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Seroprevalence of anti-SARS-CoV-2 antibodies in Senegal: a national population-based cross-sectional survey, between October and November 2020

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ABSTRACT

Objectives: A nationwide cross-sectional epidemiological survey was conducted to capture the true extent of coronavirus disease 2019 (COVID-19) exposure in Senegal.
Methods: Multi-stage random cluster sampling of households was performed between October and November 2020, at the end of the first wave of COVID-19 transmission. Anti-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibodies were screened using three distinct ELISA assays. Adjusted prevalence rates for the survey design were calculated for each test separately, and thereafter combined. Crude and adjusted prevalence rates based on test performance were estimated to assess the seroprevalence. As some samples were collected in high malaria endemic areas, the relationship between SARS-CoV-2 seroreactivity and antimalarial humoral immunity was also investigated.
Results: Of the 1463 participants included in this study, 58.8% were female and 41.2% were male; their mean age was 29.2 years (range 0.20–84.8.0 years). The national seroprevalence was estimated at 28.4% (95% confidence interval 26.1–30.8%). There was substantial regional variability. All age groups were impacted, and the prevalence of SARS-CoV-2 was comparable in the symptomatic and asymptomatic groups. An estimated 4 744 392 (95% confidence interval 4 360 164–5 145 327) were potentially infected with SARS-CoV-2 in Senegal, while 16 089 COVID-19 RT-PCR laboratory-confirmed cases were reported by the national surveillance. No correlation was found between SARS-CoV-2 and *Plasmodium* seroreactivity.
Conclusions: These results provide a better estimate of SARS-CoV-2 dissemination in the Senegalese population. Preventive and control measures need to be reinforced in the country and especially in the south border regions.

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Research in context

Evidence before this study

Coronavirus disease 2019 (COVID-19), first identified in December 2019 in Wuhan, China, is an acute respiratory infectious disease caused by a newly discovered coronavirus named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Globalization, urbanization, and environmental changes have greatly accelerated this pandemic emergence and spread, generating an unprecedented global pandemic. Almost all countries and territories around the world (with the exception of 22 island states/territories, including Greenland, Tuvalu, Tonga, Tokelau, and Saint Helena) have been affected. By June 6, 2021, SARS-CoV-2 had infected more than 172 million people worldwide and had claimed the lives of more than 3.7 million people, with the European and American regions being the most affected and accounting for nearly 80% of all cases and deaths. The African region has reported around 3.5 million cases and 87 731 deaths since the first case of COVID-19 was declared on February 15, 2020 in Egypt. With only 2% of reported cases and 3% of recorded deaths, the African region has surprisingly been less impacted than the rest of the world. Although low testing rates have impacted the true extent of COVID-19 prevalence in Africa, there are no tangible indications that a large number of COVID-19 cases and deaths have been missed.

The first case in Senegal was declared on March 2, 2020. Despite the early implementation of prevention and control measures, the virus has gradually spread in the population. As of June 6, 2021, 41 581 confirmed cases and 1144 deaths had been reported. The control strategy in Senegal is largely based on a molecular testing system. As COVID-19 vaccines are being slowly implemented in Africa and in Senegal, it has become crucial to better evaluate the actual level of population exposure to SARS-CoV-2 through seroprevalence studies.

Added value of this study

In Africa, several seroprevalence surveys have already been conducted in specific population groups and targeted areas. The present study is the first cross-sectional population-based study conducted in all administrative regions of an African country. The study results show that the national surveillance system, mostly based on passive detection of symptomatic cases of COVID-19, only captured a tiny part of the virus transmission within the population. With an estimated national seroprevalence of 28.4%, this study describes a significant disparity between regions. Alongside the expected high seroprevalence in regions such as Dakar (44%, 11 016 confirmed cases) and Thiès (24.3%, 1974 confirmed cases), the study data showed a strong and silent circulation of the virus in regions such as Ziguinchor (56.7%), Sédhiou (48.0%), Kaolack (33.1%), and Kaffrine (26.9%). This latter region recorded only 20 COVID-19 confirmed cases during the survey period. All age groups were impacted and the prevalence of SARS-CoV-2 seropositive people was similar between symptomatic (27.8%) and asymptomatic (28.1%) people.

Implications of all the available evidence

This first African nationwide sero-epidemiological survey reveals that even if the COVID-19 outcomes have been less severe among African populations, the spread of SARS-CoV-2 among the population has been, to date, heterogeneous, extended, and silent. Therefore, African countries must not relax their prevention and surveillance efforts (including repeated cross-sectional serological surveys), as the emergence of several variants that transmit more easily, thus contributing to a more rapid spread, may cause a more severe pathology, specifically among the young population, leading to overloading of fragile healthcare systems.

1. Introduction

Classified as a global pandemic on March 11, 2020, coronavirus disease 2019 (COVID-19) is present in almost all countries and territories of the world, with more than 158 million confirmed cases and 3.2 million deaths reported by May 10, 2021 (Johns Hopkins, n.d.; World health Organization 2021). While European and American regions continue to account for nearly 80% of all cases and deaths, the African region has been surprisingly less impacted, with only 2% (3 320 786) of reported cases and 3% (83 650) of recorded deaths. Among African countries, South Africa has been the most affected (with >1.5 million confirmed cases and 54 700 deaths), followed by Ethiopia and Nigeria (Lukman et al., 2020; World Health Organization, 2020).

Worldwide reported cases have been based on molecular diagnostic assays (real-time reverse transcription PCR, qRT-PCR) performed on nasopharyngeal or oropharyngeal swabs, and these have mainly been done for symptomatic carriers or their contacts; these people represent only the tip of the COVID-19 transmission iceberg. Indeed, the number of laboratory-confirmed cases does not fully reflect the true extent of infection. Several epidemiological studies have estimated that the proportion of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-infected people who are asymptomatic or paucisymptomatic is between 20% and 50% (Al-Qahtani et al., 2021; Buitrago-Garcia et al., 2020; Syangtan et al., 2021). In Africa, COVID-19 statistics are largely underestimated, in part because of the limited laboratory testing capacity and changing health authority strategies, but also because of the stigmatization associated with this new pathology and fear of attending health facilities. Consequently, studies measuring the prevalence of antibodies directed against SARS-CoV-2 proteins are important to strengthen pandemic surveillance and to guide timely public health strategies. This is needed especially in the context of emerging new variants of concern, the complexity of COVID-19 clinical presentations, and the slow rollout of an effective vaccine in Africa.

