NIPES
Journal of Science and Technology Research
Journal homepage: www.nipesjournals.org.ng

Epidemiology of Asymptomatic COVID-19 Infection in Nigeria

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Article Info

***Keywords*:**
Adults; Asymptomatic infection; Children; COVID-19; Nigeria; RT-PCR

Received 09 May 2023
Revised 15 June 2023
Accepted 19 June 2023
Available online 11 August 2023

https://doi.org/10.5281/zenodo.8229780

ISSN-2682-5821/

Abstract

There is a high proportion of asymptomatic positive COVID-19 patients at testing sites in Nigeria, with the possibility for disease transmission. Therefore, this study aimed to describe and identify the contextual factors associated with asymptomatic COVID-19 infection in Nigeria. We retrospectively analysed the Nigerian surveillance and laboratory data between February 27 and June 6, 2020, defining asymptomatic children (<18 years) and adults (≥18 years) as those who tested positive for COVID-19 by RT-PCR but reported no symptoms of illness at testing. Multivariable logistic regression analyses were performed to identify factors independently associated with asymptomatic infection. Of 11,437 study participants, 1,048 (9.2%) and 10,389 (90.8%) were children and adults, respectively; 71.3% of children and 64.1% of adults had an asymptomatic infection. The adjusted odds for asymptomatic infection was 62% higher in children than in adults [OR 1.62, 95% CI: 1.40-1.88]. In adults, Quranic education [OR 2.27, 95% CI: 1.40-3.68], high-risk profession (healthcare) [OR 1.84, 95% CI: 1.46-2.33], South-East [OR 1.98, 95% CI: 1.37-2.86] and North-East [OR 1.25, 95% CI: 1.02-1.52] residency, and close contact with a COVID-19 case [OR 1.76, 95% CI: 1.52-2.04] were positively associated with asymptomatic infection. In both children [OR 3.7, 95% CI: 1.41-9.78] and adults [OR 1.30, 95% CI: 1.07-1.59], reporting to tertiary hospitals was positively associated with asymptomatic infection. In conclusion, the findings suggest that asymptomatic COVID-19 infection in Nigeria is associated with age and sociodemographic factors; thus, such individuals should not be dismissed as being COVID-19-negative just on the basis of the absence of symptoms.

1.0.Introduction

As at August 2, 2020, the Coronavirus Disease 2019 (COVID-19) pandemic had infected more than 17 million people globally, resulting in over 600,000 deaths [1] and a case-fatality ratio of 3.9%. During the same period, the Nigeria Centre for Disease Control (NCDC) recorded over 40,000 confirmed COVID-19 cases and over 800 deaths [2]. As at the time of writing, there is neither a definitive COVID-19 treatment nor vaccine for prevention, although early findings from a phase 1/2, single-blind, randomised controlled trial involving 1,077 healthy adults in the UK, present an optimistic outlook for a vaccine [3]. Prevention of human-to-human transmission of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) via minimising respiratory droplets and close contact remains the primary public health

intervention [4]. Preventive public health measures include physical distancing [5], use of facemask in public [6], specialised personal protective equipment in healthcare facilities, and isolating or quarantining COVID-19 patients and contacts as the case may be [7]. Implementation of these non-pharmaceutical measures is even more important given emerging evidence supporting the transmission of SARS-CoV-2 by pre-symptomatic (detection of SARS-CoV-2 virus before symptom onset) or asymptomatic (detection of SARS-CoV-2 virus without any symptoms) COVID-19 patients [8]–[13]; however, compliance with such measures in the general population is challenging. Furthermore, evidence suggests high viral shedding in asymptomatic carriers of SARS-CoV-2 [4] and their capacity to transmit the virus, thus contributing to the COVID-19 pandemic [13]. It is worth noting, however, that as at June 11, 2020, the World Health Organisation's stance on COVID-19 transmission by asymptomatic cases is that asymptomatically infected individuals are much less likely to transmit SARS-CoV-2 than those who develop symptoms [14].
Evidence from the literature indicates that asymptomatic COVID-19 cases account for about 40% to 45% of SARS-CoV-2 infections and that they may be capable of transmitting SARS-CoV-2 to others for up to 14 days or more [15]. The review also noted that asymptomatic infection might be associated with subclinical lung abnormalities based on findings from computed tomography. In Nigeria, the proportion of asymptomatic COVID-19 cases at testing was found to be as high as 66% (8,150/12,289) [In Press]. Generally, the transmission of COVID-19 by asymptomatic cases has serious public health implications and could pose a challenge to the implementation of control measures [16]. Firstly, the omission of asymptomatic COVID-19 cases due to narrow screening criteria could underestimate the ate disease burden and misguide public health planning and interventions. For instance, there is evidence suggesting that the global COVID-case fatality may be lower than the current estimates when asymptomatic SARS-CoV-2 infections are identified and taken into account [17], [18]. Secondly, asymptomatic COVID-19 cases could limit the surveillance utility of COVID-19 case definitions (suspected, probable and confirmed) and indeed the Integrated Disease Surveillance and Response (IDSR) framework which has been leveraged on response in Africa [19]. For instance, the case definitions developed by NCDC is largely centred on symptoms (fever, cough, difficulty in breathing or shortness of breath) with history of international travel, contact, or epidemiology [20]. Active community case search also make use of this stringent case definitions, thereby excluding asymptomatic or pre-symptomatic cases.

It is imperative, therefore, that COVID-19 testing programmes capture asymptomatic persons given their potential to transmit the disease unwittingly [15]. The value of early identification of asymptomatic COVID-19 cases is emphasised in the WHO research roadmap for COVID-19, and is exemplified by how the elimination of SARS-COV-2 infection in northern Italy was achieved, with a significant decrease in disease symptoms by over 90% within 10 days following implementation of active search and isolation of asymptomatic persons [21]. Oran and Topol have suggested the adoption of prompt and innovative tactics for public health surveillance (crowdsourcing digital wearable data and monitoring sewage sludge) in order to supplement traditional diagnostic testing which is often constrained by limited capacity and cost [15]. However, adopting these measures may not be readily feasible, given competing demand for limited resources and technical requirements in African countries, including Nigeria [19]. Alternatively, exploring contextual sociodemographic factors associated with asymptomatic status would be of paramount importance in addressing this gap. To the best of our knowledge however, there seems to be a dearth of evidence in this regard in our context, especially in light of increasing community transmission of COVID-19 across the country.

This study therefore aims to describe asymptomatic COVID-19 cases and to identify sociodemographic factors associated with asymptomatic status at testing in Nigeria.

