





REVIEW

Seroprevalence of anti-SARS-CoV-2 antibodies in Africa: A systematic review and meta-analysis

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Abstract

We estimated the seroprevalence of anti-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibodies in residents of African countries and explored its associated factors. We searched PubMed, EMBASE, PsycINFO, AMED, CINAHL, DOAJ and Google Scholar databases for peer reviewed articles and pre-prints that reported anti-SARS-CoV-2 antibody seroprevalence of general or specific human populations resident in Africa. The eligible studies were evaluated using Joana Briggs Institute prevalence critical appraisal tool. Twenty-three studies involving 27,735 individuals were included in our paper. The pooled seroprevalence of anti-SARS-CoV-2 antibodies in Africa was 22% (95%CI: 14–31) with very high heterogeneity ($I^2 = 100\%$, $p < 0.001$). Seroprevalence was highest in studies conducted in Central Africa compared to Southern Africa, West Africa, North Africa and East Africa respectively. The number of days between the first reported coronavirus disease 2019 case in each country and when a seroprevalence study was conducted was a significant moderator of seroprevalence. Seropositivity was numerically influenced by gender and age of the participants with males and those aged below 50 years being most affected with SARS-CoV-2 infection. The highest pooled seroprevalence in Africa reported in this review should be interpreted cautiously due to high heterogeneity between studies. Continued seroprevalence surveillance is warranted to establish Africa's transition towards herd immunity.

KEYWORDS

Africa, antibody, Covid-19, SARS-CoV-2, seroprevalence

1 | INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and its concomitant disease coronavirus disease 2019 (Covid-19) has been declared a pandemic.¹ Currently, over 122 million Covid-19 positive cases and over 2.7 million deaths have been reported globally representing a case fatality rate of 2.2%.² The detection of SARS-CoV-2 in nasopharyngeal swabs using real time-polymerase chain reaction (qRT-PCR) has been recommended by WHO as a gold standard method for ascertaining positivity in symptomatic patients.³ However, the method fails to provide the extent of the population or community exposure to SARS-CoV-2 infection.⁴ This underestimation of the extent of exposure of the population to SARS-CoV-2 by RT-PCR has been reported by several studies⁵⁻⁷ and has greatly affected implementation and uptake of infection control and prevention strategies.⁸ Serological tests that detect IgG and/or IgM serum antibodies through enzyme-linked immunosorbent assays (ELISAs), chemiluminescence immunoassays and lateral flow immunoassays (LFIA) remain the only plausible platforms for providing the collective population exposure to SARS-CoV-2 infection.^{5,9,10}

Globally, population based and group targeted seroprevalence studies have been conducted with a reported seroprevalence ranging from 0.08% to 31.5% at 95% confidence interval (CI).^{4,8} However, Africa's anti-SARS-CoV-2 antibodies seroprevalence has been hugely under-represented as few countries were included (1-3). Seroprevalence studies have the ability to establish the number of people who have at any time been infected. Recently, studies have shown that the rate of reinfection is very low as immunity is able to protect the already infected individuals against repeat SARS-CoV-2 infections.^{11,12} As the pandemic progresses, with efforts being tailored to mass vaccination of the global population including Africa, it is imperative and crucial that a well-focused and quick estimate of the anti-SARS-CoV-2 seroprevalence be undertaken in Africa. Africa generally has done fewer RT-PCR tests per population denominator due to resource constraints and hence the true number of infected individuals in Africa is not known. This systematic review and meta-analysis therefore sought to estimate the current anti-SARS-CoV-2 antibody seroprevalence in Africa.

2 | METHODOLOGY

2.1 | Search strategy and selection criteria

The study utilized the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (Figure 1). The protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO), registration number CRD42020220074.¹³ Systematic literature search was carried out in the following databases: PubMed, EMBASE, PsycINFO, AMED, CINAHL, DOAJ and Google Scholar between December 2020 and April 2021 using the following terms: Covid-19 OR Covid-19 OR Covid OR corona virus OR SARS-CoV-2 OR SARSCov2 OR SAR-CoV* OR ncov2 OR nCOV

OR 2019-nCoV or 2019-nCov or '2019 coronavirus' or '2019 corona virus' OR 'novel corona virus' or 'new corona virus' or 'nouveau corona virus', AND antibody OR anti-SARS-CoV-2 antibody OR SARS-CoV-2 IgG OR population OR Seroprevalence OR Sero-surveillance OR incidence OR extent OR magnitude AND Africa. Efforts were undertaken to identify additional published data through manual hand searching of reference lists from articles that met the inclusion criteria. All the gathered articles were imported into EndNote X9 software (Thompson and Reuters) and duplicates were removed. Article titles, abstracts and full text were independently reviewed by SR, MROC, PK, BCM and SEM for eligibility for inclusion. Any discrepancies were resolved through discussions with MC, ON, BN & EC. The reviewed articles included peer reviewed published articles, and preprints that reported anti-SARS-CoV-2 seroprevalence of the general population, or specific working group domiciled in a specific state/city/region/district of a country within the African continent. The articles were excluded if they reported SARS-CoV-2 seroprevalence of non-African countries or in animal experiments and were not written in English language. Case reports or studies, commentaries, perspectives, editorials, reviews and systematic reviews were also excluded.

