SARS-CoV-2 Antibody Seroprevalence in Yaounde, Cameroon

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# Summary

## Background

The COVID-19 pandemic has led to severe strains on health systems and unprecedented levels of societal disruption. While Sub-Saharan Africa has not been completely spared, the epidemic in this region appears to have been relatively less severe. The reasons for the mitigated impact are not fully understood. A sufficient explanation will require an accurate assessment of populations’ exposure to the virus and of the typical manifestations of infection.

## Methods

We conducted a cross-sectional, community-based serosurvey from October 14 to November 26, 2020 in a densely-populated health district (Cité Verte) of the city of Yaounde, the capital of Cameroon. Households were randomly selected from an OpenStreetMap building footprint, and inhabitants between 5 and 80 years in each household were surveyed. The Abbott Panbio IgM/IgG SARS-CoV-2 antibody rapid test was administered, along with a questionnaire on illness symptoms, health-seeking behaviour and pandemic impact. Final seroprevalence estimates were reweighted based on the age-sex distribution of the Yaoundé population, and were adjusted for test specificity and sensitivity.

## Findings

SARS-CoV-2 appears to have circulated widely in the city of Yaoundé, affecting about a third of the population in the *Cité Verte* district (adjusted IgG seroprevalence: 29.2% [24.3% - 34.1%]). More than 60% of those with antibodies reported having no acute symptoms over the pandemic period, and only one individual reported a COVID-19-related hospitalization. In addition to the severe spread of the disease, the economic impact was also severe, with 85% of households reported a drop in household income over the pandemic period.

## Interpretation

The observed anti-SARS-CoV-2 IgG seroprevalence seen in Cité Verte is much higher than suggested by official case counts...implying greater than 98% of infections went undiagnosed and unreported. The low rate of symptomatic infection and hospitalization indicate a relatively mild disease manifestation in this population. Given the low testing, some of these should be taken with some skepticism.

The widely reported reductions in household income may affect other health outcomes.

## Funding

German Corporation for International Cooperation GmbH and Canton Geneva.

# Research in context

## Evidence before this study

We used the PubMed builders to find relevant preprints or published papers available as at Feb 14, 2020. We used the search terms “SARS-CoV-2”, “seroprevalence”, “antibodies” and “Africa” (Exact PubMed search term: “'SARS-CoV-2'[Title/Abstract] AND ('seroprevalence'[Title/Abstract] OR 'antibodies'[Title/Abstract]) AND ('Africa'[Title/Abstract] or 'African'[Title/Abstract])”), and read the abstracts of the 25 returned papers. We also consulted the University of Calgary SeroTracker ([***https://serotracker.com/en/Explore***](https://serotracker.com/en/Explore)), which highlights ongoing and concluded serosurveys.

To date, very few studies have assessed the SARS-CoV-2 antibody seroprevalence in Sub-Saharan African countries. The majority of published surveys have been performed on healthcare workers and other special populations. These have found quite high seroprevalences, much higher than would be

The only studies among the lay population have been in Niger State, Nigeria (which shows a 25.4% IgG seroprevalence in June, 2020, blood donors in Kenya (population-weighted seroprevalence of 4.3% in April-June) and blood donors in South Africa

## Added value of this study

This study is one of the first to assess the prior exposure to SARS-CoV-2 of a random sample of residents of an African country. We used building footprint sampling to randomly select survey participants, and used the lateral-flow Abbot PanBio SARS-CoV-2 IgG/IgM test to assess SARS-CoV-2 seroprevalence. Our findings indicate a relatively high seroprevalence (IgG: 29.2%) and a relatively low level of symptomatic infection (< 40%).

## Implications of all the available evidence

Our findings, along with others reported on the continent, show that official PCR-confirmed case reports likely produce a manyfold underestimate of SARS-CoV-2 in African countries. The data point towards a widespread, but largely asymptomatic epidemic.

The seroprevalence found here, for all ages, was at 29.2%, is more than 50 times the official case count, indicating that the epidemic has spread much more widely than was expected. This is higher than has been seen in any other published seroprevalence study in an African country, but is line with the Nigeria data (unpublished)

In contrast to what has been found in other regions, seroprevalence here appears to increase with age, with the highest seroprevalence seen among those above 65 years of age. This may reflect the slower waning of the antibody response in these respondents.

