Asian Journal of Research in Infectious Diseases

Volume 14, Issue 4, Page 69-77, 2023; Article no.AJRID.108984
ISSN: 2582-3221

Serological Survey of Severe Acute Respiratory Syndrome Coronavirus -2 (Sars-Cov-2) among Frontline Health Workers in Northwest Nigeria

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/AJRID/2023/v14i4309

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/108984

Original Research Article

Received: 20/09/2023
Accepted: 24/11/2023
Published: 02/12/2023

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ABSTRACT

Background: Serological testing of SARS-CoV-2-specific IgG/IgM antibodies is an important complement to Real Time-PCR (RT-PCR) for surveillance and outbreak investigations. The study therefore aimed to assess the serological survey of SARS-COV-2 among frontline health workers using specific IgG/IgM antibodies.
Methods: The study was a cross-sectional design. A self-administered questionnaire was used to obtain biodata. Rapid diagnostic test kits were used for the study in which samples reacted with COVID-19 antigen-coated particles in the test cassette and the complex formed produced readable bands indicating the presence of SARS-COV19 in the tested subject. Data obtained were analyzed using Stata v15.
Results: The prevalence of SARS-CoV-2 among the study sample was 39.0% and 14.9% for IgG and IgM respectively. Prevalence was highest in the outpatient department (IgG; 70.0%, IgM; 17.1%). IgG positivity was observed more among doctors while positivity for IgG was seen in 78.6% of persons with previous diagnoses. IgM was significantly associated with contact with patients having shortness of breath, p-value < 0.05.
Conclusion: This study demonstrated a high level of SARS-COV19 IgG indicating past infection and IgM suggesting recent exposure or ongoing infection among this group of workers compared to others within the hospital settings. The role of serological testing cannot be over-emphasized in the periodic screening and prompt treatment of health workers before they manifest symptoms or become capable of spreading the disease to innocent patients and or co-health workers.

Keywords: Serological testing; IgG/IgM; SARS-COV-2; health workers; Northwest Nigeria.

1. INTRODUCTION

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a newly emerged viral pathogen that causes the coronavirus disease – 2019 (COVID-19) pandemic with over 5.5 million confirmed cases and 347,000 deaths [1]. SARS-CoV-2 infections have spread to nearly all nations globally including Nigeria. The pandemic has strained health systems capacity in affected countries through an explosive increase in demand for hospital care along with a need for personal protection of healthcare workers [2]. In addition, infection among healthcare workers reduces available manpower and has led to some hospitals closing their doors causing further scarcity of vital medical care [2].

Control of SARS-CoV-2 is extremely challenging for several reasons. While the virus is highly contagious, the majority of infected individuals are either asymptomatic or mildly symptomatic making symptom-based surveillance very challenging [3]. Also, polymerase chain reaction (PCR)-based tests, which are the standard diagnostic tests for SARS-CoV-2, are complex and require substantial human and material resources that are not widely available in Nigeria. The Nigeria Center for Disease Control (NCDC), following guidelines set by the World Health Organization (WHO), uses only PCR-based tests for SARS-CoV-2 diagnosis [4]. Inability to rapidly deploy equipment, source testing kits and train personnel has greatly limited testing capacity in the country, making estimates of mortality and prevalence unreliable.

The current guidelines apply the principle of ''Smart Testing'' which requires that only those presenting with respiratory symptoms and history of contact with a proven case will be tested, thereby reducing demand for tests.

Serological tests have the capacity to capture past (and ongoing) infections by detecting specific antibody responses [5]. Serological testing of SARS-CoV-2-specific IgG/IgM antibody is an important complement to RT-PCR for surveillance and outbreak investigations. Serological tests are up to 10X cost-effective than PCR-based tests and take much less time and manpower. Researchers have used serology to identify missing links between epidemiological clusters. For example, Yong et al applied serological testing to confirm that an individual that tested negative twice by RT-PCR was indeed the connection between two case clusters in Singapore [6]. The results of serological tests provide better estimates of infection rate by detecting individuals that have recovered from SARS-CoV-2 even if their disease was mild or asymptomatic. Similarly, serological testing can

be used to strategically deploy immune healthcare workers to COVID-19 testing and treatment units and to reduce exposure of susceptible healthcare staff to the virus. Finally, individuals who mounted a strong immunological response to the virus can be donors of valuable plasma for the treatment of severely ill patients.

