ORIGINAL ARTICLE

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

[ID] Güneş ÜNAL[1,2], [ID] Simla Dilara SEZGİN[1], [ID] Mesut SANCAR[3]*

[1]İstanbul Chamber of Pharmacists, İstanbul, Türkiye
[2]İstanbul Medipol University, Institute of Health Sciences, İstanbul, Türkiye
[3]Marmara University, Faculty of Pharmacy, Department of Clinical Pharmacy, İstanbul, Türkiye

ABSTRACT

Objectives: The aim of this study was to determine the seropositivity rate of pharmacists and pharmacy staff after the administration of two doses of the CoronaVac-SinoVac vaccine and to assess changes in their antibody levels according to sociodemographic characteristics.

Materials and Methods: This descriptive study was conducted between June 04, 2021 and September 30, 2021 in pharmacies located in Istanbul, Türkiye. The results of self-initiated immunoglobulin (Ig) G testing of the pharmacists and pharmacy staff, conducted 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 used to measure antibody levels.

Results: The study included 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 positivity rate was 95.4% in participants under 65 years of age, whereas it was 91.8% in those aged 65 years and over. There was no significant difference in the mean age between those with positive and negative antibody results ($p > 0.05$). Although antibody levels were lower older people, smokers, and those with chronic diseases, this difference was not statistically significant ($p > 0.05$).

Conclusion: Seropositivity developed following the administration of two doses of CoronaVac-Sinovac vaccines. IgG antibody levels were lower in older adults, smokers, and those with chronic diseases, although not to a statistically significant extent. Further studies are needed to better understand the reasons for the different immunological responses to COVID-19.

Key words: COVID-19, pharmacist, CoronaVac-Sinovac, seropositivity, vaccines, antibodies

INTRODUCTION

Coronavirus disease 2019 (COVID-19) 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 play a crucial role 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 severe acute respiratory syndrome (SARS-CoV-2) with vaccine-derived neutralizing antibodies.[2] The first vaccine used within the scope of the COVID-19 immunization program in Türkiye was CoronaVac. Phase III studies were completed in Türkiye, 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 World Health Organization (WHO) on 01.06.2021.

Both pre-clinical and clinical studies have revealed that the vaccine provides adequate protection for a certain period and prevents 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 was first administered to healthcare workers (HCW).[7]

CoronaVac has been demonstrated to be well tolerated in healthy adults aged 60 years and above and is immunogenic with neutralizing antibody responses against live SARS-CoV-2 having been shown to not decrease in said healthy adults over 60 years. Further studies are needed on the efficacy of this vaccine in preventing COVID-19 in older adults.[8]

HCWs, older adults, and those with underlying health problems are especially at higher risk.[9,10] HCWs 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 delivered uninterrupted services to their patients. Moreover, the vaccine has been administered to community pharmacists and pharmacy staff in Türkiye, and they 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.

MATERIALS AND METHODS

Study design and participants

This descriptive study was conducted between June 04, 2021 and September 30, 2021 in pharmacies located in Istanbul, Türkiye. After informing the pharmacists and pharmacy staff about the study, all individuals aged over 18 years were invited to participate in the study (5,234 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 of the Istanbul Chamber of Pharmacists. The results of the tests (for which the pharmacists and pharmacy staff volunteered and which occurred in diagnostic laboratories contracted by the Istanbul Chamber of Pharmacists) were collected through an online data collection tool developed by the researchers according to the literature.[11]

The study was based on the results of COVID-19 spike antibody [immunoglobulin (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 used to measure antibody levels.

In accordance with the central limit theorem, parametric tests were used without testing for normality. For data analysis, the mean and standard deviation along with 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 variables. Student's t-test was used to compare the means of two independent groups, and the chi-square test was used to evaluate the categorical variables. Statistical significance was set at $p < 0.05$. For data analysis, the www.e-picos.com New York software and MedCalc statistical package program were used.[12]

The study received ethical approval from the Institute of Health Sciences Ethical Committee of Marmara University (approval number: 17.05.2021-82). Permission for the study was obtained from the Ministry of Health of the Republic of Türkiye. Online informed consent was obtained from all participants.

