
Tertiary education		214 (28%)
Occupation	1,151*	
Aged <18 years		383 (33•3%)
Employed/self-employed		284 (24•7%)
Unemployed		236 (20•5%)
Unskilled labour		167 (14•5%)
Student		64 (5•6%)
Healthcare worker		17 (1•5%)
Presence of comorbidities	1,164	96 (8•2%)
Respiratory illness		
Individuals with acute respiratory illness at time of study visit	1,158*	54 (4•7%)
Individuals with acute respiratory illness in last 2 weeks	1,158*	136 (11•7%)
Individuals with acute respiratory illness in past year	1,006*	349 (34•7%)
Individuals with acute respiratory illness among their household members at the time of study visit	1,163*	112 (9•6%)

*Variable had missing values

seropositive resident. Surprisingly, the seroprevalence observed in Nairobi was higher than or in some cases comparable to those documented in countries that experienced much more severe morbidity and mortality from COVID-19 at a similar stage of the pandemic (Bajema et al., 2020; Lai et al., 2020).

In a few cities that conducted population-based COVID-19 serosurveys 6 to 9 months after the first reported case, antibody prevalence ranged 5-23% (Bajema et al., 2020; Lai et al., 2020; Pollán et al., 2020; Poustchi et al., 2020). In Africa, few population-based seroprevalence studies have been published (Kleynhans et al., 2021; Mulenga et al., 2021; Wiens et al., 2021), while most published studies from the early phase of the pandemic are from non-representative samples such as blood donors, healthcare workers, and patients attending health facilities (Adetifa et al., 2021; Chibwana et al., 2020; Kempen et al., 2020; Ndaye et al., 2021; NICD, 2020; Shaw et al., 2021; Uyoga et al., 2021). A study among >9,000 blood donors in Kenya estimated that SARS-CoV-2 seroprevalence was 22.7% in Nairobi by the end of September 2020 (Adetifa et al., 2021). This study was limited to recruitment of healthy individuals aged 15-64 years and relied on detection of IgG rather than total Ig. Given that the sample collection period coincided with the first epidemiologic peak in the country, the investigators may have slightly underestimated SARS-CoV-2 exposure in the country by failing to detect IgM. Similarly, a population-based study conducted earlier on in the pandemic in six districts in Zambia in July 2020 and designed to detect SARS-CoV-2 IgG in the population reported a much lower seroprevalence of 2.1%. However, when antibody testing was combined with PCR testing, SARS-CoV-2 population prevalence in Zambia increased to 10.6% (95% CI 7.3–13.9) (Mulenga et al., 2021). In Juba, South Su-

Table 2
Seroprevalence of SARS-CoV-2 antibodies among Nairobi city county residents, November 2020.