2.2 | Data extraction and quality assurance

Data were extracted from articles that met the eligibility criteria as per the adapted and modified Table S1 which was developed in Microsoft Excel 2016. A data extraction table itemized with the name of the author, country, study period, sample selection methods, participants, age range in years, sample size, biological sample used, serological test method, seroprevalence, sensitivity and specificity of serological method was used to collect data (Table S1). Data collation and evaluation from eligible studies was performed by SR, MROC, PK, BCM and SEM. The quality of the eligible studies was assessed using Joana Briggs Institute (JBI) prevalence critical appraisal tool.¹⁴ The individual articles were appraised with a 'yes' or 'no', 'unclear' or 'not' 'applicable' for their appropriateness of sample frame, sampling technique, sample size, study setting, validity of the immunoassay used, adjustment for non-response and sound statistical analysis. The number of 'yes' answers for each individual study across the nine checklist selection criteria was counted and used for the overall inclusion of the study to reduce the risk of study bias. The higher the number of 'yes' answers, the higher the chance of inclusion in the review. Thus, using the JBI scale, the scores of 8-9, 5-7 and ≤ 4 indicated good quality, moderate quality and poor quality studies, respectively.¹⁵ Where there were discrepancies in rating, it was resolved through discussion with all authors (MROC, SR, SEM, AK, PK, MC, ON, BN, EC, & BCM).

2.3 | Summary of outcomes and statistical analysis

Meta-analysis was performed by SEM and AK. The primary outcome of the meta-analysis was the seroprevalence of anti-SARS-CoV-2

