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RESEARCH ARTICLE

Evaluation of Antibody Levels After Vaccination (Sinovac-CoronaVac) in Healthcare Workers

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ABSTRACT

Objectives: This study aims to evaluate the effectiveness of the inactivated SARS-COV-2 vaccine (Sinovac-CoronaVac), first administered to healthcare professionals in Turkey on January 14, 2021.

Methods: Healthcare professionals without a history of COVID-19, PCR test positivity, or chronic disease were included in the study. The antibody levels for S1 RBD antigen were measured with the Siemens SARS-CoV-2 IgG (sCOVG) kit one month and six months after the two-dose CoronaVac vaccine.

Results: A total of 108 health professionals, 35 women and 73 men, were included in this study. The mean age of the participants was 37.5 ± 10.7 years. A total of 103 (95.3%) individuals had positive antibody values, and five (4.6%) had negative values after the second vaccination. After the second vaccine dose, 11 (10.1%) participants were diagnosed with COVID-19. There was a significant decrease in antibody values in the sixth month compared to the first month ($p < 0.001$). The first-month measurements showed a significant negative correlation between age and antibody levels. Likewise, there were no significant differences in antibody levels between men and women in the first and sixth months. However, there was a significant difference in antibody levels in the first month for occupational groups ($p=0.015$). The nurses' antibody levels in the first month were significantly higher than the doctors ($p=0.05$).

Conclusion: Although the antibody level of the CoronaVac vaccine decreased significantly for the first six months, the infection was mild in 10 % of the participants. Large-scale studies are needed for the protectiveness of vaccines and the prevention of COVID-19. *J Microbiol Infect Dis 2022; 12(4):154-159.*

Keywords: *COVID-19, healthcare professionals, vaccination*

INTRODUCTION

The third major Coronavirus outbreak of the twenty-first century appeared for the first time in a group of patients who developed respiratory symptoms in late December in China's Wuhan province. Coronavirus Disease 2019 (COVID-19) was identified on January 13, 2020. In the following months, it spread rapidly throughout the world. On March 11, 2020, the World Health Organization declared it a pandemic [1]. The Turkish Ministry of Health reported the first case in Turkey on the same day [2]. The International Committee on Virus Taxonomy named the agent "Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2)" because of its close association with the 2003 SARS Coronavirus [3]. SARS-CoV-2 is a single-stranded, positive polarity, non-segmented, and enveloped RNA virus that belongs to the Betacoronavirus (β-CoV) subgroup of the Coronaviridae family [4]. The SARS-CoV-2 genome, like other pathogenic human coronaviruses, codes four main structural proteins [spikes (s), envelope (e), membrane (m), and nucleocapsid (n)] and about 16 non-structural proteins. Among them, the S protein plays a crucial role in viral

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binding fusion, input, and transmission. The S protein is a common target antigen for antibodies and vaccine development [5,6]. The COVID-19 pandemic has caused significant morbidity and mortality worldwide and also caused social, educational, and economic deterioration. There was no specific antiviral drug or vaccine against the newly emerging SARS-COV-2 [7]. Therefore, the urgency in developing a vaccine was significant to curb the pandemic and prevent further outbreaks. Various vaccine designs were evaluated during the development of SARS-COV-2 vaccines [8,9]. SARS-CoV-2 vaccines currently authorized for use include; inactivated and protein subunit vaccines, viral vector vaccines, and mRNA vaccines [10,11]. One of the interventions initiated by the Turkish Ministry of Health during the COVID-19 pandemic is the mass COVID-19 vaccination. Vaccination is particularly significant to protect people at high risk of COVID-19, such as healthcare workers, older adults, and individuals with other chronic diseases. In this study, we aimed to evaluate the effectiveness of the inactivated SARS-COV-2 (Sinovac-CoronaVac) vaccine on health workers administered since January 2021. Additionally, we aimed to determine the serological status after the vaccination of healthcare professionals using the anti-SARS-CoV-2 IgG (sCOVG) antibody test to further contribute to vaccination research and ensure the continuation of its use.

