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Analysis of total antibody levels in university hospitals health workers vaccinated against COVID-19 in Abidjan (Côte d'Ivoire)

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Abstract

Discovered in China in December 2019, coronavirus disease-19 (COVID-19) has confronted the world with an unprecedented crisis. Healthcare workers, the first line of defense against this pandemic, have been severely affected. Clinical trial results of the emergency vaccines showed that they all produced IgG antibodies against severe acute respiratory syndrome corona virus-2 (SARS-CoV-2) with high rates of seroconversion. While immunization against natural challenge (COVID-19 infection) and artificial challenge (vaccination) in health care workers is relatively well described in the West, the issue is not well understood in Sub-Saharan Africa, particularly in Côte d'Ivoire, where populations are genetically distinct from Caucasians. Our aim was to investigate the magnitude of post-vaccination IgG responses to SARS-CoV-2 in healthcare workers in our African epigenetic context. A cross-sectional, multicenter, analytical study was conducted from March to May 2022 among health workers employed at the University Hospital of Abidjan and vaccinated against COVID-19. The study included 77 health workers. IgG immunoassays were performed with an enzyme-linked fluorescent assays. Data were analyzed using SPSS version 22.0 software, with a p-value < 0.05 considered as a significant difference. All enrolled subjects developed anti-SRAS-Cov-2 IgG, of which 88.3% had a strong response (titer ≥ 250 Binding Antibody Units/ml). IgG titers varied significantly by gender (p=0.04). Vaccine type and number of doses did not affect IgG titers. However, a history of COVID-19 infection was associated with a 5-fold greater likelihood of developing a strong IgG response after vaccination. In conclusion, humoral IgG responses developed after vaccination against SARS-CoV-2 were robust and would be influenced by a variety of factors..

Keywords: : IgG, SARS-CoV-2, COVID-19, Healthcare workers, Vaccination

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Introduction

Coronavirus disease 2019 (COVID-19) infection remains a major public health concern since the World Health Organization (WHO) pandemic declaration in March 2020. Medical advances have identified severe acute respiratory syndrome corona virus-2 (SARS-CoV-2) as the virus responsible for this disease. The lack of a specific treatment has made it imperative to implement effective preventive measures to combat the pandemic. Vaccination has therefore emerged as the best option to achieve universal immunity. It is recognized that the pre-pandemic situation will not be restored until a safe and effective vaccine strategy is available.

As a result, many vaccines against SARS-CoV-2 have been developed and licensed. Results from clinical trials of vaccines developed against SARS-CoV-2 had shown that they all produced binding and neutralizing antibodies (Ac) to SARS-CoV-2 with high rates of seroconversion.[1] However, the intensity of the responses varied from subject to subject. A report by Lynch et al., 2021, suggested that not all serological responses are equivalent.[2] In addition, there are few studies investigating antibody responses following vaccination with validated commercial SARS-CoV-2 serology kits.[3] Similarly, the urgent need for information on this novel coronavirus continues to result in the proliferation of conflicting research data, preventing the complete elucidation of humoral response development.[2] In addition, studies investigating antibody responses following vaccination with validated commercial SARS-CoV-2 serological kits are scarce.[3] Similarly, the urgent need for information on this new coronavirus continues to result in the proliferation of conflicting research data, preventing full elucidation of humoral response development.[2]

Like other countries, Côte d'Ivoire has opted for targeted vaccination strategies for frontline health workers. As part of the COVID-19 Vaccines Global Access facility, four vaccine platforms (AstraZeneca, BioNTech Pfizer, Johnson & Johnson, Sinopharm) have been deployed across the country. However, questions have been raised about the immune status of these agents. While immunization of health care workers against natural and artificial challenges is relatively well described in the West, the issue is not well understood in sub-Saharan Africa, particularly in Côte d'Ivoire, where populations are genetically distinct from Caucasians. The aim of our study was therefore to analyze the magnitude of the SARS-CoV-2-specific total antibody vaccine response in health care workers.

Subjects and Methods

We conducted a prospective cross-sectional study involving 77 health workers from three university hospitals in Abidjan Centre Hospitalo-Universitaire (CHU) or University Hospital Center (Cocody, CHU Angré, and CHU Treichville). It was conducted over a 3-month period between March and May 2022 and was part of a larger project on the carriage and immunogenicity of SARS-CoV-2 in health workers in Côte d'Ivoire. The study protocol was reviewed and approved on February 21, 2022, by the National Ethics Committee of Life Sciences and Health (N° reference: 007-22/MSHPCMU/CNESVS-km).