2.0. Materials and Methods

2.1. Study design and setting

This is a retrospective analysis of Nigeria surveillance and laboratory data between February 27 and June 6, 2020. Nigeria is a Federal Republic located in West Africa bordering Niger in the north, Chad in the northeast, Cameroon in the east, and Benin in the west. It is divided into 36 states and the Federal Capital Territory (FCT), which are further clustered into six geopolitical zones: South-South, South-East, South-West, North-Central, North-West, and North-East. The provision of health care in Nigeria is the responsibility of the three tiers of government with significant private sector involvement. [22]. In brief, the primary health care system is primarily managed by local governments; the secondary health care system is more advanced and is primarily managed by the state governments through the ministry of health; and the tertiary health care is managed by the federal government via teaching hospitals and specialist hospitals.

2.2. Study population

The study population comprised of children (<18 years) and adults (≥18 years) who were tested for COVID-19. The decision to study children and adults separately was based on emerging evidence that asymptomatic infection appears to be age-dependent, with more children tending to be asymptomatic than adults [23], [24].

2.3. Data source

The Surveillance, Outbreak Response Management and Analysis System (SORMAS) served as the data source for this study. It is an open-source real-time electronic health surveillance and laboratory database which was adopted in 2017 by the NCDC as its primary digital surveillance platform for implementing the IDSR system [25]. A COVID-19 module was developed and added to the SORMAS platform in January 2020.

2.4. Data collection

Irrespective of symptomatic status (i.e., symptomatic or not), eligibility for a RT-PCR test during this study period was based on meeting the NCDC COVID-19 suspect case definition operational during the study period (Table 1) [26], although provisions were made to accommodate the testing of individuals concerned about COVID-19 upon reporting to healthcare facilities. Therefore, asymptomatic cases were tested for COVID-19 due to meeting the prevailing case definition or concern about possibly contracting/exposed to the disease at designated testing centres in the community or healthcare facility.

Table 1: COVID-19 case definitions in Nigeria, February 27-June 6, 2020

Case category	Definition/criteria
Suspected COVID-19 case	**1. Symptoms with international travel** Anyone with acute respiratory symptoms (fever and either cough, difficulty breathing or shortness of breath) OR new respiratory symptoms (cough, difficulty breathing or shortness of breath) without fever and no other explanation, **AND** a history of travel to or residence in a country reporting cases within 14 days before symptom onset; Or new respiratory symptoms with contact to a confirmed case in the last 14 days before symptom onset; OR **2. Symptoms with contact to confirmed case** Anyone with new respiratory symptoms (cough, difficulty breathing or shortness of breath, with or without fever), **AND** contact with a confirmed or

	probable COVID-19 case in the last 14 days prior to symptom onset; OR **3. Acute respiratory illness in an area of moderate or high COVID-19 prevalence with no other explanation** Anyone with acute respiratory illness within the last 10 days (fever and either cough, difficulty breathing or shortness of breath), **AND** absence of an alternative diagnosis that explains the clinical presentation **AND** residing or working in the last 14 days in an area identified by NCDC as a moderate or high prevalence region.
Probable case	Any suspected case: • For whom testing for COVID-19 is indeterminate test results; • For whom testing was positive on a pan-coronavirus assay; OR • Where samples were not collected prior to the demise of a suspect case
Confirmed case	Anyone with laboratory confirmation of SARS-CoV-2 infection with or without signs and symptoms.
Contact	Defined as anyone who experienced any one of the following exposures during the 2 days before and/or within 14 days after the onset of symptoms of a probable or confirmed case: • Face-to-face contact with a probable or confirmed case within 1 metre and for more than 15 minutes; • Direct physical contact with a probable or confirmed case; • Direct care for a patient with probable or confirmed COVID-19 disease without using proper personal protective equipment; OR • Other situations as indicated by local risk assessments. For confirmed asymptomatic cases, the period of contact is measured as the 2 days before, through the 14 days after the date on which the sample was taken which led to confirmation.

Generally, respiratory sample (a minimum of either one nasopharyngeal or nasal swab, and one oropharyngeal swab) collection, transportation, and laboratory analysis were performed by trained health workers in accordance with the NCDC guidelines [27]. Triple-packed specimens were transported aseptically in viral transport media to NCDC-certified laboratory for COVID-19 within a temperature range of 2-4^{o}C. Based on WHO guidelines,[28] RT-PCR was used for the laboratory diagnosis of COVID-19. Laboratory results, sociodemographic and clinical data (signs and symptoms in the 14 days prior to diagnosis) were submitted in real-time to the NCDC through the SORMAS platform (installed on Tablets or Laptops) by designated state health personnel or health workers.

2.4. Data management and definition of key study variables

It was decided *a priori* that variables with missing data will be handled using the missing-indicator approach, which involves giving persons with a missing value a missing indicator code (e.g. -9) to ensure that they were included in the analyses. Consequently, the estimates obtained by using this approach tend to be more transparent than those obtained by the complete case analysis [29]. A flowchart showing the selection processes for the final dataset for this study is shown in Figure 1.

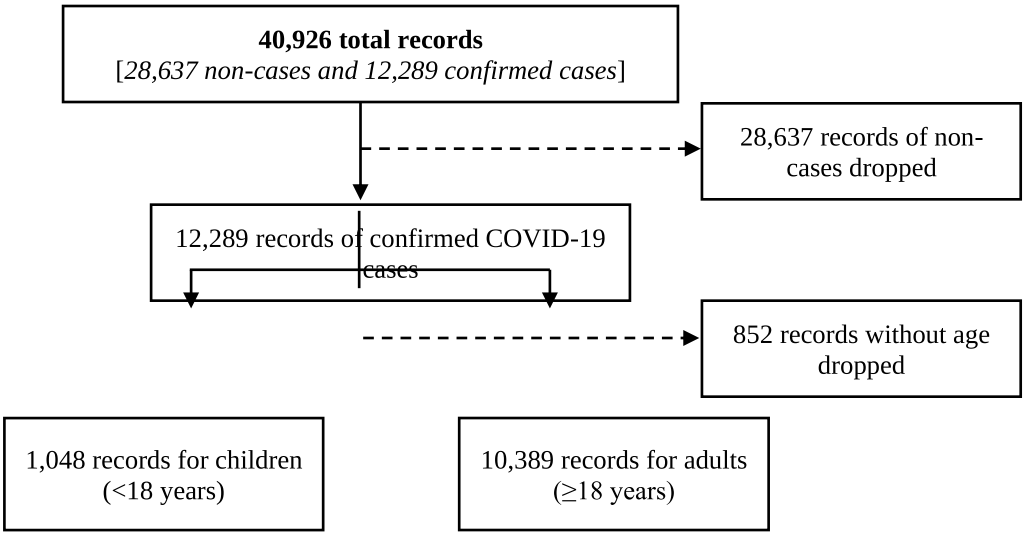


Figure 1: A flow chart showing the selection processes for study records

2.5. Outcome variable

An asymptomatic person was defined as one diagnosed with COVID-19 by RT-PCR but who did not report signs or symptoms before or at testing. The comparator population was symptomatic COVID-19 cases, defined as individuals with symptoms indicative of COVID-19 as well as RT-PCR confirmation of SARS-CoV-2.

