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Article

Effectiveness of the Booster Dose in Protecting against COVID-19, Colombia 2022

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Abstract: Vaccination has proven to be one of the most effective strategies against the COVID 19 pandemic. Several studies have evaluated and confirmed its effectiveness in different populations, particularly in reducing severe outcomes such as hospitalization and death. However, the potential of vaccination to protect against infection itself has been overlooked. The aim of this study was to determine the effectiveness of the booster dose in a sample of Colombian patients during the fourth wave of COVID-19 pandemic, which was associated with the emergence and predominance of the Omicron variant. A cross-sectional study was conducted on individuals who underwent RT-PCR testing for COVID-19 detection in a dedicated laboratory in Bogotá, Colombia, between December 30th 2021 and February 7th 2022. A total of 1,468 subjects were included in the study. The comparison between fully vaccinated individuals with a booster dose and those without the booster dose revealed a 28% reduction in the odds of infection (OR = 0.719 CI 0.531 - 0.971). Age (OR = 1,009 CI 1,001 - 1,018) and low economic status (OR= 1,812 CI 1,416- 2,319) were associated with an increased risk of infection. These findings suggest the need for booster vaccination in the general population to improve the prevention rates of SARS-CoV-2 infection and mitigate severe outcomes.

Keywords: COVID-19; booster dose; effectiveness; Colombia; vaccination strategy

1. Introduction

The COVID-19 pandemic has emerged as one of the largest and most significant public health threats that medicine has faced in the 21st century.

Efforts to contain and mitigate SARS-CoV-2 infection, a novel virus characterized by high infection and fatality rates, along with unpredictable behavior, has presented considerable challenges. A wide range of social, economic, and political factors have played a crucial role in the implementation and development of strategies against this infection [1].

The global medical and scientific community has devoted substantial efforts to identifying primary and secondary prevention measures, aimed at reducing infection and minimizing morbidity and mortality. These efforts have included the development of different treatments, such as novel antivirals, serums and vaccines targeting COVID-19. Vaccines have been based on multiple platforms, including traditional approaches employing inactivated viruses, subunit protein-based methods, viral vector-based platforms, and innovative mRNA-based technologies. Several of these vaccines have been granted emergency use authorization and have demonstrated significant efficacy in preventing infection, severe illness, ICU admission, and death [1–3].

Colombia has been severely affected by the COVID-19 pandemic. As of June 21st 2023 there have been 6,371,090 confirmed cases with 142,794 deaths, reported to WHO [4].

Tracing the epidemiological trajectory and genomic characterization of variants that emerged and became predominant in Colombia during the pandemic, four waves can be identified to date,

coinciding with the identification of some WHO-designated VOC. The first wave peaked in August 2020, the second wave peaked in January 2021, the third wave, the most severe and prolonged, associated with the Delta variant and the emergence of the Mu variant (first identified in Colombia by our group) [5], peaked in June 2021, and the fourth wave peaked in January 2022. [6] The present study focuses on the fourth wave, which occurred in mid-January 2022 and reached a maximum mortality rate of 282 deaths per day on January 28. The Colombian National Institute of Health (INS) reported that 80% of these deaths were attributed to the Omicron variant [7,8], which was designated as a VOC by the WHO on November 26, 2021 [9]. This variant has a large number of mutations, with 32 affecting the Spike protein. According to the Centers for Disease Control and Prevention (CDC) in the United States, despite its increased transmissibility, the Omicron variant is associated with less severe clinical presentations [10].

In Colombia, the national vaccination plan against COVID-19 began on February 17th, 2021. One year later, on February 17th, 2022, 33.06 million individuals were fully vaccinated (58.1%), and 7.784.212 had a booster dose [11–13]. Considering the development of the national vaccination process in Colombia, one of the strategies used to address vaccine shortage and production delays was combining vaccines from different pharmaceutical companies. This heterologous vaccination approach, supported by increasing scientific evidence and international organizations, involves administering a vaccine platform different than the one used for the primary vaccine series, for the completion of the series [14]. Heterologous induction and booster strategies can offer immunological advantages in terms of the breadth and longevity of protection provided by currently available vaccines, generating robust levels of antibodies against the COVID-19 virus and a greater T-cell response and memory B-cell response, compared to a homologous viral vector vaccine regimen. Additionally, this approach simplifies the vaccine administration logistics [2,3].