Most available serological studies have been conducted in European or American countries (Lai et al., 2020; Serological evidence of human infection with SARS-CoV-2: a systematic review and meta-analysis - The Lancet Global Health 2021). In Africa, a limited number of seroprevalence surveys have been conducted in specific population groups, including blood donors, healthcare workers, and COVID-19 exposed populations or the general population in some targeted districts/states (Chibwana et al., 2020; Etyang et al., 2021; Halatoko et al., 2020; Kempen et al., 2020; Milleliri et al., 2021; Mulenga et al., 2021; Uyoga et al., 2021Wiens et al., 2021). However, it appears that, to date, no population-based studies at a country level have been performed in Africa.

Since the first COVID-19 confirmed case reported in Senegal on March 2, 2020, the country has implemented a range of lockdown measures aimed at spatial and physical distancing (Dia et al., 2020). However, the virus gradually spread to all regions, with a recorded 41 713 COVID-19 confirmed cases and up to 1148 deaths on June 7, 2021 (Sitrep 98 : Coronavirus 2021).

Senegal faced the first wave of COVID-19 between March and September 2020, with a peak of transmission recorded in June–July. Surveillance associated with COVID-19 has mostly focused on symptomatic patients and their close contacts. To better understand the epidemiological characteristics of the COVID-19 outbreak in Senegal, a population-based sero-epidemiological survey was conducted in all regions with the aims of assessing the level of population exposure to SARS-CoV-2 and guiding public health interventions. In this study, the seroprevalence results were also compared with the reported COVID-19 confirmed case rates within the same population during the same period.

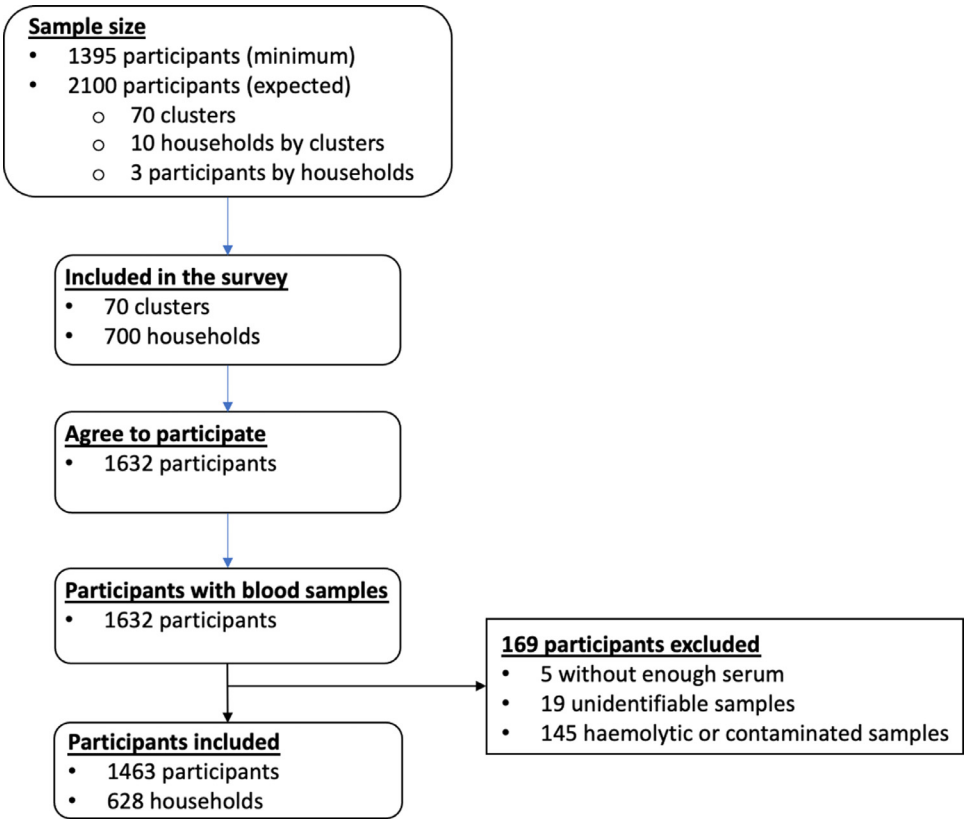


Figure 1. Flowchart of participant enrolment in the anti-SARS-CoV-2 antibody national seroprevalence study in Senegal.

2. Methods

2.1. Study design and sampling

Senegal is located in West Africa, is bordered by Mauritania, Mali, Guinea, and Guinea-Bissau, and surrounds The Gambia. Senegal has around 16.7 million inhabitants, a quarter of whom live in the Dakar region (0.3% of the territory). The country is administratively divided into 14 regions.

To evaluate the seroprevalence of anti-SARS-CoV-2 antibodies, a cross-sectional sero-epidemiological survey at the national level was conducted in all regions of Senegal at the end of the first COVID-19 transmission wave (from October 25 to November 26, 2020; Figure 1. A multi-stage cluster sampling was applied to randomly select 70 clusters, provided by the National Agency for Statistics and Demography (ANSD). In the first stage, areas were selected across Senegal by identifying the number of clusters by region according to the population size and using sampling proportional to the probability by size (PPS). In the second step, systematic random sampling to select 10 households in each selected area chosen was performed. Finally, for each selected household, a simple random sampling was done to systematically enroll two people over 5 years old and one child under 5 years old. The geographical localizations of the investigated clusters are shown in Figure 1. The study was designed following the World Health Organization (WHO) protocol for COVID-19 population-based sero-epidemiological studies (World Health Organization, 2020).

All field workers were trained in protocol procedures, how to complete the questionnaires, and sample collection procedures under COVID-19 biosafety guidelines.

