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Current profile of post-vaccination humoral signature of SARS-CoV-2 in Abidjan healthcare workers vaccinated against COVID-19 after the COVAX initiative in Côte d'Ivoire

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COVID-19, caused by SARS-CoV-2, has been the subject of unprecedented research, leading to a pandemic that urgently required effective vaccines to stop its spread. Despite the effectiveness of these vaccines, SARS-CoV-2 transmission continued, prompting questions about the immune response to SARS-CoV-2. Two years after the COVAX initiative in Cote D'ivoire, a study was conducted to assess the humoral response induced by vaccination among health workers in Abidjan. This was a cross-sectional study that included 350 health workers, examining factors such as age, gender, workstation, and body mass index, history of COVID-19, existence of comorbidity, job stress and antibody titers. Anti-SARS-CoV-2 IgM and IgG titers were determined using VIDAS® SARS-CoV-2 assays, and SARS-CoV-2 anti-S1 neutralizing antibodies were measured using the Chorus SARS-CoV-2 "Neutralizing" Ab tests. The population studied had an average age of 40.65 years, with a female predominance (57.1%). About 48.0% of healthcare workers were at moderate risk of exposure to COVID-19, and a history of SARS-CoV-2 infection was found in 29.7% of workers. Overall, 91.4% showed strong serological responses. Age, history of SARS-CoV-2 infection, vaccination status, and existence of comorbidity significantly influenced antibody titers. There was no significant association between antibody titers and COVID-19 stress. In conclusion, the humoral response to the SARS-CoV-2 vaccine was robust among healthcare professionals, and a history of SARS-CoV-2 infection boosted the humoral response.

Key words: SARS-CoV-2, Anti-COVID-19 vaccination, Healthcare workers, IgM, IgG, neutralizing antibody, humoral response.

INTRODUCTION

The COVID-19 pandemic has been the focus of unprecedented research. The infectious agent responsible for the disease is a virus that was rapidly identified through medical advances. This virus has genetic similarities with the previous Severe Acute Respiratory Syndrome Corona Virus (SARS-CoV) (Shah et al., 2020).

Safe and effective vaccines against SARS-CoV-2 were urgently needed to combat this pandemic. Thus, various vaccines have been developed in different countries, with a shortening of their development time (Jeyanathan et al., 2020). The first licensed mRNA vaccines were Pfizer-BNT162b2 and Moderna-mRNA 1273 (Psichogiou et al., 2021). Subsequently, other vaccines have been licensed, including recombinant protein vaccines (AstraZeneca-AZD1222 Vaxzevria, Serum Institute of India-Covishield, Janssen-Ad26.COV2.S) and inactivated virus vaccines (Sinopharm-InCoV, Sinovac-Coronavac) (OMS, s. d.-b).

The humoral response to SARS-CoV-2, like other coronavirus infections, involves the production of characteristic IgM and IgG antibodies (Cheng et al., 2021; Shah et al., 2020). IgM is the vanguard of the anti-infective mechanism and is the precursor antibody that appears in primary immunization before switching to IgG, which is the major antiviral antibody in serum (Cheng et al., 2021; Xiang et al., 2020; Xie et al., 2020). The SARS-CoV-2 spike (S) protein is known to promote viral entry into human cells via the ACE2 receptor. Neutralizing antibodies to this protein can therefore block viral infection in human cells and prevent viral replication (Cheng et al., 2021). Preliminary studies have shown that SARS-CoV-2 vaccines are effective, inducing the production of binding antibodies, high titers of SARS-CoV-2 neutralizing antibodies, and strong antigen-specific Th1 cellular responses (Sahin et al., 2021; Xu et al., 2021). Similarly, higher levels of neutralizing and binding antibodies have been associated with increased clinical severity of infection in several studies (Hall et al., 2021; Heffron et al., 2021; Lucas et al., 2020). However, the mechanism by which SARS-CoV-2 interacts with the immune response is not well understood (Cheng et al., 2021). Healthcare workers were a high-risk group for infection. In Europe, WHO estimated that 19% of all cases of infection were among healthcare workers (OMS, s. d.-a; WHO, s. d.). Following the example of other countries, Côte d'Ivoire has opted for the targeted vaccination of frontline health workers. As part of the COVAX Facility led by Gavi (The Vaccine Alliance), UNICEF, and WHO, four vaccine platforms (AstraZeneca, BioNTech Pfizer, Johnson and Johnson, Sinopharm) have been deployed throughout the country since February and March (MSHPCMU, s. d.). Despite the effectiveness of the vaccines, SARS-CoV-2 continues to be transmitted (Abdullahi et al., 2022a). While immunization against natural challenge (COVID-19 infection) and artificial challenge (vaccination) in healthcare 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 genetically distinct from Caucasians live in a different epigenetic context. At present, the adaptive immune response to SARS-CoV-2 antigenicity remains unclear. Would vaccination or infection protect against re-infection? Two years after the COVAX initiative, while vaccination is ongoing in our country, our aim was to characterize the humoral signature of the COVID-19 vaccine in healthcare workers in Abidjan and to identify potential factors that might influence this humoral response.