The booster strategy began in October 2021 for adults older than 70 years old and patients with a history of organ transplant, but it was rapidly expanded to include adults with other risk factors and healthcare personnel. By February 2022, the booster was accessible to the entire adult population [15].

As of June 2nd, 2023, Colombia had administered 90.506.612 vaccine doses, with 37.019 million people completing the primary vaccine series and, despite the efforts, only 14.792 million individuals had received a booster dose.

The future impact of the SARS-CoV-2 virus will be determined by a complex interaction of factors, including population protection mediated by natural immunity (recovery rate) and acquired immunity (vaccination rate), the availability of new medications and interventions, the biological behavior of new variants, and population behavior. Therefore, it is essential to study each of these factors and their impact on the course of the pandemic. Several studies have evaluated and confirmed the effectiveness of vaccination in various populations, particularly in terms of reducing serious outcomes such as hospitalization and death [16–19]. However, the potential of vaccination to protect against infection has been overlooked.

This study aims to explore the effectiveness of a booster dose regimen compared to other vaccination statuses (incomplete or complete) in terms of the probability of infection. Additionally, the study seeks to describe the behavior of cases according to other variables such as age group and gender.

2. Materials and Methods

Study Design and Participants

We conducted a cross-sectional study that included individuals who underwent a RT-PCR test for COVID-19 detection at a specific laboratory in Bogotá, Colombia, between December 30th, 2021 and February 7th, 2022. A total of 1468 subjects were included in the study.

Data collection

Data was collected using the mandatory national notification form, which was filled out by every individual who underwent an RT-PCR test for the diagnosis of SARS-CoV-2 infection at the time of

sampling. Only cases that provided information about their vaccination status were included in the study. Demographics, clinical and vaccination variables were included in the final database.

The result of the RT-PCR for SARS-CoV-2 infection was considered the dependent variable and categorized as positive or negative based on the test result. Independent variables included socio-demographic factors, clinical variables and vaccination status. Vaccination status was categorized as complete (two doses of BNT162b2, CoronaVac, mRNA-1273 or ChAdOx1 vaccines, or one dose of Ad26.COVS vaccine) or incomplete, according to Colombian regulations. Booster vaccination was defined as the receipt of an additional booster dose after completing the recommended vaccination regimen[20].

We also considered the health insurance affiliation. The Colombian health system is universal, and all citizens must join one of three insurance schemes: a contributory plan for formal employees and self-employed workers with the capacity to pay; a subsidized plan for informal workers and low-income individuals who are unable to pay; and a special plan for teachers and military personnel. Only 5% of the population is uninsured.

Data analysis

Both the dependent and independent variables obtained from the national notification forms were analyzed using SPSS version 21 software [21]. Descriptive statistics were calculated for the variables, and simple and multiple logistic regressions were performed to correlate the COVID-19 test results with vaccination status, taking into account sociodemographic and clinical variables.

Ethical aspects

This study was approved by an ethics committee with the code DVO005 1973-CV1560. The research was conducted without any risk (Resolution 8430 of 1993), as it employed a retrospective observational methodology without any intervention on the research subjects. Prior to sample collection, participants provided a signed informed consent, granting permission for the use of their information and test results for research purposes. Data was protected according to law 1581 of 2012.

3. Results

This study included 1468 participants, of whom 36.6% (n=538) were confirmed to have COVID-19 infection via PCR. The socioeconomic characteristics of the participants are described in Table 1. The sample included individuals ranging from 1 to 93 years old, with a mean of 36 years (SD 16.2). Among the participants, 57.9% (n=850) were women, and 92.4% (n=1356) were from Colombia, predominantly from Bogotá (67.7%, n=994). In terms of occupation, 26.4% (n=387) identified themselves as having a high level of education, and 33.70% (n=495) reported to be employees. Additionally, 29.8% (n=438) of the participants belonged to the middle economic level. Furthermore, 23.6% (n=347) of the participants reported having traveled prior to taking the COVID 19 test.