2.6. Independent variables

A global literature review of factors potentially associated with asymptomatic infection did not yield relevant articles at writing. As such, selection of variables was based on availability and biological plausibility. The definitions of key study variables are presented in Table 2.

Table 2: Definition of key study variables

Variable	Definition/classification
Sex	Classified as either male or female.
Type of education	Classified according to the Nigerian educational system: primary, secondary, and tertiary education. In addition, an alternative educational system (i.e. Almajiranci or Quranic schooling) was given a separate category. Briefly, Almajiranci is a system of Islamic education practised (predominantly in northern Nigeria) which encourages parents to leave parental responsibilities to the Islamic school [30]. Colloquially, the term has expanded to refer to any young person who begs on the streets and does not attend secular school [31]. Persons without any form of education were classified under the 'none' category.
COVID-19 risk level	Defined based on the chances of contracting COVID-19 in relation to an individual's occupation. For instance, students were at home during this study period, as such would be classified as being at low risk of contracting COVID-19. The variable was classified as follows: low risk [i.e. student, child, and housewife]; medium risk [i.e. trader/business, animal-related work (e.g. butcher/hunter), farmer, religious/traditional leader and transporter]; and high risk [i.e. healthcare worker (doctor, nurse, laboratorian, hospital cleaner etc.)]. 'Other risk' referred to persons whose occupation was neither specified by the respondent nor omitted by the healthcare worker.

Residential setting	Classified based on population size and administrative/ legal criteria for reporting Local Government Areas (LGA), in line with standard classification criteria for urban and rural areas in Nigeria [32]. An LGA is classified as urban if any of the following criteria is met: (1) State capital; (2) an estimated population size of ≥20,000; (3) >75% of its population is engaged in non-agricultural occupations; (4) availability of infrastructure, good transportation system and a broad array of economic, social and recreational activities.
Geopolitical zone of residence	To minimise unstable estimates of effect from small sample size (which was the case for some States such as Kogi and Cross-River States), we combined individual States into their respective geopolitical zones: South-West (Ekiti, Lagos, Ogun, Ondo, Osun and Oyo States); South-South (Akwa-Ibom, Bayelsa, Cross-River, Rivers, Delta and Edo States); South-East (Abia, Anambra, Ebonyi, Enugu and Imo States); North-Central (Benue, Kogi, Kwara, Nasarawa, Niger, and Plateau States as well as the Federal Capital Territory); North-West (Jigawa, Kaduna, Kano, Katsina, Kebbi, Sokoto and Zamfara States); and North-East (Adamawa, Bauchi, Borno, Gombe, Taraba and Yobe States).
Health facility where cases reported for testing	Classified as primary healthcare facility; secondary hospital; and tertiary hospital.
Travel history	Defined as having had local, international or no travel in the 14 days prior to COVID-19 diagnosis. It was based on self-report.
Close contact with a COVID-19 case	Based on self-report, defined as having stayed within 2 metres of COVID-19 case for at least 15 minutes, within the 14 days prior to COVID-19 testing; it was coded as a binary variable (no/yes).
Direct contact with a COVID-19 case	Defined as self-report of direct contact with a COVID-19 case in the 14 days prior to COVID-19 testing (no/yes). It was based on self-report.
Hospitalisation	Defined as either hospitalised (yes) or not (no). In our setting, a positive RT-PCR test can trigger hospitalisation, irrespective of symptomatic status. For instance, an asymptomatic COVID-19 patient might be hospitalised to prevent potential spread of COVID-19 or to ensure adequate monitoring of the patient, especially if an underlying condition is present.
Clinical outcome	Defined as a COVID-19 case with known clinical outcome (survival or death) during the study period. A survivor was defined as a COVID-19 case who was officially discharged as per the discharge criteria in use during the study period [33], [34].

2.7. Statistical analyses

All analyses were conducted using Stata version 13 (Stata Corp. LP, College Station, TX, United States of America). A p-value of less than 0.05 was considered statistically significant. Sociodemographic characteristics in relation to the outcome variable were described using frequencies and percentages (%) for binary/categorical variables and mean and standard deviation (SD) for normally distributed continuous variables. The association between the individual covariates and the outcome variable (asymptomatic infection) in children and adults was assessed by performing unadjusted logistic regression analyses, with findings presented as unadjusted odds ratios (ORs) with 95% Confidence Intervals (CIs). Subsequently, multivariable analyses using a stepwise multiple logistic regression approach were performed to assess the association between the outcome variable and each statistically significant covariate from the unadjusted analyses (p-values from the Likelihood Ratio Test and Wald's test were used to ascertain statistical significance for categorical variables and binary variables, respectively). Findings from the multivariable model were presented as adjusted ORs with 95% CIs. Similar analyses were performed for adults separately. The spatial distribution of asymptomatic cases was presented accordingly by the states they were found positive for COVID-19. The total counts of asymptomatic cases per state were calculated simply by aggregating the individual-level data to a state-level, and linking the aggregated data to a shapefile which contain the geometries for the 37 States in Nigeria. All geospatial analysis was carried out in RStudio (version 1.2.1335).

3.0. Results

3.1. Description of the study participants

Overall, there were 11,437 persons in this study, 1,048 (9.2%) and 10,389 (90.8%) of whom were children (<18 years) and adults (≥18 years), respectively. About 71% (747/1,048) of children and 64.1% (6,656/10,389) adults were asymptomatic at testing. Geographically, a higher number of asymptomatic COVID-19 cases, irrespective of age group, seemed to be broadly concentrated in the following states: Lagos, Kano, FCT, Oyo, Kaduna, Bornu, Bauchi, Gombe and Rivers, in that order (Figure 2). Specifically, in children, asymptomatic COVID-19 cases were more concentrated in Lagos, Kano, Kaduna and to a lesser degree in the FCT and Bauchi (Figure 3a). In adults, asymptomatic COVID-19 cases appear to be more pronounced in Lagos, Kano, FCT, Borno, Gombe, Ogun, Rivers, Bauchi, Kaduna and Ebonyi and Kwara States, indicating a broader distribution of asymptomatic COVID-19 cases at testing across the country as compared to children (Figure 3b). In general, among children, those aged 10-14 years of both sex accounted for the highest number of asymptomatic infection (Figure 4a) while among adults. those aged 26-35 years of both sex accounted for the highest number of asymptomatic infection, followed by those aged 36-45 years (Figure 4b).