Characteristics	Total sample tested	Seropositive individuals	Unweighted seroprevalence[a] (95% CI)	Weighted seroprevalence[b] (95% CI)	Adjusted seroprevalence[c] (95% CI)
Overall	1,164	384	33•0% (30•4-35•7)	32•7% (30•1-35•5)	34•7% (31•8-37•6)
Sex					
Female	750	247	32•9% (29•6-36•3)	33•3% (29•5-37•1)	35•3% (31•2-39•3)
Male	414	137	33•1% (28•6-37•6)	32•0% (28•2-35•9)	34•0% (30•0-38•1)
Age group in years					
0-9	179	34	19•0% (13•2-24•7)	18•5% (13•7-23•3)	19•5% (14•6-24•7)
10-19	244	74	30•3% (24•6-36•1)	31•6% (25•0-38•2)	33•4% (26•6-40•3)
20-29	265	100	37•7% (31•9-43•6)	37•1% (31•7-42•5)	39•4% (33•8-45•3)
30-39	241	95	39•4% (33•2-45•6)	40•8% (34•4-47•3)	43•3% (36•4-50•1)
40-49	134	51	38•1% (29•8-46•3)	38•4% (29•5-47•3)	40•5% (31•2-50•3)
50-59	61	21	34•4% (22•5-46•3)	36•6% (23•2-50•0)	38•6% (25•0-53•0)
60+	40	9	22•5% (9•56-35•4)	22•6% (7•0-38•1)	23•5% (10•3-43•2)
Subcounty					
Embakasi North	105	42	40•0% (30•6-49•4)	39•8% (30•6-49•0)	42•2% (32•7-52•5)
Makadara	103	32	31•1% (22•1-40•0)	33•3% (24•1-42•5)	35•2% (25•6-45)
Embakasi East	98	30	30•6% (21•5-39•7)	30•7% (21•7-39•8)	32•5% (23•2-42•3)
Embakasi Central	89	24	27% (17•7-36•2)	26•1% (16•7-35•4)	27•7% (18•4-38•5)
Kibra	83	37	44•6% (33•9-55•3)	42•8% (32•4-53•3)	45•3% (34•1-56•1)
Kasarani	80	11	13•8% (6•2-21•3)	15•4% (7•3-23•4)	16•2% (8•6-25•2)
Ruaraka	76	33	43•4% (32•3-54•6)	43•4% (32•2-54•7)	46•2% (34•1-57•3)
Dagoretti North	73	28	38•4% (27•2-49•5)	36•6% (26•2-47•1)	38•6% (27•7-49•1)
Kamkunji	71	28	39•4% (28•1-50•8)	34•1% (23•1-45•2)	36•1% (25•0-48•5)
Mathare	67	31	46•3% (34•3-58•2)	50•1% (37•7-62•5)	52•7% (39•1-65•8)
Dagoretti South	61	19	31•1% (19•5-42•8)	31•8% (19•6-44•0)	33•9% (21•3-46•3)
Roysambu	59	8	13•6% (4•8-22•3)	12•5% (4•1-20•8)	13•2% (5•7-23•4)
Embakasi South	45	13	28•9% (15•6-42•1)	27•1% (13•9-40•3)	28•7% (15•7-41•9)
Westlands	44	8	18•2% (6•8-29•6)	18•2% (6•7-29•7)	19•0% (8•5-30•9)
Embakasi West	42	24	57•1% (42•2-72•1)	57•3% (41•9-72•7)	60•4% (42•8-74•7)
Langata	39	10	25•6% (11•9-39•3)	21•9% (9•8-34•0)	23•3% (11•7-36•2)
Starehe	28	6	21•4% (6•2-36•6)	22•9% (7•0-38•8)	25•9% (11•7-46•4)
Highest completed education level among adults enrolled					
No formal education	40	14	35•0% (20•2-49•8)	36•8% (20•8-52•9)	38•8% (22•3-54•5)
Primary education	247	91	36•8% (30•8-42•9)	37•2% (30•7-43•7)	39•6% (32•7-46•5)
Secondary eduation	268	105	39•2% (33•3-45•0)	39•0% (33•2-44•8)	41•4% (35•2-47•7)
Tertiary education	214	74	34•6% (28•2-41•0)	36•6% (30•3-42•9)	38•8% (32•1-45•7)
Missing data					
Occupation					
Aged <18 years	383	94	24•5% (20•2-28•9)	23•3% (19•2-27•4)	24•5% (20•4-29•0)
Employed/self-employed	284	120	42•3% (36•5-48•0)	43•0% (37•2-48•8)	45•6% (39•3-51•7)
Unemployed	236	77	32•6% (26•6-38•6)	33•3% (26•9-39•7)	35•4% (28•7-42•2)
Unskilled labour	167	56	33•5% (26•4-40•7)	33•3% (26•2-40•4)	35•2% (27•8-43•2)
Student	64	23	35•9% (24•2-47•7)	37•0% (25•5-48•5)	39•1% (27-52•2)
Healthcare worker	17	6	35•3% (12•6-58•0)	37•6% (12•8-62•3)	38•9% (15•0-64•3)
Presence of comorbidities					
Yes	96	36	37•5% (27•8-47•2)	36•9% (26•6-47•2)	39•1% (28•8-50•5)
No	1,068	348	32•6% (29•8-35•5)	32•3% (29•6-35•2)	34•3% (31•3-37•3)
Individuals with acute respiratory illness in last 2 weeks					
Yes	136	45	33•1% (25•2-41•0)	33•1% (25•3-40•9)	35•1% (26•9-43•3)
No	1,022	334	32•7% (29•8-35•7)	32•3% (29•4-35•2)	34•2% (31•2-37•3)
Individuals with acute respiratory illness in past year					
Yes	349	129	37•0% (31•9-42•0)	36•7% (31•6-41•8)	39% (33•6-44•5)
No	657	200	30•4% (27•0-34•1)	30•0% (26•5-33•6)	31•8% (28•1-35•5)
Individuals with acute respiratory illness among their household members at the time of study visit					
Yes	112	41	36•6% (27•7-45•5)	35•7% (26•9-44•5)	37•8% (28•6-46•9)
No	1,051	343	32•6% (29•8-35•6)	32•4% (29•6-35•3)	34•3% (31•3-37•4)