Three levels of exposure risk have been defined, depending on the department and workplace. For staff not in contact with patients, the exposure risk was assumed to be low. For staff in contact with patients with unknown or suspected COVID-19 status, the risk was defined as intermediate. Staff in contact with known COVD-19 patients were defined as at high risk.

Recruited healthcare workers were vaccinated (one or more doses), employed regularly at the selected centers, and gave informed consent to participate in the study. Epidemiological, clinical and vaccination data were collected using a questionnaire.

Peripheral venous blood samples were collected on red-capped or dry tubes. The samples were transported to the laboratory in coolers with accumulators (with a medical thermometer) to keep them at a temperature of +4°C for 2 hours.

Serological testing was performed on an automated immunoassay system (Mini VIDAS® BioMérieux - France). The commercial enzyme-linked fluorescent assay kits (VIDAS® SARS-CoV-2 IgM or IgG Ref 423834 – BioMérieux, France) were used according to the manufacturer's instructions. The VIDAS® SARS-CoV-2 IgM or IgG test is an enzyme-linked fluorescent assay. It combines a two-step sandwich enzyme immunoassay procedure that ends with fluorescence detection. This test is intended for the qualitative detection of IgM and IgG antibodies to SARS-CoV-2.

The results are expressed as an "i" index. At i < 1, the result is negative (no detection of anti-SARS-Cov-2 IgM or IgG) and if i ≥ 1, the result is positive (detection of anti-SARS-Cov-2 IgM or IgG). If the result is positive, in accordance with the WHO call for harmonization of serological tests for SARS-CoV-2, quantification was obtained by converting VIDAS SARS-CoV-2 immunoglobulin index units to binding antibody units, where 1 threshold index = 20.33 Binding Antibody Units (BAU)/ml [4]. According to international standards established by the WHO [5], an antibody level < 250 BAU/ml defines a weak serological response and an antibody level ≥ 250 BAU/ml defines a strong serological response.

The variables selected for the study were age and age ranges, sex, occupational category, work position, body mass index (BMI), history of SARS-CoV-2 infection, SARS-CoV-2 vaccines, number of vaccine doses, infection-to-sample and vaccination-to-sample times, anti-SARS-CoV-2 IgM, IgG, and total IgG concentration.

Statistical analysis

Data were entered into a spreadsheet program (Excel 2013) and then analyzed using the Statistical Package for the Social Sciences (SPSS) software Version 22.0. Descriptive and analytical statistical methods were used depending on the type of variable. A p-value < 0.05 (two-tailed) was considered statistically significant.

Results

Sociodemographic characteristics of study subjects are shown in Table 1.

The most common age group among health workers was 37-46 years (50.6%). The mean age was 40.26 years. The BMI was normal in 54.5% of cases, between 18 and 25 kg/m2. Our population was predominantly female (59.7%). The most represented professional category was physicians (26%). Emergency room personnel were the most common (32%). Healthcare workers had a medium risk of exposure to COVID-19 in 44.2% of cases, a high risk in 32% of cases, and a low risk in 23.4% of cases.

Table 1. Distribution of the study population by age, BMI, sex, occupational category, workplace, and exposure risk.

		Frequency	Percentage (%)
Age range (years)	[25 – 37]	22	28,6
	[38 – 46]	39	50,6
	≥ 47	16	20,8
	Mean age = 40,26 +/- 7,51 [27 – 58]		
BMI range (kg/m2)	[18 – 26]	42	54,5
	≥ 26	35	45,5
	Mean BMI = 25,78 +/- 4,60 [18 – 39]		
Gender	Male	31	40,3
	Female	46	59,7
	Sex-ratio (M/F) = 0,67		

Table 1. Continued.