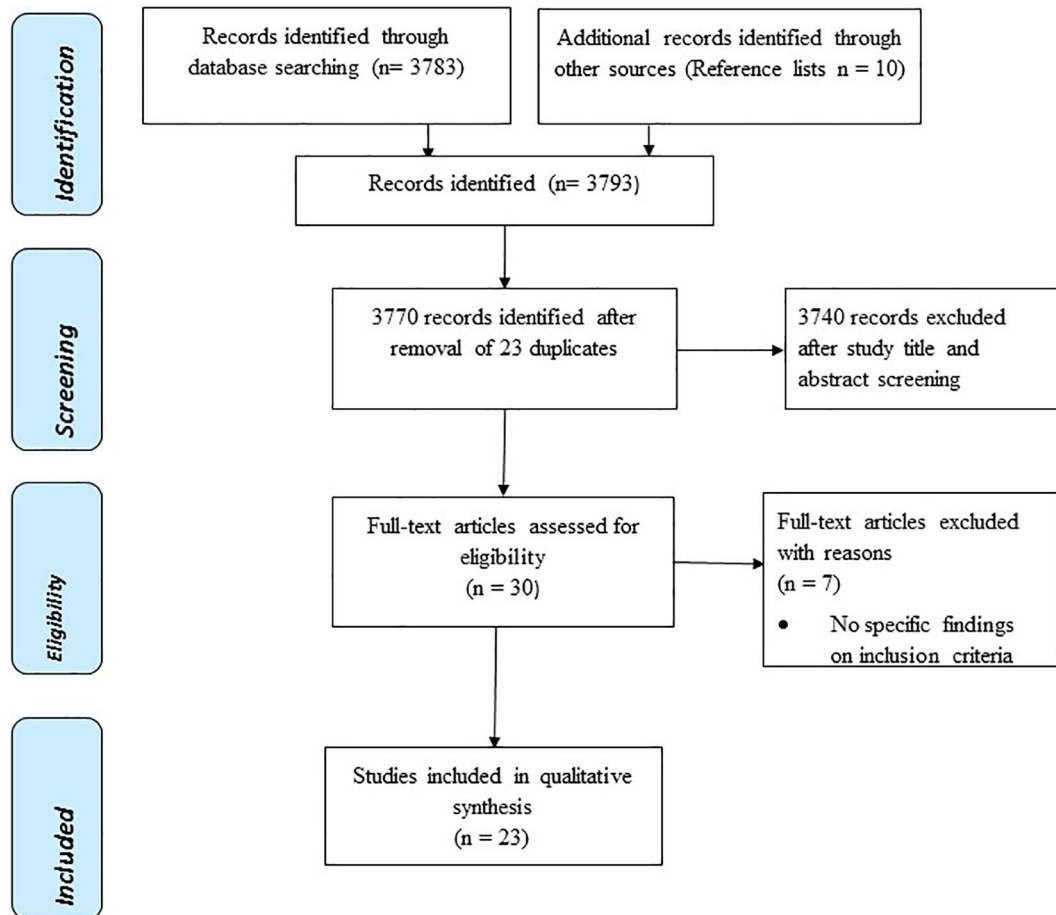


FIGURE 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram

antibodies in African countries. We calculated the weighted-pooled seroprevalence with a random effects model and assessed heterogeneity with the Hedges Q test and I^2 statistic. The statistical significance for Hedges Q statistic was set at $p < 0.1$ and I^2 values of greater than 75% indicated a higher heterogeneity between studies.¹⁶ The sample size, sensitivity, specificity, study region in Africa, number of days between the first Covid-19 reported case and the study period within a specific country, quality of the included studies and publication status were regarded as predetermined sources of heterogeneity and this was explored in subgroup and meta-regression analyses. The robustness and conclusiveness of the results was assessed using Jackknife sensitivity analysis which omits one study at a time to determine the influence of each study on the overall prevalence. The risk of publication bias and small study effect were detected through assessing the symmetry of a funnel plot, and its significance was assessed using the Egger's test. A non-significant Egger's test and symmetrical funnel plot indicated low possibility of publication bias. Therefore, $p < 0.05$ for Egger's test indicated publication bias. The meta-analysis was not performed for demographic characteristics associated with seroprevalence as the data was not enough and varied across different studies. The statistical analysis was conducted in STATA version 15.1 using the (metareg, metafunnel,

metaprop, metaninf, metabias commands) and R-software version 4.0.5 (meta and metaphor packages).

3 | RESULTS

The search strategy identified 3783 articles, and 10 additional articles were identified through review of reference lists. After screening 23 duplicates, 3740 and seven full text articles were successfully excluded; Figure 1 provides the reasons for exclusion. Accordingly, the meta-analysis of our study included 23 datasets from 23 unique studies. Of these, three were from Nigeria.¹⁷⁻¹⁹ Two were conducted in each of the following countries: Republic of South Africa,^{20,21} Ethiopia,^{22,23} Libya^{24,25} Kenya²⁶ and Democratic Republic of Congo (DRC).²⁷ One study was conducted in each of the following countries: Malawi,²⁸ Togo,²⁹ Ivory Coast,³⁰ Zambia,³¹ Egypt,³² Gabon,³³ Congo Brazaville,³⁴ South Sudan,³⁵ Cameroon^{36,37} and Guinea Bissau.³⁸

The study participants in 10 studies were recruited from the general population,^{18,22-24,31-36} four studies were from health workers,^{17,27,28,38} one study combined health workers and community,²⁵ one study combined health workers, air transport, police and drivers,²⁹ three studies recruited blood donors,^{19,20,39} one study recruited water front workers,²¹ one study involved travelers,⁴⁰ one

study recruited drivers and their assistants,²⁶ while the other one recruited gold miners.³⁰ All studies were conducted in the period between April 2020 and April 2021 except one study by Olayanju et al. (2021)¹⁷ in Nigeria which did not indicate the time/period of the study.

The overall quality of the studies as assessed using the JBI appraisal tool was high based on the rating system, with 74% classified as high quality, 22% moderate quality and 4% low quality (Table S2, Supplementary file).

In terms of biological samples, 15 studies used whole blood, while eight studies used serum samples (Table S1, Supplementary file). The commonly used type of serological test was LFIA, which was performed in nine studies, followed by ELISA in eight studies (Table S1, Supplementary file). Two studies used both the ELISA and LFIA tests, while one study used MN. The largest sample size was 4858 while the least was 98 (Table S1, Supplementary file). The highest anti-SARS-CoV-2 antibody seroprevalence was 63%²⁰ in the Republic of South Africa (RSA), while the lowest anti-SARS-CoV-2 seroprevalence recorded was 0%²⁴ in Libya (Figure 2). The sensitivity of test kits reported in this review ranged from 71.1/61.7% to 100.00%, while the specificity ranged from 85.02% to 100.00% (Table S1, Supplementary file) and were within acceptable ranges.⁴¹ However, two studies^{32,35} did not report on sensitivity. Two studies^{31,32} did not report on specificity. Twenty studies indicated that their tests were validated, thus two were not validated and one was not indicated (Table S1, Supplementary file). The sensitivity, specificity and the validation results from the included studies showed that the reported prevalence could be relied upon.

