

Seroprevalence of COVID-19 and Its Associated Factors Among Nigerian University Students: A Cross-Sectional Study

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Abstract: Universities were potential hubs for SARS-CoV-2 transmission in Nigeria; however, empirical data on the infection burden among students have been limited. The study assessed the seroprevalence of SARS-CoV-2 and associated factors among undergraduates at a public University to inform educational and public health policy. The study used a cross-sectional design and was conducted among systematically sampled students at the University of Benin City, Nigeria, between February and December 2022. Sociodemographic and behavioural data were collected using a structured tool. Nasal swabs and venous blood were tested for SARS-CoV-2 antigen and IgM/IgG antibodies using rapid diagnostic assays. Seroprevalence was estimated with 95% Confidence Intervals (CIs), and associated factors were explored using logistic regression, with the findings presented as adjusted odds ratios (aORs). Among 677 participants (mean age, 21.5 years), all antigen tests were negative. Of 670 valid serological results, 79.6% tested positive for IgG and 14.0% for IgM. IgG positivity was independently associated with the use of mixed transportation (aOR 2.32; 95% CI: 1.31-4.09) and attendance at religious gatherings twice a week (aOR 1.82; 95% CI: 1.07-3.10). IgM positivity was higher among students residing in rural settings and lower among those using mixed transportation. In conclusion, no active COVID-19 infection was detected, but most students had evidence of past infection during the post-omicron period. These findings underscore the substantial cumulative exposure among young adults and highlight the importance of strengthening prevention strategies in university settings.

Key word: COVID-19, Nigeria, Seroprevalence, Students

INTRODUCTION

As in most parts of the world, the coronavirus disease 2019 (COVID-19) pandemic profoundly impacted various spheres of Nigeria's national life, including the health, economy, and educational sectors, with its largely youthful population significantly affected (Amzat *et al.*, 2020). Universities and other institutions of higher learning, in particular, are recognised as hotspots for the transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the aetiologic agent of COVID-19 (Brooks-Pollock *et al.*, 2021). This is due to the predominantly young adult population (students continue to transmit the disease even when asymptomatic), as well as the prevalence of social activities and congregate settings (Brooks-Pollock *et al.*, 2021). On 23 March 2020, less than a month after the confirmation of the first COVID-19 case in the country, the Nigeria Ministry of Education ordered the unscheduled closure of primary and secondary schools, as well as Universities nationwide, to minimise the

direct impact of COVID-19 and the potential spread of the disease by asymptomatic persons (Ndejjo *et al.*, 2023). Despite school closures and other community mitigation strategies implemented with varying degrees of success, the pandemic persisted (Dan-Nwafor *et al.*, 2021). Without research evidence, there was uncertainty regarding the added benefits of school closure. Therefore, most Nigerian Universities, especially government-owned, fully reopened in January 2021, following directives to ensure robust implementation of non-pharmaceutical interventions, including physical distancing, handwashing, and the use of face masks (Akande *et al.*, 2021a).

While the prompt closure of Universities is believed to have decreased the rapid transmission of COVID-19 in Nigeria and elsewhere, the negative consequences on the country's educational system may have been underestimated. These harmful effects, which disproportionately affected public universities, included disruption of the academic calendar, truncation of learning,

especially due to poor technological infrastructure supporting virtual education, faculty attrition, an increased student dropout rate, and psychological/mental health effects on students (Okagbue *et al.*, 2023). By the end of January 2022, most West African countries had experienced four recognisable COVID-19 pandemic waves, each dominated by a SARS-CoV-2 variant of concern (Julienne Selb Ndiaye *et al.*, 2023). Although less harmful in terms of disease severity and case fatality than previous variants, the omicron variant (B.1.1.529), which predominated during the fourth wave, displayed higher transmissibility (Manathunga *et al.*, 2023). However, there remains little to no evidence of the cumulative impact of COVID-19 on Nigerian students in higher education institutions (Akande *et al.*, 2021b). Furthermore, it is unclear to what extent the public health measures instituted in Universities were adhered to and, consequently, curbed transmission in these institutions of higher learning, particularly during the highly contagious fourth wave. Therefore, this study aimed to determine the seroprevalence of SARS-CoV-2 infection among undergraduate students at a large public University in Nigeria and to identify the sociodemographic and behavioural characteristics associated with seropositivity.