MATERIALS AND METHODS

This was a prospective, cross-sectional, multicenter, three-month study, part of a larger project on the carriage and immunogenicity of SARS-CoV-2 in healthcare workers in Côte d'Ivoire, approved by the National Ethics Committee for Life Sciences and Health (No. 007-22/MSHPCMU/CNESVS-km). Participants were recruited and sampled in three University Hospitals (CHU) located in Abidjan (Cocody, Angré, and Treichville). Depending on the workstation, we defined three levels of exposure risk: (i) low-risk personnel: no contact with patients (administrative staff, etc.); (ii) intermediate-risk personnel: contact with unknown or suspected COVID-19 patients; (iii) high-risk personnel: contact with known COVID-19 patients. The study population was based on a random sample of 350 COVID-19 vaccinated health workers included in the large project mentioned earlier. They gave informed consent to participate in the study.

A questionnaire was used to collect epidemiological, clinical, and vaccine-related data. Venous blood samples were collected in dry tubes. This study included the following parameters: age, sex, workstation, body mass index (BMI), COVID-19 history (SARS-CoV-2 infection, vaccination status, name of SARS-CoV-2 vaccination, time between SARS-CoV-2 infection and blood collection, time between vaccination and blood collection), presence of comorbidity (asthma, diabetes, hypertension, sickle cell disease, etc). The existence of work-related stress due to COVID-19, the titers of IgM, IgG, and total anti-SARS-CoV-2 Abs, and the titer of total anti-S1 SARS-CoV-2 Abs were assessed. The history of SARS-CoV-2 infection was confirmed by the result of a positive RT-PCR test (reverse transcription followed by a polymerase chain reaction). Vaccination status and names of vaccines were obtained by checking the agent's vaccination record. For the determination of the existence of professional stress, "The job content questionnaire of KARASEK with 26 items" (Questionnaire de Karasek! Mesure du stress professionnel, s. d.) was used. The anti-SARS-CoV-2 IgM and IgG titers were determined on a mini-VIDAS (bioMérieux SA, France) using the VIDAS® SARS-CoV-2 IgM and IgG tests. These tests are sensitive (approximately 100%) and specific (greater than or equal to 99%). It is a fluorescent enzyme-linked immunosorbent assay (ELFA) that combines a two-step sandwich enzyme-linked immunosorbent assay with fluorescence detection. The test is used for the qualitative detection of IgM and IgG antibodies to SARS-CoV-2.

The results were expressed as an index 'i' of antibody detection. If 'i' was below 1 (antibody detection threshold), the result was negative; if greater than or equal to 1, the result was positive. If the result was positive, quantification was performed by converting VIDAS SARS-CoV-2 immunoglobulin index units to binding antibody units, with 1 threshold index = 20.33 BAU/ml, in accordance with the WHO call for the harmonization of serological

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tests for SARS-CoV-2 (19) (WHO/BS.2020.2403). An antibody level < 250 BAU/ml defined a weak serological response; an antibody level ≥ 250 BAU/ml defined a strong serological response, according to international standards established by the WHO (RecommandationSFGM_ac_monoclonaux_D4_200921_final - Recherche Google, s. d.).

With a CHORUS TRIO DIESSE (DIESSE Diagnostica Senese S.p.A., Italy) automaton, SARS-CoV-2 total anti-S1 antibodies was quantified using the Chorus SARS-CoV-2 "NEUTRALIZING" Ab test. This is a sensitive (99.6% [95% CI: 97.7 - 99.99]) and specific (99.8% [95% CI: 99.2 to 99.9]) kit that allows 36 immunoassays to be performed. This was a ready-to-use competitive enzyme immunoassay test, allowing the quantitative determination of total anti-S1 antibodies to SARS-CoV-2. The results were expressed as Binding Antibody Units (BAU/ml), calculated with reference to the first WHO International Standard 20/136 for anti-SARS-CoV-2 (Chorus Diesse, s. d.) and according to a graph based on the lot stored in the analyzer. The tested serum was interpreted as: (i) positive if the result > 50.0 BAU/ml; (ii) negative if the result < 20.0 BAU/ml; (iii) equivocal if the result is between 20.0 and 50.0 BAU/ml. In the case of an equivocal result, we repeated the test and/or re-sampled the patient according to the manufacturer's recommendations. SPSS V29.0 software was used for statistical analysis. Depending on the type of variable, descriptive and analytical statistical methods were employed. Pearson's correlation was used to compare two quantitative variables. The Chi^2 test and Fisher's exact test were utilized to examine the relationship between two qualitative variables and to create contingency tables. The Student T-test and the one-way ANOVA test were applied to compare means between a quantitative and a qualitative variable in cases of equal variance and normal distribution of observations. Non-parametric tests such as the Mann-Whitney U test were used in cases of unequal variance. GraphPad Prism version 9 software was used to generate the graphs. A p-value < 0.05 (two-tailed) was considered a statistically significant difference.

RESULTS

Descriptive study

Using a survey form and informed consent, this study identified a population of 350 health professionals. The most represented age group was 24-36 years (40.6%). The mean age of the respondents was 40.65 years. Our population was 54.3% overweight, with an average BMI of 26.44 kg/m^2. A female predominance of 57.1% (sex ratio=0.75) was observed. Emergency and inpatient departments had the highest number of workers (26.1% each). The majority of healthcare workers were at moderate risk of exposure to COVID-19 (48.0%) (Table 1).

Few healthcare workers had a history of SARS-CoV-2 (29.7%). The COVID-19 context was not a source of additional stress for 57.7% of healthcare workers. Pfizer and AstraZeneca vaccines were most administered in our population, at 53.1 and 34.9% respectively. The majority of workers were fully vaccinated in 84.6% of cases. For 30.9% of healthcare workers, the interval between vaccination and sampling varied from 4 to 6 months. The average was 7.95 months.

