

Respuesta inmune a la vacunación contra SARS-CoV-2 en adultos de Cali, Colombia: experiencia de 2022

Immune response to SARS-CoV-2 vaccination in adults from Cali, Colombia: a 2022 experience

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Resumen

Introducción: La inmunización es una medida protectora contra SARS-CoV-2. Este estudio evaluó los niveles de anticuerpos de IgG anti-S y su asociación con características clínicas, demográficas y del esquema de vacunación en adultos en Cali, Colombia (2021-2022).

Abstract

Introduction: Immunization is a protective measure against SARS-CoV-2. This study assessed IgG anti-S antibodies levels and their association with clinical, demographic and vaccination-related factors in adults from Cali, Colombia (2021-2022).

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Objetivo: Analizar los factores asociados con niveles de anticuerpos enlazantes con esquema completo contra SARS-CoV-2, en una ciudad de un país de medianos ingresos.

Métodos: Estudio transversal realizado entre diciembre de 2021 y febrero de 2022 en Cali, Colombia. Los adultos elegibles fueron identificados a partir de una base de datos de salud local y reclutados mediante muestreo aleatorio y convocatoria a través de medios de comunicación. Se incluyó un total de 394 participantes. La información sobre datos demográficos, vacunación e historial de infección por COVID-19 fue recopilada mediante entrevistas y verificada con registros oficiales. Los anticuerpos IgG contra la proteína Spike del SARS-CoV-2 se midieron utilizando una prueba ELISA estandarizada, y los resultados se expresaron en BAU/mL, de acuerdo con la calibración de la OMS. Se utilizó un punto de corte de 1000 BAU/mL para definir una respuesta elevada de anticuerpos. Los análisis estadísticos se realizaron con GraphPad Prism y Stata 14, utilizando modelos de regresión logística para explorar asociaciones. El estudio fue aprobado por el Comité de Ética de la Universidad Libre y se obtuvo consentimiento informado de todos los participantes.

Resultados: El 70% de los participantes presentó títulos de anticuerpos específicos ≥ 1000 BAU/mL (por sus siglas en inglés binding antibodies units). Se encontraron asociaciones con: a) Tipo de vacuna (aOR 2,40; 95% IC [0,99-5,84]; $p < 0,053$) para vacunas ARNm; b) Esquema heterólogo (aOR 2,39; 95% IC [1,14-5,02]; $p < 0,021$); y c) ≥ 21 días desde la dosis de refuerzo (aOR 2,62; IC 95% [1,29-5,30]; $p < 0,007$). Las mujeres mostraron una mayor respuesta con esquemas heterólogos (aOR 3,27; 95% IC [0,99 - 5,84]; $p < 0,008$) y vacunas mRNA (aOR 3,03; 95% IC [0,99 - 5,84]; $p < 0,048$); en hombres, el tiempo transcurrido ≥ 21 días post-refuerzo también se asoció con elevados niveles de anticuerpos (aOR 2,62, 95% IC [1,29-5,30]; $p < 0,007$).

Conclusiones: Las vacunas de ARNm, los esquemas de vacunación heterólogos y el tiempo post-refuerzo se asociaron con mayores niveles de anticuerpos IgG anti-S. Estos hallazgos, relevantes en un país de ingresos medios, respaldan estrategias de vacunación adaptadas a características poblacionales específicas.

Palabras clave: SARS-CoV-2, vacunas, anticuerpos IgG, inmunización, respuesta inmune, esquema heterólogo, anticuerpos enlazantes.

Objective: To analyze factors associated with binding antibodies levels in adults with a complete SARS-CoV-2 vaccination schedule in a middle-income country city.

Methods: A cross-sectional study was conducted between December 2021 and February 2022 in Cali, Colombia. Eligible adults were identified from a local health database and recruited through random sampling and media outreach. A total of 394 participants were included. Data on demographics, vaccination, and COVID-19 history were collected via interviews and verified with official records. IgG antibodies against the SARS-CoV-2 Spike protein were measured using a standardized ELISA, and results were expressed in BAU/mL following WHO calibration. A cut-off of 1,000 BAU/mL defined high antibody response. Statistical analyses were performed with GraphPad Prism and Stata 14, using logistic regression to explore associations. The study was approved by the Universidad Libre Ethics Committee, and informed consent was obtained from all participants.