2.2. Ethical considerations

All randomly selected individuals who fulfilled the study inclusion criteria were invited to participate. All participants consented to participate in the study. For those younger than 18 years of age, a legal representative provided informed consent. The study was approved by the Senegalese National Ethics Committee for Research in Health (reference number N°0176/MSAS/DPRS/CNERS, 10 October 2020).

2.3. Sample size calculation

The sample size needed to estimate prevalence in all regions was assessed to be 1215 individuals (with a minimum sample size of 1395 and a maximum sample size of 2100), based on a design effect of 3 to account for intra-household clustering of cases, with an absolute error of ±5%, a power of 90%, and a seroprevalence rate of 50%. The sample size calculation took into account a 10% non-response rate and 5% non-valid samples.

2.4. Blood sampling and data collection

For each participant, a whole blood sample was collected into a dry vacutainer tube by standard venipuncture technique. Blood samples were immediately stored at 4°C and quickly directed to Institut Pasteur de Dakar within 24–72 hours, according to the routing conditions required for potentially infectious samples. Tracking procedures were established to ensure temperature-controlled delivery to Institut Pasteur de Dakar. After a centrifugation step, serum samples were collected, aliquoted, and stored at −20°C until use. Sociodemographic information such as age, sex, region, place of residence, occupation, education level, contact with COVID-19 confirmed cases, and history of symptoms during the 6 months prior to the survey, were also collected.

2.5. COVID-19 serological assays (ELISA)

The antibodies specifically directed against SARS-CoV-2 proteins were detected by ELISA. In this study, three CE-marked, indirect semi-quantitative commercially available ELISA kits were used: (1) the

Table 1
Main characteristics of the study population

	Overall (*N* = 1463)
Age (years)	
Missing (*n*)	17
Mean (SD)	29.20 (20.64)
Range	0.20–84.8
Age group (years), *n* (%)	
Missing (*n*)	17
0–5	283 (19.6%)
>5–15	179 (12.4%)
>15–30	337 (23.3%)
>30–45	297 (20.5%)
>45–60	233 (16.1%)
>60	117 (8.1%)
Sex, *n* (%)	
Female	860 (58.8%)
Male	603 (41.2%)
Occupation, *n* (%)	
Missing	281
Traders	81 (6.9%)
Schoolchild – student	230 (19.5%)
Housewife	325 (27.5%)
Workers	65 (5.5%)
Jobless	364 (30.8%)
Others	117 (9.9%)
Level of education, *n* (%)	
Missing	52
None	615 (43.6%)
Primary school	251 (17.8%)
Secondary school	298 (21.1%)
Koranic school	247 (17.5%)
Region, *n* (%)	
Dakar	302 (20.6%)
Diourbel	121 (8.3%)
Fatick	76 (5.2%)
Kaffrine	80 (5.5%)
Kaolack	116 (7.9%)
Kedougou	21 (1.4%)
Kolda	60 (4.1%)
Louga	119 (8.1%)
Matam	45 (3.1%)
Saint-Louis	94 (6.4%)
Sédhiou	57 (3.9%)
Tambacounda	112 (7.7%)
Thiès	210 (14.4%)
Ziguinchor	50 (3.4%)
COVID-19 symptomatic[a], *n* (%)	
Missing	41
No	464 (32.6%)
Yes	958 (67.4%)
COVID-19 symptoms, *n* (%)	
Fever	707 (73.8%)
Headache	311 (32.4%)
Cough	286 (30.0%)
Rhinorrhea	187 (19.5%)
Fatigue	148 (15.4%)
Myalgia	72 (7.5%)
Sore throat	34 (3.5%)
Diarrhea	33 (3.4%)
Taste or smell lost	27 (2.8%)

SD, standard deviation.
[a] History of symptoms compatible with COVID-19 less than 6 months before the survey.

Omega Diagnostics COVID-19 IgG ELISA Kit (Mologic Ltd and Omega Diagnostics Ltd, Cambridgeshire, UK; Ref. ODL150/10), which detects IgG directed against the nucleocapsid (NP) and spike (subunit S2) proteins (Staines et al., 2021); (2) the ID Screen SARS-CoV-2-N IgG Indirect ELISA (IDVet; Innovative Diagnostics, France; Ref. SARSCOV2S), which detects IgG directed against only the SARS-CoV-2 NP (Krüttgen et al., 2021); (3) the Wantai SARS-CoV-2 Ab ELISA (Beijing Wantai Biological Pharmacy Enterprise, Beijing, China; Ref. WS-1096) recommended by the WHO for sero-epidemiological studies, which detects total antibodies (including IgM and IgG) binding the SARS-CoV-2 spike protein receptor-binding domain (S1/RBD) (GeurtsvanKessel et al., 2020). The main characteristics of each immunoassay are depicted in **Supplementary Material** Table S8. Serum samples were analyzed in duplicate according to the recommendations of the suppliers.

The diagnostic performance (sensitivity and specificity) of each ELISA assay was re-evaluated with a panel of 40 archived, well-documented serum or plasma samples, and the data obtained were used to adjust the seroprevalence. According to the performance obtained, in order to limit the rate of false IgG-positive results, after an evaluation of IgG directed against virus proteins using the OMEGA assay, all positive and doubtful samples were validated using the IDVet kit. In parallel, the Wantai kit was used to capture the whole antibody (including IgG and IgM) reactivity to SARS-CoV-2. The flowchart used to analyze the serum samples is described in **Supplementary Material** Figure S1.

2.6. Plasmodium falciparum *antigen preparation and ELISA assay*

Cross-reactivity on SARS-CoV-2 serological tests usually validated in high-income countries with pre-pandemic samples taken in malaria endemic areas have been reported by several studies. Therefore, cross-reactivity was explored in the study samples following the technique described below.

Crude schizont antigens from the *P. falciparum* 0703 field-adapted strain were prepared from in vitro continuous culture on O^+ erythrocytes in RPMI medium containing 0.5% AlbuMAX. Schizont stage parasites were harvested and lysed in three volumes of sterile distilled water and stored in aliquots in liquid nitrogen. The ELISA assay was performed as described previously by Diop et al. and detailed in **Supplementary Material** Methods (Diop et al., 2015). Finite mixture models, assuming two underlying distributions of 'negative' (unexposed) and 'positive' (exposed) individuals, were created from log-transformed Median Fluorescence Intensity (MFI) values to determine the seropositivity cut-off. Finite mixture models were fit with the flexmix package in R version 3.5.1 (Comprehensive R Archive Network, Vienna, Austria).