METHODS

Healthcare professionals working at Haseki Training and Research Hospital without a previous history of COVID-19, PCR positivity, or chronic disease were included in the study along with approvals from the Ministry of Health (Hatice Erdogan-2021-02-18T12_30_05) and ethics committee (Haseki Training and Research Hospital Clinical Research Ethics Board of Directors 21.04.2021/01-2021). All participants signed voluntary consent forms. After two doses of the Sinovac vaccine four weeks apart, blood samples were taken in the first and sixth months, and serums were separated. Sera stored under appropriate storage conditions were studied with the Quantitative ADVIA Centaur® SARS-CoV-2 IgG kit (Siemens, USA). This method is a two-stage, fully automated sandwich immunoassay using chemiluminescence technology. The detection range of the kit is the 0.50–150.00 index; values greater than 1 index are considered positive, <1 index are negative, and 1 index=1U/mL.

The SPSS 15.0 for Windows (SPSS Inc., Chicago, Illinois, USA) program has been used for statistical analysis. Descriptive statistics for categorical variables were given as numbers and percentages, and numerical variables were presented as mean, standard deviation, and minimum and maximum. Comparisons of numerical variables in two dependent groups were made with Wilcoxon analysis since the data did not meet the normal distribution condition. Independent groups' skewed numerical variables were compared with the Mann-Whitney U test in two groups and the Kruskal-Wallis test in more than two groups. The rates were compared with the Chi-Square test in independent groups and the McNemar test independent groups. Correlations between numerical variables were checked using Spearman correlation analysis since the parametric test condition was not met. The statistical significance level was accepted as $p < 0.05$.

RESULTS

A total of 108 healthcare professionals, 35 females, and 73 males, were included in the study one month after the second dose of the CoronaVac vaccine. The mean age of the participants was 37.5 ± 10.7 years (range between 22 and 61 years). Forty-three (39.8) of the participants were doctor, 40 (37.0) nurse and 25 (23.1) other auxillary health-care workers (paramedic, technician, medical secretary and IT staff).

One month after the second vaccination, the first antibody level was positive in 103 (95.3%) and negative in 5 (4.6%) participants. The first antibody means ± SD (Min-Max) was 10.8 ± 16.0 (0.24-150).

After the second vaccine dose, 11 (10.6%) participants were diagnosed with COVID-19 infection. Nine of these individuals became infected with COVID-19 in the second month, one in the third month, and one in the sixth month. These individuals had the infection with mild symptoms.

The Turkish Ministry of Health started the third dose vaccine studies early due to the intensity of the COVID-19 infection. Therefore,

participants who received the third dose earlier were excluded.

Six months after the second dose, a decrease in antibody levels was detected. Antibodies were negative (<1 index) in 21 (37.5%) participants and positive in 35 (62.5%). The 6th-month antibody positivity rate was significantly lower than the 1st ($p < 0.001$). The second antibody means ± SD (min-max) was 10.6 ± 34.6 (0.2-150). There was a significant decrease in antibody values in the sixth month compared to the first month ($p < 0.001$).

When the changes in the first and second antibody levels were examined, the first antibody values showed a negative correlation with age.

The first antibody positivity rate was low over the age of 40. There were no significant differences in antibody levels between women and men in the first and sixth months (the percentage of antibody change by sexes is shown in Table 1).

A significant difference was found in occupational group antibody levels in the first month ($p= 0.015$). In addition, the antibody level of nurses in the first month was significantly higher than that of doctors ($p=0.05$) (Table 2).

DISCUSSION

Specific antibodies have been shown to play a significant role in the vaccine development and approval process and the follow-up of vaccinated individuals after active vaccination under the management of the COVID-19 pandemic [12].

In our study, 96.1% antibody positivity was obtained one month after two doses of the CoronaVac vaccine in healthcare workers who did not have a history of COVID-19 or a chronic disease.

Sinovac has conducted randomized and placebo-controlled clinical studies in Brazil, Indonesia, and Turkey for adults aged 18-59. The activity estimates in these studies were different. The vaccine efficacy in Brazil, Indonesia, and Turkey is 50.65%, 65.30%, and 83.50%, respectively. The binding and neutralizing antibodies have been shown to develop 14 days after the second dose and are safe [13-16].

In two studies conducted in Turkey, antibody positivity was 97.7% and 98.5% 28 days after two doses of the CoronaVac vaccine, similar to our study (17,18). In the studies carried out among healthy adults, the CoronaVac vaccine was evaluated with a short follow-up of up to 56 days and showed a better antibody response to the participants who had a COVID-19 history before vaccination (19-22).