MATERIALS AND METHODS

Study design and setting: This cross-sectional study was conducted at the University of Benin in Edo State, southern Nigeria. The University has an average student population of 40,000. Students were engaged in the study at various strategic points within the University.

Sampling approach: The study used systematic sampling to recruit students. Beginning sampling at a randomly selected starting point within the University, the study team approached every fifth student to determine their eligibility. In the case of ineligibility, the study repeated the sampling approach until the study's end date.

Study participants: Students aged ≥ 18 years who were willing to sign an informed consent form were eligible to participate in the study, regardless of prior COVID-19 infection status, COVID-19 symptoms, or vaccination status. Those who are unwilling to consent or who experienced difficulty providing samples were excluded.

Sample size estimation: Sample size was estimated thus:

$$n = \frac{3.84\pi(1-\pi)}{w^2}$$

Where n =sample size; w =precision (confidence interval); and π =COVID-19 seroprevalence. The seroprevalence of COVID-19 among University-going students in the study context was assumed to be 20% ($\pi = 0.2$), and the study aimed to estimate the sample size to be within 2.5% ($w = 0.025$) with 95% certainty. Therefore, the sample size was estimated at 983; however, to account for non-response, a 10% contingency was added, resulting in a final sample size of 1,091, approximated to 1,000 students, given financial and time constraints.

Data collection: The data collection team was trained to use the Open Data Kit App, which enhanced the capacity for real-time data transmission and data quality monitoring. Before data collection, the study questionnaire was piloted with 20 students to assess its comprehensibility and the timeliness of administration. All identified gaps were addressed, such as making some questions mandatory. Each systematically selected student was approached and informed about the study, including ethical considerations, the requirement for blood samples for serological tests and socioeconomic data. Following screening for eligibility, only those who met the study's predefined inclusion criteria were recruited. After completing the consent form, there was an opportunity to ask questions as needed. Firstly, a questionnaire on socioeconomic and clinical data was administered to the student by a trained data collector. Some of the variables captured at

this stage included age, sex, state of residence, ethnicity, religion, accommodation type, hostel type, size and sharing facilities, parental occupation, mode of transportation to school, signs and symptoms of COVID-19, and pre-existing medical conditions. Secondly, the student was referred to a phlebotomy station within the data collection venue to withdraw 5 mL of venous whole blood and collect nasal swabs, as per the predefined study standard procedures. Testing for SARS-CoV-2 antigen was conducted on campus at the point of data collection, while observing standard precautions and performing intermittent environmental decontamination. A rapid lateral flow antigen detection device (SD Biosensor, Republic of Korea) targeting the SARS-CoV-2 nucleoprotein was used. Arrangements were made to refer students with a positive antigen result to the University Healthcare Centre. The collected blood samples were transported to the Medical Microbiology Laboratory at the University of Benin Teaching Hospital, Benin City, Nigeria, where samples were processed and tested according to the manufacturer's instructions for SARS-CoV-2 IgG and IgM (SD Biosensor, Republic of Korea). The test kit is a rapid antibody detection kit that detects antibodies formed against the SARS-CoV-2 nucleoprotein (Ndejjo *et al.*, 2023).

Duration of data collection: Data collection for this study commenced in February 2022 and concluded in December 2022, as the fourth wave, dominated by the omicron variant, began to subside. However, data collection stopped between March and October due to an eight-month industrial action by the Academic Staff Union of Universities (ASUU). Data collection resumed in November 2022 and ended in December 2022.

Data management and analyses: Data management and statistical analyses were performed using Stata version 16 (College Station, TX: StataCorp LLC). A seropositive student was defined as one who is IgM+/IgG-, IgM-/IgG+ or IgM+/IgG+. A

positive antigen test was considered an active infection, necessitating follow-up at the University of Benin Staff Clinic. Covariates were managed accordingly, using definitions consistent with the existing literature. The 'missing indicator' approach was used to handle missing data, which is epidemiologically more robust than the complete-case analysis. Descriptive statistics were used to summarise the students' baseline and demographic characteristics. These statistics included frequencies and percentages for binary/categorical variables, as well as means (SD) for normally distributed continuous variables.