Serological tests are currently recommended for research purposes by the WHO and have been applied for large-scale population surveys in the states of New York, California and Indiana in the United States, in Germany, and several other locations [7]. Going forward, we expect PCR will continue to be vital for identifying acute infection while serological tests will become increasingly important for understanding the extent of the pandemic and to help calibrate control strategies.

Despite the importance of serological studies in understanding the extent and burden of SARS-CoV-2, there are very limited published serological surveys of SARS-CoV-2 from Africa. To our knowledge, there is no published serological study from Nigeria. Several rapid serological tests that have been validated by the manufacturers are now commercially available in Nigeria. Our recent verification study which assessed the validity of five rapid serological test kits found a range of 96.86% sensitivity and 98% specificity. The study aimed to measure the serological prevalence of anti-SARS-CoV-2 antibodies among healthcare workers in Katsina.

2. METHODOLOGY

2.1 Study Population

The study included participants from the Accident & Emergency (A&E) section, Out Patient Department (OPD), wards, clinical laboratories and central administration department were recruited from the Federal Teaching Hospital Katsina Nigeria.

2.2 Sample Size

The required sample size to estimate the serological prevalence of SARS-CoV-2 with a 5% level of statistical significance was estimated as four hundred however, three hundred and ninety participated in the study.

2.3 Procedure

The rapid diagnostic technique was used as an onsite diagnostic tool to screen for SARS-COV19 IgG/IgM antibodies using the detection principle below. A drop of whole blood sample was placed into the test cassette with a drop of buffer solution provided. Reactions were allowed and readings were taken after a minute.

2.4 Detection Principle

COVID-19 IgG/IgM Rapid Test is a qualitative membrane-based immunoassay for the detection of COVID-19 antibodies in whole blood, serum, or plasma. This test consists of two test lines, an IgG line and an IgM line. In the IgG line, anti-human IgG is coated in the IgG test line region. During testing, the sample reacts with COVID-19 antigen-coated particles in the test cassette. The mixture then migrates upward on the membrane chromatographically by capillary action and reacts with the anti-human IgG in the IgG test line region. If the sample contains IgG antibodies to COVID-19, a colored line will appear in the IgG test line region. In the IgM line, anti-human IgM is coated in IgM test line region. During testing, the sample reacts with antihuman IgM. IgM antibodies to COVID-19, if present in the sample, react with the anti-human IgM and the COVID-19 antigen-coated particles in the test cassette, and this complex is captured by the anti-human IgM, forming a colored line in IgM test line region.

2.5 Data Analysis

Data analyses were conducted using Stata v15 using a raw percentage, two-tailed t-tests and ANOVA with a 5% significance level for specific, univariable and multivariable logistic regression models to achieve the study aim.

3. RESULTS

The prevalence of SARS-CoV-2 among the study population was 39.0% and 14.9% for IgG and IgM respectively. Prevalence was highest in the GOPD unit (IgG; 70.0%, IgM; 17.1%) followed by Medical Ward (IgG; 57.5%, IgM; 45.0%) and then the A&E unit (IgG; 57.5%, IgM; 17.5%) (Fig. 1).

There was no significant difference in the prevalence of SARS-CoV-2 for IgG between OPD unit and medical wards, OPD unit and A&E unit, p-value > 0.05. However, there was a significant difference in the prevalence of SARS-CoV-2 for IgM between OPD unit and medical ward, A&E unit and medical ward, p-value < 0.05 (Table 1).