2.7. Statistical analysis

Crude and standardized seroprevalence rates were calculated with the 95% confidence interval (CI). The 95% CI for seroprevalence were estimated using the Clopper–Pearson method. Weighted prevalence estimates were assessed using 2020 population data from ANSD and direct standardization on the observed seroprevalence and population weights by age andsex. For combined seroprevalence results, samples were counted as positive if they were positive with one of the two tests and negative if they were negative with both tests. The performance of combined tests was calculated using the performance of both tests (Weinstein et al., 2005). A multiple regression analysis was conducted. Statistical significance was assumed at a p-value <0.05. All statistical analyses were done with R version 4.0.4. The spatial distribution of seroprevalence was mapped using mapplots R package.

3. Results

3.1. Population characteristics

All of the Senegalese administrative regions were investigated. Among the 70 clusters initially targeted, only 66 were included in the study. One cluster in Sédhiou, in the south of the country, did not agree to participate in the study, and blood samples from three remote clusters in the Diourbel region were not delivered in compliance with the laboratory requirements. Of the 700 randomly selected households, 628 (89.7%) for which the head of the household consented to participate were included in the study. Hemolytic and under-filled blood samples

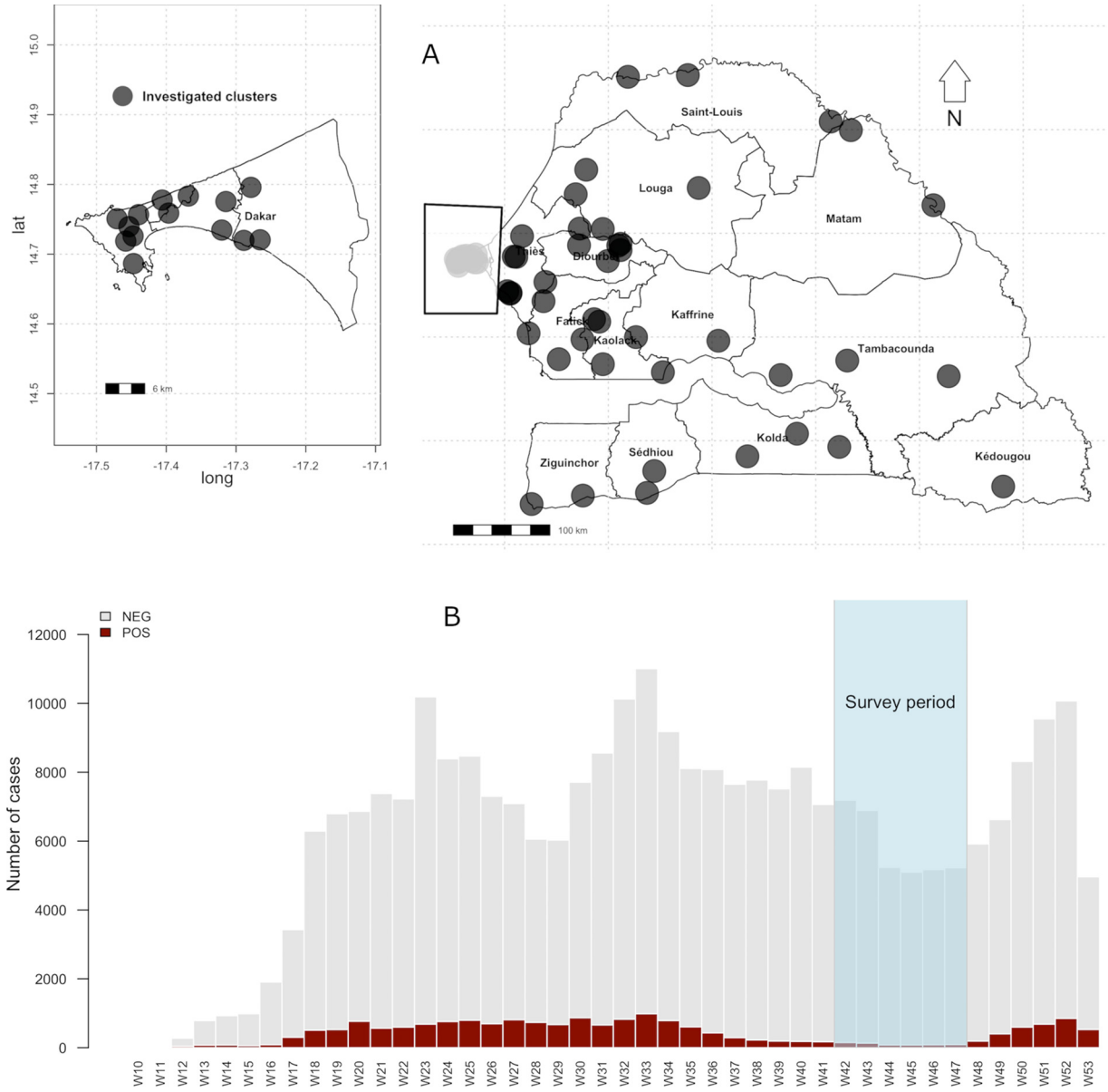


Figure 2. Mapping of clusters investigated and the Senegal COVID-19 epidemic curve from March 2 to December 31, 2020 (Data sourced from the Ministry of Health).

were excluded from the serological analysis. Overall, 1632 people were enrolled, among whom 1463 (89.4%) with complete sociodemographic data and an eligible blood sample were included in the serological analysis (Figure 2).

This cross-sectional household survey was initiated just after the first wave of COVID-19 transmission (March to October 2020) (Figure 1). The mean age of the participants was 29.2 years, ranging from 0.20 to 84.8 years. There were significantly more female participants than male participants (58.8% vs 41.2%; $P < 0.001$). During the survey, a high number of people ($n = 958$; 67%) declared having a history of symptoms compatible with COVID-19 during the 2–3 months prior to the survey. Fever (73.8%), headaches (32.4%), and cough (30.0%) were the most often described COVID-19-related symptoms (Table 1). Anosmia and/or ageusia was only reported by 2.8% of the participants.