Among workers with a history of SARS-CoV-2 infection, the time between infection and sampling was 4 to 6 months for 28.8%, and 13 months or more for 25.0%, with an average of 9.74 months. Healthcare workers had no comorbidity in 54.3% of cases (Table 2).

Healthcare workers with an IgM titer below 21 BAU/ml (negative) represented most of the study population (92.0%). The average IgM level was 8.17 BAU/ml. Anti-SARS-CoV-2 IgGs were detected in 100% of healthcare workers, with strong serological responses (titer ≥ 250 BAU/ml) in 91.4% of cases. The IgG mean was 490.47 BAU/ml. IgG was the predominant isotype of the total antibody count. Almost all healthcare workers (99.4%) had a positive titer for neutralizing antibodies with an average of 1365.56 BAU/ml (Table 3).

Analytical study

The authors correlated total and neutralizing antibody levels and observed a weak positive and significant correlation ($p = 0.002$) between total and neutralizing antibody levels (Figure 1).

Then, we looked for factors that might influence the humoral response. A strong neutralizing antibody response was more significantly observed in healthcare workers aged 24-36 years (Table 4). There was a highly significant relationship ($p<0.001$) between mean total antibody levels and the presence or absence of a history of SARS-CoV-2 infection among healthcare workers. However, there was no statistically significant association between the mean levels of neutralizing antibodies and the history of infection (Figure 2). All subjects with a history of SARS-CoV-2 infection developed a significantly strong total antibody response ($p = 0.004$) (Table 5). Although we observed no significant association between neutralizing antibody response and history of infection, there was a 2.61-fold increased risk of developing a strong neutralizing antibody response if one had a history of SARS-CoV-2 infection (Figure 3).

By comparing the means of total and neutralizing antibodies according to the vaccination status, we noted a significant relationship between the mean levels of total antibodies and the vaccination status (Figure 4). Most fully vaccinated subjects had non-significantly strong total (86.3%) and neutralizing (85.1%) antibody responses. However, there was a 3-fold increased risk of developing a strong total antibody response and a 2-fold increased risk of developing neutralizing antibodies (Figure 5).

The co-morbidities presented by the workers were mainly high blood pressure (21.3%), asthma (18.8%), diabetes (10.0%) and the combination of high blood pressure and diabetes (3.8%). A significant relationship was found between mean total antibody levels and having or not having a comorbidity ($p=0.046$) (Figure 6). 47.5% of workers with comorbidity had a high total antibody response. Existence of comorbidity was associated with a 2.49 increased risk of developing a high total antibody response (Figure 7).

A significant association was found between a history

Table 1. Distribution by age and BMI groups, workstation, and workstation risk.

Parameter	Rate (%)
Age range (years)	
[24 - 37[	142 (40.6)
[37 - 46[	132 (37.7)
≥ 47	76 (21.7)
Mean age = 40.65 ± 7.97 [25 - 59]	
BMI range (kg/m^2)	
[17.30- 25]	160 (45.7)
≥ 25	190 (54.3)
Mean BMI = 26.44 ± 4.53 [18.49 - 39.56]	
Sex	
Male	150 (42.9)
Female	200 (57.1)
Sex ratio = 0.75	
Workstation	
Emergency	92 (26.3)
Hospitalizations	92 (26.3)
Consultation services	54 (15.4)
Laboratories	76 (21.7)
Administrative services	22 (6.3)
Others services	14 (4.0)
Workstation risk	
High	88 (25.1)
Intermediate	168 (48.0)
Low	94 (26.9)

of SARS-CoV-2 infection (p=0.033) and work-related stress, although no significant association was found between stress and humoral response. In addition, a history of SARS-CoV-2 infection increased the risk of work-related stress by 1.95 (Table 6).

DISCUSSION

Immunization programs around the world have prioritized healthcare workers as one of the main groups for SARS-CoV-2 vaccination since the approval of the first available vaccines. Two years after the initiation of the COVAX initiative in our country, our aim was to contribute to identifying factors that could impact the humoral response to the anti-SARS-CoV-2 vaccine among healthcare personnel in Côte d'Ivoire. It's worth noting that some non-significant results, including gender, BMI, workstation, workstation risk, vaccine type (name), and work-related stress, among others, have not been presented in this document. In general, our findings align with the observations of other researchers regarding the serological response following vaccination against SARS-CoV-2. Our results indicated that all healthcare workers included in this study developed antibodies against SARS-CoV-2. Studies have demonstrated that humoral responses to SARS-CoV-2 infection or COVID-19 vaccination are independent of sex and age (Adamczuk et al., 2022; Lau et al., 2021). Moreover, SARS-CoV-2 infection induces a robust neutralizing antibody response in most individuals (Lau et al., 2021). Terpos et al. (2021) reported that a stronger immune response in healthcare workers vaccinated with the BNT162b2 mRNA vaccine against COVID-19 was predicted by female sex and younger age (Terpos et al., 2021). Another study in healthcare workers revealed a more robust humoral response in young individuals and women after vaccination with the BNT162b2 vaccine (Pellini et al., 2021).

The study results support the assertion that the humoral response induced by SARS-CoV-2 is not gender-dependent. The study series included all vaccines from the COVAX Facility. Additionally, no significant correlation was found between serological test titers and

Table 2. Distribution of study population according to presence of history of SARS-CoV-2 infection, stress related to COVID-19 context, name of vaccines, vaccination status, delays between samples and infection and vaccine, and presence of comorbidity.