		Frequency	Percentage (%)
Professional category	**Physician**	20	26,0
	Pharmacist	2	2,6
	Nurse	14	18,2
	Midwife	8	10,4
	Nursing Assistant	15	19,5
	Medical Biology Technician	1	1,3
	Others.	17	22,1
Workplace	Laboratory	12	15,6
	Consultation	13	16,9
	Hospitalization	21	27,3
	Administration	6	7,8
	Emergency	25	32,5
Risk of exposure	High risk	25	32,5
	Medium risk	34	44,2
	Low risk	18	23,4
Total		77	100

Clinical and vaccine characteristics data are shown in Table 2.

There were few healthcare workers with a history of COVID-19 infection (36.4%). COVID-19 did not cause stress at work for 57.1% of healthcare workers. The Pfizer vaccine was the most commonly administered vaccine in our population (57.1%). Most had received two doses (80.5%), followed by one dose (16.9%). Only 2.6% had received three doses (Table 2).

Table 2. Distribution of subjects according to history of COVID-19 infection, work stress status, type of vaccine and number of doses received.

		Frequency	Percentage
Previous COVID-19 infection			
Infected	Women	19	24,7
	Men	9	11,7
Non-infected		49	63,6
Type of vaccine			
AstraZeneca		26	33,8
Pfizer		44	57,1
Sinopharm		1	1,3
Johnson & Johnson		2	2,6
AstraZeneca/Moderna		1	1,3
AstraZeneca/Pfizer		3	3,9
Number of doses received			
1 dose		13	16,9
2 doses		62	80,5
3 doses		2	2,6
Mean = 1,86 + /- 0,42 [1-3]			
Total		77	100

Serological characteristics of study subjects are shown in Tables 3, 4 and, 5.

Healthcare workers with IgM titers less than 21 BAU/mL, i.e., negative, made up the majority of our study population (92.2%). SARS-CoV-2 IgG was detected in 100% of health care workers, with strong responses (titers ≥ 250 BAU/mL) in 88.3% of health care workers and weak responses in 11.7% of cases. The time between vaccination and sampling varied from 4 to 7 months in 39% of the personnel. The mean was 7.56 months (+/- 3.76), with a minimum of 3 months and a maximum of 26 months. Study of the parameters influencing IgG titers (Table 3).

Table 3. Distribution of subjects according to anti-SARS-CoV-2 IgG and IgM titers and post-vaccination sample delays.

	Frequency	Percentage
IgG titer (BAU/ml)		
< 21	71	92,2
≥ 21	6	7,8
Mean = 9,50 +/- 20,40 [1,02 – 128,69]		
IgG titer (BAU/ml)		
[21 – 250 [	9	11,7
≥ 250	68	88,3
Mean= 464,58 +/- 188,49 [21,55 – 799,17]		
Vaccination - sampling period (months)		
[0 – 4]	7	9,1
[4 – 7]	30	39,0
[7 – 10]	18	23,4
[10 – 13]	17	22,1
≥ 13	5	6,5
Mean: 7,56 +/- 3,76; range [3 – 26]		
Total	77	100

BAU: Binding Antibody Units.

The IgG level was highest in personnel aged 25 to 36 years (482.97 BAU/ml), followed by those aged 47 years and over (467.28 BAU/ml). The lowest mean value was observed in personnel aged between 36 and 47 years (453.10 BAU/ml). However, the differences observed were not significant. The mean IgG level in women (500.72 +/- 185.39 BAU/ml) was significantly higher than in men (410.95 +/- 183.06 BAU/ml). Administrative staff had the highest mean IgG level (506.96 BAU/ml) and emergency room staff had the lowest mean IgG level (444.90%). The differences observed were not significant. Paradoxically, the mean IgG level was higher in personnel with a low risk of exposure to COVID-19 (486.07 BAU/ml) than in those with a high risk of exposure (444.90 BAU/ml). However, the differences observed between the groups were not statistically significant. The mean IgG levels were 405.3 BAU/ml, 473.86 BAU/ml, and 562.23 BAU/ml in the one, two and three dose groups, respectively, with non-significant differences (Table 4).

Personnel with a history of COVID-19 infection were 5 times more likely to develop a strong post-vaccination IgG response (Table 5).

Table 4. Comparison of IgG titer by age group, gender, workstation, exposure risk and number of vaccine doses received.

