RESEARCH ARTICLE / ARAŞTIRMA

DOI: 10.4274/mjima.galenos.2022.2021.24
Mediterr J Infect Microb Antimicrob 2022;11:24
Erişim: http://dx.doi.org/10.4274/mjima.galenos.2022.2021.24

Anti-nucleocapsid Antibody Response After Two Doses of CoronaVac® Among Healthcare Workers

Sağlık Çalışanlarında İki Doz CoronaVac® Sonrası Anti-Nükleokapsid Antikor Yanıtı

Ayşin KILINÇ TOKER[1], Duygu ÇERÇİOĞLU ÖZDEMİR[1], Esma EREN[1], Ayşe TURUNÇ ÖZDEMİR[1], Azade KANAT[1], İlhami ÇELİK[1], İbrahim TOKER[2]

[1]Kayseri City Hospital, Clinic of Infectious Disease and Clinical Microbiology, Kayseri, Turkey
[2]Kayseri City Hospital, Clinic of Emergency Medicine, Kayseri, Turkey

Abstract

Introduction: The Coronavirus disease-2019 (COVID-19) pandemic that started over two years ago has led to high mortality and morbidity. Vaccine studies have been initiated worldwide to end the pandemic, and the CoronaVac® vaccine was first administered to healthcare workers at high risk of COVID-19 in Turkey. In our study, we aimed to investigate serum antibody levels after vaccination.

Materials and Methods: Volunteer healthcare workers without COVID-19 disease who received two doses of CoronaVac® vaccine 28 days apart and were at least 14 days after the last dose of vaccine were included in this study. Assessment of antibodies against Severe acute respiratory syndrome-Coronavirus-2 (SARS-CoV-2) in blood samples from participants was performed using the Elecsys® anti-SARS-CoV-2 electrochemiluminescence immunoassay. Samples with a cut-off index (COI) (COI; signal sample/cut-off) <1.0 were considered negative; whereas samples with COI≥1.0 were deemed positive.

Results: A total of 269 healthcare workers, 168 women (62.5%), were included in our study. The mean age of the participants was 37.7±8.6 (minimum-maximum: 21-62). Antibody levels were positive in 188 (69.9%) of the participants. The median antibody level was 9.2 COI (interquartile ranges=3-34.7). In terms of mean age, the mean age of participants with negative antibodies was higher with a statistically significant difference (p=0.001). The antibody positivity rate of women was higher than that of men (p<0.001). No statistically significant association was found between the time elapsed after vaccination, presence of comorbidities, development of post-vaccine side effects, and antibody levels. It was found that one or more side effects developed in 45.7% of the participants after vaccination.

Conclusion: Our study showed that seropositivity developed significantly in healthcare workers after the CoronaVac® vaccine. It emphasizes the importance of maintaining infection prevention and control measures and administering the SARS-CoV-2 vaccine for healthcare workers at high risk.

Keywords: COVID-19, SARS-CoV-2 antibody, vaccine, side effect

Öz

Giriş: Yüksek mortalite ve morbiditeye sahip olan Koronavirüs hastalığı-2019 (COVID-19) pandemisi iki yılı aşkın süredir devam etmektedir. Pandeminin son bulması için tüm dünyada aşı çalışmaları başlamış ve ülkemizde ilk olarak CoronaVac® aşısı yüksek risk grubundaki sağlık çalışanlarına yapılmıştır. Çalışmamızda aşılama sonrası serum antikor düzeylerinin araştırılması hedeflenmiştir.

Gereç ve Yöntem: Çalışmaya COVID-19 geçirmemiş, 28 gün ara ile iki doz CoronaVac® aşısı yapılan ve son doz aşısından sonra en az 14 gün geçmiş olan gönüllü sağlık personeli dahil edilmiştir. Katılımcılardan alınan kan örneklerinin Şiddetli akut solunum sendromu-Koronavirüs-2'ye (SARS-

Cite this article as: Kılınç Toker A, Çerçioğlu Özdemir D, Eren E, Turunç Özdemir A, Kanat A, Çelik İ, Toker İ. Anti-Nucleocapsid Antibody Response After Two Doses of CoronaVac® Among Healthcare Workers. Mediterr J Infect Microb Antimicrob. 2022;11:24.