3.2. Seroprevalence of anti-SARS-CoV-2 antibody

The prevalence data were weighted according to the age and sex distribution of the general population and adjusted according to the performance of each immunoassay. In accordance with the serological analysis strategy, seroprevalence data were given first using the results obtained with the OMEGA/IDVet ELISA (**Supplementary Material** Tables S3 and S4) and Wantai ELISA (**Supplementary Material** Tables S5 and S6) separately, and subsequently after a combination of both results (Tables 2 and 3). At the country level, the overall seroprevalence was estimated at 22.5% (95% CI 20.4–24.7%) with the OMEGA/IDVet ELISA targeting IgG directed against SARS-CoV-2 proteins, and at 28.1% (95% CI 25.8–30.5%) with the Wantai ELISA measuring both IgG and IgM against the SARS-CoV-2 S1/RBD proteins. Combining the two approaches, OMEGA/IDVet and Wantai ELISA results, the global seroprevalence was estimated at 28.4% (95% CI 26.1–30.8%). SARS-CoV-2 combined seroprevalence data are presented below (**Supplementary Material** Figure S2).

SARS-CoV-2 transmission occurred in all age groups investigated, with the 15–30 years group showing the highest seroprevalence at 37.3% (95% CI 32.2–42.8%) (Table 2). The lowest weighted prevalence of 16.1% (95 CI 12.2–21.1%) was observed in children under 5 years

Table 2
Seroprevalence of anti-SARS-CoV-2 IgG per age group and sex: combined results obtained with OMEGA/IDVet and Wantai ELISA

	All samples	Seropositive samples	Crude seroprevalence		Senegal population (2020)	Standardized seroprevalence		Adjusted seroprevalence	
			%	(95% CI)		%	(95% CI)	%	(95% CI)
Age group (years)									
0–5	283	45	15.9	11.8–20.7	3 224 935	15.9	11.8–20.7	16.1	12.2–21.1
>5–15	179	44	24.6	18.5–31.6	4 096 096	24.6	18.5–31.6	24.9	19–32.2
>15–30	337	124	36.8	31.6–42.2	4 423 193	36.5	31.3–41.9	37.3	32.2–42.8
>30–45	297	81	27.3	22.3–32.7	2 687 369	29.9	24.8–35.5	27.6	22.6–33.1
>45–60	233	70	30.0	24.2–36.4	1 418 953	30.0	24.2–36.4	30.4	24.6–36.8
>60	117	29	24.8	17.3–33.6	855 062	24.9	17.3–33.6	25.1	17.3–33.6
Sex									
Female	850	235	27.6	24.7–30.8	8 391 358	27.6	24.7–30.8	28.0	25–31.2
Male	596	158	26.5	23–30.2	8 314 250	27.2	23.6–30.9	26.9	23.3–30.6

CI, confidence interval.

Table 3
Seroprevalence of anti-SARS-CoV-2 IgG per region: combined results obtained with OMEGA/IDVet and Wantai ELISA

Region	All samples (*n*)	Seropositive samples (*n*)	Crude seroprevalence		Adjusted seroprevalence		Population per region	Estimated COVID-19 infection	Confirmed COVID-19 cases	Ratio of reported cases to estimated infection
			%	(95% CI)	%	(95% CI)				
Dakar	295	128	43.4	37.7–49.3	44.0	38.3–49.9	3 835 011	1 687 405	11 016	1:153
Diourbel	117	22	18.8	12.2–27.1	19.0	12.2–27.1	1 859 503	353 306	754	1:469
Fatick	75	13	17.3	9.6–27.8	17.5	9.6–27.8	900 800	157 640	325	1:485
Kaffrine	79	21	26.6	17.3–37.7	26.9	17.3–37.7	728 951	196 088	20	1:9804
Kaolack	113	37	32.7	24.2–42.2	33.1	24.2–42.2	1 191 577	394 412	291	1:1355
Kedougou	21	4	19.0	5.4–41.9	19.2	05.4–41.9	190 509	36 578	219	1:167
Kolda	52	12	23.1	12.5–36.8	23.4	12.5–36.8	822 003	192 349	216	1:891
Louga	118	13	11.0	6–18.1	11.1	6–18.1	1 061 612	117 839	75	1:1571
Matam	45	5	11.1	3.7–24.1	11.2	3.7–24.1	732 863	82 081	51	1:1609
Saint-Louis	94	15	16.0	9.2–25	16.2	9.2–25	1 091 735	176 861	319	1:554
Sédhiou	57	27	47.4	34–61	48.0	34–61	572 101	274 608	151	1:1819
Tambacounda	106	25	23.6	15.9–32.8	23.9	15.9–32.8	872 155	208 445	111	1:1878
Thiès	200	48	24.0	18.3–30.5	24.3	18.7–31.1	2 162 833	525 568	1974	1:266
Ziguinchor	50	28	56.0	41.3–70	56.7	41.3–70	683 955	387 802	567	1:684
National	1422	398	27.9	25.7– 30.4	28.4	26.1–30.8	16 705 608	4 744 393	16 089	1:295

CI, confidence interval.

old. Adjusted prevalence by sex was similar for female and male participants: 28.0% (95% CI 25.0–31.2%) and 26.9% (95% CI 23.3–30.6%), respectively (Table 2).

Regarding SARS-CoV-2 seroprevalence at the regional level, substantial variability was observed (Table 3, Figure 3). As expected, a high seroprevalence was recorded for the regions of Dakar, with 44.0% (95% CI 38.3–49.9%) of people harboring antibodies against SARS-CoV-2. Interestingly, two south border regions displayed the highest seroprevalence: Ziguinchor with 56.7% (95% CI 41.3–70.0%), followed by Sédhiou with 48.0% (95% CI 34.0–61.0%). The two regions located in the center north of Senegal, Louga and Matam, presented the lowest COVID-19 prevalence rates of 11.1% (95% CI 6.0–18.1%) and 11.2% (95% CI 3.7–24.1%), respectively. Of note, in Kaffrine, only 20 qRT-PCR confirmed cases were recorded during the survey period, while the seroprevalence was up to 26.9% (95% CI 17.3–37.7%), which was similar to that found in Thiès (24.0%, 95% CI 18.7–31.1%), the second most impacted region (after Dakar) with 1974 COVID-19 qRT-PCR confirmed cases.