RESULTS

Three hundred and 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, while 17 were 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).

The antibody results of 62 individuals under the other category were not further evaluated for descriptive characteristics
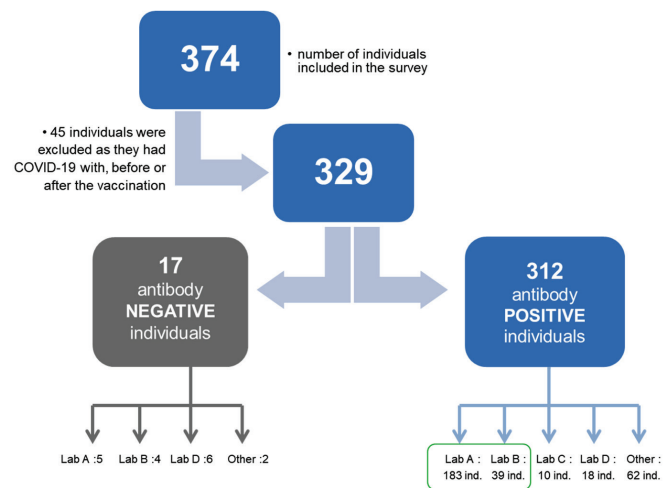

Figure 1. Flow chart of the study
(Because of the small number of individuals, the results of Lab C and Lab D were not further evaluated for descriptive characteristics)

because they were obtained from different institutions 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. 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 Sinovac to determine antibody response. The participants with negative and positive antibody test results had no statistically significant differences in the descriptive parameters listed in Table 1 ($p > 0.05$).

Comparison of antibody levels according to sociodemographic characteristics of individuals with a positive antibody response after vaccination is provided in Table 2. These results were analyzed only internally without comparing the two laboratories. Although antibody levels were lower in smokers, older people, and the ones with chronic diseases, this difference was not statistically significant.

DISCUSSION

Following the vaccination during the COVID-19 pandemic, many studies have assessed the antibody levels of HCWs worldwide including Türkiye. Most of these studies 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. In other studies conducted with healthcare professionals in Türkiye, seropositivity rates of 99.6%, 99.4%, and 97%, respectively, were observed after four weeks in individuals vaccinated with two doses of the CoronaVac.[13] The slightly lower positivity rate in our study may be related to antibody level measurements being made over a wider time interval after two doses of the vaccine.

A subject we investigated was the 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 older participants was lower than that in younger individuals; however, the difference was not statistically significant. In a study conducted with HCWs vaccinated with the CoronaVac in Türkiye, the antibody level was found to be highest in the group aged 30-39 years, but this finding was not statistically significant.[13] In Xia et al.'s[14] study, neutralizing antibody titers were lower in the group aged ≥ 60 years compared with the group aged 18-59 years. Similarly, in a study performed in Türkiye by Şenol Akar et al.,[15] the antibody response was significantly higher in participants aged 18-64 years.

The association with age was shown not only in studies of the CoronaVac-SinoVac 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 conducted with two age groups: < 60 years and > 80 years. Although most participants produced titers of specific IgG antibodies in response to the SARS-CoV-2 spike protein, titers 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 HCWs in Japan were higher in individuals aged 20-29 years than in those aged 60-79 years.[6]

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

Descriptive characteristics		Antibody test status after 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

Table 2. Comparison of antibody levels according to 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: < 1 BAU/mL negative; ≥ 1 BAU/mL positive
SD: Standard deviation

In this study, it was observed that comorbid disease and chronic medication use had no effect on antibody response. A study on HCWs 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 Güzel et al.[17] found that the presence of comorbidities (diabetes mellitus and cardiovascular disease) decreased COVID-19 IgG antibody levels.