Address for Correspondence/Yazışma Adresi: Ayşin Kılınç Toker MD, Kayseri City Hospital, Clinic of Infectious and Clinical Microbiology, Kayseri, Turkey
Phone: +90 352 315 77 00 **E-mail:** dr.aysin@gmail.com
Received/Geliş Tarihi: 12.12.2021 **Accepted/Kabul Tarihi:** 24.03.2022 **ORCID ID:** orcid.org/0000-0002-6775-1234

Published: 10 April 2022

Öz

CoV-2) karşı antikor değerlendirmesi Elecsys®anti-SARS-CoV-2 elektrokemilüminesans immünolojik testi kullanılarak yapılmıştır. Cut-off indeksi (COI) (COI; sinyal numune/eşik) <1,0 olan numuneler negatif, ≥1,0 olan numuneler pozitif olarak kabul edildi.

Bulgular: Çalışmamıza 168'i kadın (%62,5) olmak üzere toplam 269 hastane personeli dahil edildi. Katılımcıların ortalama yaşı 37,7±8,6 (minimum-maksimum: 21-62) idi. Katılımcıların 188'inin (%69,9) antikor düzeyi pozitif idi. Ortanca antikor değeri 9,2 COI (çeyrekler arası aralık=3-34,7) idi. Yaş ortalaması açısından bakıldığında antikoru negatif olan kişilerin yaş ortalaması istatistiksel anlamlı farkla daha yüksekti (p=0,001). Kadınların antikor pozitiflik oranı erkeklere göre daha yüksekti (p<0,001). Aşıdan sonra geçen süre, komorbidite hastalık varlığı ve aşı sonrası yan etkisi gelişimi ile antikor düzeyleri arasında istatistiksel anlamlı farklılık saptanmadı. Aşı sonrası, katılımcıların %45,7'sinde bir veya daha fazla yan etki geliştiği bulundu.

Sonuç: Çalışmamızda, CoronaVac® aşısı sonrası sağlık çalışanlarında önemli ölçüde seropozitiflik geliştiği gözlendi. Çalışmamız yüksek riskli olan sağlık çalışanları için enfeksiyon önleme ve kontrol önlemlerinin sürdürülmesi ve SARS-CoV-2 aşısının uygulanmasının önemini vurgulamaktadır.

Anahtar Kelimeler: COVID-19, SARS-CoV-2 antikor, aşı, yan etki

Introduction

The Coronavirus disease-2019 (COVID-19) pandemic, which has been ongoing for over a year, has led to high mortality and morbidity. As of July 12, 2021, there were 186 million confirmed cases worldwide, resulting in approximately 4 million deaths[1].

Vaccine studies have been started worldwide to end the pandemic. According to their technological features, inactivated virus vaccines, live virus vaccines, vaccines containing recombinant viral carriers, nucleic acid-based vaccines, protein subunit vaccines, and many vaccines containing virus-like particles are under development[2]. At least 13 different vaccines have already been developed, in addition to vaccines that are still undergoing clinical trials[3]. In a meta-analysis of 51 studies, various COVID-19 vaccines were highly protective against Severe acute respiratory syndrome-Coronavirus-2 (SARS-CoV-2) related mortality and morbidity worldwide.

CoronaVac® is an inactivated vaccine obtained from African green monkey kidney cells inoculated with the SARS-CoV-2 strain CN02. After the incubation period in the cell, the virus is collected, inactivated with p-propiolactone, concentrated, purified, and finally absorbed onto aluminum hydroxide to complete its production[4].

In Turkey, the CoronaVac® vaccine, which we are involved in its phase-3 studies and is approved for emergency use by the Turkish Medicines and Medical Devices Agency, was first administered to high risk healthcare workers (HCWs). The vaccine was administered in two doses, 28 days apart.

Our study aimed to investigate serum antibody levels at least 14 days after the last dose of vaccine, which indicates post-vaccination humoral immunity.

Materials and Methods

This study was conducted at Kayseri City Hospital from March 1 to March 15, 2021. All volunteer HCWs without COVID-19 disease, who received two doses of CoronaVac® vaccine with an interval of 28 days, and who received their last dose of vaccine at least 14 days prior were included in the study. Participants were asked to complete a questionnaire that included medical history and recent or current symptoms. The Bio-speedy SARS-CoV-2 (2019-nCoV) reverse transcription-quantitative polymerase chain reaction (PCR) detection kit (Bioeksen, İstanbul, Turkey) was used to conduct the SARS-CoV-2 PCR test on nasopharyngeal swabs to determine the presence of SARS-CoV-2 infection.

