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Evaluation of anti-spike IgG response after inactivated COVID-19 vaccine in healthcare workers

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ABSTRACT

Aim: This study purposed to determine anti-spike IgG levels at the fourth week after the second dose in healthcare workers (HCWs) who had two doses of the CoronaVac vaccine (Sinovac Life Sciences, Beijing, China). The second purpose of the study was to evaluate several factors that may affect antibody levels.

Material and Method: The study was performed at Kastamonu Training and Research Hospital. A total of 197 HCWs of both genders aged 20-63 were included in this study. Antibody levels that neutralize the SARS-CoV-2 spike protein S1 subunit were determined using the SARS-CoV-2 IgG II Quant kit from serum samples collected from the subjects between 10-16 March 2021. Also, a questionnaire containing information about demographic and clinical data was administered to all subjects. It was statistically investigated whether these data affected the anti-spike IgG levels.

Results: All subjects had anti-spike IgG levels positive. The median value of the subjects' anti-spike IgG levels was calculated as 860.2 AU/mL (Q25: 519.1 AU/mL, Q75: 1674.1 AU/mL). Anti-spike IgG levels were statistically higher in non-smokers and Rh-positive subjects versus the smokers and Rh-negative subjects ($p=0.001$ and $p=0.046$, respectively). However, age groups, gender, COVID-19 history, blood type, and seasonal influenza vaccine did not significantly affect anti-spike IgG levels in the subjects ($p>0.05$).

Conclusion: Anti-spike IgG responses were positive in all HCWs who received the CoronaVac vaccine. Besides, the results showed that smoking and Rh-factor affect the anti-spike IgG response. On the other hand, further studies need to examine more parameters with a larger number of subjects.

Keywords: CoronaVac, COVID-19, healthcare worker, SARS-CoV-2 spike protein

INTRODUCTION

COVID-19 is a disease caused by the SARS-CoV-2 virus of the Coronaviridae family (1). COVID-19 was declared a pandemic by the World Health Organization (WHO) on March 11, 2020. COVID-19 is a severe public health problem that continues to be important today and needs attention (2). Scientists are working tirelessly to discover and develop antiviral agents against SARS-CoV-2. Unfortunately, no definitive antiviral agent to combat COVID-19 has yet been found (3). Therefore, hygiene and vaccines continue to be our most important weapons in the fight against COVID-19 (4). Fortunately, thanks to the vaccines developed in a short time and with great success, the pandemic could be partially controlled.

COVID-19 vaccines are classified as inactivated vaccines, live attenuated vaccines, subunit vaccines, viral vector vaccines, and nucleic acid vaccines based on the way they are prepared (5). However, the common purpose of all is to create neutralizing antibodies against the spike antigen on the virus and to inhibit the virus by blocking it (6). CoronaVac (Sinovac Life Sciences, Beijing, China), one of the inactivated COVID-19 vaccines, was first started to be used in healthcare workers (HCWs) on January 14, 2021, after it was approved for emergency use in Türkiye (7). Since then, millions of people have been vaccinated with CoronaVac in Türkiye. A detailed study in Brazil showed that two doses of the vaccine administered 14 days apart were 51% protective against symptomatic COVID-19 infection and almost 100% protective against hospitalization (8).

This study purposed to determine the anti-spike IgG levels after the second dose in HCWs who received the CoronaVac vaccine in Kastamonu Training and Research Hospital. In

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addition, the effects of various factors (age, gender, body mass index, smoking, COVID-19 history, blood type, Rhesus (Rh) factor, and seasonal influenza vaccine) on the antibody level were evaluated in this study.

MATERIAL AND METHOD

This study was approved by the Kastamonu University, Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (Date: 11.03.2021, Decision no: 2020-KAEK-143-70). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Healthcare Workers Cohort

The present study was conducted in a training and research hospital in Kastamonu province, northwest Türkiye. A total of 197 HCWs of both genders, aged 20-63, who received two doses of the CoronaVac vaccine (Sinovac Life Sciences, Beijing, China) were included in this study.

Study Design

Blood samples were gotten from all subjects in the fourth week after the second dose of the CoronaVac vaccine. Blood samples were collected between 10 and 16 March 2021. A questionnaire containing information about demographic and clinical data was administered to all subjects. Accordingly, all subjects' gender, age, height, weight, blood type, Rh-factor, smoking, and whether they had seasonal influenza vaccine in the three months before CoronaVac were recorded. In addition, subjects who had a prior PCR-confirmed diagnosis of COVID-19 were included in the "COVID-19 recovered group", while had not a prior PCR-confirmed diagnosis of COVID-19 were included in the "no COVID-19 history" group.