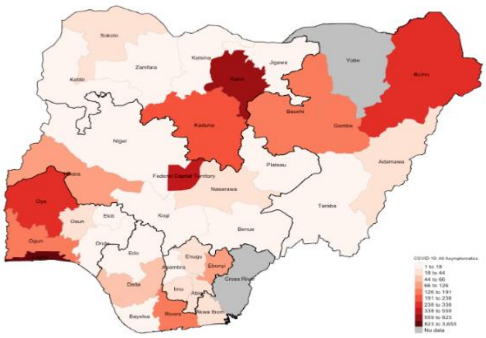
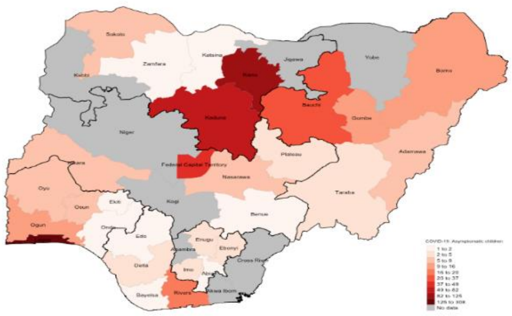
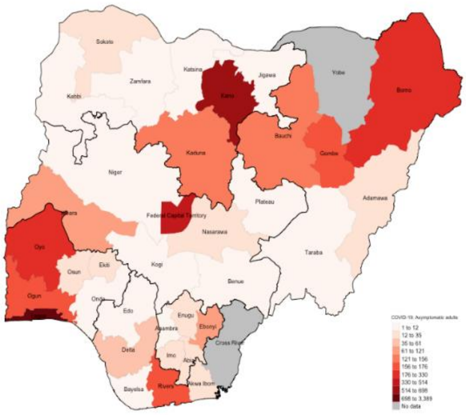


Figure 2: Map showing the overall number of asymptomatic Covid-19 cases for each state in Nigeria

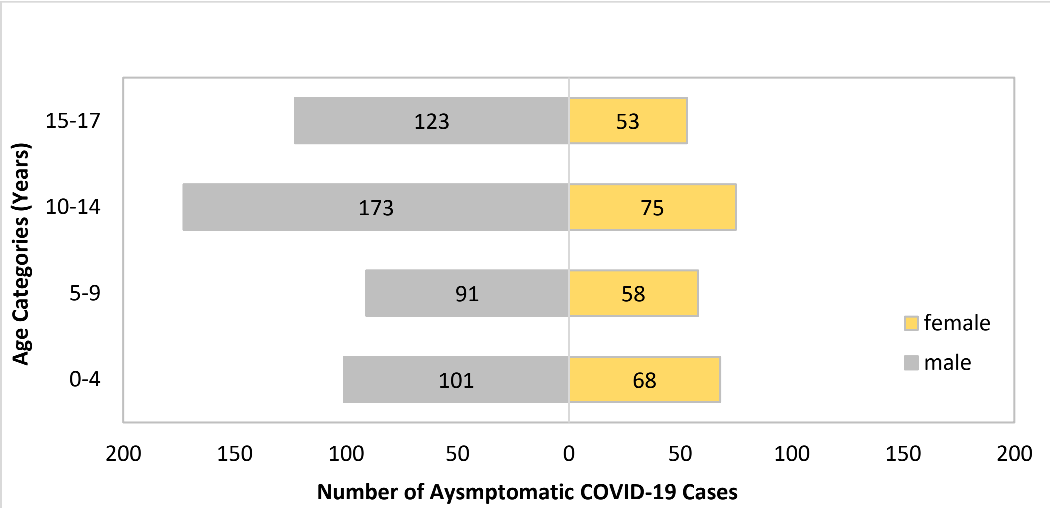


a) Distribution of asymptomatic COVID-19 cases in children (<18 years)

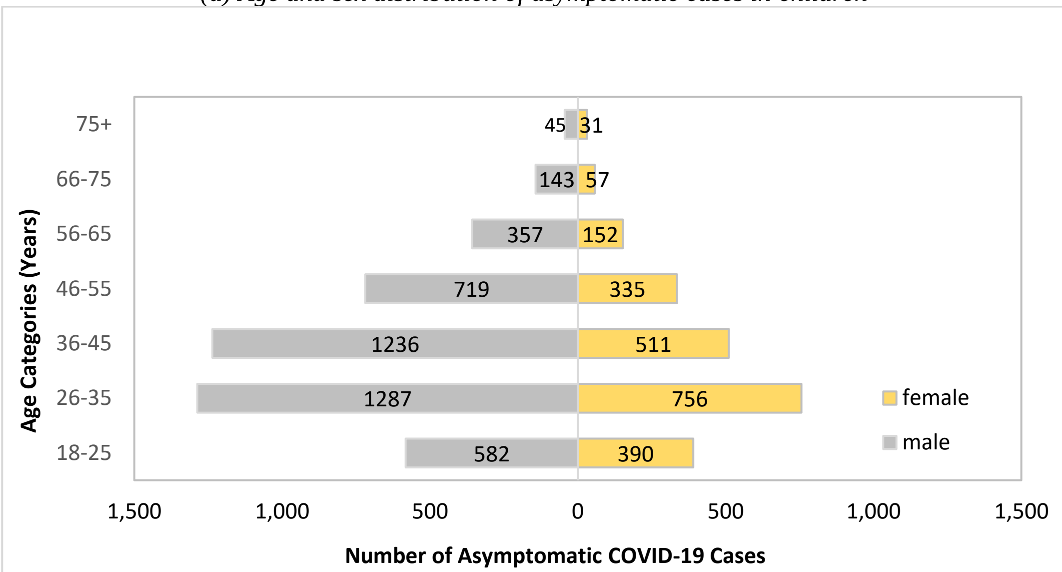


b) Distribution of asymptomatic COVID-19 cases among adults (≥18 years)

Figure 3: Map showing asymptomatic COVID-19 cases in the children (a) and adult (b) population for each State in Nigeria



(a) Age and sex distribution of asymptomatic cases in children



(b) Age and sex distribution of asymptomatic cases in adults

Figure 4: Age and sex distribution of asymptomatic cases in children (a) and adults (b)

The distribution of children's and adults' characteristics in relation to symptomatic status at testing is presented in Table 3. The mean (SD) age of all children diagnosed with COVID-19 was 10.1 (5.4) years, and 9.7 (5.5) years for those who were asymptomatic when tested. Males accounted for 66.9% of the 1,048 children. The majority (42.8%; 448/1,048) of children were classified as being at low risk for SARS-CoV-2 infection. Only 6.3% (66/1,048) of children were hospitalized in a health facility, but the proportion of asymptomatic cases admitted to a health facility was lower at 3.6% (27/747). All childhood COVID-19-related deaths (4/1,048) were recorded among those who presented as asymptomatic at testing.