Results: Seventy percent of participants showed specific antibodies titers ≥ 1000 BAU/mL (binding antibodies units). Associations were observed with: a) mRNA vaccines (aOR: 2.40; 95% CI: 0.99-5.84; $p = 0.053$); b) heterologous vaccination schemes (aOR: 2.39; 95% CI: 1.14-5.02; $p < 0.021$); and c) ≥ 21 days since the booster dose (aOR: 2.62; 95% CI: 1.29-5.30; $p < 0.007$). Women showed a stronger response with heterologous schemes (aOR: 3.27; 95% CI: 0.99-5.84; $p = 0.008$) and mRNA vaccines (aOR: 3.03; 95% CI: 0.99-5.84; $p = 0.048$). Among men, antibodies levels were higher when measured ≥ 21 days after the booster dose (aOR: 2.62; 95% CI: 1.29-5.30; $p < 0.007$).

Conclusions: mRNA vaccines, heterologous vaccination schedules, and a longer interval since the booster dose were associated with higher anti-S IgG antibodies levels. These findings, relevant to middle-income countries, support the adaptation of vaccination strategies to specific population characteristics.

Keywords: SARS-CoV-2, vaccines, IgG antibodies, immunization, immune response, heterologous vaccination, binding antibodies levels.

INTRODUCTION

The COVID-19 pandemic, declared a global health emergency by the World Health Organization (WHO), posed an unprecedented challenge to healthcare systems worldwide (1). Mass vaccination quickly became the main strategy to mitigate the spread and severity of the disease (2,3). Colombia's national vaccination plan included the vaccines: BNT162b2 (Pfizer-BioNTech), ChAdOx1-S/nCoV-19 (Oxford/AstraZeneca), mRNA-1273 (Moderna TX, Inc), CoronaVac (Sinovac), Ad26.COV2-S (Janssen, Johnson & Johnson) (4).

The city of Cali reported its first case in March 2020 (5). By 2022, approximately 40% of the adult population had received a complete vaccination schedule or booster dose (6). Although the efficacy of these vaccines ranges between 50% and 95% protection (7), various studies have reported a decrease in humoral immune response over time, potentially reducing clinical protection (8,9).

Despite widespread vaccine implementation, there is limited local evidence on the magnitude and duration of humoral immune response after vaccination in urban populations of middle-income countries like Colombia, hindering informed public health decision-making. This gap underscores the need to understand how demographic, clinical and vaccination-related factors influence antibodies levels in the context.

Therefore, this study, conducted in 2022, aimed to evaluate the humoral immune response by measuring anti-S SARS-CoV-2 IgG antibodies induced by vaccination in adults in Cali. It is also sought to explore the relationship of this response with variables such as age, sex, vaccine type and schedule, booster dose, and time elapsed since vaccination, thereby contributing evidence to optimize immunization programs in similar populations.

METHODS

Study design

This was a cross-sectional analytical study conducted in Cali, Colombia, between December 15, 2021, and February 25, 2022, at two vaccination centers: Hospital Primitivo Iglesias ESE Centro and the Welfare Service of Universidad Libre, Seccional Cali. This design was chosen to estimate associations between vaccination-related variables and antibodies levels at a single time point, as a part of a strategy to maximize sample size instead of dividing participants across multiple time points.

Population and sample

In 2021, the city of Cali had a population of 2 264 748 inhabitants, distributed across 22 administrative communes, according to data from the National Administrative Department of Statistics (DANE) (10). A consolidated dataset identified 1 509 150 potential participants based on sources such as Sismuestras (11), Sivigila (12), SegCOVID-19 Adress (13), PAI web (14), PISIS (15) and DANE (10), following a methodology similar to that used in previous COVID-19 studies conducted in Colombia (7).

The sample size was determined using version 3 of the Open-Source Epidemiological Statistics for Public Health equation (16), based on a population of over 1 000 000 vaccinated individuals, assuming a vaccination rate of 50% and a 95% confidence interval. The required number of participants to achieve 80% power was 384.