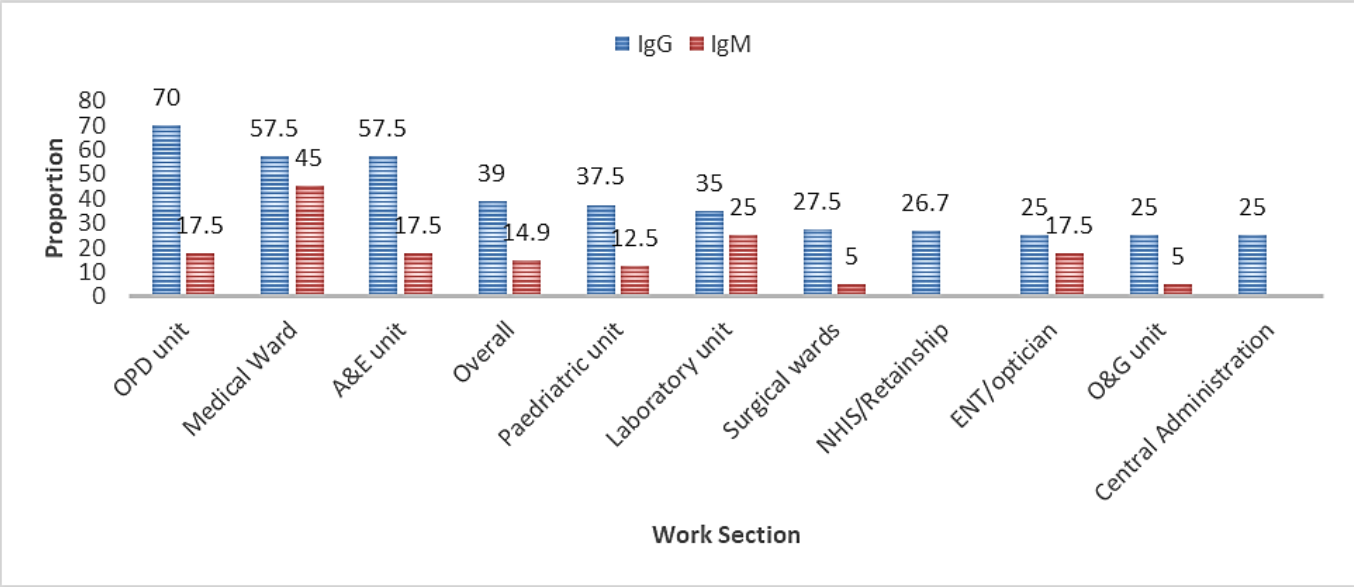

Fig. 1. Prevalence of IgG and IgM against Work section

Table 1. Comparison of IgG and IgM proportion between OPD unit, medical wards and A &E units

Work Section	SARS-CoV-2	
	IgG n(%)	IgM n(%)
OPD unit	28 (18.4)	7 (12.1)
Medical wards	23 (15.1)	18 (31.0)
A&E unit	23 (15.1)	7 (12.1)
X^2	0.807	9.267
p-value	0.668	0.010

X^2: Chi square statistic, p-value < 0.05 indicates significance.

Table 2. Relationship between IgG, IgM by demographic characteristics and work schedule

Variable	IgG				IgM			
	Positive n(%)	**Negative n(%)**	**Total**	**X^2(p-value)**	**Positive n(%)**	**Negative n(%)**	**Total**	**X^2(p-value)**
Age (Years)								
< 30	35 (35.0)	65 (65.0)	100 (25.6)	1.163 (0.762)	19 (19.0)	81 (81.0)	100 (25.6)	2.763 (0.430)
30-39	68 (40.5)	100 (59.5)	168 (43.1)		25 (14.9)	143 (85.1)	168 (43.1)	
40-41	37 (38.9)	58 (61.1)	95 (24.4)		10 (10.5)	85 (89.5)	95 (24.4)	
50 and above	12 (44.4)	15 (55.6)	27 (6.9)		4 (14.8)	23 (85.2)	27 (6.9)	
Occupation								
Civil servant	151 (39.3)	233 (60.7)	384(98.5)	1.275 (0.259)	58 (15.1)	326 (84.9)	384(98.5)	1.065 (0.302)
Student	1 (16.7)	5 (83.3)	6 (1.5)		0 (0.0)	6 (100.0)	6 (1.5)	
Marital status								
Single	47 (41.2)	67 (58.8)	114 (29.2)	0.920 (0.821)	22 (19.3)	92 (70.7)	114 (29.2)	7.246 (0.064)
Married	98 (37.5)	163 (62.5)	261 (66.9)		33 (12.6)	228 (87.4)	261 (66.9)	
Divorced	4 (50.0)	4 (50.0)	8 (2.1)		3 (37.5)	5 (62.5)	8 (2.1)	
Widow	3 (42.9)	4 (57.1)	7 (1.8)		0 (0.0)	7 (100.0)	7 (1.8)	
Job title								
Doctors	64 (49.2)	62 (50.8)	126 (32.3)	18.087 (0.003)	23 (18.3)	103 (81.7)	126 (32.3)	8.205 (0.145)
Admin officer	26 (28.9)	64 (71.4)	90 (23.1)		14 (15.6)	76 (84.4)	90 (23.1)	
Medical scientist	11 (44.0)	14 (56.0)	25 (6.4)		4 (16.0)	21 (84.0)	25 (6.4)	
Technician	8 (47.1)	9 (52.9)	17 (4.4)		4 (23.5)	13 (76.5)	17 (4.4)	
Nurse	37 (37.4)	62 (62.6)	99 (25.4)		13 (13.1)	86 (66.9)	99 (25.4)	
Others	6 (18.2)	27 (81.8)	33 (8.5)		0 (0.0)	33 (100.0)	33 (8.5)	
Level of education								
Primary Education	0 (0.0)	2 (100.0)	2 (0.5)	6.443 (0.040)	0 (0.0)	2 (100.0)	2 (0.5)	6.443 (0.040)
Secondary Education	18 (26.9)	49 (73.1)	67 (17.2)		9 (13.4)	58 (86.6)	67 (17.2)	
Tertiary education	134 (41.7)	187 (58.3)	321 (82.3)		49 (15.3)	272 (84.7)	321 (82.3)	
Previous Diagnosis								
Yes	11 (78.6)	3 (21.4)	14 (3.6)	9.573 (0.002)	1 (7.1)	13 (92.9)	14 (3.6)	0.685 (408)
No	141 (37.5)	325 (62.5)	376 (96.4)		57 (15.2)	319 (84.8)	376 (96.4)	
Direct contact								
Yes	145 (39.9)	218 (60.1)	363 (93.1)	2.077 (0.150)	57 (15.7)	306 (84.3)	363 (93.1)	2.858 (0.091)
No	7 (25.9)	20 (74.1)	27 (6.9)		1 (3.7)	26 (96.3)	27 (6.9)	