Serological Test

Serum samples obtained after centrifugation (at 4000 rpm for 20 min) of blood samples were analyzed using the SARS-CoV-2 IgG II Quant (Abbott Laboratories, Chicago IL, USA) test on the Architect i2000SR (Abbott) instrument. The SARS-CoV-2 IgG II Quant assay detects neutralizing immunoglobulin G (IgG) antibodies versus the receptor binding site (RBD) of the COVID-19 spike protein S1 subunit (9). The results were evaluated per the manufacturer's instructions, and <50 AU/mL and ≥50 AU/mL were determined to be negative and positive values, respectively.

Statistical Analysis

The statistical analyses were performed using the SPSS 23.0 (IBM SPSS Statistics, IBM Corporation, Chicago, IL) software for Windows. The data were analyzed for normality using the Shapiro-Wilks test. Mann-Whitney U and Kruskal Wallis tests were used to compare two independent groups, and more than two independent groups, respectively. Tha data were presented as the median and the interquartile range [Me (Q25–Q75)] and $p<0.05$ was recognized as statistical significant.

RESULTS

The median age of the subjects was 37 years (IQR, 31–44; range, 20–63 years). The cohort had 45.7% male and 54.3% female. The age distribution of the subjects was as follows: 48 (24.4%) in the 20-30 age group, 72 (36.5%) in the 31-40 age group, 61 (31.0%) in the 41-50 age group, and 16 (8.1%) in the ≥51 age group. Anti-spike IgG level was above 50 AU/mL in all subjects and the median value was calculated at 860.2 AU/mL (519.1-1674.1 AU/mL).

Anti-spike IgG levels in HCWs vaccinated with CoronaVac, according to age, gender, body mass index (BMI), smoking, COVID-19 history, blood type, and seasonal influenza vaccine history are presented in Table 1. Anti-spike IgG levels were statistically higher in non-smokers and Rh-positive subjects compared to the smokers and Rh-negative subjects ($p=0.001$ and $p=0.046$, respectively). However, age groups, gender, COVID-19 history, blood type, and seasonal influenza vaccine did not affect the anti-spike IgG production in a significant manner ($p>0.05$).

Table 1. Anti-spike IgG level in healthcare workers vaccinated with CoronaVac. The data were presented as the median and the interquartile range (Q25–Q75).

	N	Anti-spike IgG (AU/mL)	p value
Age group			0.253*
20-30	48 (24.4%)	995.7 (588.1-1648.3)	
31-40	72 (36.5%)	797.0 (481.7-1625.7)	
41-50	61 (31.0%)	836.8 (339.7-2009.5)	
≥51	16 (8.1%)	1009.9 (774.3-2655.2)	
Gender			0.145**
Male	90 (45.7%)	856.0 (399.2-1639.2)	
Female	107 (54.3%)	860.2 (585.4-1711.5)	
BMI, kg/m²			0.552*
<18.5 (underweight)	2 (1.0%)	637.3 and 2108.1	
18.5-24.9 (normal weight)	87 (44.2%)	776.5 (484.2-1667.8)	
25-29.9 (pre-obesity)	74 (37.5%)	971.9 (481.7-1508.8)	
≥30 (obesity)	34 (17.3%)	820.5 (602.2-2263.5)	
Smoking			0.001**
Yes	71 (36.0%)	697.0 (331.5-1307.1)	
No	126 (64.0%)	1012.5 (606.3-1716.5)	
COVID-19 history			0.050**
COVID-19 recovered group	101 (51.3%)	1115.4 (482.9-1912.3)	
No COVID-19 history	96 (48.7%)	814.6 (522.9-1326.4)	
Blood type			0.301*
O	60 (30.5%)	755.7 (397.9-1373.0)	
A	92 (46.7%)	929.5 (524.3-929.5)	
B	31 (15.7%)	926.5 (665.5-1821.1)	
AB	14 (7.1%)	851.5 (354.1-2013.0)	
Rh-factor			0.046**
Rh-negative	25 (12.7%)	672.9 (324.9-1113.6)	
Rh-positive	172 (87.3%)	928.2 (540.2-1703.8)	
Seasonal influenza vaccine history			0.682**
Yes	29 (14.7%)	926.5 (426.6-1566.8)	
No	168 (85.3%)	847.5 (534.6-1703.8)	

N: number, BMI: Body mass index, *Kruskal Wallis test ** Mann-Whitney U test

DISCUSSION

COVID-19 has spread rapidly and become a global crisis. Fortunately, the pandemic has now been relatively contained with herd immunity. COVID-19 vaccines have played a significant role in the formation of herd immunity (10). In Türkiye, the COVID-19 vaccine was first administered to HCWs with CoronaVac in January 2021. This study examined the anti-spike IgG response and the factors affecting this response in 197 HCWs who received two doses of the CoronaVac vaccine.