All participants were informed about the study objectives and procedures prior to enrollment, following the guidelines established by the Declaration of Helsinki. They were notified in advance of the dates and locations for participation. Each participant provided a single blood sample and demographic and clinical records were collected. All the data were anonymized to protect participant confidentiality.

Inclusion criteria

Adults aged 18 and over, who had completed a full SARS-CoV2 vaccination schedule and were registered in the consolidated dataset provided by the Secretary of Health of Santiago de Cali were eligible. Individuals with a history of autoimmune diseases or using immunosuppressive treatments were excluded. Exclusion criteria only applied to individuals who declined to participate voluntarily in the study after being invited.

Data collection

Initially, a random sampling strategy was used to contact eligible individuals via telephone, yielding a low response rate of 112 volunteers. To complete the targeted number of participants, a second recruitment phase was conducted using outreach strategies through local television, social media, and vaccination centers. These additional efforts aimed to ensure representativeness of the vaccinated population and minimize selection bias. A total of 581 interested individuals responded to the call, from which 394 were selected for analysis.

Information was obtained through interviews, which included questions on age, sex, vaccination dates, prior COVID-19 infection, type of vaccine received, and whether the booster dose was homologous or heterologous. Homologous vaccination was defined as the use of the same vaccine platform for both the primary series and the booster, whereas heterologous vaccination referred to the use of different vaccine platforms. This information was supplemented and cross-checked with a consolidated dataset compiled from multiple databases managed by the Secretary of Health of Santiago de Cali.

Anti-SARS-CoV-2 measurement techniques

Serum IgG level against the Spike (S) protein of SARS-CoV-2 were measured using a quantitative enzyme-linked immunosorbent assay (ELISA) from the manufacturer GSD Novalisa SARS-CoV-2 (COVID-19) Quantitative IgG (LNOVA TEC IMMUNODIAGNOSTICA GMBH, Dietzenbach, Germany; Product No.: CVGQ0970, Lot: CVGD-004). Reported repeatability was 5.93%, 6.37% and 5.0% at concentrations of 6.22, 14.40 and 32.03 AU/mL, respectively. Reproducibility was 14.11%, 8.37% and 5.52% at the same concentration. Borderline sensitivity was 96.05%, with specificity ranging from 98.16 to 99.94%.

Blood samples were collected in vacuum tubes with a silica gel separator and clot activator. Serum was separated by centrifugation ($2\ 000 \times g$ for 15 minutes) and stored at $-80\ ^\circ\text{C}$ until analysis. The assay was calibrated using the First WHO International Standard for anti-SARS-CoV-2 immunoglobulin (human) (NIBSC 20-136) (17,18). Results in arbitrary units (AU/mL) were converted to binding antibodies units per milliliter (BAU/mL) based on WHO standardization (17). A threshold value of 1 000 BAU/mL was adopted, based on evidence available at that time, correlating this level with high neutralizing activity in the PRNT50 microneutralization assay. This cut-off was used in the analysis to dichotomize antibodies response levels.

Statistical Analysis

Antibodies levels were quantified using GraphPad Prism version 9.1.1 (GraphPad Software, San Diego, CA, USA), while the other study variables were organized using Excel (Microsoft Corporation, 2019). Data quality was verified prior to analysis. Descriptive statistics were used to characterize the study population. The Shapiro-Wilk test was applied to assess the distribution of variables.

Quantitative variables were reported as medians with interquartile range (IQR), while categorical variables were summarized as proportions and presented in frequency tables.

For univariate analysis, antibodies levels were dichotomized based on a cut-off value of $\geq 1\ 000$ BAU/mL. Associations between independent variables and the outcome (high antibodies level) were assessed using Chi-square tests for categorical variables and log-binomial regression models for continuous variables. Odds Ratios (OR) with 95% confidence intervals (CI) were calculated to estimate the strength of the association.