This study fills an important gap in the knowledge of the burden of COVID-19 in Cameroon, providing the first data on a random sample of households in the country, and one of the first in the African continent.

# Introduction

Given the severe burden that the SARS-CoV-2 virus has implied for many countries, it has become

burden spread of the epidemic in Europe and the Americas, and the handicapped response by countries with the richest health systems, the outlook for less developed countries, and sub-Saharan Africa in particular, seemed dire. High numbers of deaths were expected due to weaknesses in health systems, difficulties in enforcing hygiene measures, and perceived health vulnerabilities of the population.1,2 But the trajectory of the epidemic on the continent appears to have gone against expectation. Despite having over 2,200,200 infections as of December 1,3 Africa remains the least affected region and the mortality rate, even if not well documented, remains lower than expected.2

Multiple hypotheses have been advanced to explain the seemingly mild trajectory of the COVID-19 epidemic in Africa: researchers have pointed to the warm climate conditions across sub-Saharan Africa (apart from South-Africa), the continent’s young population (median age of 19 years), and cross-reactive or non-specific immunity from other infections as possible mitigating factors.2 But an informed explanation of the epidemic trajectory requires, first and foremost, accurate numbers on the actual extent of population infection. And, as has been observed elsewhere,4 the officially reported case counts in Africa may significantly underestimate the extent of the viral propagation.2 In this context, the use of serological antibody tests to detect exposure to SARS-CoV-2 is valuable. Was the spread of the virus largely impeded, or has virus spread widely without the majority of the population exhibiting clinical symptoms?

In this context, the use of serological antibody tests to detect exposure to SARS-CoV-2 is valuable. Point-of-care lateral-flow immunoassays offer the opportunity to test representative samples of individuals

A number of validated SARS-CoV-2 antibody tests now exist on the market,5 and some of these are which are affordable, easy to use and provide quick results. Although concerns about sensitivity and specificity remain, these antibody tests offer the opportunity to more accurately assess the prior infection rate of populations in regions where PCR-based testing has been uncommon.4

This report presents the protocol and results of our study using a lateral-flow immunoassay to assess the seroprevalence of anti-SARS-CoV-2 IgG and IgM antibodies in a region of Yaounde, the capital of Cameroon.

Notable serological studies on the continent include a study of blood banks in Kenya in April-June 2020, which showed an IgG seroprevalence of 4.3% (2.9% to 5.8%)6, or from Niger State in Nigeria in June 2020 which showed a seroprevalence of 25.4%7, healthcare workers in Ibadan 45%9 , healthcare workers in urban Malawi in May-June 2020 showed an IgG seroprevalence of 12.3% (8.2% to 16.5%)8, and blood donors in South Africa in January 2021 (a range from 31.8% in cities in provinces in South Africa to 62.5%). Only 38.9% of participants experience acute flu-like symptoms since the start of the pandemic.

These indicate that infection rates could be higher in some settings, but only the latter was designed as a representative sample and serology-based estimates are sparse in SSA.

# Methods

## Sampling

Based on power calculations with an assumed prevalence of 20%, a precision of 5% and a confidence level of 95% we estimated a required sample of 245 participants. The final target population was increased to 1000 people (250 households) to improve precision.

Households were randomly selected [**HOW? Dr. Ray**] from a pre-processed set of residential buildings on an OpenStreetMap footprint10. In cases where non-residential buildings were encountered by the surveyors, or households were unwilling to participate, the residential building to the right of the sampled one was used as a replacement.

In each household, all individuals between 5 and 80 years were included if they: (a) were living in the selected household, (b) had been present in the household for at least 14 days, and (c) could give written informed consent (or had an adult guardian who could give consent). People with severe psychiatric illness or temporary visitors to the household were not considered for inclusion.

## Testing

Study surveyors used the Abbott Panbio™ COVID-19 IgG/IGM Rapid Test Device, an immunochromatographic test for the qualitative detection of IgG and IgM antibodies to SARS-CoV-2 (with a manufacturer-estimated sensitivity and specificity of the test are 95.8% and 94% respectively).

