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Evaluation of SARS-CoV-2 Antibody Levels in Pharmacists and Pharmacy Staff Following CoronaVac Vaccination

Short Title in English: Evaluation of the SARS-COV-2 Antibody Levels

Gunes Unal, Simla Dilara Sezgin, Mesut Sancar
Department of Clinical Pharmacy, Marmara University, Istanbul, Turkey

Corresponding Author Information
Mesut Sancar
sancarmesut@yahoo.com
+905322625808
https://orcid.org/0000-0002-7445-3235
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Abstract
OBJECTIVE: The aim of this study was to determine the seropositivity rate of pharmacists and pharmacy staff after administration of two doses of the CoronaVac-SinoVac vaccine, and to assess changes in their antibody levels according to sociodemographic characteristics.
METHODS: This descriptive study was conducted between 04 June 2021 and 30 September 2021 in pharmacies located in Istanbul, Turkey. The results of self-initiated IgG testing of the pharmacists and pharmacy staff, carried out at diagnostic laboratories contracted by the Istanbul Chamber of Pharmacists, were obtained using an online data collection tool. IgG measurements taken from 15 days up to 120 days after the two vaccine doses were included in the study. Participants were asked whether they smoked, had any chronic diseases (hypertension, chronic obstructive pulmonary disease, asthma, diabetes, etc.), or took any medications. Subgroup analyses were performed for each method that was used to measure antibody levels.
RESULTS: The study included a total of 329 pharmacists/pharmacy staff (298 pharmacists and 31 pharmacy staff). The mean age of the participants was 49.7±13.7 years, and 71.4% were female. The antibody positivity of the 329 participants was 94.9% following the two doses. The rate of positivity was 95.4% in participants aged 65 years and younger, while it was 91.8% in those above 65 years of age. There was no significant difference in mean age between those with positive and negative antibody results ($p > 0.05$). Although antibody levels were lower in individuals over 65 years of age, smokers and those with chronic diseases, this difference was not statistically significant ($p > 0.05$).
CONCLUSION: Seropositivity developed following two doses of CoronaVac- Sinovac vaccines. IgG antibody levels were lower in older adults, smokers, or those with chronic diseases, although not to a statistically significant extent. Further studies are needed to better understand the reasons for different immunologic responses to COVID-19.
KEYWORDS: COVID-19, pharmacists, CoronaVac-Sinovac, seropositivity, vaccines, antibodies

INTRODUCTION

COVID-19 (Coronavirus Disease 2019) is caused by a virus belonging to the Coronavirus family (HCoV-229E, HCoV-OC43, HCoV-NL63, HKU1-CoV), a family that often causes epidemics in the winter months and is responsible for one-third of common cold cases (1).
Vaccines have a crucial role to play in increasing herd immunity, preventing severe diseases, and controlling ongoing health crises. CoronaVac (Sinovac Life Sciences, Beijing, China) is an inactivated vaccine against COVID-19 that shows good immunogenicity in animal trials and can neutralize SARS-CoV-2 with vaccine-derived neutralizing antibodies (2). The first vaccine used within the scope of the COVID-19 immunization program in Turkey was CoronaVac, the Phase III studies of which were completed in Turkey, Brazil, Chile, and Indonesia. The positive neutralizing antibody rate was reported to be higher than 90% (3). In addition, the results of phase III clinical trials conducted in Brazil showed that two doses of the Sinovac vaccine protected 50.7% of symptomatic COVID-19 patients and all moderate-to-severe cases (4). The vaccine was approved for emergency use by WHO on 01.06.2021.
Both pre-clinical and clinical studies have revealed that the vaccine has provided adequate protection for a certain period and prevented hospital admissions to a great extent (1,5,6). The Turkish Ministry of Health