The mean (SD) age of all adults diagnosed with COVID-19 was 39.8 (13.7) years, and males accounted for a higher proportion of the population at 66.8%. Tertiary education (35.7%) was the most common type of education completed by adults during the study period. High COVID-19 risk level (i.e. health care profession) among adults was 10.8% (1,128/10,389). About 11% (1,098/10,389) adults were hospitalized during this study period; however, the proportion of asymptomatic adult cases who were hospitalized was lower at 6.8% (450/6,656). In total, there were 324 COVID-19-related deaths among adults (3.1% of 10,389), 115 of which were accounted for by those classified as asymptomatic at testing.

3.2. Association between COVID-19 patients' characteristics and asymptomatic status at testing

The odds of asymptomatic status at testing in children as compared to adults

The association between different age groups (children vs adults) and asymptomatic status at testing is presented in Table 4. The unadjusted odds ratio suggests that the odds of asymptomatic status at testing was 39% higher in children than in adults [OR 1.39, 95% CI: 1.21-1.60]. However, after adjusting for the confounding effect of geopolitical zone of residence, the odds of asymptomatic status at testing became even higher in children when compared with adults [OR 1.62, 95% CI: 1.40-1.88].

Table 4: The odds of asymptomatic status at testing in relation to different age groups (n=11,437)

Variable	Unadjusted OR (95% CI)	Wald's p-value	Adjusted OR (95% CI)†	Wald's p-value
Age group				
Adults	1.00	<0.001	1.00	<0.001
Children	1.39 (1.21-1.60)		1.62 (1.40-1.88)	

†: Adjustment for geopolitical zone of residence (the only confounding variable that changed the unadjusted OR by more than 10%).

3.3. Children's characteristics associated with asymptomatic status at testing

The unadjusted and adjusted odds ratios for children' and adults' characteristics associated with asymptomatic status at testing are presented in Table 5. In children, the unadjusted odds ratios for presenting at testing without symptoms was significantly associated with the type of current education (p<0.0001) and risk of exposure to SARS-CoV-2 infection (p<0.0001). In general, children who reported at secondary and tertiary hospitals had higher odds ratios for being asymptomatic at testing than those who reported at primary healthcare facilities. The adjusted model contained education, risk of exposure to SARS-CoV-2 infection, geopolitical zone of residence, type of residence (rural vs urban), type of health facility, self-report of close and direct contact with COVID-19 patient(s). Compared with children who reported at primary healthcare facilities for testing, those who reported at tertiary hospitals had about four-fold [OR 3.7, 95% CI: 1.41-9.78] increased odds of being asymptomatic. Risk of exposure to SARS-CoV-2

Table 3: The distribution of children's and adults' characteristics in relation to symptomatic status at testing between February 27and June 6 2020 in Nigeria

Variable	Children (<18 years)			Adults (≥18 years)		
	Symptomatic at testing [n=301 (%)*]	Asymptomatic at testing [n=747 (%)*]	Total [N=1,048 (%)*]	Symptomatic at testing [n=3,733 (%)*]	Asymptomatic at testing [n=6,656 (%)*]	Total [N=10,389 (%)*]
Mean (SD) age, years	11.2 (4.8)	9.7 (5.5)	10.1 (5.4)	41.1 (14.4)	39.1 (13.2)	39.8 (13.7)
Mean (SD) temperature, °C	37.4 (1.0)	36.4 (0.8)	36.9 (1.0)	37.3 (1.1)	36.6 (0.7)	37.0 (1.0)
Sex						
Female	87 (28.9)	254 (34.0)	341 (32.5)	1,146 (30.7)	2,232 (33.5)	3,378 (32.5)
Male	213 (70.8)	488 (65.3)	701 (66.9)	2,568 (68.8)	4,369 (65.6)	6,937 (66.8)
Missing	1 (0.3)	5 (0.7)	6 (0.6)NS	19 (0.5)	55 (0.8)	74 (0.7)†
Current education						
None	19 (6.3)	65 (8.7)	84 (8.0)	52 (1.4)	54 (0.8)	106 (1.0)
Primary	29 (9.6)	112 (15.0)	141 (13.5)	56 (1.5)	78 (1.2)	134 (1.3)
Secondary	38 (12.6)	108 (14.5)	146 (13.9)	382 (10.2)	515 (7.7)	897 (8.6)
Tertiary	11 (3.7)	18 (2.4)	29 (2.8)	1,379 (36.9)	2,327 (35.0)	3,706 (35.7)
Alternative/Islamic	11 (3.7)	74 (9.9)	85 (8.1)	92 (2.5)	281 (4.2)	373 (3.6)
Missing	193 (64.1)	370 (49.5)	563 (53.7)‡	1,772 (47.5)	3,401 (51.1)	5,173 (49.8)‡
COVID-19 risk level						
Low risk	117 (38.9)	331 (44.3)	448 (42.8)	242 (6.5)	250 (3.8)	492 (4.7)
Medium risk	5 (1.7)	4 (0.5)	9 (0.9)	508 (13.6)	379 (5.7)	887 (8.5)
High risk	0 (0.0)	2 (0.3)	2 (0.2)	374 (10.0)	754 (11.3)	1,128 (10.9)
Other	21 (7.0)	131 (17.5)	152 (14.5)	1,631 (43.7)	2,922 (43.9)	4,553 (43.8)
Missing	158 (52.5)	279 (37.4)	437 (41.7)‡	978 (26.2)	2,351 (35.3)	3,329 (32.0)‡
Geopolitical zone of residence						
South-west						
South-south	51 (16.9)	341 (45.7)	392 (37.4)	1,553 (41.6)	3,945 (59.3)	5,498 (52.9)
South-east	31 (10.3)	27 (3.6)	58 (5.5)	627 (16.8)	260 (3.9)	887 (8.5)
North-central	0 (0.0)	14 (1.9)	14 (1.3)	40 (1.1)	200 (3.0)	240 (2.3)
North-west	54 (17.9)	67 (9.0)	121 (11.6)	506 (13.6)	679 (10.2)	1,185 (11.4)
North-east	155 (51.5)	219 (29.3)	374 (35.7)	838 (22.5)	910 (13.7)	1,748 (16.8)
	10 (3.3)	79 (10.6)	89 (8.5)‡	169 (4.5)	662 (10.0)	831 (8.0)‡
Type of residential setting						
Rural	19 (6.3)	99 (13.3)	118 (11.3)	177 (4.7)	412 (6.2)	589 (5.7)
Urban	63 (20.9)	256 (34.3)	319 (30.4)	1,630 (43.7)	2,729 (41.0)	4,359 (42.0)
Missing	219 (72.8)	392 (52.5)	611 (58.3)‡	1,926 (51.6)	3,515 (52.8)	5,441 (52.4)†