The tests were performed on capillary blood which was collected from a finger prick from all the consenting participants. A questionnaire was also administered in tandem with the testing.

## Data analysis

### Seroprevalence estimation

Seroprevalence values were weighted within each age or sex stratum to match the age-sex distribution of the Yaounde population, as sourced from the 2018 Cameroon DHS11.

We used the Rogan-Gladen formula to adjust IgG seroprevalence estimates to account for test performance.12 sensitivity estimate provided by Batra and others’ validation study of the Abbott test, which found a sensitivity of 91.5% (75 correct diagnoses out of 82 samples) when applied on sera collected from hospitalized COVID-19 patients 14 – 56 days post symptom onset.13 We measured specificity by applying the test on a panel of 246 pre-pandemic (2017) samples from hospital patients in Yaounde. The IgG test correctly diagnosed 230 of 246 samples (93.5% specificity).

### Risk factor analysis

For seropositivity risk factor analysis, we used logistic models with household random effects to account for within-household clustering. In the logistic models, the following prospective risk factors were analysed: sex, age, education, BMI group, occupation, contact with an international traveller since March 1st, contact with a suspected or confirmed COVID case since March 1st, presence of comorbidities (combining hypertension, respiratory illness, diabetes, tuberculosis, HIV, cardiovascular illness and “other illnesses” which were not explicitly listed in questionnaire), whether or not the respondent is the breadwinner, adherence to social distancing rules, location of the household (one of nine health zones), number of household members, and whether or not there are children in the household. Each variable was first analysed in a univariate model. Then variables with p < 0.10 for at least one factor level were entered into the multivariable analysis. All such variables are shown in the regression tables.

## Ethical considerations

The study protocol obtained the ethical clearance and the administrative authorization of the Ministry of Health of Cameroon. Every adult participant (21 years or above) signed an informed consent. For minors, a person with parental authority was asked to sign the consent form and, if the age was equal to or above 15 years, an assent was also requested. Questionnaires were coded and names of participants were recorded in a confidential list available only to the study team. Before starting the study, all the team members were trained on research ethics, good clinical practices and study protocol and procedures.

# Results

Out of 255 household visited during the survey period, 192 (75%) agreed to participate in the study,

for a total of 1,007 respondents (figure 1). However, in 37 cases (4%), some members of the household, despite responding to the questionnaire, refused the test. Data was collected from

However, for 37 (4%) individuals,

Of the 192 included households, 128 were the originally sampled by the random method, while the remaining 64 (33%) were replaced through standard procedures because the identified buildings were non-residential (Figure 1). All participants were to be tested for SARS-CoV2-antibodies, but

Participants reflected the age-sex distribution of the Yaounde population: Participants had a median age of 26 (IQR 14-38) years and 570 (56.6%) were women, which closely reflects the distribution of the Yaounde population (Supplementary Fig 1). The demographic characteristics of respondents are summarized in Table 2.

Of the 970 respondents tested for IgG and IgM antibodies, 340 (35.1%) were seropositive for at least one of the antibodies (Figure 1). IgM seropositivity was quite low, and the overlap between IgG and IgM seropositivity was minimal; among the 32 individuals who were IgM positive, only 6 were also IgG positive.

Figure 3 shows distribution of positive serology in the different areas of *Cité Verte* district. This distribution may be partly explained by household size. The figure makes clear that the zone with the smallest households, Cité Verte (mean size 5.5 residents), is also the zone with the lowest prevalence. Therefore, spread within the household or living environment is a driving factor for exposure to SARS-CoV-2 in the Cameroonian community.

Adjustments for diagnostic test performance slightly increased the Tables 3 and 4 show the seroprevalence adjustments for the age-sex distribution of the Yaounde population and for diagnostic test performance. Since women were oversampled as compared to their proportion in the general population (56.6% of sample was female), and women also showed a lower seroprevalence, the crude estimates were downwardly biased. Thus, population weighting increased the overall estimate of seropositivity in nearly all age categories for both the IgG and IgM assays. Adjustments for specificity and sensitivity also increased the estimates slightly.