Anti-spike IgG response was positive in all subjects. Anti-spike IgG levels were more in the ≥51 age group than in other age groups and higher in females than in males in the current study.

However, no significant difference was found between age groups and genders for anti-spike IgG levels. Kaya et al. (11) investigated the anti-spike IgG levels in 102 HCWs who had been vaccinated with CoronaVac and found that age groups and genders did not significantly affect the antibody level, as in this study. On the contrary, Yigit et al. (12), Şenol Akar et al. (13), and Vural et al. (14) stated that the anti-spike IgG levels were higher in females than in males and young adults compared to the elderly. Relatively higher antibody levels are expected in young adults, as the immune system can weaken with aging (15). However, the oldest subject in this study was 63 years old. In addition, the number of subjects in the ≥51 age group (n=16) was lower than in other age groups. For these reasons, anti-spike IgG levels might have been high in the ≥51 age group in this study.

In this study, subjects were classified as <18.5 (underweight), 18.5-24.9 (normal weight), 25-29.9 (pre-obesity), and ≥30 (obesity) kg/m² according to the WHO reference range for BMI (16). It is known that being overweight negatively affects the cellular and humoral immune response (17). Şenol Akar et al. (13) reported that being overweight negatively affected the anti-spike IgG response in HCWs who had been vaccinated with CoronaVac. However, it was found that BMI did not significantly affect the anti-spike IgG response in this study. Demir Tekol et al. (18) investigated the factors affecting the antibody level in HCWs who had received two doses of the CoronaVac vaccine and reported that BMI did not significantly affect the anti-spike IgG response, consistent with this study. In addition, Pellini et al. (19) performed a similar study with the BNT162b2 messenger RNA (mRNA) vaccine and reported that there was no relationship between BMI and vaccine-related antibody response.

The negative effects of smoking on the immune system are obvious. Studies investigating the effect of smoking on post-vaccine anti-spike IgG levels emphasized that smokers generally have lower antibody levels than non-smokers (20). The effect of smoking on anti-spike IgG levels was also investigated in the current study. The subjects were separated into two groups smokers and non-smokers, ignoring the number of cigarettes they smoked, in this study. Anti-spike IgG levels were significantly higher in non-smokers than in smokers, consistent with the literature.

It is known that antibodies formed as a result of COVID-19 infection maintain their neutralizing properties for about six months (21). Many studies reported that post-vaccination antibody levels are significantly higher in the COVID-19 recovered group than in the no COVID-19 history group (13, 22-24). In the presented study, the median anti-spike IgG level in the subjects with a prior PCR-confirmed diagnosis of COVID-19 was found to be higher than the subjects in the no-COVID-19 history group. However, this difference was not statistically significant (p=0.05).

There are four main blood type: A, B, AB, and O. Another important blood type system is the Rh-factor. Rh-factor refers to an antigen molecule called protein D that is carried on the surface of erythrocytes. If the erythrocyte has the D antigen, it is Rh-positive (25). Some studies stated that the A blood type may increase susceptibility to COVID-19 infection, O blood type and Rh-negative blood type may be protective against the disease (26). However, this mechanism has not yet been elucidated. On the other hand, some researchers hypothesized that blood type (A, B, AB, O) might play a role in the immune response to COVID-19 vaccines (27). It was determined that blood group antigens (A, B, AB, O) did not significantly affect the anti-spike IgG level in this study. However, Rh positive subjects had higher anti-spike IgG levels than Rh negative subjects (p=0.046).

Recent research has suggested that the seasonal influenza vaccine might potentiate the COVID-19 vaccine response. A recent study reported that subjects who had recently been vaccinated with influenza had a better antibody response to the BNT162b2 mRNA vaccine than others (28). Another study similarly emphasized that the response to the BNT162b2 mRNA vaccine was better in subjects who had previously been vaccinated against influenza and pneumococcus (29). Şenol Akar et al. (13) reported that the neutralizing antibody response after the second dose of the CoronaVac vaccine was statistically higher in those who received the influenza vaccine that year. In this study, it was investigated how the seasonal influenza vaccine affected the antibody response to the CoronaVac vaccine. Contrary to other studies, no significant difference was found in anti-spike IgG levels between subjects with and without the influenza vaccine.

CONCLUSION

As a result, anti-spike IgG responses were positive in all HCWs who received the CoronaVac vaccine. Besides, the results showed that smoking and Rh-factor affect the anti-spike IgG response. On the other hand, further studies need to examine more parameters with a larger number of subjects.

ETHICAL DECLARATIONS

Ethics Committee Approval: This study was approved by the Kastamonu University, Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (Date: 11.03.2021, Decision no: 2020-KAEK-143-70).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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