Watanabe et al.[18] conducted an observational study with 86 HCWs who received Pfizer-BioNTech COVID-19 vaccines and showed that higher waist circumference, smoking, and the presence of hypertension were associated with lower antibody titers. Two studies conducted in Indonesia on HCWs vaccinated with the CoronaVac concluded that the presence of hypertension negatively affects antibody levels.[19]

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

A study including a group of HCWs 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 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]

Study limitations

This study has several limitations. The foremost limitation was the lower-than-expected number of participants, as the participants did their antibody testing voluntarily and at their own expense. Individuals with positive and negative antibody results were not compared because this was not a purpose of this study. Because 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. Because of 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; however, 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 the 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 effects of smoking, old age, and the presence of chronic diseases on the immunological response to the COVID-19 vaccine have been clinically proven by other studies, there is still a need for trials with a higher number of individuals and longer follow-ups.

REFERENCES

1. Özçelik B, Orhan İE. Eczacılar için Covid-19 Aşıları Kitapçığı. 1st ed. Kitapçığı (1st ed). Ankara; 2020.

2. Gao Q, Bao L, Mao H, Wang L, Qin C. Development of an inactivated vaccine candidate for SARS-CoV-2. Science. 2020;369:77-81.

3. Zhu FC, Guan XH, Li YH, Huang JY, Jiang T, Hou LH, Li JX, Yang BF, Wang L, Wang WJ, Wu SP, Wang Z, Wu XH, Xu JJ, Zhang Z, Jia SY, Wang BS, Hu Y, Liu JJ, Zhang J, Qian XA, Li Q, Pan HX, Jiang HD, Deng P, Gou JB, Wang XW, Wang XH, Chen W. Immunogenicity and safety of a recombinant adenovirus type-5-vectored COVID-19 vaccine in healthy adults aged 18 years or older: a randomized, double-blind, placebo-controlled, phase 2 trial. Lancet. 2020;396:479-488.

4. Palacios R, Patiño EG, de Oliveira Piorelli R, Conde MTRP, Batista AP, Zeng G, Xin Q, Kallas EG, Flores J, Ockenhouse CF, Gast C. Double-blind, randomized, placebo-controlled phase III clinical trial to evaluate the efficacy and safety of treating healthcare professionals with the adsorbed COVID-19 (inactivated) vaccine manufactured by Sinovac - PROFISCOV: a structured summary of a study protocol for a randomized controlled trial. Trials. 2020;21:853.

5. Thanh Le T, Andreadakis Z, Kumar A, Gómez Román R, Tollefsen S, Saville M, Mayhew S. The COVID-19 vaccine development landscape. Nat Rev Drug Discov. 2020;19:305-306.

6. Nomura Y, Sawahata M, Nakamura Y, Kurihara M, Koike R, Katsube O, Hagiwara K, Niho S, Masuda N, Tanaka T, Sugiyama K. Age and smoking predict antibody titres at 3 months after the second dose of the BNT162b2 COVID-19 vaccine. Vaccines (Basel). 2021;9:1042.

7. Dinc HO, Saltoglu N, Can G, Balkan II, Budak B, Ozbey D, Caglar B, Karaali R, Mete B, Tuyji Tok Y, Ersoy Y, Ahmet Kuskucu M, Midilli K, Ergin S, Kocazeybek BS. Inactive SARS-CoV-2 vaccine generates high antibody responses in healthcare workers with and without prior infection. Vaccine. 2022;40:52-58.

8. Ferrara P, Ponticelli D, Agüero F, Caci G, Vitale A, Borrelli M, Schiavone B, Antonazzo IC, Mantovani LG, Tomaselli V, Polosa R. Does smoking have an impact on the immunological response to COVID-19 vaccines? Evidence from the VASCO study and need for further studies. Public Health. 2022;203:97-99.