The Kayseri City Hospital Ethics Committee approved this study (approval no: 140121/500, date: 14.01.2021), and a signed informed consent form was obtained from all participants.

Antibody Measurement

Elecsys anti-SARS-CoV-2 electrochemiluminescence immunoassay was used in this study. This assay is intended for use on Cobase analyzers (Roche Diagnostics International Ltd, Rotkreuz, Switzerland) for the *in vitro* qualitative detection of antibodies (both IgA and IgG) to SARS-CoV-2 in human serum and plasma. The Elecsys anti-SARS-CoV-2 test uses the double antigen sandwich test principle and a recombinant protein representing the nucleocapsid antigen to detect SARS-CoV-2 antibodies. Regarding anti-SARS-CoV-2 antibody positivity, samples with a cut-off index (COI) (COI; signal sample/cut-off) <1.0 were considered negative, whereas samples with COI ≥1.0 were deemed positive, as per the manufacturer's instructions. A measured antibody level magnitude above the cut-off value was not considered an indicator of the sample's total amount of antibody present.

Statistical Analysis

Statistical analyses were performed using the IBM Statistical Package for the Social Sciences (version 26) program. In the statistical evaluation of the data obtained from the study, categorical data were summarized as frequency and percentage, continuous data with normal distribution as mean±standard

deviation, and data with skewed distribution as median [25-75% interquartile range (IQR)]. Normality controls of continuous measurements were tested using the Shapiro-Wilk test. Independent samples t-tests were used to compare two groups of continuous variables with a normal distribution. The non-parametric Mann-Whitney U test was used to perform two-group comparisons for variables not consistent with the normal distribution. The chi-square test was used to compare categorical variables. The statistical significance level was considered as 0.05.

Results

A total of 269 hospital personnel, 168 women (62.5%), were included in our study. The mean age of the participants was 37.7±8.6. Of the participants, 144 (53.7%) were nurses, 42 (15.6%) were medical secretaries, and 32 (11.9%) were physicians. At least one comorbid disease was present in 77 (28.6%) of the study participants. The most common comorbid disorders were hypertension (7.8%), diabetes (3.7%), and cardiovascular diseases (2.6%).

Comorbid diseases and occupational distribution are shown in Table 1.

Antibody levels were negative in 81 (30.1%) participants, while 188 (69.9%) were positive. The median antibody value of SARS-CoV-2 antibody-positive HCWs was 9.2 COI (IQRs=3-34.7).

A comparison of the participants' antibody levels according to mean age reavealed a statistically significant difference, and the mean age of particiapants with negative antibodies was higher (p=0.001) (Table 2).

A comparison of the participants' antibody levels in terms of gender revealed a statistically significant difference, and the antibody positivity rate of women was higher than that of men (p<0.001) (Table 2).

There was no statistically significant association of antibody levels with the time elapsed after vaccination and the presence of comorbid diseases was found (p values: 0.147 and 0.408, respectively). Similarly, no statistically significant association

Table 1. Basic characteristics of healthcare workers

Age, mean (±standard deviation)	**37.7±8.6**	
Gender	**n**	**%**
Female	168	62.5
Male	101	37.5
Occupation	**n**	**%**
Doctor	32	11.9
Nurse	144	53.7
Administrative staff	4	1.5
Laboratory staff	11	4.1
Medical secretary	42	15.6
Cleaning/directing staff	6	2.2
Security personal	5	1.9
Others*	25	9.3
Comorbidity	77	28.6
Hypertension	21	7.8
Diabetes mellitus	10	3.7
Cardiovascular diseases	7	2.6
Chronic lung diseases	11	4.1
Chronic kidney diseases	2	0.7
Immunosuppressive diseases	5	1.9
Others**	24	7.9