approved the use of CoronaVac (Sinovac) on 13.01.2021, after which the vaccine first began to be administered to healthcare workers (HCW) (7).
CoronaVac has been shown to be well tolerated in healthy adults aged 60 years and above, and has been shown to be immunogenic, with neutralizing antibody responses against live SARS-CoV-2 having been shown to not decrease in said healthy adults over 60. Further studies are needed on the efficacy of this vaccine in preventing COVID-19 in older adults (8).
Healthcare workers, older adults, and those with underlying health problems are especially at higher risk (9,10). Healthcare workers have continued to work on the front line to care for their patients throughout the COVID-19 pandemic, and despite changes in routine practices, community pharmacists have also delivered uninterrupted services to their patients. Moreover, the vaccine has been administered to community pharmacists and pharmacy staff in Turkey, and pharmacists and pharmacy staff have, to a large degree, taken part in vaccination campaigns. Although there are studies in the literature on the changes in antibody levels in society and, more specifically, health workers created by Covid-19 vaccines and the factors affecting these changes, for these changes to be better understood, more studies need to be conducted with pharmacists and pharmacy staff. The aim of the present study was to measure the presence of antibodies produced following vaccination in pharmacists and pharmacy staff and to investigate the association between quantitative antibody values and age, underlying chronic diseases, smoking, and use of medications.

METHODS

Study design and participants

This descriptive study was performed between 04 June 2021 and 30 September 2021 in pharmacies located in Istanbul, Turkey. After informing the pharmacists and pharmacy staff about the study, all individuals aged over 18 years were invited to participate in the study (5234 pharmacists and pharmacy staff in these pharmacies). A stratified sampling method was used, with the target of accessing data from 500 participants. For data collection, an e-mail was sent to all members by the Istanbul Chamber of Pharmacists. The results of the tests (for which the pharmacists and pharmacy staff volunteered and which took place in diagnostic laboratories contracted by the Istanbul Chamber of Pharmacists) were collected through an online data collection tool that the researchers developed according to the literature. (11)
The study was based on the results of COVID-19 spike antibody (IgG) tests performed at the following centers contracted by the Istanbul Chamber of Pharmacists: Biruni Laboratories, Datalab Laboratory, Gelişim Tıp Laboratories, Türk Kızılay Sağlık A.Ş. (Turkish Red Crescent Health Co.), and Yaşar Hospital, IgG measurements taken from 15 days up to 120 days after the two vaccine doses were included in the study. Participants were asked whether they smoked, had any chronic diseases (hypertension, chronic obstructive pulmonary disease, asthma, diabetes, etc.), or took any medications. Subgroup analyses were performed for each method that was used to measure antibody levels.
In accordance with the central limit theorem, parametric tests were used without testing for normality. For data analysis, mean and standard deviation, minimum and maximum values of characteristics were used for statistics of the continuous variables, while frequency and percentage values were used to describe the categorical valuables. Student's t-test was used for comparing the means of two independent groups, and the Chi-Square test was used for evaluating the categorical variables. Statistical significance was accepted $p < 0.05$. For data analysis, www.e-picos.com New York software and MedCalc statistical package program were used. (12)
The study received ethical approval by the Marmara University Institute of Health Sciences Ethical Committee (approval number of 17.05.2021-82). Permission for the study was also obtained from the Ministry of Health of the Republic of Türkiye. Online informed consent was obtained from all participants.

RESULTS

Three hundred seventy-four pharmacists/pharmacy staff participated in the study; however, 45 of them were excluded due to COVID-19 diagnoses, and analyses continued with 329 participants (298 pharmacists and 31 pharmacy staff). Of these, 312 had positive antibody levels, and 17 measured negative. In the evaluation of the relationship between antibody levels and sociodemographic parameters, only positive patients were considered, the results of laboratories with small sample numbers were not included, and the antibody levels of 222 individuals were evaluated in the two laboratories where most of the tests were performed (Figure 1).