[a] Sample seroprevalence
[b] Seroprevalence adjusted for county population age and sex structure
[c] Weighted seroprevalence further adjusted for test performance (i.e. sensitivity and specificity)

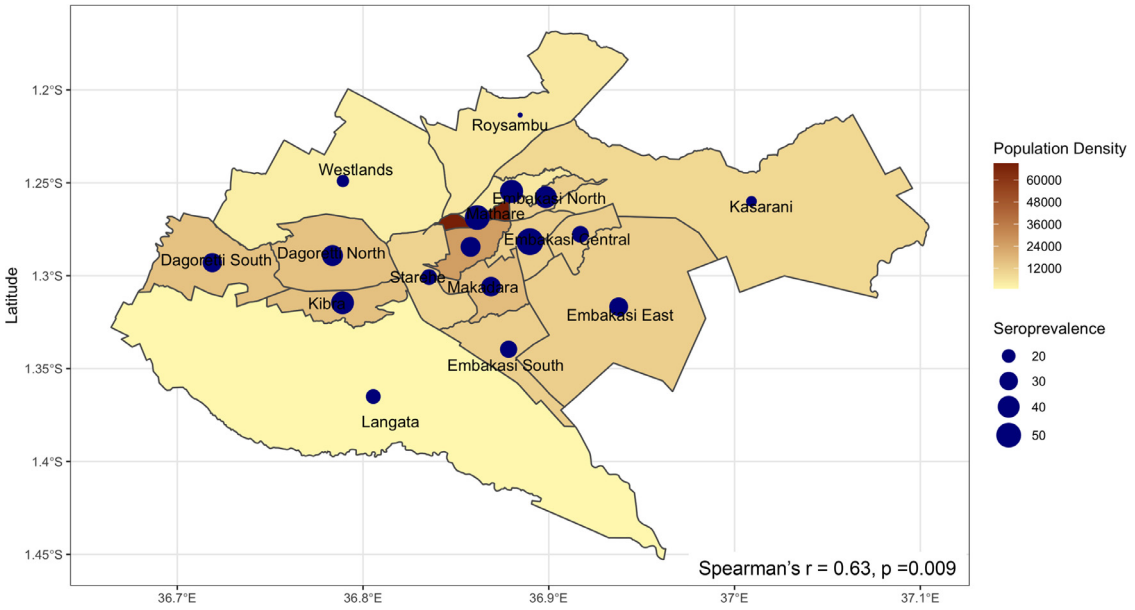

Figure 2. Sub-county seroprevalence positivity and population density per kilometre^2.

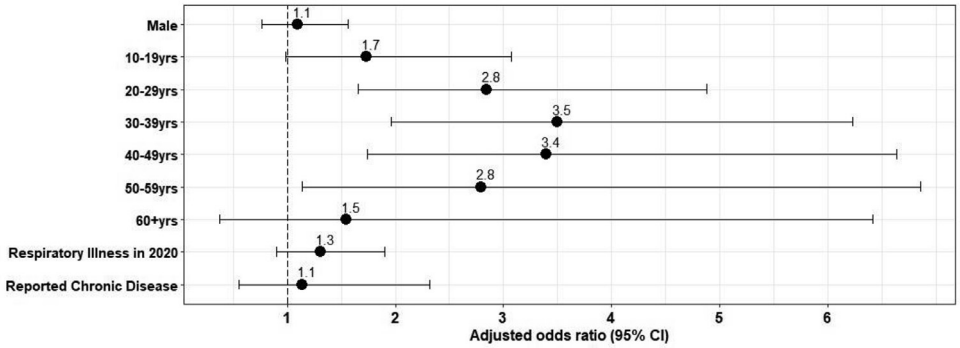

Figure 3. Multivariable mixed effects logistic regression of factors associated with SARS-CoV-2 seropositivity, Nairobi city county.
The 0-9 years group was used as the reference age category. The adjusted odds ratios for each variable are indicated as a black dot, with the confidence intervals on either side.

Table 3
Estimated age-specific infections, case ascertainment probabilities, and infection fatality rates in Nairobi city county, November 2020.