The seroprevalence of SARS-CoV-2 antibodies (IgM/IgG) and antigen was determined using proportions with 95% Confidence Intervals (CIs). The seroprevalence of COVID-19 by age group, sex, accommodation type, and faculty of study was also calculated. The factors associated with SARS-CoV-2 IgG and IgM were determined using logistic regression models. First, we assessed the association between each covariate and serological test outcomes using the Chi-squared test, with *p*-values <0.05 considered statistically significant. Then, a univariable logistic regression model for each outcome variable was developed, and the findings were presented as odds ratios (ORs) with 95% CIs. *P*-values from Wald tests were presented for binary or continuous variables, and those from the likelihood ratio tests for categorical variables. Only statistically significant covariates were entered into the adjusted model, and the findings were presented as adjusted ORs (aORs) with 95% CIs. The report was structured according to the STROBE checklist for a cross-sectional study (Cuschieri, 2019).

Ethics approval and consent to participate:

Before commencing the study, ethical approval was obtained from the University of Benin College of Medical Sciences Research Ethics Committee (approval number: CMS/REC/2021/247). The purpose of the study was explained to all the participants before seeking informed

consent, ensuring that anonymity and confidentiality were maintained throughout the study.

RESULTS

Baseline characteristics of the study participants

Six hundred and seventy-seven (N=677) students were recruited for this study. The proportion of students aged 18-22 was the highest at 71.1%, while that of males was slightly higher than that of female students (52.4% vs 47.6%). Regarding residency while in school, about three-quarters (77.7%) of the students reported off-campus as their residency, while over half (58.1%) described their accommodation as self-contained off-campus. The most common mode of transportation during studies was walking (36.3%), followed by bus or tricycle. Only about 22% of the students expressed concern about contracting COVID-19, while the majority (61.2%) reported discomfort wearing a face mask as a preventive measure against COVID-19 infection. The most frequently reported clinical signs and symptoms seven days before participation in the study were headache (26.0%), cough (11.8%), and runny nose (11.5%).

Seroprevalence of COVID-19 among students

Seven of the 677 serological tests (IgG and IgM) were deemed invalid per the manufacturer's protocol, leaving 670 records for subsequent analysis. All the antigen tests were negative; therefore, the focus shifted to serological tests. Eighty per cent (95% CI: 76.3-82.4) of the study participants tested positive for SARS-CoV-2 IgG, while 14% (95% CI: 11.6-16.9) tested positive for SARS-CoV-2 IgM (Table 1). The seroprevalence of SARS-CoV-2 IgG and IgM, in relation to students' demographic and academic characteristics, is presented in Table 2. The highest seroprevalence of SARS-CoV-2 antibodies was recorded among students aged 23-27 for IgG at 83.5% and among those aged ≥ 28 for IgM at 25.0%. Female students recorded the highest

SARS-CoV-2 IgG and IgM positivity at 80.4% and 14.5%, respectively. Year 4 and 3 students recorded the highest SARS-CoV-2 IgG and IgM prevalence, respectively. Regarding accommodation type at school, students who reported living in a shared apartment or self-contained accommodation off-campus had the highest prevalence of SARS-CoV-2 IgG and IgM, respectively.