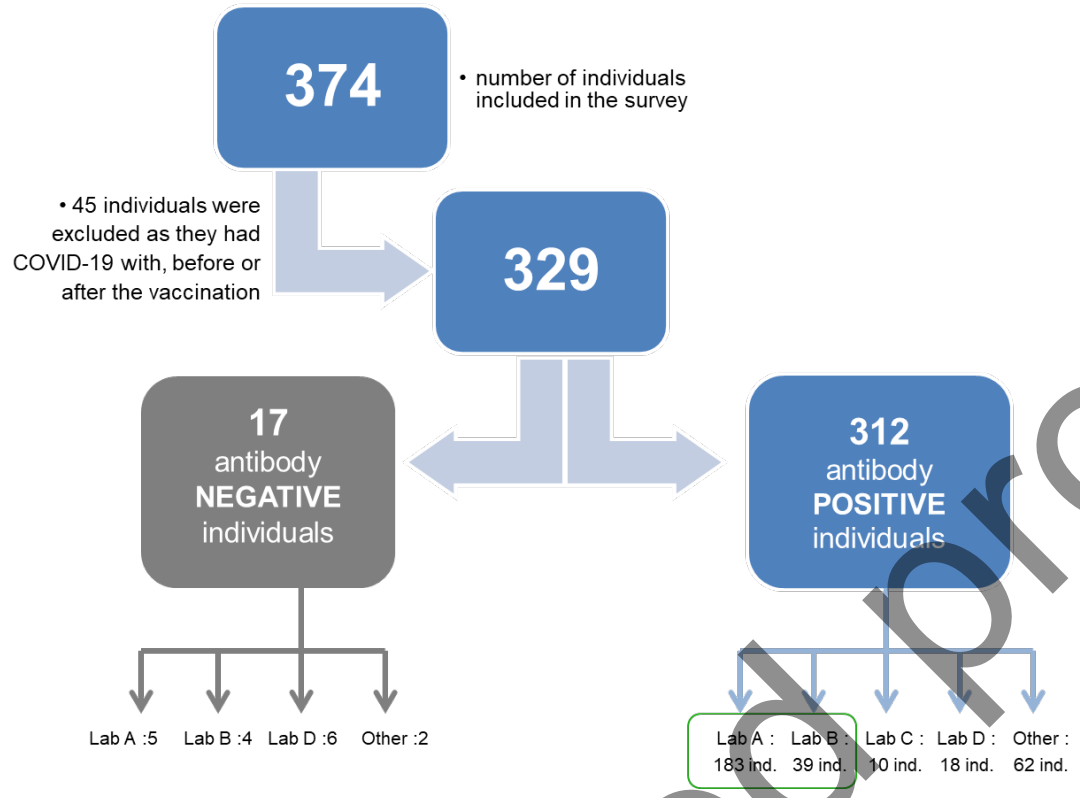

Figure 1. Flow chart of the study

Due to the small number of individuals, the results of Lab C and Lab D were not further evaluated for descriptive characteristics.

The antibody results of 62 individuals under the Oher category were not further evaluated for descriptive characteristics because they were obtained from different laboratories.

The mean age of the 329 participants was 49.7±13.7 years; 71.4% were female, and 94.9% had positive antibody levels following two doses of the CoronaVac vaccine. The rate of positivity was 95.4% in participants aged ≤65 years and 91.8% in those aged >65 years. Fifty percent of the participants were tested within 45 days following the second dose of the Sinovac vaccine to determine the antibody response. The participants with negative and positive antibody test results had no statistically significant differences in the descriptive parameters listed in Table 1 ($p > 0.05$).

Table 1. Comparison of antibody test results by descriptive characteristics (n = 329)

Descriptive characteristics		**Antibody test status following vaccination**			
		Total (n = 329)	**Negative (n = 17)**	**Positive (n = 312)**	**P value**
Sex, n (%)	Female	235 (71.4)	11 (4.7)	224 (95.3)	0.58
	Male	94 (28.6)	6 (6.4)	88 (93.6)	
Disease status, n=212, n (%)	Yes	139 (65.6)	8 (5.8)	131 (94.2)	0.56
	No	73 (34.4)	6 (8.2)	67 (91.2)	
Medication use, n=104, n (%)	Yes	81 (77.9)	4 (4.9)	77 (95.1)	0.61
	No	23 (22.1)	2 (8.7)	21 (91.3)	