	A	B	C			
Age category	**No. of estimated infections as at November 2020 from seroprevalance study Mean (95% CI)**	**No. of COVID cases captured by surveillance system as at 30 November 2020**	**No. of deaths captured by surveillance system as at 31 December 2020**	**Proportion of infected cases reported by surveillance system (B/A x 100%)**	**Multiplication factor (A/B)**	**Estimated Infection Fatality Ratio (C/A)**
0-9	188,053 (187,883-188,224)	1,858	18	1•0%	101	0•010%
10-19	244,156 (243,979-244,333)	1,313	3	0•5%	186	0•001%
20-29	452,978 (452,744-453,211)	7,702	28	1•7%	59	0•006%
30-39	363,887 (363,684-364,091)	11,183	73	3•1%	33	0•020%
40-49	174,372 (174,228-174,516)	6,932	96	4•0%	25	0•056%
50-59	74,197 (74,103-74,291)	4,381	126	6•2%	17	0•177%
60+	27,069 (27,010-27,128)	2,812	269	12•1%	10	1•153%
Overall	1,524,886 (1,524,439-1,525,333)	36,354*	613	2•4%	42	0•040%

*Included 173 reported cases without date of birth data

dan, researchers detected significant SARS-CoV-2 IgG titres in one-third of residents by August 2020, suggesting that the Ministry of Health detected <1% of all SARS-CoV-2 infections in the country. In South Africa, 5-9% of rural residents and 23-31% of urban residents had detectable SARS-CoV-2 antibodies by November-December 2020, and it was estimated that the surveillance system only detected 5% of all SARS-CoV-2 infections (Kleynhans et al., 2021). The high prevalence of SARS-CoV-2 infections in Nairobi, Juba, South Africa, and Zambia suggests that the widely held perception that the pandemic was less severe in Africa was likely not the result of lower virus transmission. Instead, the current findings suggest that >40-fold underestimation of cases by the na-

tional surveillance system, and lower morbidity and mortality in the relatively younger African population may be the primary contributing factors to the perceived lower severity of the pandemic in the continent (Diop et al., 2020; Maeda and Nkengasong, 2021; Njenga et al., 2020; Tso et al., 2021)

Overall, the Kenya national surveillance system detected one case for every 42 SARS-CoV-2 infections (2.4%) in Nairobi, a number that decreased to less than one for every 100-190 infections among individuals aged <20 years, who constitute most of the population in the country (median age 20 years) (Kenya National Bureau of Statistics, 2019b). This suggests that the mitigation measures that the government implemented, such as isolation of known positive cases, probably had minimal effectiveness in slowing the pandemic, partly because most of the infections were likely mild or asymptomatic and thus not detected by preferential testing for symptomatic cases. This was further compounded by low turnout for testing, which was attributed to low healthcare utilization in Kenyan urban communities, as has been shown in previous studies (Otieno et al., 2020).

The estimated IFR in this study (40 deaths per 100,000 infections) was at least 10 times lower than previous estimates for East Africa and 20-25 times lower than Europe or the USA (Ghisolfi et al., 2020). These findings suggest that despite high SARS-CoV-2 transmission, Kenya's youthful population may have contributed to lower rates of severe COVID-19 (Kenya National Bureau of Statistics, 2019b). An important finding was that the estimated IFR for individuals aged ≥60 years was >28-fold higher than the average IFR for other age groups and twice as high as the estimated COVID-19 IFR for East Africa, suggesting that the elderly population may be more severely affected than previously thought and underscoring the urgent need for vaccination in this group (Ghisolfi et al., 2020). The other possible factors that may contribute to the low morbidity and mortality of COVID-19 in Africa include the presence of cross-reacting antibodies to other coronaviruses that have not been adequately investigated (Diop et al., 2020; Njenga et al., 2020; Tso et al., 2021).

The population included in this survey represented a broad range of demographics and socioeconomic statuses, including residents in affluent and less densely populated sub-counties and residents in crowded sub-counties largely comprising informal settlements. Higher seroprevalence was observed in more densely populated areas, which likely lack improved sanitation facilities and basic infrastructure, suggesting higher transmission associated with challenges in applying mitigation measures such as social distancing and good hygiene practices. The data suggest lower than expected transmission within households. In seropositive households where more than one household member had been tested, 40% of households had more than one seropositive household member. Although SARS-CoV-2 transmission is higher in indoor settings compared with outdoor settings (Bulfone Tc et al., 2021), household secondary attack rates are estimated to be 16.6% (Madewell et al., 2020), which is in keeping with the current findings of what appeared to be low transmission within households.