The anti-SARS-CoV-2 seroprevalence varied numerically across some demographic characteristics. Six articles reported that seroprevalence was higher among males than females while 12 articles showed that the prevalence was higher in females than males (Table S3, Supplementary file). For those studies that reported age among the Covid-19 positive cases, the highest seroprevalence was among those who were 50 years or less. For the studies that were conducted in the general population (Table S1, Supplementary file), health care workers (HCW) were not the top most affected group, except in a study by Benn et al. (2021) in which more medical staff and laboratory technicians were infected than other staff (Table S3). Those living in urban settings were numerically more affected (27.82%) than in rural setting (21.41%), in a study by Majiya et al. (2020) in Nigeria.¹⁸ A study by Shaw et al. (2021) in RSA found that seroprevalence was higher in participants with hypertension (15 [15.6%]) than diabetes (10 [10.4%]).^{21,42} Alemu et al. (2020), in Ethiopia found that prevalence was higher in married 13 (9.8%), compared to single 9 (6.8%), or divorced/widowed 1 (2.8%).²² Additionally, Alemu et al. (2020) also reported higher seroprevalence of 11 (5.7%) among those with high school and above education compared to those without formal education 1 (6.3%), or primary education (1–8).

A random effects model was utilized to estimate the pooled Anti-SARS-CoV-2 antibody seroprevalence since the heterogeneity between studies was very high ($I^2 = 100\%$, $p < 0.001$). The overall

estimated pooled seroprevalence of anti-SARS-CoV-2 antibodies in Africa involving 27,735 individuals was 22% (95%CI: 14–31; Figure 2). Between African countries the seroprevalence ranged from 0% to 63% (Figure 3)

Based on subgroup analysis with respect to study region, seroprevalence of anti-SARS-CoV-2 antibodies was higher in studies conducted in Central Africa (41%, CI: 14–72) compared to Southern Africa (34%, CI: 13–59), West Africa (25%, CI: 13–39), North Africa (13%, CI: 2–32) and East Africa (12%, CI: 2–28; Figure 4). Furthermore, there was a higher seroprevalence of anti-SARS-CoV-2 antibodies in blood donors (33%, CI: 12–60) compared with health care workers (28%, CI: 10–50) and the general population (18%, CI: 8–30; Figure S7, Supplementary File). The seroprevalence of non-peer reviewed studies (Pre-prints) was 28% (95%CI: 16–41) higher than that of peer reviewed published studies which was 18% (Figure S8, Supplementary File). Additionally, the seroprevalence was higher for studies of high quality (25%, 95%CI: 17–35) followed by moderate quality (16%, 95%CI: 4–34) and the least were low quality studies (3%, 95%CI: 0–34; Figure S9, Supplementary File). The increase in anti-SARS-CoV-2 antibody seroprevalence was independent of study sample size, sensitivity and specificity of serological tests and their combined interaction effect (Table S7, Supplementary File). Similarly, study quality did not influence the overall seroprevalence (Table S9, Supplementary File). The number of days between the first reported Covid-19 case in each country and when a seroprevalence study was conducted was a significant moderator of seroprevalence including in its multivariable interaction effect (Tables S8 and S10, Supplementary File).

The meta-influence of each study on overall seroprevalence based on Jackknife sensitivity analysis revealed that omitting a high quality study had a proportionate effect on overall anti-SARS-CoV-2 antibody seroprevalence than a low quality study with a range from 18.04 (CI –96.13 to 132.22) to 30.34 (CI: –88.72 to 149.41; Table S15, Supplementary File). The meta-bias of number of days between the first reported Covid-19 case in each country and when a seroprevalence study was conducted on overall seroprevalence based on Egger's test and asymmetrical funnel plot was significant ($p < 0.001$; Table S14, Supplementary File). Nevertheless, the study sample size, sensitivity and specificity of serological tests had no influence on overall anti-SARS-CoV-2 seroprevalence based on Egger's test and symmetrical funnel plots ($p > 0.05$; Tables S11–S13, Figures S4–S6, Supplementary File).