Smoking status, n=208, n (%)	Yes	63 (30.3)	6 (9.5)	57 (90.5)	0.20
	No	145 (69.7)	7 (4.8)	138 (95.2)	
Age, n=311, n (%)	<65 years	262 (84.2)	12 (4.6)	250 (95.4)	0.30
	≥65 years	49 (15.8)	4 (8.2)	45 (91.8)	
Time from the second vaccine to antibody, mean±SD (days)		68.7±51.4	80.8±54.2	68.1±51.2	0.32

SD: Standard deviation

Comparison of the antibody levels according to sociodemographic characteristics of individuals with a positive antibody response after vaccination is provided in Table 2; these results were analysed only internally, without comparing the two laboratories. Although antibody levels were lower in smokers, individuals over 65 years of age, and individuals with chronic diseases, this difference was not statistically significant.

Table 2. Comparison of antibody levels according to the sociodemographic characteristics of participants with a positive antibody response

Descriptive characteristics	**Antibody level (AU/mL) after vaccination**		
		Lab A results (n = 183)	**Lab B results (n = 39)**
	Groups	**Mean±SD**	**Mean±SD**
Sex	Female	575.12±528.65	31.25±52.17
	Male	580.57±502.17	15.98±34.1
	p	0.56	0.40
Age	<65 years	595.37±552.93	32.91±23.84
	≥65 years	577.33±434.54	9.42±8.21
	p	0.86	0.26
Disease status	Yes	527.13±469.41	32.78±39.8
	No	550.67±507.82	42.36±64.03
	p	0.87	0.67
Medication use	Yes	491.99±423.81	62.27±81.09
	No	815.19±754.37	6.85±62.28
	p	0.12	0.44
Smoking status	Non-smoker	583.38±531.32	61.07±58.92
	Smoker	446.44±392.31	15.24±16.86
	p	0.23	0.07

Lab A SARS-CoV-2 IgG quantitative antibody, reference value: <50 AU/mL negative; ≥50 AU/mL positive

Lab B COVID-19 IgG antibody (against spike protein), reference value: 0-0' <1 negative; ≥1 positive

DISCUSSION

Following vaccination during the COVID-19 pandemic, many studies have assessed the antibody levels of healthcare workers in Turkey and worldwide. Most of these studies have included doctors and healthcare staff working in hospitals and clinics. The present study is the first to investigate community pharmacists' and pharmacy staff's post-vaccine antibody levels and their association with age, smoking status, and chronic diseases.

We found antibody positivity to be approximately 95% after two doses of the CoronaVac vaccine. In other studies conducted with healthcare professionals in Turkey, seropositivity rates of 99.6%, 99.4%, and 97%, respectively, were observed after four weeks in individuals vaccinated with two doses of the CoronaVac vaccine (13). The slightly lower positivity rate in our study may be related to antibody level measurements being made in a wider time interval after two doses of the vaccine.

One of the subjects we aimed to investigate was possible factors affecting the vaccine antibody response. Although it is well known in other vaccines that the antibody response is affected by decreasing T cell-derived antibody production and B lymphocyte production with age, more data are needed on the COVID-19 vaccine. In this study, the antibody level in individuals over 65 years of age was lower than that in younger individuals; however, the difference was not statistically significant. In a study conducted with healthcare workers vaccinated with the CoronaVac vaccine in Turkey, the antibody level was found to be highest in the group aged 30–39 years, but this finding was not statistically significant (13). In Shengli et al.'s study, the neutralizing antibody titres were lower in the group aged ≥60 years compared to the group aged 18–59 years (14). Similarly, in a study performed in Turkey by Şenol Akar et al., the antibody response was significantly higher in participants aged 18–64 years (15).