9. Flaxman S, Mishra S, Gandy A, Unwin HJT, Mellan TA, Coupland H, Whittaker C, Zhu H, Berah T, Eaton JW, Monod M; Imperial College COVID-19 Response Team; Ghani AC, Donnelly CA, Riley S, Vollmer MAC, Ferguson NM, Okell LC, Bhatt S. Estimating the effects of non-pharmaceutical interventions on COVID-19 in Europe. Nature. 2020;584:257-261.

10. Sanche S, Lin YT, Xu C, Romero-Severson E, Hengartner N, Ke R. High contagiousness and rapid spread of severe acute respiratory syndrome coronavirus 2. Emerg Infect Dis. 2020;26:1470-1477.

11. Hansen CH, Michlmayr D, Gubbels SM, Mølbak K, Ethelberg S. Assessment of protection against reinfection with SARS-CoV-2 among 4 million PCR-tested individuals in Denmark in 2020: a population-level observational study. Lancet. 2021;397:1204-1212.

12. Norman G. Likert scales, levels of measurement and the "laws" of statistics. Adv Health Sci Educ Theory Pract. 2010;15:625-632.

13. Uysal EB, Gümüş S, Bektöre B, Bozkurt H, Gözalan A. Evaluation of antibody response after COVID-19 vaccination of healthcare workers. J Med Virol. 2022;94:1060-1066.

14. Xia S, Zhang Y, Wang Y, Wang H, Yang Y, Gao GF, Tan W, Wu G, Xu M, Lou Z, Huang W, Xu W, Huang B, Wang H, Wang W, Zhang W, Li N, Xie Z, Ding L, You W, Zhao Y, Yang X, Liu Y, Wang Q, Huang L, Yang Y, Xu G, Luo B, Wang W, Liu P, Guo W, Yang X. Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBIBP-CorV: a randomized, double-blind, placebo-controlled, phase 1/2 trial. Lancet Infect Dis. 2021;21:39-51.

15. Şenol Akar Ş, Akçalı S, Özkaya Y, Gezginci FM, Cengiz Özyurt B, Deniz G, Karadağ Yalçın F, Özer D, Dündar Erbay P, Eser E. Factors affecting side effects, seroconversion rates and antibody response after İnactivated SARS-CoV-2 vaccination in healthcare workers. Mikrobiyol Bul. 2021;55:519-538.

16. Müller L, Andrée M, Moskorz W, Drexler I, Walotka L, Grothmann R, Ptok J, Hillebrandt J, Ritchie A, Rabl D, Ostermann PN, Robitzsch R, Hauka S, Walker A, Menne C, Grutza R, Timm J, Adams O, Schaal H. Age-dependent immune response to the Biontech/Pfizer BNT162b2 coronavirus disease 2019 vaccination. Clin Infect Dis. 2021;73:2065-2072.

17. Güzel EÇ, Çelikkol A, Erdal B, Sedef N. Immunogenicity after CoronaVac vaccination. Rev Assoc Med Bras (1992). 2021;67:1403-1408.

18. Watanabe M, Balena A, Tuccinardi D, Tozzi R, Risi R, Masi D, Caputi A, Rossetti R, Spoltore ME, Filippi V, Gangitano E, Manfrini S, Mariani S, Lubrano C, Lenzi A, Mastroianni C, Gnessi L. Central obesity, smoking habit, and hypertension are associated with lower antibody titres in response to COVID-19 mRNA vaccine. Diabetes Metab Res Rev. 2022;38:e3465.

19. Rifai A, Wahono CS, Pratama MZ, Handono K, Susianti H, Iskandar A, Diyah N, Santoningsih D, Samsu N, Gunawan A. Association between the effectiveness and immunogenicity of inactivated SARS-CoV2 vaccine (CoronaVac) with the presence of hypertension among health care workers. Clin Exp Hypertens. 2022;44:233-239.