Table 1. Socioeconomic characteristics.

	Variable	Frequency	Percentage
Age		Min 1 - Max 93 Mean 36 (SD 16.2)	
Nationality	Other	112	7,60%
	Colombian	1356	92,40%
Origin	Other	474	32,30%
	Bogotá	994	67,70%
Gender	Male	618	42,10%
	Female	850	57,90%
	Housewife	123	8,40%
Occupation	Salesman	40	2,70%
	Freelance	72	4,90%
	Health professional	85	5,80%
	High level education	387	26,40%

	Student	141	9,60%
	Employee	495	33,70%
Economic status	Low	383	26,10%
	Medium	438	29,80%
	High	144	9,80%
	Contributory	965	65,70%
	Uninsured	66	4,50%
Health regimen	Special	11	0,70%
	Subsidized	54	3,70%
	Undetermined	313	21,30%
	Foreign	59	4,00%

Table 2 presents the clinical characteristics of the participants. Only 1.1% of the included records pertained to hospitalized individuals. Among the reported symptoms, the most common were cough 17.7% (n=550), odynophagia 15.5% (n=437), and headache 11.9% (n=336). Regarding the comorbidities, hypertension was the most common, affecting 5.3% of the participants (n=82).

Table 2. Clinical Characteristics.

	Variable	Frequency	Percentage	
Hospitalized		16	1,10%	
	Some symptom	796	54,20%	
Symptoms	Cough	500	17,70%	
	Fever	212	7,50%	
	Odynophagia	437	15,50%	
	Dyspnoea	76	2,70%	
	Fatigue/adynamia	156	5,50%	
	Rhinorrhea	240	8,50%	
	Conjunctivitis	37	1,30%	
	Headache	336	11,90%	
	Diarrhea	78	2,80%	
	Anosmia	25	0,90%	
	Others	52	1,80%	
	Asymptomatic	512	18,1%	
	Medical History	Any	280	19,10%
		No Medical History	819	53,2%
Asthma		39	2,50%	
COPD		6	0,40%	
Diabetes		35	2,30%	
HIV		3	0,20%	
Heart disease		13	0,80%	
Cancer		21	1,40%	
Obesity		24	1,60%	
Renal insufficiency		8	0,50%	
Immunosuppression		4	0,30%	
Smoker		32	2,10%	
Hypertension		82	5,30%	
Tuberculosis		1	0,10%	
Others		82	5,30%	

COPD Chronic Obstructive Pulmonary Disease
HIV Human Immunodeficiency Virus

Of the individuals, 97.7% were vaccinated (n=1434), and 90.3% (n=1326) had completed the full vaccination scheme. However, only 20.8% (n=306) of vaccinated individuals had completed the vaccination scheme with a booster dose. The most frequently administered vaccine among the population was BNT162b2, accounting for 30.9% (n=467) of the cases (Table 3).

Table 3. Vaccination Characteristics.

Variable	Frequency	Percentage
Vaccinate	1434	97,70%
Booster vaccination scheme	306	20,80%
Complete vaccination scheme	1326	90,30%
Vaccine dose		
1	231	15,70%
2	913	62,20%
3	278	18,90%
4 or more	3	0,20%
Vaccine type		
BNT162b2	467	30,90%
CoronaVac	325	21,50%
mRNA-1273	281	18,60%
ChAdOx1	203	13,40%
Ad26.COVS.2.S	182	12%
Other	10	0,70%

In the multivariate analysis, lower infection rates were associated with the booster dose compared to the complete vaccination scheme (OR =0.719 CI 0.531 - 0.971), while higher infection rates were associated with age and lower socio-economic status (Table 4).

Table 4. Variables associated with the booster vaccination scheme.