Multivariable analysis was performed using binomial logistic regression models. The initial model included variables with p-values ≤ 0.25 during bivariable analysis. A backward stepwise strategy was applied, and sex was controlled as a potential confounder. Final model selection was based on the likelihood ratio test (LR test), and variables with p-values ≤ 0.05 or clinical relevance were retained. In cases of collinearity, the most clinically meaningful variable was prioritized. Model fit was evaluated using the Hosmer-Lemeshow goodness of fit test. All statistical analyses were performed using the statistical software package Stata version 14 TM (StataCorp, College Station, TX, USA).

Ethical considerations

This study was approved by the Research Ethics and Bioethics Committee of the Faculty of Health Sciences of the Universidad Libre, Colombia, and was classified as risk-free research under to Act No. CEB-013-2021 of December 12, 2021.

RESULTS

Participant selection and follow-up

A total of 1 509 150 individuals were identified as eligible for inclusion. Among these, 581 responded to the recruitment process. However, 187 did not meet the selection criteria and were excluded. Consequently, 394 participants were included in the analysis (Figure 1). Vaccine type was considered during categorization.

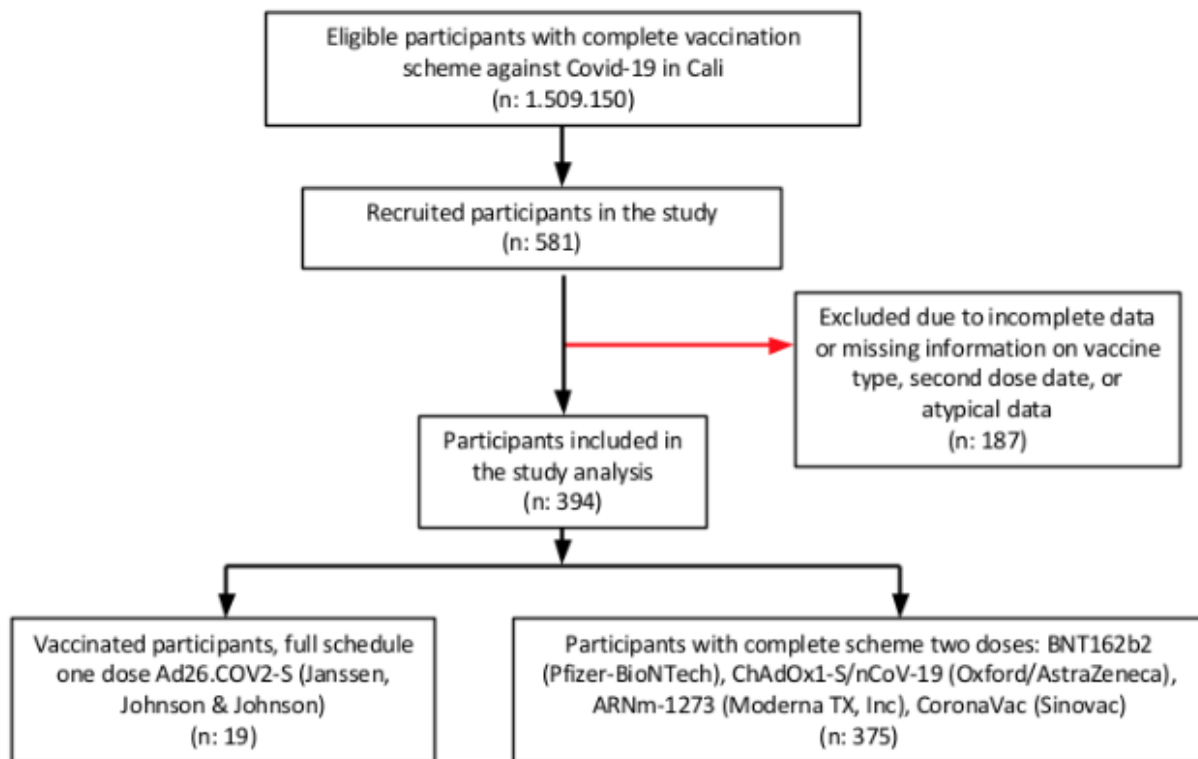


Figure 1. Flowchart, patient recruitment.

Descriptive characteristics

Participants were categorized into three age groups: <40, 40-60, and >60 years. The median age was 31 years (IQR 21-57). Women comprised 67.0% of the sample; 77.2% reported no history of COVID-19 symptoms; 62.2% of participants received mRNA vaccines, and 50.8% had received a booster dose.