4 | DISCUSSION

Covid-19 is still the number one public health concern globally. This study provides a comprehensive appraisal of SARS-CoV-2 antibody seroprevalence in the human population from the African continent perspective from the available literature (up to 30th April 2021). This was necessitated upon observing that most globally published reviews on this topic critically under represented the Africa's Covid-19 burden.^{4,8,43,44}

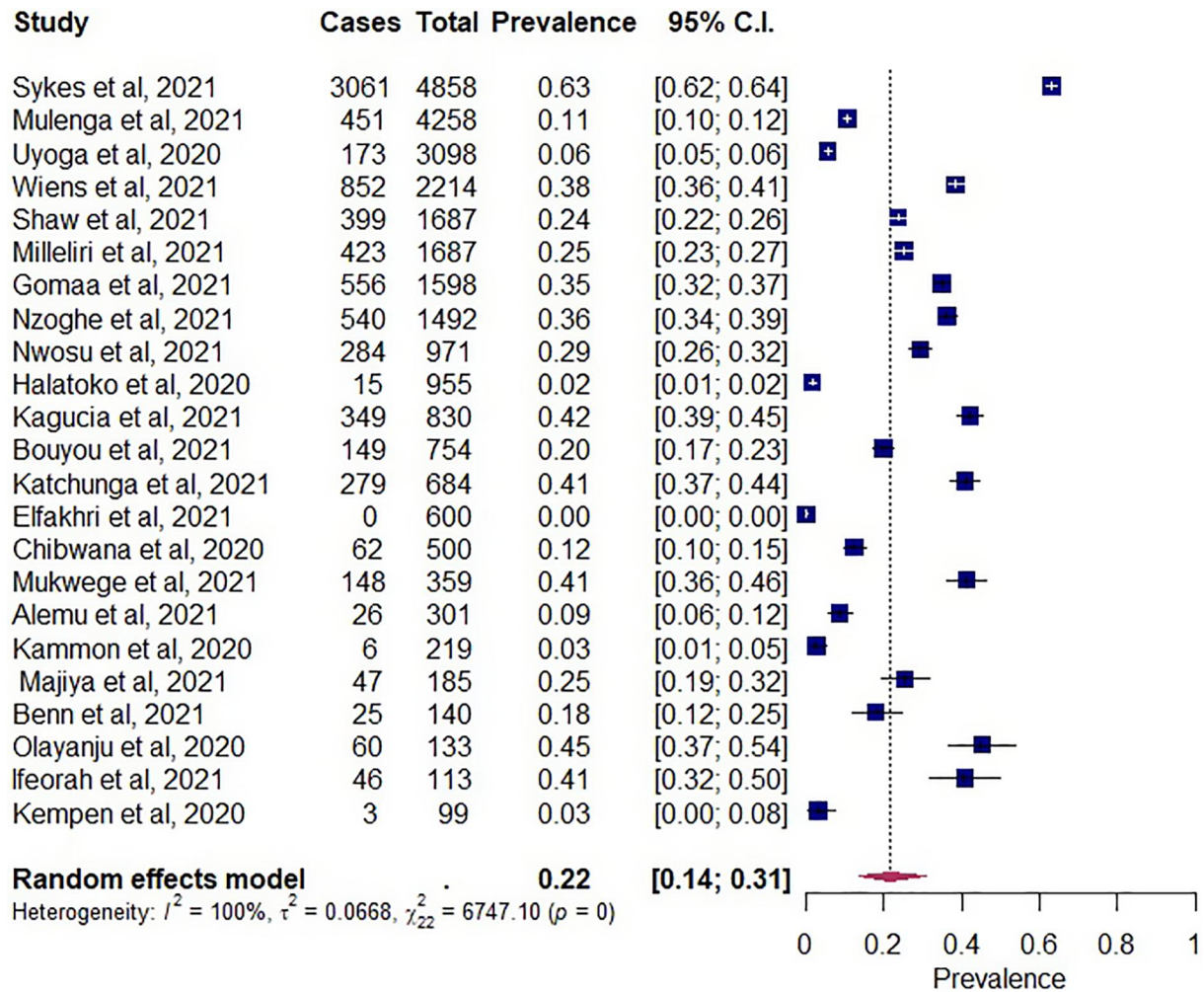


FIGURE 2 Forest plot of the seroprevalence of anti-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibodies with corresponding 95% confidence intervals in African countries. The proportional weight assigned to a study is shown by the size of the box and the horizontal lines symbolize the 95% confidence intervals (CIs) according to the random effects analysis

Overall seroprevalence varied markedly among and between countries (4–8), socio-demographic and health related characteristics. This review established that the estimated pooled seroprevalence of SARS-CoV-2 antibodies in Africa is 22% (95%CI: 14–31) with a seroprevalence range of 0% to 63% between countries which is higher than all global reviews estimates.^{4,8,43,44} However, the findings from this review are relatively low as compared to some studies conducted in India.^{45–47} Nevertheless, this could mean that even though Africa has experienced lower case morbidities and mortalities as compared to other continents, transmission of Covid-19 locally is very high.