The association with age was shown not only in studies of the CoronaVac-SinoVac vaccine but also in studies of other COVID-19 vaccines produced using different methods. To compare the antibody responses against the first and second doses of Biontech/Pfizer BNT162b2, a cohort study was carried out with two age groups: <60 years and >80 years. Although most participants produced titres of specific immunoglobulin G antibodies in response to the SARS-CoV-2 spike protein, titres were found to be significantly lower in older individuals (16). It was observed that antibody levels measured three months after the second dose of the Biontech/Pfizer BNT162b2 vaccine in healthcare workers in Japan were higher in individuals aged 20–29 years than in those aged 60–79 years (6).

In the present study, it was observed that comorbid disease and chronic medication use had no effect on antibody response. A study on healthcare workers vaccinated with the Biontech/Pfizer BNT162b2 vaccine in Japan found that other diseases, such as diabetes and allergic diseases, were not associated with low antibody levels (6). However, a study by Çelik Güzel et al. found that the presence of comorbidities (Diabetes mellitus and cardiovascular disease) decreased COVID-19 IgG antibody levels (17).

Watanabe et al. carried out an observational study with 86 healthcare workers who received Pfizer-BioNTech COVID-19 vaccines and showed that higher waist circumference, smoking, and the presence of hypertension were associated with lower antibody titres (18). Two studies conducted in Indonesia on healthcare workers vaccinated with the CoronaVac vaccine concluded that the presence of hypertension negatively affects antibody levels (19).

In the present study, lower antibody levels were observed in smokers; however, this was not statistically significant. A study conducted by Uysal et al. in Turkey found that antibody levels were lower in smokers than in non-smokers ($p = 0.032$) in healthcare workers vaccinated with the CoronaVac vaccine (13). In another study conducted with healthcare professionals in Turkey, antibody levels following CoronaVac vaccination were found to be significantly higher in non-smokers (15). Nomura et al. reported that age and smoking habits were the most important factors associated with low antibody titres. They highlighted that being a smoker was associated with lower antibody titres and that quitting smoking before vaccination may improve the individual efficacy of the vaccine (6).

A study including a group of healthcare workers in Italy examined the effects of smoking on the humoral response produced by the BioNTech-Pfizer COVID-19 vaccine. In the study, antibody levels were lower in smokers than in non-smokers 60 days after vaccination ($p = 0.002$). According to the authors, although the pathophysiological basis of the effect of smoking on the dynamics of vaccine-induced anti-SARS-CoV-2 antibodies is not yet clear, previous studies have reported that antibody response decreases more rapidly in smokers who receive other vaccines, such as vaccines for hepatitis B and influenza. Exposure to smoking impairs the immune system's ability to form memory cells, which are critical for maintaining the protective immune response induced by vaccines (8).

The present study has several limitations. The foremost limitation was the lower-than-expected number of participants, as participants did their antibody testing voluntarily and at their own expense. Individuals with positive and negative antibody results were not compared, as this was not one of the purposes of this study. Since the study evaluated post-vaccination antibody levels, it is likely that some individuals with negative results did not participate. Another limitation was conducting the study on a specific occupational group. Due to this specificity, the data cannot be generalized. In this study, only the COVID-19 spike antibody (IgG) response to the vaccine was assessed, and no information on cellular immunity was provided. Therefore, it cannot be assumed that our results provide adequate evidence regarding the level of protection from the disease that this vaccine offers individuals. Age, smoking, and the presence of diseases that may affect antibody response were examined, but due to difficulties in collecting data from patients, parameters such as obesity and distribution of existing diseases and drugs could not be evaluated.

CONCLUSION

CoronaVac, an inactive SARS-CoV-2 vaccine administered to community pharmacists and pharmacy staff, produced seropositivity within two months in approximately 95% of participants. The antibody response was higher in participants younger than 65 years, non-smokers, and those without a chronic disease; however, the differences were not statistically significant. Further studies are needed to determine how much the vaccine protects individuals from the disease. Although the effect of smoking, old age, and the presence of chronic diseases on the immunologic response to the COVID-19 vaccine has been clinically proven by other studies, there is still a need for trials with a higher number of individuals and longer follow-up.

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