Parameter	Rate (%)
SARS-CoV-2 infection history	
Infected	104 (29.7)
Not infected	246 (70.3)
Work-related stress in the COVID-19	
Stress	148 (42.3)
Unstressed	202 (57.7)
Name of vaccine	
Astra Zeneca	122 (34.9)
Pfizer	186 (53.1)
Sinopharm	8 (2.3)
Johnson and Johnson	14 (4.0)
Moderna	2 (0.6)
AstraZeneca/Moderna	6 (1.7)
AstraZeneca/Pfizer	12 (3.4)
Vaccination status	
Fully vaccinated	296 (84.6)
Partially vaccinated	54 (15.4)
Time vaccination - collection (months)	
[0 - 3]	44 (12.6)
[4 - 6]	108 (30.9)
[7 - 9]	84 (24.0)
[10 - 12]	60 (17.1)
≥ 13	54 (15.4)
Average time = 7.95 ± 4.19 [1 - 26]	
Time infection - collection (months)	
[0 - 3]	4 (3.8)
[4 - 6]	30 (28.8)
[7 - 9]	14 (13.5)
[10 - 12]	20 (19.2)
≥ 13	26 (25.0)
Unspecified	10 (9.6)
Average time = 9.74 ± 5.24 [2 - 24]	
Existence of comorbidity	
Yes	160 (45.7)
No	190 (54.3)

age. In contrast, Tawinprai et al. (2022) reported a significant correlation between age and RBD antibody levels after a single dose of the ChAdOx1 (AZD1222) vaccine in a general population. However, a stronger neutralizing antibody response was observed in individuals aged 24 to 36, regardless of previous SARS-CoV-2 infection. In general, immunogenicity is better in younger subjects than in older subjects. However, in a report on the antibody response in COVID-19 patients, Ozgocer et al. (2021) found that the anti-SARS-CoV-2 antibody titer was significantly higher in the elderly than in the young. Our population was, on average, overweight.

Table 3. Distribution of the subjects according to the serological test titer (IgM, IgG, total anti-SARS CoV-2 and neutralizing anti-S1).

Parameter	Rate (%)
IgM level (BAU/ml)	
< 20.33 (Negative)	322 (92.0)
≥ 20.33 (Positive)	28 (8.0)
Mean = 8.17 ± 15.95 [1.02 - 128.69]	
IgG level (BAU/ml)	
20.33 - 249.99	30 (8.6)
≥ 250	320 (91.4)
Mean = 490.47 ± 176.62 [21.55 - 799.80]	
Total Ab (IgM + IgG)	
IgM Negative + Positive IgG	322 (92.0)
Positive IgM + Positive IgG	28 (8.0)
Mean = 498.64 ± 180.41 [23.58 - 808.70]	
Neutralizing Ab level (BAU/ml)	
< 20 (Negative)	2 (0.6)
≥ 20 (Positive)	348 (99.4)
Mean = 1365.56 ± 400.80 [19.90 -1983.25]	

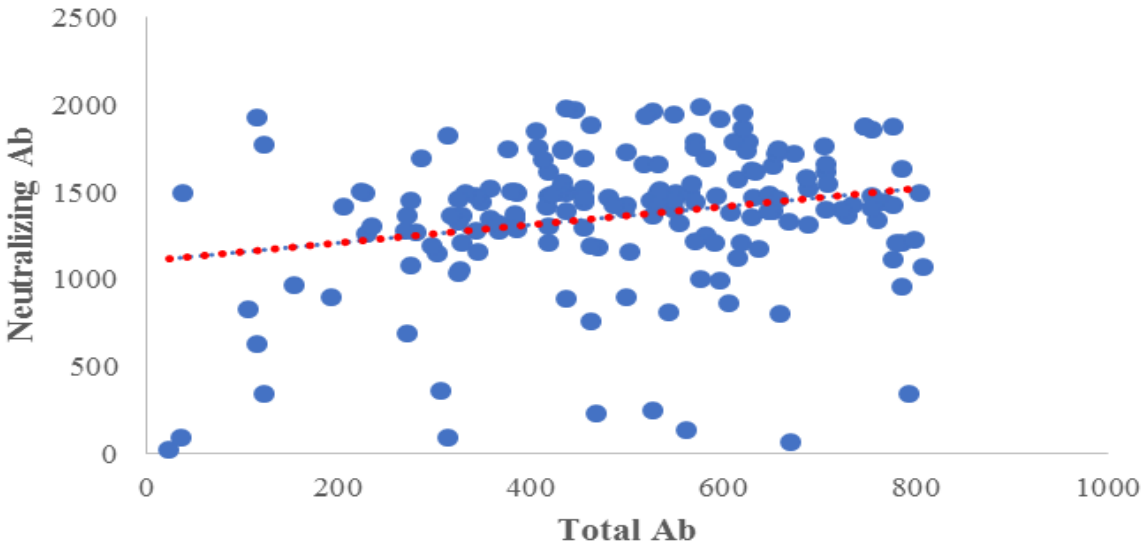

Figure 1. Analysis of correlation of anti-SARS-Cov-2 total and neutralizing antibodies titer. Pearson correlation: r = 0.232; p = 0.002.

Table 4. Relationship between neutralizing antibody response and age groups.