Variables that were associated with SARS-CoV-2 seropositivity in univariable analyses included sex, educational level, BMI group, contact with an international traveler, contact with a suspected or confirmed COVID case, health zone, and number of household members (Table 5). Age, sex, and any variables where a p-value below 0.1 was observed, were carried over into the multivariate analysis. The results are shown in the last two columns of Table 5. These are largely in line with the findings from the univariate analysis.

Three hundred and two respondents (30%) reported having at least one symptom compatible with SARS-CoV-2 infection (frequency of symptoms is reported in Figure 4).

Among those who tested positive for anti-SARS-CoV-2 IgG, 40% reported at least one symptom. Among these, the most common symptoms reported were fever (18.5%), headache (17.5%), cough (17.9%) and runny/stuffy nose (12.3%), and all four were significantly more common in seropositive than in seronegative individuals (Figure 5). Surprisingly, anosmia or ageusia was only experienced by 4.3% of the seropositive respondents (versus 1.9% of seronegative respondents).

Based on the WHO criteria for COVID-suspect symptoms13, 51 of 328 IgG/IgM seropositive individuals (15.6%) and 64 of 642 seronegative individuals (10%) reported COVID-suspect symptoms, suggesting that the WHO criteria may lack specificity for identifying true COVID-19 symptoms—these might be common symptoms with other respiratory infections or similar pathologies.

Concerning the effect of the epidemic on the households, 163 households (85%) reported that their income had fallen since March 1st. Households where the head was a salaried worker or had a university degree appeared to be least financially affected, with only 67% and 63% reporting an income reduction (Figure 10).

# Discussion

These seropositivity estimates seen here are in line with observed values in other regions. Many countries have now conducted large seroprevalence studies in the general and specific populations, and seropositivity has ranged from as low as 3% to more than half of those studied. In the African context, a few studies have been reported. A survey in Kenya among blood donors found a global adjusted prevalence of 4.3% very early in the epidemic. Another report in Niger State, Nigeria (data not yet published) reported a prevalence of 25.4%.

Notably, there is evidence of pre-existing reaction to SARS-CoV-2 antibody testing in African populations: 23.7% (32/135) of pre-pandemic samples from a study in Gabon (a neighbouring country to Cameroon) were found to have humoral cross-reactivity to SARS-CoV-2. Thus, adjusting for test specificity, as we have done here, is crucial to arrive at accurate findings about population exposure to SARS-CoV-2

It is important to note that because anti-SARS-CoV-2 immunoglobulins wane over time (one study has reported a 90% decline in levels 3 months from exposure), antibody seroprevalence is not a perfect proxy for past infection with the virus.

Finally, the seroprevalence results here should be interpreted with some caution, since our study was not able to validate the test sensitivity on local PCR-positive sera, relying instead on a validation study from a European population

Therefore, being of male sex, being obese (as defined by a BMI >30), and having five or more household members, are the three independent factors related to anti-SARS-CoV-2 IgG seropositivity. Evidence-based interventions for epidemiological surveillance may choose to focus on these individuals within the communities.

11 households reported a death during the period of the pandemic, of which none was reported to be known COVID-19 related. And \_\_ individuals reported hospitalization, of which only one was reported to be COVID-19 related. This would imply a hospitalization rate of < 0.3%, although this should be interpreted with caution, since self-reports of COVID-19 hospitalization may be subject to stigma avoidance bias, and the shortage of tests may mean that individuals with COVID-19 went undiagnosed.

“Concerns have been raised regarding the use of pointof-contact antibody tests for clinical decision making and for so-called immune passports. However, use of such tests for large-scale, population-based, seroprevalence studies is less controversial, provided that sensitivity and specificity are sufficiently high and appropriately corrected for.37,38 “ - https://www.thelancet.com/pdfs/journals/langlo/PIIS2214-109X(20)30387-9.pdf

“Our results have strong face validity, showing a high correlation with reported death rates, an increase over time as the pandemic progressed, and distribution by age, socioeconomic status, and household size that would be expected. “ https://doi.org/10.1016/ S2214-109X(20)30387-9

Important doubts exist regarding the use of rapid point-of-care antibody tests in clinical settings, due to their far-from-perfect specificity values (CITE). This is valid as a worry regarding clinical use, but it less important for population-based surveys, where estimates can be adjusted for sensitivity and specificity, as we have done here.