		Moyenne +/ ET	*p* value
Mean IgG concentration (BAU/ml)	Age ranges (years)		
	[25 -36]	482,97 + /- 177,80	NS
	[36 -47]	453,10 +/- 190,35	
	≥ 47	467,28 +/- 207,68	
	[25 -36]	482,97 + /- 177,80	
	Gender		
	Male	410,95 + /- 183,06	0,040
	Female	500,72 +/- 185,39	
	Workstation		
	Laboratories	475,62 +/- 250,8	NS
	Consultations	438,77 +/- 177,66	
	Hospitalizations	485,58 +/- 162,48	
	Emergencies	444,90 +/- 184,91	
	Administration	506,96 +/- 220,71	
	Risk of exposure to COVID-19		
	Low	486,07 +/- 234,78	NS
	Medium	467,68 +/- 167,36	
	High	444,9 +/- 184,91	
	Vaccine dose received		
	One	405,3 +/- 180,04	NS
	Two	473,86 +/- 190,35	
	Three	562,23 +/- 176,09	

P > 0.05 is not significant (NS).

Table 5. IgG response and history of SARS-CoV-2 infection.

		History of infection		Total
		Yes	No	
IgG response	High response	27	41	68
	Low response	1	8	9
Total		28	49	77

Odds ratio = 5,27.

Discussion

Healthcare workers, the first line of defense against SARS-CoV-2, have suffered many casualties since the beginning of the pandemic. Vaccination programmes around the world have therefore made them a priority target since the first available SARS-CoV-2 vaccines were licensed. The aim of our study was to analyze the IgG and IgM titers developed against the artificial challenge in health care workers in Côte d'Ivoire.

The predominant age range in our study population was 36-45 years, with a mean age of 40 years. There was a female predominance and a normal mean BMI of 25.78 kg/m2, with most of our subjects (54.5%) below 25 kg/m2. Our results were like those of Lustig et *al*., 2021, in their study of immune correlates of post-vaccination COVID-19 in Israeli health care workers. They reported a predominance of young adults under 46 years of age in their study population, a clear female predominance of 72%, and a mean BMI of 25.6 kg/m2.[6] These

results suggest that vaccination is acceptable to the young adult females present among our healthcare workers.

In our study, the most represented professional category was physicians (26%), followed by orderlies (19.5%) and nurses (18.2%), most of whom worked in emergency departments (32.5%), a position with a high risk of exposure to COVID-19. These health workers would therefore have a greater propensity to be vaccinated, as they have more frequent contact with patients. Furthermore, our results are in line with the work of Kabamba et al., 2020, in Congo, who reported that acceptance of vaccination was related to profession, with doctors and nurses being the most supportive.[7]

In the present study, 36.4% of vaccinated healthcare workers had a history of SARS-CoV-2 infection. The low proportion of subjects with a previous infection could be explained by the fact that they thought they were already protected by the immune response induced by natural infection. The COVID-19 was not an additional burden in 57.1% of cases because the services surveyed were not necessarily specialized in the management of the disease.

The most widely administered vaccines were those from Pfizer and AstraZeneca because they were the first vaccines to arrive in Côte d'Ivoire, facilitated by the COVID-19 Vaccines Global Access initiative, and the vaccination policy included health care workers as one of the priority groups.[8] The majority received two doses of vaccine according to the established vaccination schedule. Some of the workers who received only one dose were those who had received the Johnson & Johnson vaccine, which requires only one dose. The others were discouraged by the side effects of the first dose they received.

Our tests were performed at an average of 7.56 months after the last vaccine doses, with a minimum of 3 months and a maximum of 26 months, and the majority in the 4-6-month range. IgM levels were undetectable in 92.2% of vaccinated healthcare workers. This can be explained by the kinetics of anti-SARS-CoV-2 antibodies. Indeed, IgM appears earlier and then declines dramatically as IgG peaks, as reported by Higgins et al., 2021, in their longitudinal study of SARS-CoV-2 antibodies, where more than 50% of IgM was negative between 91 and 144 days after symptom onset.[9] Lustig et al., 2021, excluded IgM antibodies from their analysis because they were induced in only a small proportion of vaccinated healthcare workers and declined rapidly.[6] In our study, however, IgG was detectable in all workers. Strong responses with concentrations ≥ 250 BAU/ml were seen in 88.3% of workers and weak responses in a minority (11.7%). These results reflect the efficacy of vaccination-induced seroconversion and the persistence of the humoral response beyond 6 months.