	OR	95% C.I.		Sig.
		Low	High	
Booster vaccination scheme	0,719	0,531	0,971	0,032
Age	1,009	1,001	1,018	0,027
Low Stratum	1,812	1,416	2,319	0,000
Medium - High Stratum		Comparison categories		
Health professional	1,500	0,947	2,375	0,084
Student	1,037	0,670	1,603	0,871
Other occupation		Comparison categories		
Unknown Vaccine	1,270	0,635	2,539	0,499
CoronaVac	1,518	1,079	2,135	0,016
BNT162b2	1,147	0,831	1,582	0,405
ChAdOx1	1,224	0,833	1,799	0,303
Ad26.COVS.2.S	1,691	1,137	2,514	0,010
Other Vaccine	0,237	0,029	1,919	0,177
mRNA-1273		Comparison category		

4. Discussion

This study provides supportive evidence of the effectiveness of the COVID-19 vaccine, specifically in a sample of the Colombian population. External proof of this, is the fact that, at the time patients for this analysis were recruited, the Colombian National Vaccination Plan had been in place for 10 months, showing a significant reduction in the number of severe and fatal cases of SARS-

CoV-2 infection. By February 2022, it was estimated that 35,047,468 Colombians had received the first or only dose, 27,057,045 had completed the vaccination scheme, and 7,784,212 had received a booster dose. This may explain the decrease in mortality rates despite the high number of cases observed during the fourth peak [13]. This data is not limited to Colombia, as it has been widely described the way COVID-19 vaccines application played a major role in the final and successful control of the pandemic worldwide. [22]

Considering the above, it is important to highlight that an essential factor in maintaining the effectiveness of these vaccines is the booster dose. According to our results, people with a booster dose of the vaccination scheme, had a 28% reduced odds of developing a COVID-19 infection.

According to WHO's Strategic Advisory Group of Experts on immunization (SAGE) most recent statement, there are three priority-use groups for COVID-19 vaccination: high, medium and low, based on risk of severe disease and death. The high priority group includes older adults; younger adults with significant comorbidities; people with immunocompromising conditions; pregnant women; and frontline health workers. The medium priority group includes healthy adults (under 50-60 years) without comorbidities and children and adolescents with comorbidities. The low priority group includes healthy children and adolescents between 6 months to 17 years [23].

The medium and high risk groups are the ones with an explicit recommendation for a booster dose. For people outside these categories, countries have established different recommendations depending on factors such as the national disease burden, cost-effectiveness, epidemiological situation, among others.

Due to the fact that in our sample the mean age was 36 years old and 53.2% were healthy participants, our findings suggest that the WHO recommendation of a booster dose in Colombia could be considered to be expanded to other sociodemographic groups in addition to those already recommended by SAGE.

From a biological point of view, the effectiveness of the booster dose could rely on the previously reported seroconversion rates of antibodies against the spike protein and the receptor binding domain, as well as the neutralization antibody by Plaque Reduction Neutralization Tests, achieved one and six months after administration of the booster shot [24]. Furthermore, it has been also described that this seroconversion includes the increase in antibodies against specific SARS-CoV-2 lineages like Delta and Omicron variants, specially six months after the booster [25,26].

Additionally, Vadrevu et al, reported an increase in the Th1:Th2 and the media IgG secreting memory B cells when comparing populations with and without booster, while, Chiu et al, reported an enhancement of the cellular immune response for the Delta variant and the wildtype when receiving a booster dose [25,27].

It is worth noting that circulating lineages at the time this study was performed, are important factors that could impact these results. As previously mentioned, during the time frame when the sample was collected, the Omicron variant was predominant in Colombia, and by the same moment [28], the administered vaccines were monovalent, mainly targeting the original strain of the virus with proven coverage against the Alpha and Delta variants [3].

According to Lauring et al, in the United States winter of 2021-2022, three doses of an mRNA monovalent vaccine were necessary to achieve effectiveness against the Omicron variant, while only two doses achieved the same results for Alpha and Delta variants earlier in the same year. This evidence overlaps the same time period evaluated by the authors, leading them to consider that these results could also be explained by the type of vaccines used at the time the sample was collected [3].