Variable	IgG				IgM			
	Positive n(%)	**Negative n(%)**	**Total**	**X^2(p-value)**	**Positive n(%)**	**Negative n(%)**	**Total**	**X^2(p-value)**
Level of contact								
1-2patients	9 (31.0)	20 (69.0)	29 (7.4)	3.602 (0.308)	4 (13.8)	25 (86.2)	29 (7.4)	3.564 (0.313)
3-5patients	26 (34.2)	50 (65.8)	76 (19.5)		7 (9.2)	69 (90.8)	76 (19.5)	
6-10patients	27 (35.1)	50 (64.9)	77 (19.7)		10 (13.0)	67 (87.0)	77 (19.7)	
11 and more	90 (43.3)	118 (56.7)	208 (53.5)		37 (17.8)	171 (82.2)	208 (53.5)	
Contact with known COVID 19 patient								
Yes	60 (58.3)	43 (41.7)	103 (26.4)	21.870 (0.000)	19 (18.4)	84 (81.6)	103 (26.4)	1.413 (0.235)
No	92 (32.1	195 (67.9)	287 (73.6)		39 (13.6)	248 (86.4)	287 (73.6)	
Contact with patient having: Fever symptoms								
Yes	103 (46.8)	117 (53.2)	220 (56.4)	13.056 (0.000)	35 (15.9)	185 (84.1)	220 (56.4)	0.429 (0.513)
No	49 (28.8)	121 (71.2)	120 (43.6)		23 (13.5)	147 (86.5)	120 (43.6)	
Cough symptoms								
Yes	96 (45.7)	114 (54.3)	210 (53.8)	8.690 (0.003)	34 (16.2)	176 (83.8)	210 (53.8)	0.625 (0.429)
No	56 (31.1)	124 (68.9)	180 (46.2)		24 (13.3)	156 (86.7)	180 (46.2)	
Shortness of breath								
Yes	84 (52.5)	76 (47.5)	160 (41.0)	20.686 (0.000)	31 (19.4)	129 (80.6)	160 (41.0)	4.346 (0.037)
No	68 (29.6)	162 (70.4)	230 (59.0)		27 (11.7)	203 (88.3)	230 (59.0)	
Pneumonia/respiratory symptoms								
Yes	82 (50.3)	81 (41.7)	163 (41.8)	15.121 (0.000)	29 (17.8)	134 (82.2)	163 (41.8)	1.886 (0.170)
No	70 (30.8)	157 (69.2)	227 (58.2)		29 (12.8)	198 (87.2)	227 (58.2)	

Table 2 shows the socio-demographic and work schedule correlation of SARS-CoV-2. IgG was significantly associated with Job title, level of education, previous diagnosis for COVID-19, contact with known COVID patients, contact with patients having fever, cough, shortness of breath, pneumonia and other respiratory challenges, p-value < 0.05. IgG positivity was seen more in doctors (49.2%), nurses (37.4%) and admin officers (28.9%), increased with literacy level ((secondary education; 26.9% and tertiary education; 41.7%). Additionally, positivity for IgG was seen in 78.6% of persons with previous diagnosis, 58.3% who have been in contact with a known COVID-19 patient, 46.8%, 45.7%, 52.5% and 50.3% of persons with symptoms of fever, cough, shortness of breath, and pneumonia/respiratory challenges respectively.