Our results corroborated those of Lustig et al, 2021, who reported that 99.9% of healthcare workers developed IgG antibodies to SARS-CoV-2 after the second dose of Pfizer vaccine.[6] Havervall et al., 2022, also reported detectable anti-SARS-CoV-2 antibodies in 99.8% and 7 months after the first vaccination series (Pfizer and AstraZeneca) in Swedish healthcare workers.[10] Doria-Rose et al., 2021, found persistent antibodies after the second vaccination with COVID-19 mRNA-1273.[11] Our results support those of Lustig et al., 2021 who reported that healthcare workers from different backgrounds responded differently to vaccination. Significant differences in outcomes that did not show clear dose effects included hypertension, heart disease, autoimmune disease and diabetes compared with healthy individuals.[6] However, these results did not include all the medical conditions listed in our study.

The number of doses had no effect on IgG responses in our study population. Contrary to our results, Lustig et al., 2021, found that each dose elicited specific antibody responses[6] and Sahin et al., 2021, published in their study on the effects of the BNT162b2 vaccine (Pfizer) that the second dose boosted the first. The IgG response was therefore dose dependent.[12] However, the tests were performed between 29 and 43 days after vaccination. The differences observed could be explained by the different sampling times after vaccination in our study, on one hand, and by the progressive decrease of antibodies over time, on the other hand.

Among the demographic factors, significant differences in mean IgG levels were observed according to sex. However, there was no significant difference when the population was divided into age groups. Our results were similar to those of Remy et al., 2021, who reported that of the demographic factors, only sex had a significant effect on IgG production.[13] Kontopoulou et al., 2021, in a study in Greece, on the other hand, found that although there was no difference by sex, there was a statistically significant difference in antibody titers between age groups.[14] The differences observed by age could be explained by the fact that comparisons were made between subjects under and over 60 years of age, whereas the maximum age in our study population was 58 years. The relationship between gender and IgG production in our study could be explained by the fact that women generally have higher IgG titers than men and that in the subpopulation of persons with a history of SARS-CoV-2 infection, women represented the majority. Personnel with a history of COVID-19 infection were five times more likely to develop a strong IgG response after vaccination than those without such a history. Vaccination therefore enhances the response obtained after natural infection. Our results are like those reported by other authors.

For insistence, Turner et al., 2021, showed that individuals with a history of infection with COVID-19 were able to maintain a certain level of antibodies.[15] Anichi et al., 2021, found significantly higher mean titers in previously infected subjects than in naive subjects after use of the BNT162b2 vaccine (Pfizer).[16] Havervall et al., 2022, showed that vaccination after SARS-CoV-2 infection resulted in an improved humoral response of greater magnitude than vaccination in naive subjects.[10] The difference between these two subpopulations could be explained by the notion that both natural infection and vaccination can produce high titers of anti-SARS-CoV-2 IgG.

However, our study had several limitations. For reasons of feasibility, we limited ourselves to quantifying IgG and IgM levels in healthcare workers. In a second phase of our study, the determination of neutralizing antibodies correlated with vaccine efficacy and the study of the kinetics of these antibodies and Th2 cytokines could better elucidate the post-vaccination humoral response to COVID-19.

In conclusion, we observed a robust humoral response to SARS-CoV-2 in healthcare workers after vaccination. Vaccination appeared to enhance the humoral response in personnel with a history of COVID-19 infection. In view of these results, it seems important to determine the protection afforded by this vaccine response by measuring neutralizing antibodies and the pool of memory effector cells (TCD3 - TCD8 - TCD45RO).

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Author Contributions

DSR conceptualized and designed the study. DSR and SKL drafted the manuscript; NK, AAH, YOR, AAUA critically reviewed it and contributed to its design. DSR coordinated the study. SYJ, KAP, AAUA, MLCR, MS, OD contributed to recruit healthcare workers employed regularly at the selected centers and they collected, transported to the laboratory the peripheral venous blood samples. SYJ, MS, OD performed on the Mini VIDAS the serological testing IgG/IgM anti-SARS-CoV-2 antibodies.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical approval

The study protocol was reviewed and approved on February 21, 2022, by the National Ethics Committee of Life Sciences and Health (No reference: 007-22/MSHPCMU/CNESVS-km).

Informed consent

A signed consent form was obtained from each study participant.

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