This study had several limitations. A few studies have reported loss of SARS-CoV-2 antibodies in previously seropositive individuals, perhaps associated with a weak immunologic response or low infecting viral load (Dobi et al., 2020). While it used a validated total antibody test kit, asymptomatic and mild cases that more commonly occur in younger individuals have been shown to evoke lower titers of antibodies, which may be missed by EIA tests, such as that used in this study. It may also have missed acutely infected individuals who had not yet developed IgM or IgG antiviral antibodies. These limitations would bias towards underestimating population prevalence. Conversely, cross-reactivity from pre-existing antibodies may have resulted in false positives and higher seroprevalence estimates. Although the ELISA assay used in this study was not assessed for cross-reactivity, an evaluation of COVID-19 serological assays reported specificity of 99% for the Wantai SARS-CoV-2 total Ig assay that was used; therefore, the number of false-positives was likely minimal (GeurtsvanKessel et al., 2020; Lassauniere et al., 2020).

The study approach may have included fewer individuals who spent most of the daytime hours at work, thus introducing selection bias, particularly if such individuals were at higher risk of exposure. Due to a nighttime curfew, participant enrollment could not take place past the evening hours. One-fifth of the households that were approached declined participation, which could have led to bias if the households had characteristics related to SARS-CoV-2 exposure that were different from those households that were enrolled. The total population size for each ward was used to determine the number of households to be sampled from each sub-county. It is possible that the use of ward population rather than the number and size of households per ward to determine the number of households to be enrolled per ward/sub-county may have resulted in differences in the likelihood of an individual being selected for the study, particularly if there were significant differences in household size across sub-counties. However, this risk was determined to be minimal, as there is little difference in average household size between sub-counties in Nairobi.

In determining presence of respiratory illness, a broad definition of respiratory illness was used that did not include loss of taste or smell, which could have led to an underestimation of COVID-19-like illness. Finally, although it was assumed that detection of COVID-19-related deaths among deceased individuals in Nairobi was adequately captured by the surveillance system, a postmortem study conducted in Lusaka, Zambia, observed that six of 70 COVID-19-related deaths identified between June and September 2020 had been tested for SARS-CoV-2 before death and up to three-quarters of all COVID-19-related deaths occurred in the community where none had been tested for SARS-CoV-2 before death (Mwananyanda et al., 2021). Similarly, the WHO and other studies estimate that global COVID-19 deaths are underreported by a factor of between 1.1-1.7, even in countries with the best mortality surveillance systems (IHME, 2021; WHO, 2021b).

Therefore, the low IFRs described in this study, which probably represent floor estimates, should be interpreted with caution, as the magnitude of underreporting of COVID-19-related deaths cannot be confidently determined (Tembo et al., 2021).

In conclusion, this study demonstrates extensive SARS-CoV-2 transmission in Nairobi during the first eight months of the pandemic, resulting in more than one-third of residents and half of the identified households being exposed to the virus. There was significant underreporting of infections by the national surveillance system and a lower than expected mortality rate, attributed in part to the youthful Kenyan population.

Disclaimer

The findings and conclusions in this study are those of the authors and do not necessarily represent the official position of the US NIH, KEMRI, Kenya MOH, or US Centers for Disease Control and Prevention.

Author contributions

Conceptualization: IN, JD, NO, PA, LM, CNW, BN, OO, CN, MKN, EO. Data curation: DM, EO. Formal analysis: IN, JD, BN, DM, MKN, EO. Funding acquisition: EH, MKN, MB, AHR, EO. Investigation: IN, JD, EH, NO, MM, CN, HM, DM, DO, MDA, EO. Methodology: IN, JD, NO, PA, LM, CNW, BG, BN, OO, CN, HM, DM, OA, MKN, EO. Project administration: IN, JD, HM, EO. Resources: EH, MM, OA, MKN, MB, AHR, EO. Software: DM. Supervision: IN, JD, PA, LM, CNW, OO, CN,

OA, MKN, EO. Validation: IN, JD, MM, BG, JG, MKN, EO. Visualization: IN, JD, CNW, JG, DM, MKN. Writing – original draft: IN, JD, CNW, DM, RB, JG, MKN, EO. All authors reviewed and edited the manuscript.

Competing interests

The authors declare that they have no competing interests.

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Role of the funding source

The funder did not play any role in the study design, collection, analysis and interpretation of data, manuscript writing or the decision to submit the paper for publication.

Ethics approval and consent to participate

This study was reviewed and approved by the Kenya Medical Research Institute Scientific and Ethical Review Committee (number SSC 4098), National Commission for Science Technology and Innovation (number 827570), U.S. CDC (number CGH-ET-4/12/21-f3b82), and a reliance approval provided by Washington State University Institutional Review Board. All participants provided written consent or assent before enrollment.

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