Of the 958 (67.4%) participants who reported a history of symptoms compatible with COVID-19, 28.1% ($n = 269$) were COVID-19 seropositive. The prevalence of anti-SARS-CoV-2 antibodies among participants without documented COVID-19 symptomatology history ($n = 464$) was comparable (27.8%, $n = 169$). The seroprevalence of antibodies to SARS-CoV-2 among people reporting a history of COVID-19-related symptoms was variable: 27.0% (191 of 707) for fever, 31.1% (97 of 311) for headache, 24.8% (71 of 286) for cough, 29.2% (21 of 72) for myalgia, and 40.7% (11 of 27) among participants with anosmia and/or ageusia. No significant correlation was observed between reported COVID-19 symptoms and the serostatus (**Supplementary Material** Table S7).

3.3. Risk factors associated with COVID-19 transmission

Participants aged 15–30 years (odds ratio (OR) 2.49, 95% CI 1.57–3.98; $P < 0.001$) and 45–60 years (OR 1.79, 95% CI 1.12–2.89; $P = 0.016$) were around two times more infected than children aged 0–5 years. No association was observed between SARS-CoV-2 seroprevalence and sex. The Dakar region was more at risk than all of the other regions except Sédhiou (OR 1.07; $P = 0.832$) and Ziguinchor (OR 1.42; $P = 0.286$) (**Supplementary Material** Table S1, Figure 4). No association was observed between COVID-19 seropositivity and occupation. Interestingly, a significant association was identified between SARS-CoV-2 seroprevalence and attendance at Koranic schools (OR 1.54; $P = 0.030$).

3.4. Estimation of the national prevalence of COVID-19 in Senegal

Seroprevalence estimate results highlighted a strong discrepancy with the reported prevalence of COVID-19 based on RT-PCR-confirmed COVID-19 cases (Table 3). Indeed, the analyses estimated that 4 744 392 cases of SARS-CoV-2 infection (95% CI 4 360 164–5 145 327) potentially occurred, while only 16 089 cases were detected in the country during the survey period, with important variability between regions. At the national level, the ratio of reported cases to estimated infections was 1:295 and ranged between regions from 1:153 in Dakar to 1:9804 in Kaffrine.

3.5. Relationship between SARS-CoV-2 seropositivity and malaria seropositivity

To explore the impact of malaria seropositivity on immune reactivity to the SARS-CoV-2 proteins used in the serological tests, the im-

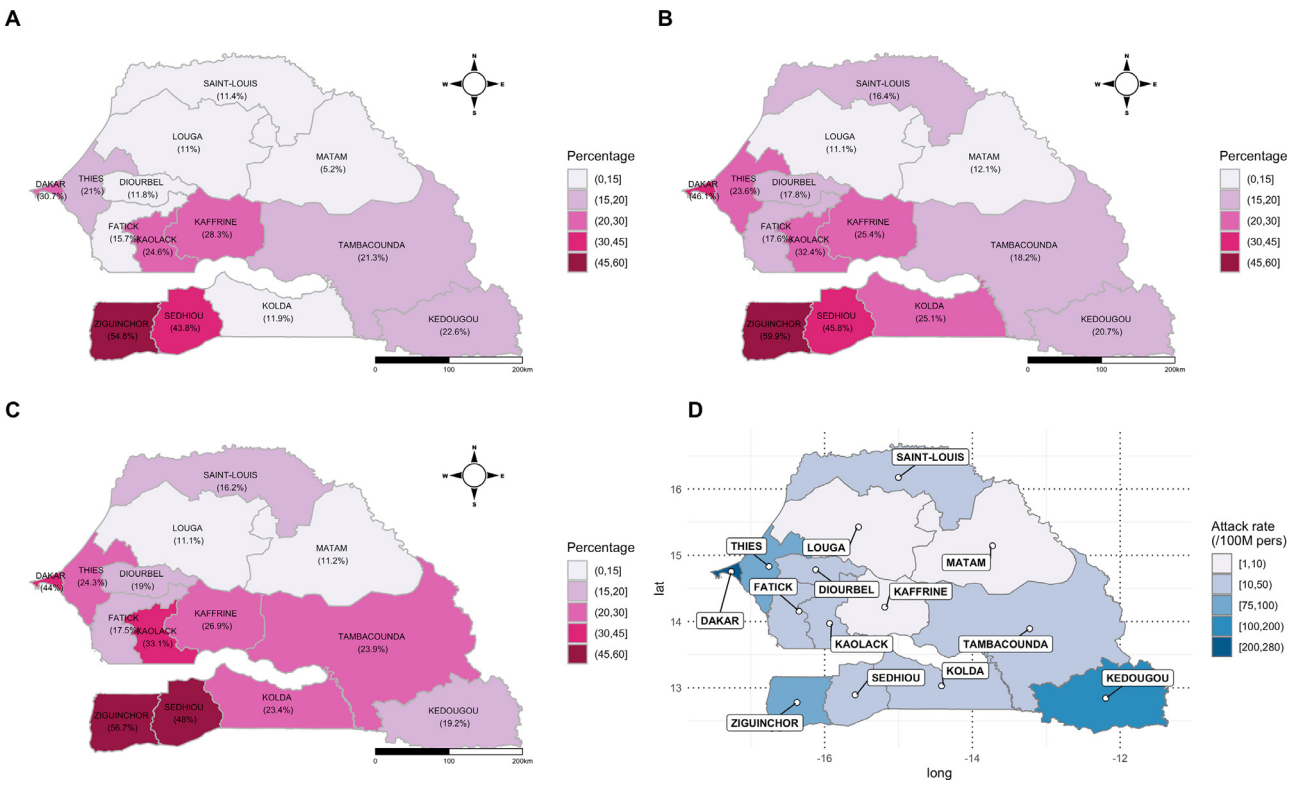


Figure 3. Mapping of the seroprevalence data obtained by ELISA (panels A, B, and C) and COVID-19 attack rate cases at the time of the household sero-survey (panel D).