Students' characteristics associated with SARS-CoV-2 IgG positivity

In both the unadjusted and adjusted models, only students' mode of transportation while in school (walking, bus/tricycle, private taxi, or mixed transportation platform) and their weekly attendance at religious gatherings (more than twice, twice, once, and never) were significantly associated with IgG positivity. Specifically, the odds of IgG positivity among students who reported using a mix of transportation modes were 2-fold higher (OR 2.25; 95% CI: 1.28-3.94) than among those who primarily walked while in school. The odds of IgG positivity were also higher when using a bus or tricycle than when walking, but the difference was not statistically significant. Similarly, the odds of IgG positivity appear to increase with attendance at religious gatherings less than twice per week. Notably, attendance at religious gatherings twice a week increased the odds of IgG positivity by almost two-fold (OR 1.78; 95% CI: 1.05-3.03). In the adjusted model, the odds of IgG positivity remained significantly associated with using mixed transportation means (aOR 2.32; 95% CI: 1.31-4.09) compared to walking and attendance at religious gatherings twice per week (aOR 1.82; 95% CI: 1.07-3.10) compared to a frequency of more than twice per week.

Students' characteristics associated with SARS-CoV-2 IgM positivity

Similar variables were explored in relation to IgM positivity among the study participants. In the unadjusted model, residential settings during holidays, state of residence during holidays, the primary mode of transportation, and frequency of attending religious gatherings were significantly

associated with IgM positivity. Specifically, the odds of IgM positivity were 93% higher among students who reported a rural residential setting than those who reported an urban setting (unadjusted OR 1.93; 95% CI: 1.07-3.49). Compared with Edo State residents, the odds of IgM positivity were 71% higher and threefold higher among those from Nigeria's South-West and North-Central regions, respectively. Compared with students who primarily walk to school, the odds of IgM positivity were 64% lower among those who use multiple modes of transportation. Unlike the association with IgG positivity, the odds of IgM positivity decreased by half among students who reported attending religious gatherings twice a week compared to those who attended more than twice a week. In the adjusted model, the association between students'

state of residence and IgM positivity became non-significant; however, the residential setting, the primary mode of transportation, and the frequency of attending religious gatherings remained statistically significant. Specifically, the odds of IgM positivity were about twice as high (aOR, 1.99; 95% CI, 1.08-3.67) among rural residents compared with urban residents. The odds of IgM positivity decreased by 60% (aOR, 0.30; 95% CI, 0.15-0.60) among students who used mixed modes of transportation compared to those who walked. Additionally, the odds of IgM positivity continued to decrease by half (aOR 0.50; 95% CI: 0.26-0.95) among students who attended weekly religious gatherings, compared with those who attended twice or more.

Table 1: Seroprevalence of SARS-CoV-2

Diagnostic test	Rapid diagnostic test result (%)	95% CI
SARS-CoV-2 IgG		
Negative	20.4	17.6-23.7
Positive	79.6	76.3-82.4
SARS-CoV-2 IgM		
Negative	86.0	83.1-88.4
Positive	14.0	11.6-16.9

Table 2: Seroprevalence of SARS-CoV-2 IgG and IgM (N=670)

Variable	SARS-CoV-2 IgG		SARS-CoV-2 IgM	
	Negative	Positive	Negative	Positive
Age group, year				
18-22	21.4 (18.0-25.4)	78.6 (74.6-82.0)	85.1 (81.6-88.0)	14.9 (12.0-18.4)
23-27	16.5 (11.8-22.6)	83.5 (77.4-88.2)	89.0 (83.6-92.8)	11.0 (7.2-16.4)
≥28	41.7 (18.4-69.3)	58.3 (30.7-81.6)	75.0 (44.8-91.7)	25.0 (8.3-55.2)
Sex				
Female	19.6 (15.5-24.3)	80.4 (75.7-84.5)	85.5 (81.2-89.0)	14.5 (11.0-18.8)
Male	21.2 (17.3-25.8)	78.8 (74.2-82.7)	86.4 (82.4-89.6)	13.6 (10.4-17.6)
Year of Study				
Year 1	20.4 (14.6-27.9)	79.6 (72.1-85.4)	86.6 (78.0-91.3)	13.4 (8.7-20.0)
Year 2	22.2 (16.5-29.1)	77.8 (70.9-83.5)	85.0 (78.8-89.7)	15.0 (10.3-21.2)
Year 3	23.6 (17.8-30.4)	76.4 (69.6-82.2)	83.3 (77.0-88.2)	16.7 (11.8-23.0)
Year 4	16.0 (11.1-22.4)	84.0 (77.6-88.9)	88.3 (82.4-92.4)	11.7 (7.6-17.6)
Year 5 or higher	16.7 (6.4-37.0)	83.3 (63.0-93.6)	91.7 (72.1-97.9)	8.3 (2.1-2.8)
Accommodation type				
Self-contained (off-campus)	22.9 (19.0-27.3)	77.1 (72.7-81.0)	83.5 (79.5-86.9)	16.5 (13.1-20.5)
Shared apartment (off-campus)	14.4 (9.4-21.5)	85.6 (78.5-90.6)	92.4 (86.5-95.9)	7.6 (4.1-13.5)
School hostel (on-campus)	19.5 (13.9-26.6)	80.5 (73.4-86.1)	86.6 (80.1-91.2)	13.4 (8.8-19.9)