Based on African region subgroup analysis, seroprevalence of anti-SARS-CoV-2 antibodies was higher in studies conducted in Central Africa (41%) compared to Southern Africa (34%), West Africa (25%), North Africa (13%) and East Africa (12%). As we have shown above, the main factor determining the high seroprevalence is likely the time point at which the study sample was taken, but there are many other factors on the African continent which might contribute to this heterogeneity significantly such as

chance, cultural practices, political decision-making, policies, mitigation efforts, health infrastructure and prevention/control measures and/or the effectiveness of the implementation of such measures as well as occupations.^{4,44,48,49} Contrary to many study findings, based on subgroup analysis of participants included in our review, seroprevalence of anti-SARS-CoV-2 antibodies was higher in blood donors followed by health care workers and general population. This could possibly be due to the usage of personal protective equipment and engagements in economic activities. Furthermore, blood donors are generally a healthy subset of the general population hence being the most socio-economically active group and likely more vulnerable to contract SARS-CoV-2.

As expected, the most significant factor affecting the seroprevalence was the number of days between the first reported Covid-19 case in each country and when a seroprevalence study was conducted and was a significant moderator of seroprevalence including in its multivariable interaction effect with those being conducted earlier showing low level of prevalence.

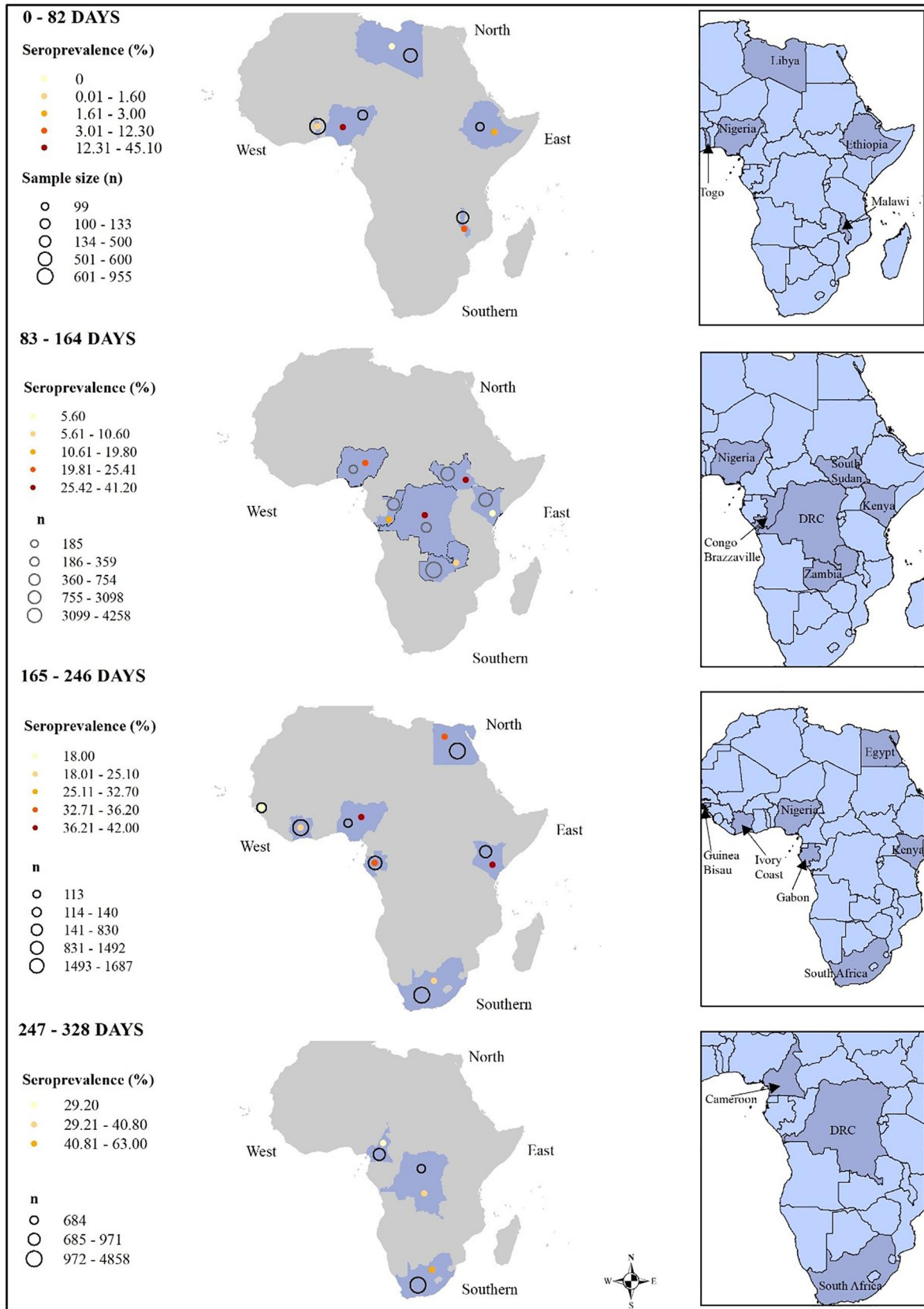


FIGURE 3 Estimated seroprevalence rates of anti-severe acute respiratory syndrome coronavirus 2 antibodies in African countries using the Arc Geographical Information System. Number of days represent days since the first reported coronavirus disease 2019 case in each study area

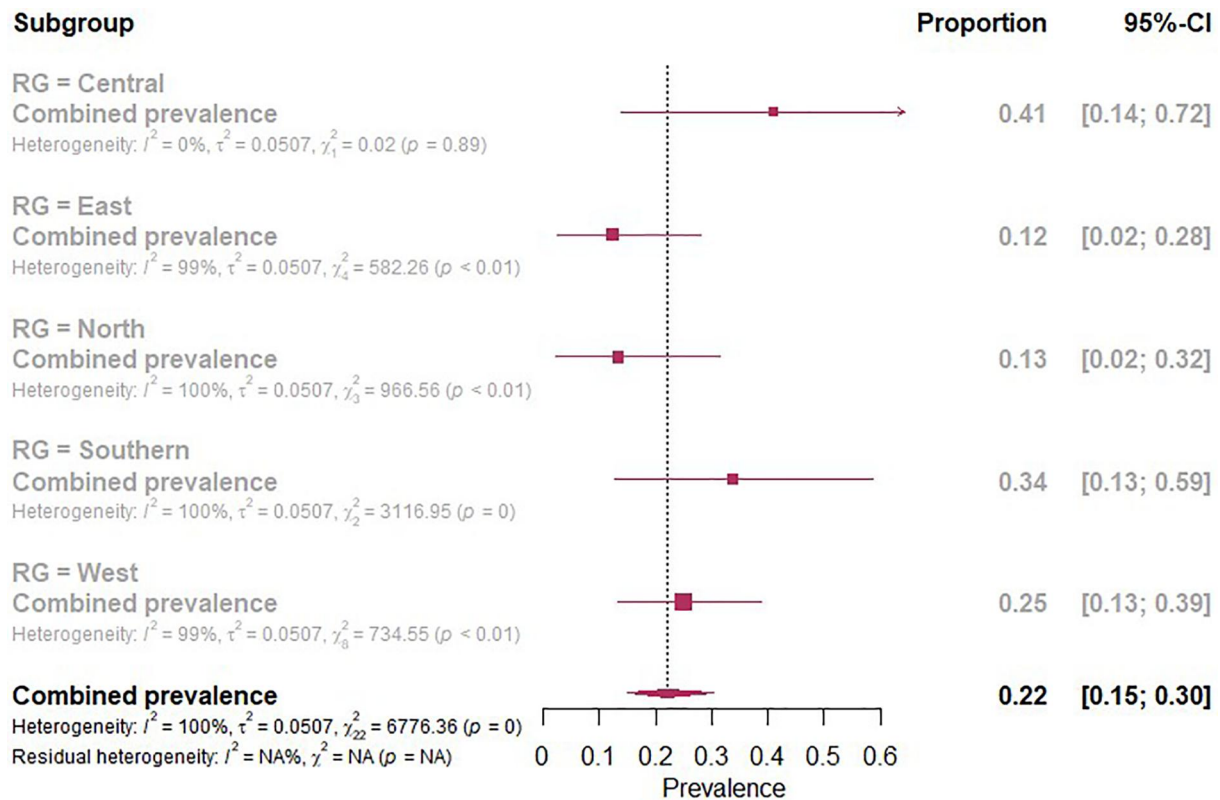


FIGURE 4 Subgroup analysis of the regions of Africa and anti-severe acute respiratory syndrome coronavirus 2 antibodies seroprevalence in Africa

Surprisingly, sample size, study quality, sensitivity and specificity of serological tests and their combined interaction effect did not influence the overall seroprevalence. This therefore shows that when evaluating the seroprevalence of anti-SARS-CoV-2 antibodies, it is imperative to always consider the effect of length of pandemic exposure period.