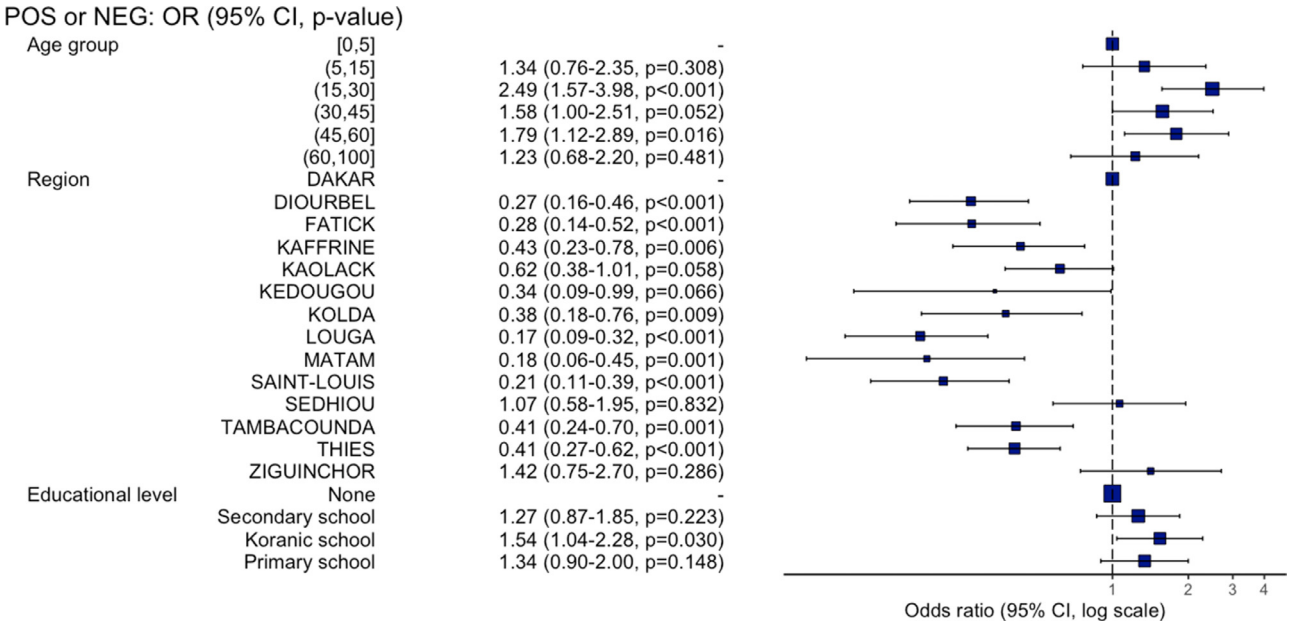


Figure 4. Association between SARS-CoV-2 prevalence and sociodemographic factors.

mune reactivity (IgG) against a crude antigen extract of *P. falciparum* and SARS-CoV-2 ELISA on 863 randomly selected samples were also analyzed. Overall, 541 participants (62.7%) had IgG against *P. falciparum* antigens. The proportion of individuals seropositive for SARS-CoV-2 by OMEGA/IDVet ELISA screening was similar between individuals with and without immune reactivity towards *P. falciparum* antigen, i.e., 60.9% (142 of 233) and 59.7% (203 of 340), respectively. Similarly, SARS-CoV-2 seropositivity did not differ significantly between subjects with (26.2%, 142 of 541) and without (28.2%, 91 of 322) *P. falciparum* antibodies ($P = 0.833$). Comparable results were obtained with the Wantai COVID-19 total Ig immunoassay (**Supplementary Material** Table S2).

4. Discussion

This study appears to be the first COVID-19 cross-sectional, sero-epidemiological survey to be performed at a national level in Africa since the beginning of the pandemic. The survey was conducted at the

end of the first wave of the COVID-19 epidemic and before the roll-out of COVID-19 vaccines in Senegal.

Several studies, including the present study, have reported cross-reactivity on SARS-CoV-2 serological tests usually validated in high-income countries with pre-pandemic samples taken in malaria endemic areas (Emmerich et al., 2021; Lapidus et al., 2021; Steinhardt et al., 2021). This cross-reactivity was detected either on SARS-CoV-2 nucleocapsid (N) or spike (S) proteins and thus complicated the use of any of the homemade or already available serological tests. They may be due to the high exposure of African populations to multiple pathogens, including one of the most prevalent parasites, *Plasmodium*. The present study results suggest no evidence of cross-reactivity interference between malaria and SARS-CoV-2 ELISA immunoassays using the double screening strategy with OMEGA/IDVet and Wantai ELISA assays (**Supplementary Material** Table S2).

The adjusted national prevalence of anti-SARS-CoV-2 IgG/IgM was estimated at 28.4%, with a great disparity between regions. Despite some areas of transmission like Dakar, Ziguinchor, and Sédhiou presenting high seroprevalence rates (>40%), the global seroprevalence suggests that a vast majority (around two in three) of Senegalese people still remained susceptible to SARS-CoV-2 infection. Indeed, it is estimated that about 4 744 392 cases of SARS-CoV-2 infection potentially occurred among the 16.7 million population. With the emergence of variants of concern in December 2020, these data may explain the rebound observed following the survey period, with a second wave that presented a higher amplitude in terms of the number of cases (41 416 compared to 16 089) and deaths (333 compare to 1139) in comparison to the first wave, as herd immunity was not reached.