IgM was significantly associated with history of contact with patients having shortness of breath and respiratory challenges, p-value < 0.05. IgM positivity among participants was found to be more among those who had contact with patients having shortness of breath (19.4%).

4. DISCUSSION

The development of effective and reliable serological detection methods is important as a tool in monitoring the vast and neutralization efficacy of antibodies among infected patients, assessing and predicting the severity of symptoms, and quantifying the quality of immune response to new vaccines [8]. In addition, a variety of serological tests are more cost-effective, convenient, and effective for commercial application. Serological tests may retrospectively assess the incidence and phase of an outbreak in an area [8]. The prevalence of SARS-CoV-2 among the study population was 39.0% and 14.9% for IgG and IgM respectively. This is comparable to 16.21% positivity among health workers reported in Spain [9].

The prevalence was highest among workers in the OPD unit followed by Medical Wards and then the A&E unit. The OPD unit is peculiar with the reception of patients on out-based treatment. The majority of patients seen in this unit are often acutely ill individuals presenting with conventional symptoms including fever, headache, cough, catarrh, body itching etc, which until proven by further laboratory and clinical assessment could be COVID-19 symptoms. These groups of frontline workers are at the highest risk of contracting the infection on account of its undistinguishable features from other common illnesses like malaria, upper respiratory tract infections etc.

Both SARS-CoV-2 IgM and IgG antibodies may be detected around the same time after infection. However, while IgM is most useful for determining recent infection, it usually becomes undetectable weeks to months following infection; in contrast, IgG is usually detectable for longer periods [10]. From this study, it was observed that IgG was significantly associated with a previous diagnosis of COVID, contact with known COVID patients, and contact with patients having symptoms like fever, cough, shortness of breath, pneumonia, and other respiratory challenges.

IgG positivity was more prevalent among doctors, followed by nurses and then admin officers. Therefore, healthcare workers are at a higher risk of exposure due to their direct contact with ill individuals seeking medical attention. The time required for clerking, and close examination of patients to elicit clinical signs put doctors at greater risk than any other healthcare workers. This agrees with a report from Pakistan [11]. where 62% of doctors were found to be positive for SARS-COVID-19 IgG antibodies compared to other healthcare workers.

Previous studies [12–14] indicate that nearly all immunocompetent persons develop an adaptive immune response following SARS-CoV-2 infection, triggering antiviral humoral and cellular immune response; antibodies directed against S and N proteins. The S1 subunit (of S-proteins) contains the receptor-binding domain (RBD) that mediates the binding of viruses to susceptible cells and is also the main target for neutralizing antibodies. Antibodies including IgM, IgG, and IgA—against S proteins and their subunits can be detected in serum within 3 weeks after infection [15]. IgM and IgG antibodies are produced nearly simultaneously; however, IgM (and IgA) antibodies decay more rapidly than IgG [15,16].

However, positivity for IgG was observed in 78.6% of persons with previous diagnosis, 58.3% who have been in contact with a known COVID-19 patient, and persons with symptoms of fever, cough, shortness of breath, and respiratory/pneumonia challenges respectively.

IgM was significantly associated with contact with patients having shortness of breath challenges and IgM positivity among participants was found to be more among those that had contact with patients having shortness of breath (19.4%). IgG antibodies, including IgG against the S and N proteins, persist for at least several months in most persons, but the precise duration of time that antibodies persist after infection is unknown [10]. Persons with the more severe disease appear to develop a more robust antibody response with IgM, IgG, and IgA, all achieving higher titers and exhibiting longer persistence [16,17].

5. CONCLUSION

Healthcare workers especially doctors and nurses who are the major front liners of the medical team are constantly at risk of exposure to covid infection as this study demonstrated a high level of SARS-COV19 IgG indicating past infection and IgM suggesting recent exposure or ongoing infection among this group of workers compared to others within the hospital setting. The role of serological testing cannot be over-emphasized in the periodic screening and prompt treatment of healthcare workers before they manifest symptoms or become capable of spreading the disease to innocent patients and or co-health workers in the line of duty. Therefore, Serological testing of SARS-CoV-2-specific IgG/IgM antibodies is an important complement to RT-PCR for surveillance and outbreak investigations.

CONSENT

An informed consent was obtained from all participants after explaining the procedure to them. Thereafter, a self-administered questionnaire was given for biodata

ETHICAL APPROVAL

Ethical clearance was sought and obtained in compliance with the Nigeria National Health Research Ethics Committee through the Institutional Review Board of Federal Teaching Hospital, Katsina

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
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