Parameter		Neutralizing Ab response		p
		Strong (%)	Weak (%)	
Age range (years)	[24 - 37]	12 (85.7)	130 (38.7)	0.018
	[37 - 46]	2 (14.3)	130 (38.7)	0.257
	≥ 47	0 (0.0)	76 (22.6)	0.349
Total		14 (100)	336 (100)	

Fisher exact test: p = 0.026.

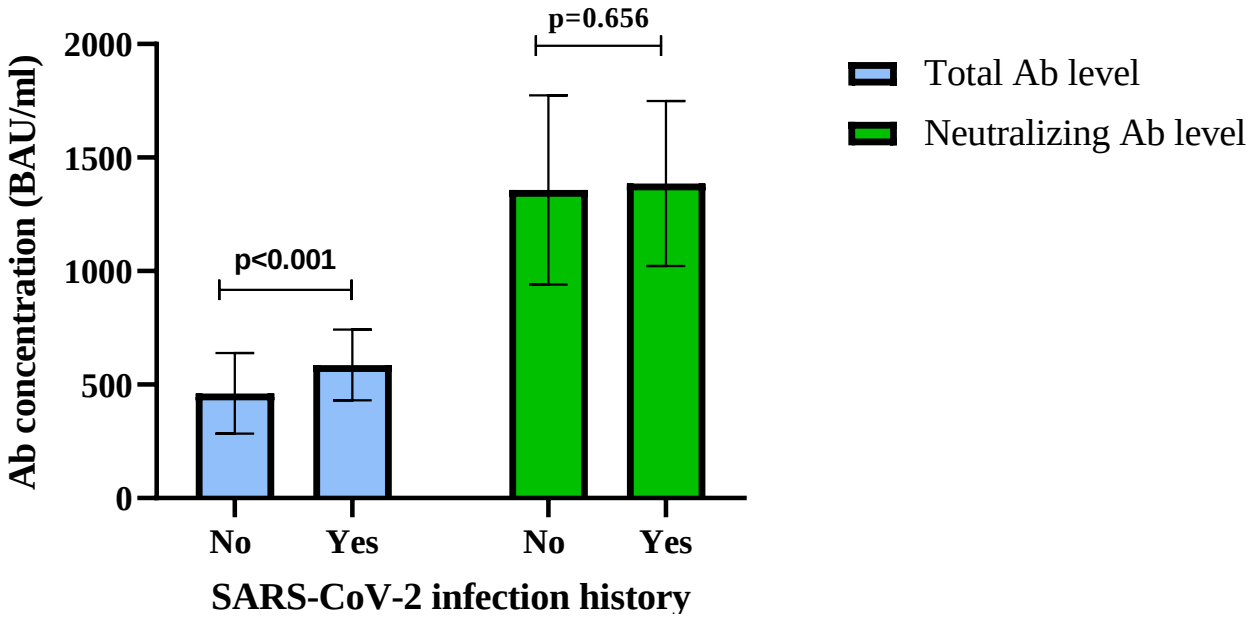

Figure 2. Comparison of the mean values of total and neutralizing antibodies according to the history of infection with SARS-CoV-2.

Table 5. Relationship between total antibody response and history of SARS-CoV-2 infection.

Parameter		SARS-CoV-2 infection history		
		Yes (%)	No (%)	Total (%)
Total Ab response	Weak	0 (0.0)	30 (100.0)	30 (100)
	Strong	104 (32.5)	216 (67.5)	320 (100)
Total		104 (29.7)	246 (70.3)	350 (100)

Fisher exact test: p = 0.004.

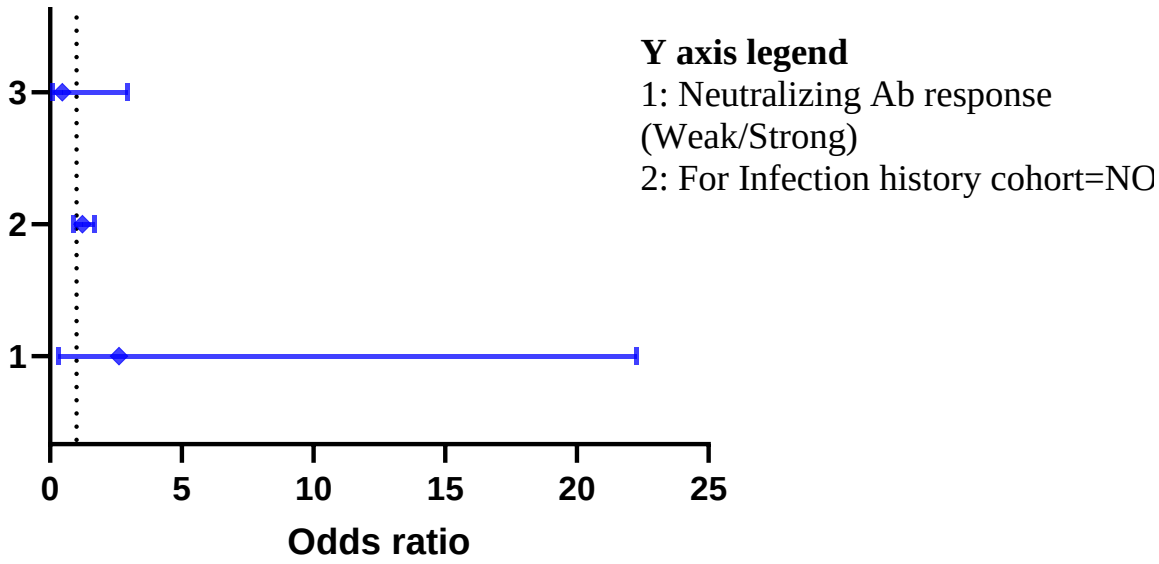

Figure 3. Forest plot between neutralizing antibody response and history of SARS-CoV-2 infection. OR = 2.615 ([95% CI: 0.307 to 22.283).