The highest prevalence was observed in the regions of Ziguinchor and Sédhiou, with seroprevalence of 56.7% (574 confirmed cases) and 48.0% (151 confirmed cases), respectively. These regions are located in the south-western part of the country, close to the borders with the neighboring countries of Guinea-Bissau and Gambia. These high seroprevalence data do not mirror the surveillance data recorded at the time of the survey. Several factors could explain these discrepancies, including (1) the lack of molecular testing at the beginning of the COVID-19 pandemic in these remote areas (on-site laboratory testing was put in place only in August 2020), (2) an airport in Ziguinchor (a tourist region) facilitating imported cases before the closure of air traffic, and (3) the difficulty controlling inter-regional and cross-border trade. Louga and Matam, with a seroprevalence of around 11%, seemed to be less impacted by the COVID-19 epidemic. After the Tambacounda region, these rural regions are the two largest regions in the country, with low population densities of around 20–30 inhabitants/km^2. These sociodemographic characteristics could explain the lower circulation of the virus. Kaffrine, one of the main commercial crossroads of the country, recorded a high seroprevalence (26.9%) with regard to the low number of COVID-19 confirmed cases (n = 20) registered. High population movement with a lack of on-site laboratory facilities for molecular testing may greatly have contributed to this underestimation of the extent of the COVID-19 burden. This underestimation can be explained by the large number of asymptomatic individuals or those with limited symptoms, not requiring medical consultation.

Other studies performed in Africa over the same period or at the beginning of 2021 have reported similar results, i.e. Juba, South-Sudan (22.6% in August–September) and neighboring Mali (54.7% in December to January 2021), although these studies involved only a part of the population or a targeted population (Sagara et al., 2021; Wiens et al., 2021). Altogether, this demonstrates an important circulation of SARS-CoV-2 in Senegal and in general in Africa. The slow SARS-CoV-2 transmission was not mirrored by the data obtained through the surveillance system, highlighting the need to assess the true exposure of COVID-19.

Given the scale of the pandemic, the Senegalese authorities quickly implemented several measures to limit the spread of the virus, such as social distancing, lockdown of markets, schools, and universities, masking in public places and public transport, hand washing, contact tracing and testing, isolation, and treatment of SARS-CoV-2-positive persons in health centers, among others. It is difficult to assess how much and how strictly these measures were followed by the population between March and July 2020. However, transmission was not stopped and social living conditions in Africa remain favorable to airborne transmissible viruses. This study clearly demonstrated the invisible and extended spread of the virus in the population regardless of age, sex, or level of education. The results are corroborated by other studies showing that the rate of infection with SARS-CoV-2 was higher than the rate announced by the surveillance systems (Sagara et al., 2021; Sykes et al., 2021). The hidden face of the progression of the virus was enhanced by the low number of molecular tests performed and a smaller proportion of severe cases of the disease as compared to European and American regions.

The severity of COVID-19 disease may have been tempered by one of the demographic features of the African population, i.e. the youth of the Senegalese population (mean age 19 years), a more robust non-specific immunity gained by multiple and abundant exposures to pathogens that protect against the severe form of COVID-19, and the absence of self-reporting of mild symptoms compatible with COVID-19 during the first wave. Indeed, a high proportion of participants (67.2%) reported having a history of COVID-19-related symptoms during the 2–3 months prior to the survey (corresponding to the peak of transmission in June–July). However, in the absence of more severe symptoms, none of them made a voluntary laboratory diagnosis of COVID-19. This observation highlights the complexity of attributing these non-specific symptoms to COVID-19, the stigmatization around this pathology, and also the fear of attending health facilities or being diagnosed as SARS-CoV-2-positive. In addition to forgetting the symptoms, all of these aspects may explain the fact that, in the present study, the seroprevalence of anti-SARS-CoV-2 antibodies was comparable between symptomatic and asymptomatic individuals.

There were more female participants than male participants; however, no significant difference in seroprevalence data was observed between the two groups. The most affected age group was 15–30 years, which is the most active age group, followed by the 45–60 years group, when compared to the under-5 years age group. The household contact mode seems to be the main transmission mode, as the <5 years age group and the >60 years age group were also impacted. No significant difference in the level of infection by occupation was noted. This could be explained by the fact that all occupations were at the same risk level, with a significant community-based transmission. Interestingly, a significant association was identified between SARS-CoV-2 seroprevalence and attendance at Koranic schools (OR 1.54, 95% CI 1.04–2.28; P = 0.030). This could reflect that schools in general (including Koranic schools) are places of favorable transmission due to the regrouping of individuals of all age groups without necessarily the required respect for social distancing measures.

This study is the first population-based representative national survey to estimate the number of SARS-CoV-2 infections in Senegal and in West Africa. The study provides an estimate of the current level of transmission of the disease, and points out the impact of community-based COVID-19 transmission and the cross-regional or cross-border transmission increased by population movement. These data also demonstrate the need to strengthen decentralized laboratories equipped with a capacity for molecular biology analysis of SARS-CoV-2 infection in all regions, in order to improve monitoring. With the emergence of SARS-CoV-2 variants, regular population-based national sero-epidemiological studies will be mandatory to guide prevention, control, and vaccination strategies. A larger number of clusters in some regions would provide a better estimate of the prevalence.

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Declarations

Data sharing: De-identified participant data used for this analysis can be requested from Institut Pasteur de Dakar. Interested researchers must submit a research proposal for consideration by the study investigators. If approved, the requestor must sign a data use agreement. Additionally, the study protocol is available upon request. All data requests should be directed to the corresponding author.

Disclaimer: The findings and conclusions in this report are those of the author(s) and do not necessarily represent the official position of the US Centers for Disease Control and Prevention.

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Author contributions

OusF, CT, AAS, JLR, JT, OF, CL, BD, MN, CTD, OP, and IVW conceived and designed the study. CT, SN, MB, AT, MD, MarD, IMK, JPD and JLR co-coordinated the survey and data collection. ON, OF, RF, AAM, IVW, BaD, MDia, and CTD performed the serological analysis. CT, IVW, and MD accessed and verified the underlying data. CT, CL, MarD, TW, MW, ON, MST, and IVW analyzed the data. CT, IVW, JLR, and BD wrote the manuscript. All authors contributed to the data interpretation, critically reviewed the first draft and approved the final version of the manuscript, and agreed to be accountable for the work. All authors had full access to all of the data in the study and had final responsibility for the decision to submit for publication.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijregi.2022.02.007.

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