Confidence in our results is increased by the fact seropositivity showed the correlations with household size and COVID-like symptoms that would be expected.

Understanding what populations have already developed antibodies to SARS-CoV-2 is vital for public health planning. It allows to understand whether large-scale spread––additional waves of infection––are still possible. It also provides data that allows us to do a retrospective review of public health prevention measures: that is, it allows us to ask questions like: to what extent were these measures effective? And, how can hygiene measures be reinforced for future epidemics.

By studying a random sample of participants in a West African city, this study gives an idea of what levels of spread might be reasonable to expect in similar cities in Africa where serosurveys have not been done. The analysis therefore provides valuable data to inform practice and research.

While the estimates arrived at in this cannot serve as a stand-in for other African cities where serosurveys have not been done, we should expect that the extent of spread here (and especially the high degree of underreporting) should not be too far from what might be expected in similarly-dense African cities with like climates.

Other studies have shown similarly high extents of spread in African cities. A preprint from Nigeria showed that up to XX% of individuals in Niger state were positive for anti SARS-CoV-2 antibodies.



**Figure 1:** Recruitment process and study profile

**Table 1:** Sociodemographic characteristics of the participants in the final sample of 1007 study participants. N is the number of individuals in each stratum. IQR: Interquartile range. BMI: Body mass index

|  |  |  |
| --- | --- | --- |
| **Characteristic** | **N** | **%** |
| Age | Median:26 | IQR:14 - 38 |
| ***Age groups*** | | |
| 5 - 14 | 248 | 24.6 |
| 15 - 29 | 339 | 33.7 |
| 30 - 44 | 218 | 21.6 |
| 45 - 64 | 156 | 15.5 |
| 65 + | 46 | 4.6 |
| ***Sex*** | | |
| Female | 570 | 56.6 |
| Male | 437 | 43.4 |
| ***BMI*** | | |
| < 18.5 (Underweight) | 164 | 16.3 |
| 18.5 - 24.9 | 414 | 41.1 |
| 25 - 30 (Overweight) | 259 | 25.7 |
| > 30 (Obese) | 166 | 16.5 |
| Unknown | 4 | 0.4 |
| ***Education Level*** | | |
| Secondary | 442 | 43.9 |
| Primary | 328 | 32.6 |
| University | 157 | 15.6 |
| No formal instruction | 53 | 5.3 |
| Doctorate | 20 | 2 |
| Other | 7 | 0.7 |
| ***Profession*** | | |
| Student | 418 | 39.5 |
| Small trader | 222 | 21 |
| Businessperson | 131 | 12.4 |
| Home-maker | 74 | 7 |
| Unemployed | 73 | 6.9 |
| Salaried worker | 60 | 5.7 |
| Retired | 35 | 3.3 |
| Other | 46 | 4.3 |
| ***Chronic conditions*** | | |
| Hypertension | 37 | 3.6 |
| Respiratory illness | 17 | 1.7 |
| Diabetes | 11 | 1.1 |
| Other | 951 | 93.6 |



**Figure 2:** **Crude IgG and IgM seroprevalence: A.** Euler diagram showing seropositivity of respondents by antibody test. **B.** Seropositivity of respondents by antibody test and age-sex stratum. Percentage labels indicate the proportion of each stratum that is IgG and/or IgM seropositive. **C.** Household and geographic variation in seropositivity. Fill colour indicates the neighbourhood seroprevalence (IgG and/or IgM). Pie charts indicate household size, household location and the proportion of the household that is seropositive. Pie charts are dodged to avoid overlap and to preserve location anonymity. Five households are not shown due to improperly-coded or missing coordinates.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **n** | **Seropos.** | **Seroprevalence (95% confidence interval)** | | |
|  |  |  | *Crude* | *Population-weighted* | *Weighted, test-adjusted* | |
| **Total** | 971 | 302 | 31.1% (28.3 - 34.1) | 31.3% (28.4 - 34.3) | 29.2% (24.3 - 34.1) | |
| **Female** | 549 | 154 | 28.1% (24.5 - 32.0) | 28.0% (24.4 - 31.9) | 25.3% (20.0 - 31.2) | |
| **Male** | 422 | 148 | 35.1% (30.7 - 39.7) | 34.6% (30.2 - 39.3) | 33.1% (27.6 - 40.5) | |
| **5 - 14** | 241 | 69 | 28.6% (23.3 - 34.6) | 28.7% (23.3 - 34.7) | 26.1% (18.9 - 34.1) | |
| **15 - 29** | 325 | 98 | 30.2% (25.4 - 35.4) | 30.7% (25.9 - 35.9) | 28.5% (21.4 - 35.1) | |
| **30 - 44** | 212 | 69 | 32.5% (26.6 - 39.1) | 32.7% (26.7 - 39.3) | 30.8% (22.9 - 39.5) | |
| **45 - 64** | 153 | 51 | 33.3% (26.4 - 41.1) | 34.1% (27.0 - 41.9) | 32.5% (22.8 - 41.8) | |
| **65 +** | 40 | 15 | 37.5% (24.2 - 53.0) | 39.4% (25.8 - 54.8) | 38.7% (20.5 - 55.8) | |