DISCUSSION

The study estimated the prevalence of SARS-CoV-2 antibodies among undergraduates attending a public University

in South-South Nigeria. Following the highly transmissible omicron wave, the study found that nearly eight out of ten students at the University had been naturally

infected, as evidenced by anti-nucleocapsid IgG antibodies to SARS-CoV-2. All antigen tests, however, were negative, ruling out any active infections. Less than one in ten of the sampled students reported ever conducting a test for COVID-19, and fewer than one in a hundred reported having a positive test result in the past. Thus, the study highlights the importance of serology in understanding infection dynamics, particularly in the context of limited testing activity, as observed in Nigeria.

There is a dearth of information about the prevalence of COVID-19 in educational settings in Nigeria. In March 2020, very early in the pandemic, a prevalence of 1.4% was recorded among students from three private Universities in Rivers State who underwent testing using the gold-standard polymerase chain reaction test (Okoro *et al.*, 2023). Upon the resumption of academic activities in 2021, zero prevalence was recorded among students returning to the University of Port Harcourt, Rivers State, Nigeria, using rapid diagnostic antigen tests (Henrietta Ogadimma Asuzu-Samuel *et al.*, 2021). These studies targeted only active infections and were conducted before the omicron wave. Contrastingly, in March 2021, a serological survey revealed that 27% of students at a University in Cameroon had SARS-CoV-2 antibodies (Essomba *et al.*, 2023). Another study conducted at a different Cameroonian campus in December 2021 reported a seroprevalence of 73.6% among the predominantly student population (Wondeu *et al.*, 2023), which was closer to the findings of this study. Collectively, these data illustrate the advantage serological studies possess over case ascertainment using tests that target the virus directly. The findings also imply that studies conducted during or after the omicron wave reported higher infection rates.

Despite the lack of seroprevalence data from educational institutions in Nigeria, it remains relevant to compare these findings with those from community-based studies. The seropositivity rate in our study is significantly higher than the rates of 17.6%

in Anambra and 18.9% in Enugu, Gombe, Lagos, and Nasarawa States across Nigeria (Audu *et al.*, 2022; Okpala *et al.*, 2021). Unlike our study, which was conducted after the highly contagious Omicron wave and involved mostly young adults, these studies were household surveys conducted in 2020 and encompassed a broader age range. Nevertheless, community-based studies conducted in 2021 demonstrated higher rates of 43.7% in Kaduna and 66.8% in Kano, as well as in Ebonyi, Imo, Oyo, and Lagos (Burbelo *et al.*, 2020; Olaleye *et al.*, 2022). The largest community-based survey in Nigeria to date was conducted between June and August 2021. It involved 12 states, with seroprevalence rates ranging from 73.6% to 85.9%; in Edo State, it was 74.0% (Matthew Kolawole *et al.*, 2022). Notably, this study utilised an enzyme-linked immunosorbent assay (BeijingWantai BioPharm) with combined IgG and IgM assays, which may have led to a higher seroprevalence. These data demonstrate that multiple factors, including the pandemic's trajectory, the target demographic, and the assay type, can influence seroprevalence rates.