A binding antibodies threshold ($\geq 1\ 000$ BAU/mL) was observed in 71.6% of participants. The median time between the final vaccine dose (complete scheme) and blood sampling was 211 (IQR 149-244), while the interval after the booster dose was 33 days (IQR 13-56.5) (Table 1).

Table 1. Characteristics of participants admitted to the study with a complete vaccination schedule against COVID-19 in Cali, December 2021- February 2022.

Demographic and clinical characteristics	Description	Outcome	
		n: 394	%
Age (years)**	31	Median	IR* 21-57
Age, n(%)	< 40	231	58.6
	40-60	92	23.4
	>60	71	18.0
Sex, n(%)	Woman	264	67.0
	Men	130	33.0
Symptoms related with COVID-19, n (%)	No	304	77.2
	Yes	90	22.8
Type of biological vaccine n (%)	Inactivated viral vector	56	14.2
	Recombinant adenoviral vector	93	23.6
	mRNA	245	62.2
Booster shot, n(%)	No	194	49.2
	Yes	200	50.8
Type of vaccination scheme n (%)	Homologous	99	25.1
	Heterologous	101	25.6
	ND	194	49.3
Antibody level (BAU/mL)	<1000	112	28.4
	≥1000	282	71.6
Time interval between full vaccination schedule and sample day (days)	≤ 120	56	14.2
	> 120	338	85.8
Time interval between booster and COVID-19 serology (days)	≤ 21	83	41.1
	> 21	119	58.9
Time interval between reporting symptoms associated with COVID-19 and serology (days)	≤ 21	5	5.6
	> 21	85	94.4
Time between complete vaccination scheme and sample day (days)	211,5	Median	IR* 149-244
Time interval between booster and COVID-19 serology (days)	33	Median	IR* 13-56.5

*IR: Interquartile range, ND: no data

Analysis

As shown in Table 2, no statistically significant correlation was found between age and achieving high antibodies levels (p 0.614). Among mRNA vaccine recipients, 62.2% reached antibodies levels ≥ 1000 BAU/mL, whereas 22.0% of those who received inactivated adenoviral vector vaccines did not reach this threshold ($p < 0.001$).

Additionally, 32.3% of participants with homologous vaccinations schemes had sub-threshold levels, compared to 14.9% with heterologous schemes ($p < 0.004$). Statistically significant differences were also observed for sex ($p < 0.018$), vaccination booster ($p < 0.028$), and time interval > 21 days post-booster ($p < 0.001$).

Table 2. Characteristics of participants and antibody levels against COVID-19.

Demographic and clinical characteristics	Description	Total (394)	Antibody level ≥ 1000 (BAU/mL) n:(282)	Antibody level < 1000 (BAU/mL) n:(112)	p - value
Age, (years) n(%)	< 40	231 (58.6)	161 (69.7)	70 (30.3)	0.614
	40-60	92 (23.4)	68 (74.0)	24 (26.0)	
	>60	71 (18.0)	53 (74.7)	18 (25.3)	
Sex, n(%)	Woman	264 (67.0)	179 (67.8)	85 (32.2)	0.018
	Men	130 (33.0)	103 (79.2)	27 (20.8)	
Symptoms associated with COVID-19, n (%)	No	304 (77.2)	70 (77.8)	20 (22.2)	0.137
	Yes	90 (22.8)	212 (70.0)	91 (30.0)	
Type of biological vaccine, n (%)	Inactivated viral vector	56 (14.2)	35 (62.5)	21 (37.5)	0.001
	Recombinant adenoviral vector	93 (23.6)	56 (60.2)	37 (39.8)	
	mRNA	245 (62.2)	191 (78.0)	54 (22.0)	
Booster shot, n(%)	No	194 (49.2)	129 (66.5)	65 (33.5)	0.028
	Yes	200 (50.8)	153 (76.5)	47 (23.5)	
Type of vaccination scheme n (%)	Homologous	99 (25.1)	67 (67.7)	32 (32.3)	0.004
	Heterologous	101 (25.6)	86 (85.1)	15 (14.9)	
Time interval between full vaccination schedule and sample day (days)	≤ 120	56 (14.2)	35 (62.5)	21 (37.5)	0.104
	> 120	338 (85.8)	247 (73.1)	91 (26.9)	
Time interval between booster vaccination and sample day (days)	≤ 21	83 (41.1)	53 (63.9)	30 (36.1)	0.001
	> 21	119 (58.9)	101 (84.9)	18 (15.13)	
Time interval between reporting symptoms associated with COVID-19 and sample day (days)	≤ 21	5 (5.6)	5 (100)	0	0.219
	> 21	85 (94.4)	65 (76.47)	20 (23.53)	