Health facility for COVID-19 testing						
Primary	24 (8.0)	45 (6.0)	69 (6.6)	406 (10.9)	609 (9.2)	1,015 (9.8)
Secondary	8 (2.7)	25 (3.4)	33 (3.2)	236 (6.3)	266 (4.0)	502 (4.8)
Tertiary	10 (3.3)	65 (8.7)	75 (7.2)	367 (9.8)	651 (9.8)	1,018 (9.8)
Missing	259 (86.1)	612 (81.9)	871 (83.1)†	2,724 (73.0)	5,130 (77.1)	7,854 (75.6)‡
Travel history						
None	280 (93.0)	672 (890.0)	952 (90.8)	3,442 (92.2)	6,268 (94.2)	9,710 (93.5)
Local	16 (5.3)	58 (7.8)	74 (7.1)	186 (5.0)	257 (3.9)	443 (4.3)
International	3 (1.0)	9 (1.2)	12 (1.2)	72 (1.9)	106 (1.6)	178 (1.7)
Missing	2 (0.7)	8 (1.1)	10 (1.0)NS	33 (0.9)	25 (0.4)	58 (0.6)‡
Self-report of direct contact with a COVID-19 case						
No	100 (33.2)	308 (41.2)	408 (38.9)	2,164 (58.0)	3,184 (47.8)	5,348 (51.5)
Yes	87 (28.9)	174 (23.3)	261 (24.9)	858 (22.9)	1,256 (18.9)	2,114 (20.4)
Missing	114 (37.9)	265 (35.5)	379 (36.2)†	711 (19.1)	2,216 (33.3)	2,927 (28.2)‡
Self-report of close contact with a COVID-19 case						
No	84 (27.9)	285 (38.2)	369 (35.2)	2,072 (55.5)	2,996 (45.0)	5,068 (48.8)
Yes	98 (32.6)	186 (24.9)	284 (27.1)	842 (22.6)	1,338 (20.1)	2,180 (21.0)
Missing	119 (39.5)	276 (37.0)	395 (37.7)†	819 (21.9)	2,322 (34.9)	3,141 (30.2)‡
Hospitalisation						
No	148 (49.2)	504 (67.5)	652 (62.2)	2,603 (69.7)	4,423 (66.5)	7,026 (67.6)
Yes	39 (13.0)	27 (3.6)	66 (6.3)	648 (17.4)	450 (6.8)	1,098 (10.6)
Missing	114 (37.9)	216 (28.9)	330 (31.5)‡	482 (12.9)	1,783 (26.8)	2,265 (21.8)‡
Clinical outcome						
Survivor	164 (54.5)	204 (27.3)	368 (35.1)	1,170 (31.3)	1,475 (22.2)	2,645 (25.5)
Dead	0 (0.0)	4 (0.5)	4 (0.4)	209 (5.6)	115 (1.7)	324 (3.1)
No outcome yet	137 (45.5)	539 (72.2)	676 (64.5)‡	2,354 (63.1)	5,066 (76.1)	7,420 (71.4)‡

NS=p-value>0.05; †=p-value<0.05; ‡=p-value<0.001
*: Percentages in some instances may be greater than 100·0% due to rounding up.

infection, geopolitical zone and type of residence were negatively associated with asymptomatic status at testing.

3.4. Adults' characteristics associated with asymptomatic status at testing

In the unadjusted model, a higher level of education appeared to be associated with higher odds of asymptomatic status at testing (p<0.0001). Adults at high risk of exposure to SARS-CoV-2 infection had higher odds [OR 1.95, 95% CI: 1.57-2.42] of being asymptomatic at testing than those classified as being at low risk. Compared to residency in the South-West, residing in the South-East [OR 1.97, 95% CI: 1.39-2.78] and North-East [OR 1.54, 95% CI: 1.29-1.84] appeared to be associated with higher odds of asymptomatic status at testing. Also associated with higher odds of asymptomatic status at testing was reporting at tertiary hospitals and self-report of close contact with a COVID-19 case. In the adjusted model, adults with an Islamic education (i.e. Almajiranci) had over two-fold [OR 2.27, 95% CI: 1.40-3.68] increased odds of being asymptomatic at testing than those with no education. Adults at higher risk of exposure to SARS-CoV-2 infection (healthcare workers) [OR 1.84, 95% CI: 1.46-2.33] and residing in the South-East [OR 1.98, 95% CI: 1.37-2.86] and North-East [OR 1.25, 95% CI: 1.02-1.52] remained positively associated with higher odds of asymptomatic infection at testing. Reporting to tertiary hospitals [OR 1.30, 95% CI: 1.07-1.59] and self-report of close contact with a COVID-19 case [OR 1.76, 95% CI: 1.52-2.04] also remained positively associated with asymptomatic status at testing.

3.5. Summary of key findings

We have described asymptomatic COVID-19 infection in children and adults, and identified their characteristics that are independently associated with an asymptomatic status at testing in Nigeria. Overall, 71% (747/1,048) of children and 64% (6,656/10,389) adults were asymptomatic at testing between February 27 and June 6, 2020. Adults with an Islamic education (Almajiranci), engaging in a high-risk profession (healthcare), residing in the South-East and North-East, and reported coming in close contact with a COVID-19 case had higher odds of being asymptomatic at testing. Reporting to tertiary hospitals was also positively associated with an asymptomatic status at testing in both adults and children.

3.6. Interpretation of key findings

As expected with respect to age and COVID-19 asymptomatic status, we found the adjusted odds of asymptomatic status at testing to be 62% higher in children than in adults. This is similar to the findings of a recent report for European countries and the UK which indicates that children (0-18 years) are more likely to have a mild or asymptomatic COVID-19 infection [35]. While an asymptomatic COVID-19 infection in children may not necessarily be considered a serious public health burden, it is a problem if they are responsible for COVID-19 transmission.