**Table 2:** Population-weighted and test-adjusted seroprevalence estimates for anti-SARS-CoV-2 IgG antibodies



**Figure 3:** **Risk factor** **analysis for IgG seropositivity among participants tested for antibodies. n = 966** OR: Odds ratio. Asterisks indicate significance at a 0.05 alpha level. 41 individuals (4%) were dropped due to variable missingness. Recent contact indicates contact since March 1st, 2020. A “COVID case“ is a confirmed *or* suspected COVID-19 case. Variables that were found to be not significant at a 0.10 alpha level, and which were not controlled for in the multivariate regression, include occupation, presence of comorbidities, breadwinner status, adherence to social distancing rules and presence of children in the household.



#### Figure 4: Acute symptoms of survey participants. Acute symptoms were any symptoms noticed by the respondent between March 1st and the date of survey, which were not related to any known pre-existing health condition. A. Euler plot showing the intersection of acute and COVID-like symptoms with seropositivity (example interpretation: 50 of 302 IgG seropositive individuals had COVID-19-suspect symptoms [WHO guideline for diagnostic suspicion], and 65 of 669 IgG seronegative individuals had COVID-19 suspect symptoms). B. Most common symptom profiles among IgG seropositive individuals. C. Comparison in frequency of symptoms between IgG seropositive and seronegative individuals. 𝝌-square: \* p < 0.05

# Discussion

## Limitations

Future serosurveys might focus on some of the limitations of the present study.

Our study is limited by our lack of knowledge of the time since infection of each of the study participants. Because of this, our sensitivity estimates are crude, time-indifferent estimates. This is an important limitation because we know that even IgG antibody levels decline over time. However, one recent study found that IgG antibodies were present up to 8 months after infection.14

# Contributors

JL, DMP, and SIH conceived and planned the study. JL wrote the computer code, and designed and carried out the analyses with input from FMS and DMP. DJWe constructed the accessibility covariate data layer. JL produced all output figures. DJWi, DAW, NR, RRdC provided intellectual inputs into aspects of this study. All authors contributed to the interpretation of the results. JL wrote the first draft of the manuscript and all authors contributed to subsequent revisions.

# Declarations of interests

The authors declare no competing interests.

# Data sharing

The study protocol and the individual partiticpant data

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# Figures and Tables

**Figure 1. Conceptual overview of vulnerability to snakebite envenoming.** Vulnerability can be considered as the intersection of populations who live within the range of venomous snakes which have no antivenoms available, cannot easily access health care, and have poor-quality health care in delivery of antivenoms or ensuring necessary stocks. The intersection of all three defines the most vulnerable peoples. The figure to the right indicates that these factors vary in space and that by overlaying these features, the most vulnerable populations can be identified spatially (represented here by the boxes outlined in black).

# Additional Files

Supplementary file 1:



**Supplementary Figure 1. Timeline for sampling for SARS-CoV-2 seroprevalence.** **A.** Weekly crude IgG and IgM seroprevalence and 95% confidence interval. **B.** Daily number of samples collected from participants in each district of Cité Verte.

**Supplementary Figure 2. Here, include a fig showing the.** **A.** Weekly crude IgG and IgM seroprevalence and 95% confidence interval. **B.** Daily number of samples collected from participants in each district of Cité Verte.

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