After assessing factors associated with generating antibodies, it was noticeable that users of mRNA vaccines had a probability of 62.2%, of reaching high levels of specific binding antibodies; the inactivated viral vector vaccine users were used as the reference group (baseline probability: 100%). Participants with heterologous vaccination had an 85.1% probability of reaching the threshold, compared to those with homologous schemes.

As shown in Table 3, the bivariate analysis revealed several variables with statistically significant association with achieving high antibodies levels. This included sex ($p < 0.018$), booster shot ($p < 0.028$), type of vaccination scheme ($p < 0.004$), time interval between booster dose and sample collection ($p < 0.001$) and type of biological vaccines ($p < 0.001$). In addition, there was an association between sex OR 1.81 (1.10 - 2.98) ($p < 0.019$), use of booster shot OR 1.64 (1.03 - 2.62) ($p < 0.028$), type of biological vaccination OR 2.74 (1.37 - 5.47) ($p < 0.004$), and the time interval between booster vaccination and sample day OR 3.18 (1.54 - 6.61) ($p < 0.0006$).

Multiple logistic regression models were performed and the parsimonious model was selected. The findings revealed that the heterologous vaccination scheme was significantly associated with high antibodies levels, with raw odds ratio (rOR) of 2.74 (1.37- 5.47) and adjusted odds ratio (aOR) of 2.39 (95% CI 1.14-5.02), ($p < 0.021$). In addition, time interval between booster vaccination and blood sample collection greater than 21 days had a rOR 3.18 (1.54 - 6.61) and aOR of 2.62 (95% CI 1.29 - 5.30), ($p < 0.007$). Both variables maintained significant associations after adjustment p -values ≤ 0.05 .

Age and the type of biologic vaccines were added to the model as clinically significant variables. The inclusion of mRNA vaccine type improved the explanatory capacity of the model, showing a rOR 2.12 (1.14 - 3.94) and aOR 2.40 (95% CI 0.99 - 5.84), ($p 0.053$). On the other hand, age was not significantly associated with antibodies levels (Table 3).

A secondary model adjusted by sex (ESM) showed that women with a heterologous vaccination had an aOR 2.84 (95% CI 1.14 - 7.04), ($p 0.024$). Women with mRNA type vaccination got OR 2.89 (95% CI 0.96 - 8.74), ($p 0.59$). Among men with more than 21 days between booster vaccinations and sampling, had an aOR 4.77 (95% CI 1.27-17.85) ($p < 0.02$). The final model correctly classified 78% of cases.

DISCUSSION

This study, conducted during the 2022 vaccination period in Cali, Colombia, found that approximately 70% of fully vaccinated adults developed high levels of IgG antibodies against the SARS-CoV-2 Spike (S) protein. These findings align with other international studies conducted during the early post-vaccination phases of the pandemic. For example, a longitudinal study in Romania reported sustained neutralizing activity in over 75% of healthcare workers six months post-vaccination (10), while a cross-sectional study in Brazil observed antibodies prevalence exceeding 70% (18).

Interestingly, we did not find significant relationship between antibodies levels and age, which is consistent with reports from studies conducted in the United States and China (3, 8, 18-20). Conversely, other research reported the impact of age on antibodies development, such as indicated some findings in Poland, Italy and Portugal showing a considerable decline in antibodies titers with increasing age, up to 63-fold in some cases (21). Similarly, studies in Israel and Bulgaria observed diminished antibodies longevity in older adults, while research from Switzerland and Brazil found no significant correlation between age and immune response (18-22), suggesting that age-related variability may be context-dependent and influenced by population characteristics, as recently has been pointed out (23).