Now that the bivalent COVID-19 vaccines are available, additional studies following similar methodologies to the one performed in this analysis should be conducted. This, in order to confirm the necessity of a third dose with the use of COVID-19 'second generation' vaccines. In addition, the Omicron variant has been described as a milder disease-causing variant of SARS-CoV-2, when compared with Alpha and Delta. These differences should be taken into account, as confounding factors when conducting further studies, highlighting the fact that controlling the Omicron or other emerging variants goes beyond reducing clinically severe COVID-19 infection, as it also contributes to preventing the emergence of other variants of concern.

Regarding the reported efficacy for each vaccine, Chi et al. reported efficacy against COVID-19 infection of 91.3% for BNT162b2, 93.2% for mRNA-1273, 74% for ChAdOx1, 52.4% for Ad26.COVS, 50.7% for CoronaVac [29]. These results are consistent with those of our study, which showed a higher infection rate in participants who received CoronaVac (OR=1.518, CI 1.079 - 2.135) and Ad26.COVS (OR=1.691, CI 1.137 - 2.514).

It is known that countries with lower socioeconomic levels have higher transmission and mortality rates. Our study identified a significant association between lower socioeconomic statuses and a higher risk of infection. This could be related to different health determinants such as living situations, education and health practices, among others. Although, the functionality of a society and its socioeconomic determinants in health may differ among nationalities, a study by Hawinkgs et al. in the United States analyzed the number of cases and fatalities, pairing them with the county level of the distressed communities index to measure socio-economic status and determinant factors. The results showed that despite a higher rate of infection among higher-income people, other factors like the lack of high school education and a higher proportion of black Americans were the strongest associations with transmission [30].

We also found an association between age and infection, with higher rates of COVID-19 in older people. This finding could be related to the fact that despite the high percentage of complete vaccination in the studied sample, it is well known that older people have a lower rate of response to vaccines [31]. A previous study in Colombia found that COVID-19 vaccine effectiveness decreased with age, regardless of the type of vaccine used, being lower in vaccines that used traditional platforms [32]. Older people have also shown a greater and faster decline in neutralizing antibodies making vaccination booster more advisable [33].

In 2021, the Ministry of Health and Social Protection conducted a population-based cohort study in adults aged 60 and older. The study aimed to estimate the effectiveness of COVID-19 vaccines in preventing hospitalization and death among older adults with complete vaccination schemes during the first five months of the National COVID-19 Vaccination Plan in Colombia. The study found that the effectiveness of vaccines in this population group was 69.9% in preventing non-fatal hospitalization, 79.4% in preventing death from COVID-19 after hospitalization, and 74.5% in preventing death from COVID-19 among those who were not hospitalized [34].

On the other hand, vaccination of the elderly has proved to be safe and effective, especially after multiple doses. Incidence of adverse events (AEs) have shown to be lower than in young adults. Despite immunosenescence, vaccine adjuvants enhance humoral response and increased serum conversion [35]. A higher incidence of infection, mortality, and serious outcomes has been reported throughout the pandemic in the elderly. Multiple studies had found that people over 60 years of age were the most affected [28,32,35]. Protection of the older population has been demonstrated to be critical in the prevention and control of the pandemic and the WHO had strongly prioritized vaccination efforts for this group [36].

Some limitations of this study were the population size of a convenience sample and the lack of epidemiological data to further identify the different homologous and heterologous vaccination schemes in order to analyze their different effectiveness. Additionally, some of the socioeconomic and demographic data could be expanded to better understand the health determinants of the population, so that they could be addressed in the future. Lastly, this was a cross-sectional study that did not follow up with the studied population, so it is not certain how the effectiveness of the booster dose scheme may change over time.

5. Conclusions

The booster vaccination schedule has demonstrated effectiveness as a strategic measure against COVID-19 infection, surpassing the results achieved through the administration of complete initial vaccination schedules. Consequently, it is imperative to enhance efforts in order to administer booster vaccines to the general population and raise awareness about their critical significance. Furthermore, it is crucial to intensify research endeavors to determine the duration of effectiveness and the necessity for additional booster doses.

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Data Availability Statement: Additional data related to this paper may be requested from the authors

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