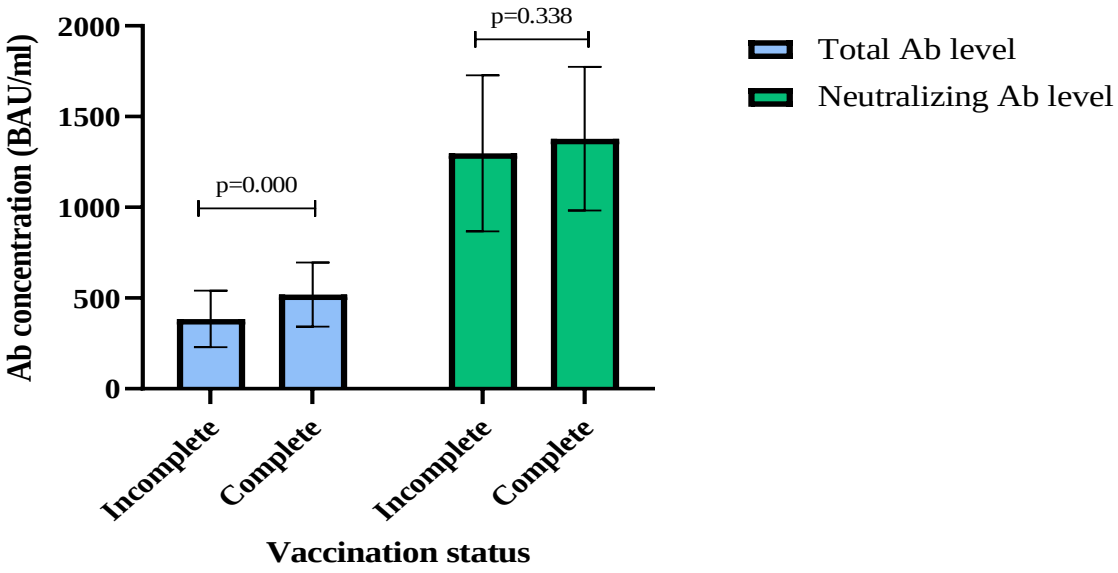

Figure 4. Comparison of the results of serological tests based on vaccination status.

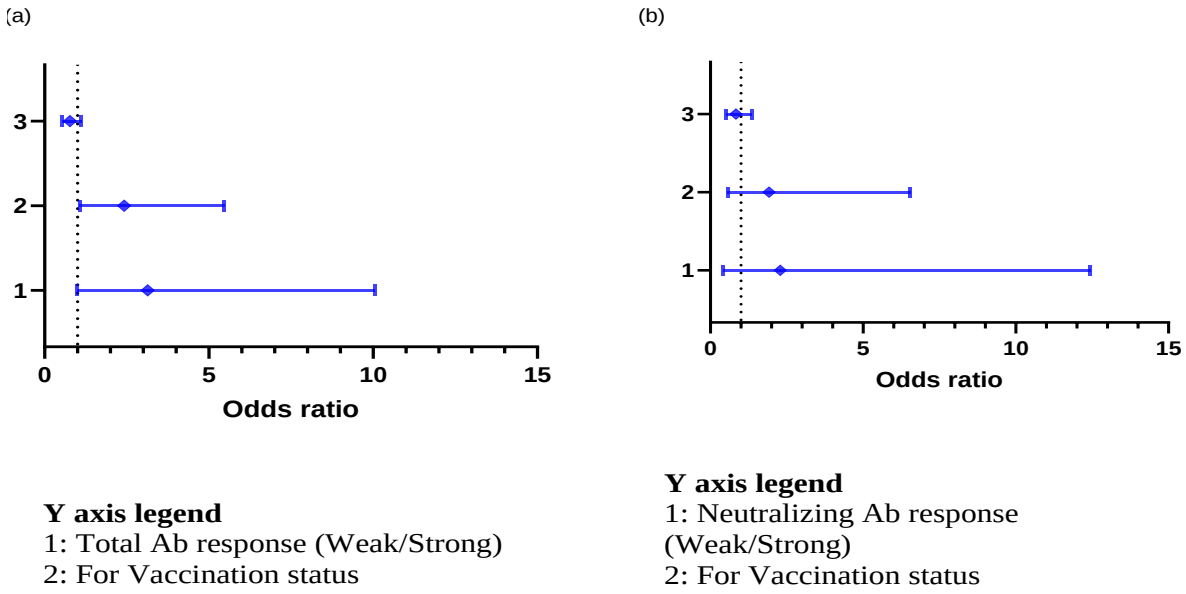

Figure 5. Meta-analysis plot between total (a) and neutralizing (b) antibody response and vaccination status.

We did not find a significant difference between the body mass index groups, nor a correlation with the anti-SARS-CoV-2 antibody titer. Studies have reported different results from ours (Pellini et al., 2021; Soffer et al., 2021). However, our results align with the findings of Ozgocer et al. (2021). Several factors may contribute to the heterogeneity of immune responses to SARS-CoV-2, including comorbidities (Bertholom, 2021).