Our results showed that heterologous vaccination schemes were associated with higher antibodies titers. This is in agreement with studies in Brazil, where higher immune responses were observed when an mRNA vaccine was used as a booster following an inactivated vaccine primary series (22, 8). Participants who received mRNA vaccines demonstrated a greater likelihood of reaching higher antibodies levels, a trend supported by the literature. mRNA vaccines have consistently shown the ability to induce strong neutralizing antibodies responses (24-30).

The duration between the booster vaccination and testing was another relevant factor influencing antibodies levels, as supported by literature reports (30-37). It has been reported that antibodies titers tend to increase in the weeks following vaccination, with peaks commonly observed from day 21 onward (16, 32, 38-40). These results reinforce the role of booster doses in sustaining a robust and long-lasting immune response against COVID-19 (41).

Table 3. Bivariable and multivariable analysis. Patients' factors related to production of high specific binding antibodies levels against COVID-19.

Demographic and clinical characteristics	Description	Total (394)	Antibody level ≥ 1000 (BAU/mL) n: (282)	rOR*	CI 95% low	Sup	p-value**	aOR*** CI 95%	p-value
Age, (years) n(%)	< 40	231 (5.6)	161 (69.7)	1					
	40-60	92 (23.4)	68 (74.0)	1.23	0.72	2.12	0.452		
	>60	71 (18.0)	53 (74.7)	1.28	0.69	2.34	0.423	-	-
Sex, n(%)	Woman	264 (67.0)	179 (67.8)	1					
	Men	130 (33.0)	103 (79.2)	1.81	1.10	2.98	0.019	-	-
Symptoms associated with COVID-19, n(%)	No	304 (77.2)	70 (77.8)	1					
	Yes	90 (22.8)	212 (70.0)	1.52	0.85	2.79	0.137	-	-
Type of biological vaccine, n(%)	Inactivated viral vector	56 (14.2)	35 (62.5)	1					
	Recombinant adenoviral vector	93 (23.6)	56 (60.2)	0.91	0.46	1.80	0.782	1.13 0.37-3.42	0.833
	mRNA	245 (62.2)	191 (78.0)	2.12	1.14	3.94	0.017	2.40 0.99-5.84	0.053
Booster shot, n(%)	No	194 (49.2)	129 (66.5)	1					
	Yes	200 (50.8)	153 (76.5)	1.64	1.03	2.62	0.028	-	-
Type of vaccination scheme n(%)	Homologous	99 (25.1)	67 (67.7)	1					
	Heterologous	101 (25.6)	86 (85.1)	2.74	1.37	5.47	0.004	2.39 1.14-5.02	0.021
Time interval between full vaccination schedule and sample day (days)	≤ 120	56 (14.2)	35 (62.5)	1					
	>120	338 (85.8)	247 (73.1)	1.63	0.85	3.05	0.104	-	-
Time interval between booster vaccination and sample day (days)	≤ 21	83 (41.1)	53 (63.9)	1					
	> 21	119 (58.9)	101 (84.9)	3.18	1.54	6.61	0.0006	2.62 1.29-5.30	0.007
Time interval between reporting symptoms associated with COVID-19 and sample day (days)	≤ 21	5 (5.6)	5 (100)						
	> 21	85 (94.4)	65 (76.47)	-	-	-	-	-	-

*rOR: raw Odds Ratio; **A statistical significance value of $p \leq 0.25$ was considered statistically significant. According to Hosmer & Lemeshow as variable selection criteria to build the model in the bivariable logistic analysis; ***aOR: adjusted Odds Ratio

Concerning previous infection, our study did not find a significant correlation between prior COVID-19 infection and the generation of antibodies levels. However, studies conducted in Brazil and Spain have reported a strong influence of previous infection on IgG antibodies levels and stability (21, 42). It has also been observed that prior SARS-CoV-2 infection leads to a broad anti-S IgG reactivity (43). It is important to note that underestimation is possible in our data due to limited testing availability during the early stages of the pandemic.