In addition, the antibody positivity rate decreased to 58.8% six months after the second vaccine. Antibody values and positivity rates were significantly lower in the sixth month compared to the first month.

Yıldız et al., in their study evaluating the CoronoVac antibody response of long-term healthcare professionals, found that responses decreased significantly on the 180th day in those over 40 years of age and without a history of COVID-19 (23).

Studies have shown that the presence of anti-spike and anti-nucleocapsid antibodies of COVID-19 within the first six months reduces the re-infection rate [10,11]. After the second dose of CoronaVac, 11 participants (10.6%) in our study had been infected with COVID-19. Of these, nine participants became infected three months after the second dose. All participants with COVID-19 infection had positive antibody values after vaccination. These participants did not develop severe illness; the disease course was mild to moderate.

There was no relationship between infection and antibody levels. CoronaVac is effective in preventing symptomatic or severe illness (24).

According to recent research, the main factors that may influence vaccine response are young age, female sex, and COVID-19 history before vaccination. (17,18,22,23).

In our study, the first antibody change is negatively correlated with age. The mean age of the participants was 37.5 ± 10.7 years (22-61). The age range of the health professionals working in our hospital is 20-65, and the majority are young. The first antibody positivity rate for people over 40 years was lower than that of other age groups. Antibody levels in nurses being higher than that of doctors can be attributed to their lower average age. Although some studies have a high positivity rate in women, there was no such difference in our study [17].

Table 1. Distribution of first and second antibody levels by genders (Median (IQR index)).

Variables	Male	Female	p-value
1. Ab	5.38 (2.10-14.78)	7.23 (4.13-14,01)	0.267
2. Ab	0.92 (0,40-2.90)	1.40 (0.78-2.95)	0.108
Difference (1.Ab-2. Ab)	5.51 (1.72-10.16)	4.66 (1.92-7.31)	0.715
Variation %	85.1 (69.8-88.5)	78,4 (59,3-87,6)	0.207
1.Abpositive (n=97)* n (%)	31 (91.2)	61 (96.8)	0.34
2.Abpositive (n=51)* n (%)	9 (50.0)	21 (63.6)	0.344

*Patients with COVID-19 after vaccination were not included in this analysis.

Table 2. Distribution of antibody levels by occupational groups (Median (IQR)).

Variables	Doctor	Nurse	Others	p-value
First antibody level	6.49 (2.98-9.36)	9.18 (5.13-19.39)	4.01 (3.07-10.26)	0.015*
Second antibody level (6th month)	1.35 (0.82-4.09)	0.73 (0.60-1.48)	1.24 (0.57-3.15)	0.169
Difference (1. Ab-2. Ab difference)	4.38 (0.99-7.25)	7.14 (4.49-13.73)	2.98 (1.66-7.30)	0.201

*The antibody level of nurses in the first month was significantly higher than that of doctors, Ab= Antibody

In another study conducted by health professionals in Turkey, the highest antibody levels were identified in women in the 19-30 age group after the inactive SARS-COV-2 vaccine (18).

Although the post-vaccine seroconversion status does not fully protect, it is considered a significant indicator of the effective immune response. It also helps in future seroepidemiological studies [25].

Our main limitation is that the study is conducted only in a specific occupational group. In addition, SARS-COV-2 IgG antibody status before vaccination was not evaluated. The duration of COVID-19 vaccine protection has yet to be discovered, and long-term studies are required. Furthermore, other parts of the immune system, such as cellular and cytokine reactions, play a primary role in vaccine activity. There is evidence that genetics, sex, extensive vaccination, comorbidities, and products such as vaccines, adjuvants, and vaccine programs strongly affect vaccination reactions. The complex interaction between these different parts of the immune system in vaccine responses has yet to be fully understood [25].

The current increase in variant strains causes a decrease in neutralizing activity over time, and the increase in transmission rates reduces the effectiveness of vaccines [26].

Conclusion

Antibody tests are helpful in diagnosis, follow-up, and serological studies. Our study showed that the CoronaVac vaccine significantly protects individuals from severe COVID-19 infection during the first six months. However, the results of our study cannot be generalized. Large-scale future studies are needed to elucidate this issue further.

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