Table 5: Association between sociodemographic characteristics of asymptomatic children and adults with COVID-19 infection

Characteristics	Children (<18 years				Adults (≥18 years)			
	Unadjusted OR (95% CI)	**P-value (LRT)**	**Adjusted OR (95% CI)**	**P-value (LRT)**	**Unadjusted OR (95% CI)**	**P-value (LRT)**	**Adjusted OR (95% CI)**	**P-value (LRT)**
Sex								
Female	1.00	0.2053	NS		1.00	0.0015	1.00	0.0203
Male	0.78 (0.59-1.05)				0.87 (0.80-0.95)		0.87 (0.80-0.96)	
Missing	1.71 (0.20-14.86)				1.49 (0.88-2.52)		1.03 (0.59-1.80)	
Type of education								
None	1.00	<0.0001	1.00	0.1421	1.00	<0.0001	1.00	<0.0001
Primary	1.13 (0.59-2.17)		1.37 (0.60-3.12)		1.34 (0.80-2.24)		0.97 (0.55-1.68)	
Secondary	0.83 (0.44-1.56)		0.76 (0.34-1.69)		1.30 (0.87-1.94)		1.09 (0.71-1.69)	
Tertiary	0.48 (0.19-1.19)		0.38 (0.13-1.14)		1.60 (1.10-2.39)		1.24 (0.81-1.88)	
Alternative/Islamic	1.97 (0.87-4.44)		1.39 (0.54-3.59)		2.94 (1.88-4.60)		**2.27 (1.40-3.68)**	
Missing	0.56 (0.33-0.96)		0.99 (0.46-2.16)		1.85 (1.26-2.72)		1.31 (0.86-2.00)	
COVID-19 risk level								
Low risk	1.00	<0.0001	1.00	<0.0001	1.00	<0.0001	1.00	<0.0001
Medium risk	0.28 (0.07-1.07)		0.13 (0.02-0.76)		0.72 (0.58-0.90)		0.64 (0.51-0.82)	
High risk	Omitted		Omitted		1.95 (1.57-2.42)		**1.84 (1.46-2.33)**	
Other	2.21 (1.33-3.66)		3.39 (1.94-5.93)		1.73 (1.44-2.09)		1.57 (1.28-1.93)	
Missing	0.62 (0.47-0.83)		1.01 (0.70-1.47)		2.33 (1.92-2.82)		1.88 (1.49-2.37)	
Geopolitical zone of residence								
South-west								
South-south	1.00	<0.0001	1.00	<0.0001	1.00	<0.0001	1.00	<0.0001
South-east	0.13 (0.07-0.24)		0.08 (0.04-0.16)		0.16 (0.14-0.19)		0.14 (0.12-0.16)	
North-central	Omitted		Omitted		1.97 (1.39-2.78)		**1.98 (1.37-2.86)**	
North-west	0.19 (0.12-0.30)		0.12 (0.07-0.20)		0.53 (0.46-0.60)		0.44 (0.38-0.52)	
North-east	0.21 (0.15-0.30)		0.13 (0.08-0.20)		0.43 (0.38-0.48)		0.32 (0.28-0.36)	
	1.18 (0.57-2.43)		0.85 (0.40-1.85)		1.54 (1.29-1.84)		**1.25 (1.02-1.52)**	
Type of residential setting								
Rural	1.00	<0.0001	1.00	<0.0001	1.00	0.0010	1.00	<0.0001
Urban	0.78 (0.44-1.37)		0.50 (0.27-0.92)		0.72 (0.60-0.87)		0.55 (0.45-0.68)	
Missing	0.34 (0.20-0.58)		0.17 (0.09-0.29)		0.78 (0.65-0.94)		0.43 (0.35-0.53)	
Health facility type								
Primary	1.00	0.0073	1.00	0.0172	1.00	<0.0001	1.00	<0.0001
Secondary	1.67 (0.65-4.26)		1.20 (0.41-3.47)		0.75 (0.61-0.93)		0.79 (0.63-1.00)	
Tertiary	3.47 (1.51-7.95)		**3.71 (1.41-9.78)**		1.18 (0.99-1.41)		**1.30 (1.07-1.59)**	

Missing	1.26 (0.75-2.11)		2.33 (1.23-4.40)		1.26 (1.10-1.44)		1.69 (1.45-1.96)	
Travel history								
None	1.00	0.4520			1.00	0.0002	1.00	0.0711
Local	1.51 (0.85-2.67)				0.76 (0.63-0.92)		0.86 (0.70-1.09)	
International	1.25 (0.34-4.65)				0.81 (0.60-1.09)		0.81 (0.59-1.13)	
Missing	1.67 (0.35-7.90)				0.42 (0.25-0.70)		0.54 (0.31-0.95)	
Self-report of direct contact with a COVID-19 case								
No	1.00	0.0365	1.00	0.3793	1.00	<0.0001	1.00	<0.0001
Yes	0.65 (0.46-0.91)		0.71 (0.43-1.15)		0.99 (0.90-1.10)		0.63 (0.54-0.72)	
Missing	0.75 (0.55-1.03)		0.84 (0.35-2.02)		2.12 (1.92-2.34)		1.17 (0.94-1.45)	
Self-report of close contact with a COVID-19 case								
No	1.00	0.0031	1.00	0.9204	1.00	<0.0001	1.00	<0.0001
Yes	0.56 (0.40-0.79)		0.93 (0.58-1.51)		1.10 (0.99-1.22)		**1.76 (1.52-2.04)**	
Missing	0.68 (0.49-0.95)		1.09 (0.47-2.53)		1.96 (1.78-2.16)		1.53 (1.24-1.87)	

NS=not statistically significant
Significant findings are in **bold fonts**

A study of children with COVID-19 in England however suggests that they may be less likely to play a significant role in SARS-CoV-2 transmission overall [36]. Nevertheless, this finding (coupled with those in Figure 4) has potential ramifications for school reopening in Nigeria which remained closed since March 23, 2020. This is particularly so for nursery, primary and secondary schools with predominantly students under 18 years old. Furthermore, this finding has value for COVID-19 testing strategy in Nigeria which is largely reliant on respiratory symptoms and epidemiological parameters [26]. The benefits of an age-dependent criterion for COVID-19 testing may therefore be worth exploring, which is in accordance with advice elsewhere [23].