Sex emerged as a significant variable, with women more likely to develop higher antibodies levels. Findings in line with a 2021 prospective study from Portugal, where women consistently exhibited stronger humoral responses compared to men in the first two weeks post-vaccination (44). The higher proportion of women in our sample may reflect a greater willingness to participate in health research, rather than follow a demographic profile in Cali.

Although our study was conducted between 2021 to 2023, the findings remain relevant for understanding post-vaccination immunity in middle-income urban populations. While several studies in Colombia have addressed efficacy, few have focused on quantifying antibodies levels or exploring demographic and immunological factors (45). This study adds evidence supporting the effectiveness of heterologous vaccination schemes and mRNA vaccines in generating strong humoral responses. Further research should explore interactions between these variables to better understand the combined effects.

Since this study focused on binding IgG antibodies due to the scope of the assay used, future research should explore additional immune components, such as neutralizing antibodies and cellular responses, to better characterize vaccine-induced protection.

Despite limitations such as potential self-selection bias, limited clinical records data and underreporting of prior infections, this research offers a meaningful snapshot of the immune landscape during a critical vaccination period. The results highlight the importance of booster doses, particularly heterologous strategies, as well as the influence of sex and timing since vaccination. These insights can inform more tailored and effective immunization strategies in post-pandemic contexts, especially in resource-constrained settings.

CONCLUSIONS

This study found that mRNA vaccines, heterologous vaccination schedules and a longer interval since the booster dose were significantly associated with higher levels of anti-SARS-CoV-2 IgG antibodies in adults. Aligned with global evidence, these findings provide context-specific insights from a middle-income country and highlight key factors that can inform more effective and equitable vaccination strategies in similar settings.

ETHICAL CONSIDERATIONS

This research was approved and classified under risk-free research by the research ethics and bioethics committee of the Faculty of Health Sciences of the Universidad Libre - Colombia, according to Act No. CEB-013-2021 of December 12, 2021.

AUTHOR CONTRIBUTIONS

MGP. Conceptualization and designed the study, funding acquisition, project administration, review, formal analysis, and original draft.

AMV. Performed experiments, data curation, methodology, review, formal analysis, and original draft.

RPL. Conceptualized the study, formal analysis.

CAR. Conceptualized the study, funding acquisition.

GA. Conceptualized the study, funding acquisition.

PR. Conceptualized the study, and funding acquisition.

MT. Conceptualized the study, and funding acquisition.

ALM. Performed experiments, methodology, review, and formal analysis. All authors reviewed and edited the draft.

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SUPPLEMENTARY MATERIAL

Supplementary Table 1: Logistic regression. Multivariable analysis adjusted for sex (Female).

Logistic regression

ac_protector	Odds Ratio	St.Err.	t-value	p-value	[95% Conf Interval]	Sig
: base Inact_vec mRNA	1 2.896
Non_recombi_vec	1.774	1.308	0.78	0.437	0.418	7.527
: base Homologous Heterologous	1 2.843
: base <=21 >21	1 1.679
Constant	0.584	0.335	-0.94	0.348	0.19	1.797
Mean dependent var			0.732	SD dependent var		0.445
Pseudo r-squared			0.080	Number of obs		123
Chi-square			11.393	Prob > chi2		0.022
Akaike crit. (AIC)			141.670	Bayesian crit. (BIC)		155.731

*** p<.01, ** p<.05, * p<.1

Supplementary Table 2. Logistic regression. Multivariable analysis adjusted for sex (Male).

Logistic regression

ac_protector	Odds Ratio	St.Err.	t-value	p-value	[95% Conf Interval]	Sig
: base Inact_vec mRNA	1 2.191
Non_recombi_vec	0.517	0.499	-0.68	0.494	0.078	3.426
: base Homologous Heterologous	1 2.041
: base <=21 >21	1 4.775
Constant	0.995	0.818	-0.01	0.995	0.199	4.982
Mean dependent var			0.818	SD dependent var		0.388
Pseudo r-squared			0.169	Number of obs		77
Chi-square			12.335	Prob > chi2		0.015
Akaike crit. (AIC)			70.682	Bayesian crit. (BIC)		82.401

*** p<.01, ** p<.05, * p<.1