A numerically higher seroprevalence was registered in females, while some studies found high seroprevalence among males.^{8,17,18,29,30,39} However, a pooled analysis of systematic and meta-analysis studies conducted with a global data representation, established that the difference is not statistically significant.^{4,8,43,44} The insignificant differences in gender is also substantiated by the absence of gender factor in WHO and African CDC reports and strategic planning agenda.^{50,51}

High anti-SARS-CoV-2 antibody seroprevalence was reported among those aged 50 years or less.^{17,22,26,27,30,33,36,39} Five of these studies^{17,20,27,30,39} showed high anti-SARS-CoV-2 antibody seroprevalence among participants with ages between 30 and 50 years. These findings are in accord with a global review with over 58 datasets where they reported high pooled seroprevalence of anti-SARS-CoV-2 among people with age range of 20 to 49 years. Accordingly, studies^{52–57} which focused on the characterization of Covid-19 admitted cases have indicated that most of the patients had ages over 50 years with those critically ill having mean ages of over 60 years and majority of deaths observed among those aged over 65

years.⁵⁸ On the other hand, studies have also shown a low prevalence of Covid-19 among children.^{8,44} It is more likely that the high involvement in economic activities among individuals of the age group of 30–50 years could have contributed to high seroprevalence rate observed.^{44,49} However, some studies have reported lack of adherence to Covid-19 preventive measures among this age group.^{59–61} Hence an increase in the enforcement of restrictions on movements, assembly or gathering of people have been strongly advocated in most settings around the world.⁶¹ Much as it is imperative to continue advocating for the prohibitions of movement, gathering, social interactions and the rest of measures, the Covid-19 battle is multifaceted, demanding well thoughtful strategies on how to practically win the trust of the population and support them to cope with these stringent measures.⁶²

Similar to other studies,^{4,63} in this review, settlements,^{18,45,46,64} comorbidities,²¹ marital status²² and level of education²² were associated with rate of anti-SARS-CoV-2 seroprevalence. Particularly, studies from India have reported very high Anti SARS CoV-2 antibody seroprevalence among the residents of slums.^{45,46} Practically Covid-19 has shown and proven to have a gross and multifaceted dynamics on pathogenesis, transmission as well as preventions hence these factors may have an influence in one way or another.^{4,65–67}

Our study calls for more comprehensive SARS-CoV-2 seroprevalence studies in African continent to monitor progressive changes

in their respective countries. In the context of epidemics and pandemics, such studies might be conducted regularly to allow authorities to assess the spread of the virus and exposure levels of populations.⁴ As most African countries are adopting and procuring vaccines which is likely to be in insufficient quantities for everyone in the shortest time period, a plan is still required to monitor SARS-CoV-2 seroprevalence to continue assisting in prevention and control efforts. Furthermore, with the emergent evidence that the rate of reinfection of SARS-CoV-2 is very low,^{11,12} we speculate that other countries may decide to exempt the confirmed anti-SARS-CoV-2 antibody seropositive people as a cost cutting measure of vaccine administration.

As the present study represents an African first 'snapshot' of SARS-CoV-2 seroprevalence based on evaluation of published information, it has a number of limitations. First, after 12 months since the Covid-19 pandemic started, there is a critical lack of peer-reviewed, population-based studies from many countries across the African continent and some studies included here lacked data on most important basic epidemiological variables like sex and age of subjects tested. Furthermore, the disease onset for each country is different hence posing a critical challenge on generalization. We are optimistic that these challenges will be addressed in the coming studies, so that future longitudinal investigations will provide better representative estimates of seroprevalence. This will ensure that conclusive decisions might be reached regarding endemic stability and instability in particular countries.

5 | CONCLUSION

Overall, anti-SARS-CoV-2 seroprevalence varied numerically among countries, socio-demographic and health related characteristics. This review has registered one of the highest pooled seroprevalence (22%) of anti-SARS-CoV-2 antibodies. However, due to inconsistency in the captured data, lack of comprehensive reporting, and methodological flaws, the existing findings should be interpreted with caution. More rigorously executed anti-SARS-CoV-2 seroprevalence studies in Africa are needed to monitor progressive changes in respective countries.

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CONFLICT OF INTEREST

The authors declare no competing interests.

AUTHOR CONTRIBUTIONS

Design of the literature review: Master R.O. Chisale, Sheena Ramazanu, Saul E. Mwale & Balwani C. Mbakaya. Protocol writing

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DATA AVAILABILITY STATEMENT

We want to confirm that the processed data associated with our results are existing within the systematic review. However, the raw data are available upon request to the Corresponding author (Saul Eric Mwale).

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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