Healthcare workers, classified as being at high risk of exposure to SARS-CoV-2, were found to have higher odds of asymptomatic infection at testing as compared to a low-risk professions. This finding could be explained by a number of factors including (1) low viral loads given the mandatory and frequent use of personal protective equipment and (2) behavioural modifications owing to increased knowledge and awareness of COVID-19. SARS-CoV-2 transmission by asymptomatic healthcare workers has been reported in the UK [37], US [38], [39] and Italy [40]. Thus, asymptomatic COVID-19 infection among healthcare workers could present significant public health challenges in our setting. For instance, the mandatory quarantining of contacts of infected persons implies that COVID-19 transmission by healthcare workers, albeit unwittingly, could result in the depletion of a fragile health workforce in the country. Routine screening of healthcare workers, irrespective of symptomatic status, before the commencement of work shift would be a worthy measure in mitigating such a scenario. A similar approach proved effective in combating COVID-19 outbreak in Lombardy in Italy [40]. Moreover, asymptomatic healthcare workers could act as ‘silent super spreaders’ in fuelling both nosocomial and community COVID-19 infection.

Adults with Almajiranci education had about two-fold increased odds of asymptomatic infection at testing as compared to those without any education—the adjusted odds was 39% higher in children with Almajiranci education, but the association was not statistically significant. While the practice of alms begging is widely denounced as child abuse in Nigeria, the almajiri tend to practice alms begging in the street out of necessity to eat (this often involves physically touching or holding a potential donor) [41], [42]. As such, their risk of contracting SARS-CoV-2 is high, especially considering the poor socioeconomic status of some who may be incapable to adopt or enforce preventive measures against COVID-19. However, their increased odds of asymptomatic status at testing could be an artefact explained by potential misclassification of status due to their: (1) inability to communicate COVID-19 symptoms to data collectors since they do not receive a secular education, including English; (2) fear of losing means of daily sustenance following quarantine or isolation; and (3) unwillingness to disclose symptoms due to fear of being stigmatised (they are often stigmatised and insulted in the course of begging [41]). The current finding also has an important implication for COVID-19 estimation in northern Nigeria where the Almajiranci system of education is predominantly practised [30]. It is, therefore, possible for COVID-19 cases in this region to be underestimated and for the community, the transmission goes unabated if existing screening strategies do not account for this population.

South-East and North-East residents had higher odds of asymptomatic infection at testing as compared South-West residents. Without robust diagnostic criteria, COVID-19 cases in adult residents of South-East and North-East could be underestimated if COVID-19 case definition remains hinged on respiratory symptoms. This was identified as possible explanation for the variation in COVID-19 cases in China, with the majority of cases attributed to Wuhan [43]. Evidence from a national survey of Nigerians’ perceptions towards COVID-19 suggests that adult residents of South-East had the highest proportion of recorded misconceptions (e.g. non-existence of COVID-19) in the country [Personal Communication with the NCDC Risk Communication Team]. It could therefore be argued that widespread misconceptions in the South-East might have contributed to adults’ unwillingness to disclose COVID-19 symptoms, especially in the absence of fever that could be measured with a thermometer. Conversely, possible reasons for the higher odds of asymptomatic status among North-East adult residents are not entirely clear, hence the finding warrants further investigation. Such research endeavours should aim to explore the (1) effect of social stigma on willingness to disclose symptoms, as noted in a WHO report [44] and (2) local understanding of COVID-19 given the reliance on patients' self-reports for data collection—this is particularly relevant considering the heterogeneity of culture and religion in Nigeria and the fact that an individual's understanding of health may not necessarily align with formal protocols for [45].

Presentation at tertiary hospitals was associated with higher odds of asymptomatic status among children and adults. A possible explanation for these findings could be due to the majority of COVID-19 treatment centres (including laboratories and trained healthcare personnel) being domiciled within tertiary hospitals in Nigeria [Personal Communication with COVID-19 Case Management Pillar]. This is also in agreement with the WHO's operational considerations for case management of COVID-19 in the health facility and community [46]. COVID-19 being an emerging viral disease with deleterious impacts, these findings could therefore be attributable, in part, to health-seeking behaviour. Local evidence indicates that preference for a health facility is informed by patients' perceived severity of an illness, with illnesses perceived to be severe (such as COVID-10) more likely to be reported to tertiary hospitals and vice-versa [47].

3.7 Strengths and limitations of the study

Identifying both children's and adults' characteristics associated with asymptomatic infection at testing is of paramount importance to surveillance, case management, and infection prevention and control measures in the Nigerian context. To our knowledge, this study supports evidence in this regard in the Nigerian context. Apart from taking concrete measures to minimise biases (e.g. separating data analysis for children and adults), the study also has the advantage of providing findings that are potentially generalisable given the geographical spread (the 36 States and the FCT in Nigeria) of data sources, albeit the high prevalence of home-based management of endemic diseases, such as malaria, with similar symptoms as COVID-19 could limit the generalisability due to non-presentation for testing by asymptomatic COVID-19 cases. Findings from this study are, however, subject to some limitations. Firstly, the lack of an extended period of close clinical observation of asymptomatic children and adults in the current study makes it difficult to generalise findings beyond the point of testing. That is, persons classified as asymptomatic COVID-19 cases in the current study might have (1) been in the incubation period, or acute phase of infection (in which case development of signs or symptoms following COVID-19 diagnosis was possible, but had not yet occurred), (2) developed signs or symptoms but were not reported at testing (this is possible given the similarity in signs and symptoms of COVID-19 with those of endemic diseases including malaria and Lassa fever in Nigeria), (3) had a sub-clinical infection such that RT-PCR result may come out negative later without experiencing signs and symptoms [48]. However, preliminary findings from our contact tracing indicate that a majority of persons remain asymptomatic after testing (findings will be reported elsewhere). Secondly, missing data—which is a pervasive problem in many public health investigations—was notably evident in our study. Although the adopted approach to handling missing data ensured that each study participant was included in the analysis, hence reducing the loss of statistical power, there is a potential for bias. However, our approach is more transparent and informative to policymakers as compared to a complete case analysis. Essentially, our approach reflects the current status of COVID-19 surveillance data in Nigeria and, importantly, underlines the need to prioritise data quality by NCDC and its technical partners.

4.0. Conclusion

Our study suggests that asymptomatic COVID-19 infection in Nigeria is influenced by age and that targeting the identified sociodemographic characteristics (education, profession, geographical location and health care) would be useful to strengthening response strategies and mitigating community transmission. Therefore, any prevention strategies should be population-based and not focused purely on symptomatic COVID-19 cases. A follow-up prospective study is recommended to ascertain the transmission capacity of asymptomatic COVID-19 cases in our setting.

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