A significant association was found between mean levels of total anti-SARS-CoV-2 antibodies and the presence of comorbidity. In contrast, Tawinprai et al. (2022) found a decreased immune response after vaccination in subjects with diabetes or hematological disease. In the presence of comorbidity, the risk of developing a strong total antibody response was multiplied by two in our population. In a longitudinal study, Lustig et al. (2021) found a decreased prevalence of IgG-positive antibodies in healthcare workers with comorbidities such as diabetes and hypertension. The differences they observed were not significant outside of immunosuppression. We did not observe an influence of occupational stress and the number of vaccine doses on the humoral response. In contrast to our results, Lustig et al. (2021) reported that each dose resulted in antibody-

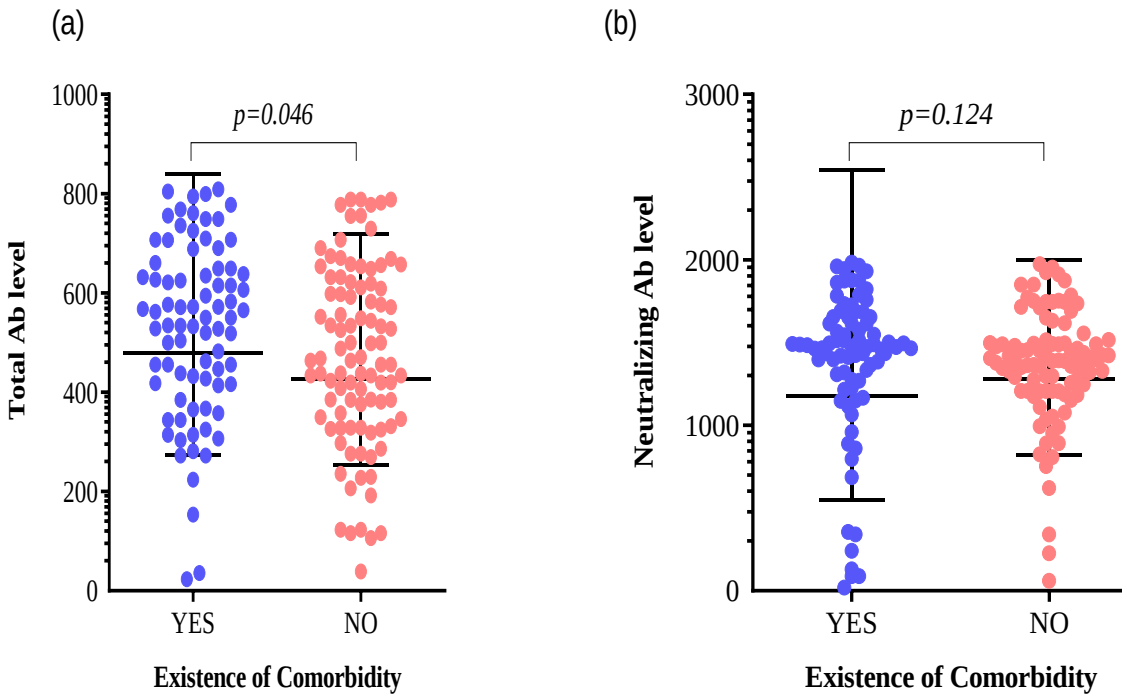

Figure 6. Comparison of mean total (a) and neutralising (b) antibodies by presence of comorbidities.

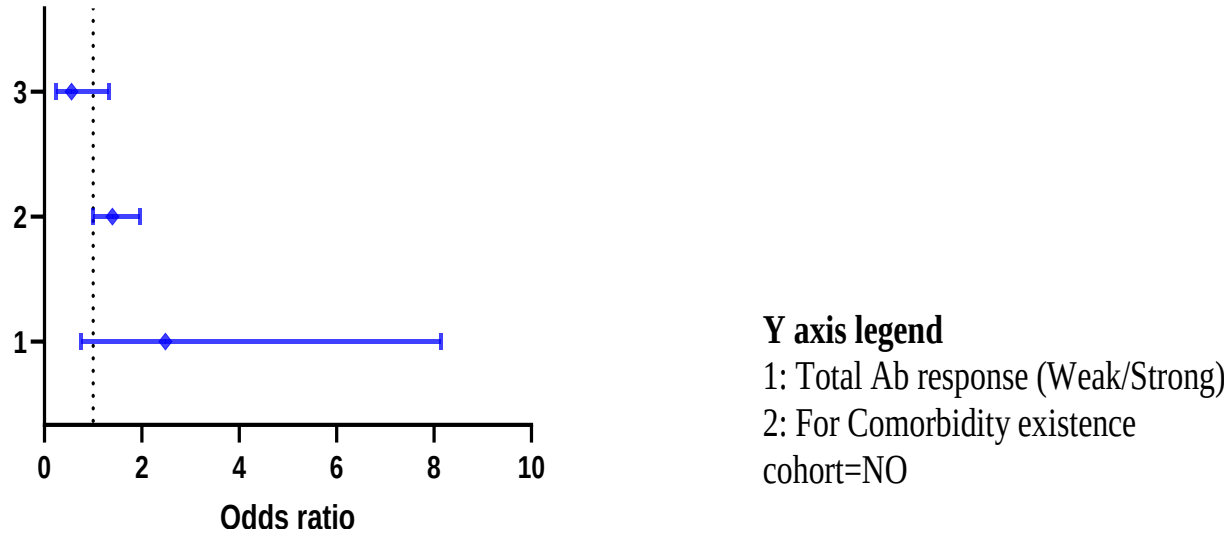

Figure 7. Forest plot between total antibody response and comorbidities. OR = 2.488 ([95% CI: 0.760 to 8.143).