As in other seroprevalence studies, sex did not significantly influence seropositivity in our study. The study also did not detect a significant relationship with age, probably because most were young adults. However, some socio-behavioural patterns associated with SARS-CoV-2 seroprevalence were identified, including an increased risk of IgG positivity among students who used mixed/multiple modes of transportation compared to those who walked. Additionally, the risk of IgG positivity increased by 82% among students who attend religious gatherings twice a week compared to those who attend more frequently. This is surprising, as one might have expected the risk to be the other way around, given that COVID-19 transmission risk tends to increase with proximity. However, the decreased risk might be explained by perceived infection risk, with students attending more religious gatherings complying more with preventive measures,

such as face masks, than their counterparts with lower attendance frequency. Another surprising finding was that the availability of COVID-19 preventive infrastructure and mitigating behaviours, such as social distancing, did not significantly affect seroprevalence. Since students were not confined to the school campus, and the effectiveness of prevention strategies outside the Universities was not assessed, it would be difficult to exclude external confounders. When mitigation strategies are practised in particular settings but ignored in others, the desired effects of reduced transmission may not be achieved. Consequently, concerted efforts are necessary to promote the comprehensive adoption of these strategies in all settings.

Although young adults, who constitute the majority of participants in the present study, are less likely to have severe disease (most participants may even remain asymptomatic) (Brooks-Pollock *et al.*, 2021), the sheer number of infected persons still raises concern. Long-term sequelae of COVID-19 (long COVID), including fatigue, impaired exercise capacity, cognitive disturbances and cardiovascular complications, have been reported in not only patients with more severe COVID-19 but also amongst non-hospitalised individuals, including those who were asymptomatic (O'Mahoney *et al.*, 2023). Moreover, about one in ten of the participants in our study had pre-existing medical conditions, including asthma, hypertension and diabetes, which have been shown to predict long COVID-19 significantly (Arjun *et al.*, 2022). Since these individuals may be particularly at risk for long-term COVID-19 sequelae, this category may benefit from long-term follow-up. Future research should investigate whether post-acute sequelae of SARS-CoV-2 infection are present in student populations and their impact on the health status and educational goals of these individuals.

Compared to the few studies on COVID-19 prevalence among University students in Nigeria (Henrietta Ogadimma Asuzu-Samuel *et al.*, 2021; Okoro *et al.*, 2023), this

study's strength lies in its methodological approach, which combines direct viral detection with serology. This enabled this study to determine the cumulative number of students infected, rather than detecting only active infections, as was done in previous studies (Henrietta Ogadimma Asuzu-Samuel *et al.*, 2021; Okoro *et al.*, 2023). Using an antibody assay targeting the nucleocapsid protein also strengthened the study's findings by addressing the confounding effects of vaccination and enabling the detection of only individuals with infection-induced immunity. Despite the strengths, the study also had some limitations. These limitations included using a rapid antibody test, which is generally less accurate than laboratory tests, such as enzyme immunoassays (Essomba *et al.*, 2023). However, the study selected assay with manufacturer-reported high sensitivity and specificity that corroborated and was adjudged to be one of the best-performing assays in a large external validation study (Lutalo *et al.*, 2021). In addition, the eight-month industrial action embarked on by the academic staff union of universities forced us to halt data collection and resulted in an unplanned phasing of the study; since antibodies to SARS-CoV-2 nucleocapsid decline at a faster rate than antibodies to spike protein (Burbelo *et al.*, 2020), some previously infected participants may have sero-reverted by the time data collection resumed in October causing an inadvertent underestimation of the burden of COVID-19. Furthermore, 68% was recruited of the estimated 1,000 students initially proposed for the study. Therefore, despite the fact that the study recruited more participants than similar studies (Asuzu-Samuel *et al.*, 2021; Essomba *et al.*, 2023; Okoro *et al.*, 2023), this should be considered when interpreting the generalisability of the findings to the University of Benin, Benin City, Nigeria.

CONCLUSION

This study found a high prevalence of antibodies from natural COVID-19 infection among students at the University of Benin,

Benin City, Nigeria, during the period following the Omicron wave. The findings may aid Universities and public health authorities in formulating policies to structure the academic calendar and limit the spread and impact of future outbreaks of this and similar infectious diseases.

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