Table 6. Relationship between history of SARS-CoV-2 infection and work-related stress.

Parameter		SARS-CoV-2 infection history		
		Infected (%)	Uninfected (%)	Total (%)
Work-related stress	Stress	56 (37.8)	92 (62.2)	148 (100)
	Unstressed	48 (23.8)	154 (76.2)	202 (100)
Total		104 (29.7)	246 (70.3)	350 (100)

Fisher exact test: p = 0.033; OR = 1.953 (95% CI: 1.013 to 3.764).

specific responses. Reporting on the effects of the BNT162b2 vaccine, Sahin et al. (2021) found a boost from the second dose over the first. Antibodies were measured between 29 and 43 days after vaccination. The differences observed with the study results could be explained, on the one hand, by a longer average time between vaccinations and assays and, on the other hand, by the progressive decrease in antibodies over time. However, significant immune responses have been reported following vaccination or infection with COVID-19. These responses have lasted for more than six months in patients (Adamczuk et al., 2022). To obtain a clear idea of the level of anti-SARS-CoV-2 antibodies or their persistence after vaccination or even natural infection, it is necessary to study the kinetics of anti-SARS-CoV-2 antibodies over a long period of time. According to Ozgocer et al. (2021) the production of specific antibodies is non-linear and cannot be predicted from any point in time and a very high level of seroprevalence was observed.

Vaccination against SARS-CoV-2 elicited a strong humoral response, even in individuals with incomplete vaccination (87.8% for total binding antibodies and 92.6% for neutralizing antibodies) or without a history of COVID-19 infection (87.8% for total binding antibodies and 95.1% for neutralizing antibodies). This raises the question of herd immunity to the COVID-19 pandemic in our country. Was it due to pre-existing immunization or cross-reactivity? IgG detection may lack specificity due to cross-reactions with other human coronaviruses (Héla, 2020; Milleliri et al., 2021). Is it true that, in our series, the 70.3% who had no history of infection really do? There have been many reports of the high prevalence of asymptomatic forms of COVID-19 (Institut Pasteur, 2020; Milleliri et al., 2021). The study found 13% of patients were contagious before symptoms appeared (Bulut and Kato, 2020). Moreover, in this context, many people are in a posture of denial of COVID-19 and have a fatalistic attitude (UNICEF, s. d.). As a result, the use of personal protective equipment (PPE) is relatively low. In addition, there is a lot of mixing of the population in our public transport conditions. This could favor contamination and contribute to the high number of asymptomatic forms. In a report on healthcare workers eligible for vaccination in Nigeria, Abdullahi et al. (2022b) reported a high prevalence of previous SARS-CoV-2 infection. Our series found a lower percentage (29.7%). Besides the significant association observed with mean total antibody concentrations, no significant relationship was observed with mean level of neutralizing antibodies. In addition, a history of SARS-CoV-2 infection doubled the likelihood of developing a strong neutralizing antibody response. In the course of infection by SARS-CoV-2, in parallel, a slower response lasting several months is set up. Through a mechanism of gene hypermutation, this leads to B-cell maturation. After positive selection, these B cells will form a compartment of memory B cells and long-lived plasma cells (as opposed to short-lived early plasma cells in the initial phase of infection) that produce high-affinity antibodies against SARS-CoV-2. Thus, following a vaccination, therefore, a re-exposure to SARS-CoV-2, this immune memory leads to the rapid and efficient production of anamnestic antibodies with amplification of the humoral response.

There are many reports that vaccination enhances the response obtained after natural infection. Turner et al. (2021) established that people with a history of SARS-CoV-2 infection can maintain some level of antibodies. A history of SARS-CoV-2 infection has been shown to be associated with high levels of neutralizing antibodies, even after a single dose and regardless of the vaccine (Cheng et al., 2021; Naranbhai et al., 2021).

Since the dawn of time, stress has not been without consequences for human health. Studies have linked stress to lowered immune defences, but the mechanisms involved are still unclear (Jacque and Thurin, 2002; Padgett, 2003; Wieduwild et al., 2020).

No significant relationship was observed between having experienced a stressor and antibody levels. However, a history of SARS-CoV-2 infection increased the risk of work-related stress by about two-fold. It has been reported that this association between stress and immunity is largely mediated by β2-adrenergic receptors expressed on the surface of immune cells. These receptors bind to stress hormones (adrenaline and noradrenaline) (Wieduwild et al., 2020).

This study has some limitations that would have allowed further elucidation of the humoral response of our population. The sample size may have influenced the results obtained. Previous asymptomatic infection in the "no history of infection" group cannot be excluded. There is a lack of a longitudinal component to study the kinetics of anti-SARS-CoV-2 antibodies and measure Th2 cytokine levels.

Conclusion

Humoral response to SARS-CoV-2 vaccine, as part of the COVAX mechanism, is robust and persistent in healthcare workers. A history of SARS-CoV-2 infection appears to enhance the humoral response. Younger age seems to be associated with a better vaccine response.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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