*Radiology technician, cafeteria staff, library staff

**Hypo/hyperthyroidism, rheumatoid arthritis, psychiatric diseases

Table 2. Comparison of basic characteristics and antibody levels of HCWs

		Antibody levels		
	n (%)	**IG<1 (n=81)**	**IG≥1 (188)**	**p value**
Age (mean±Std)	37.7±8.6	40.4±8.8	36.5±8.2	**0.001***
Female	168 (62.5%)	37 (45.7%)	131 (69.7%)	**<0.001**
Male	101 (37.5%)	44 (54.3%)	57 (30.3%)	
Comorbidity				
Absent	192 (71.4%)	55 (67.9%)	137 (72.9%)	0.408
Present	77 (28.6%)	26 (32.1%)	51 (27.1%)	
Days after vaccination (median-IQRs)	27 (24-28)	27 (25-28)	26 (24-28)	0.147**
Adverse event				
Absent	146 (54.3%)	45 (55.6%)	101 (53.7%)	0.782
Present	123 (45.7%)	36 (44.4%)	87 (46.3%)	

*p: Student's t-test, **p: Mann-Whitney U test. Other p-values were calculated using the chi-square test.

Std: Standard, IQR: Interquartile range, HCW: Healthcare worker

was found between the development of post-vaccine side effects and antibody levels (p=0.782) (Table 2).

It was found that one or more side effects developed in 45.7% of the participants after vaccination. No serious side effects were observed. The most common side effects were local side effects such as pain at the injection site (15.2%), headache (13.8%), weakness-fatigue (13.4%), and muscle-joint pains (8.6%) (Table 3).

Discussion

The first randomized controlled phase 3 trial on inactivated vaccines was conducted with 40,000 adults in China. Two inactive vaccines were examined in this study and shown to significantly reduce the risk of symptomatic COVID-19 in those vaccinated with either vaccine[5].

According to the results of the CoronaVac® vaccine phase 3 trial in Turkey, the vaccine's effectiveness is 83.5%; the rate of prevention of hospitalization was reported to be 100%, and no death was observed[6]. According to the results from Chile, where the other phase 3 study was conducted, it was shown that the vaccine reduced symptomatic infection by 67%, hospitalizations by 85%, and mortality rates by 80%[7]. The World Health Organization gave emergency use approval for the CoronaVac® vaccine on June 1, 2021. It has been reported that the vaccine prevents 51% of symptomatic diseases and 100% of severe illness and hospitalizations[8].

Table 3. Adverse events

Adverse event	n (%)
Local side effects	41 (15.2)
Headache	37 (13.8)
Fatigue	36 (13.4)
Myalgia	23 (8.6)
Dizziness	10 (3.7)
Fever	9 (3.3)
Menstrual irregularity	6 (2.2)
Sore throat	5 (1.9)
High blood pressure	5 (1.9)
Low blood pressure	3 (1.1)
Allergic reaction	3 (1.1)
Nasal discharge	3 (1.1)
Diarrhea	2 (0.7)
Ataxia	2 (0.7)
Change in taste	2 (0.7)
Amnesia	2 (0.7)
Chest pain	2 (0.7)
Blood sugar change	2 (0.7)
Change in sleep pattern	2 (0.7)
Cough	1 (0.4)
Shingles rash	1 (0.4)
Palpitation	1 (0.4)
Nausea	1 (0.4)
Lymphadenopathy	1 (0.4)

Presenting real-life data about the CoronaVac® vaccine is beneficial in providing information about the vaccine's effectiveness. Zhang et al.[9] showed that a cellular immune response with the release of Th1 cytokines and a humoral immune response with the release of Th2 cytokines were triggered by the CoronaVac® vaccine, especially in the following days after the 2nd dose. Evaluation of the antibodies formed after vaccination gives an idea about the humoral response triggered by the vaccine.

A study of multiple HCWs found that anti-spike or anti-nucleocapsid antibodies significantly reduced the risk of SARS-CoV-2 reinfection over the following six months. In this study, anti-spike and anti-nucleocapsid IgG negative HCWs had 1.08 per 10,000 days at risk, both baseline assays positive HCWs had 0.07 per 10,000 days at risk, and only one assay positive HCWs had 0.49 per 10,000 days at risk[10]. The advantage of inactivated vaccines is that all their proteins can act as antigens with the complete inactivation of the virus.

In a study conducted with 264 HCWs in Turkey, antibody levels developed after the CoronaVac® vaccine were examined by measuring anti-RBD anti-SARS-CoV-2 IgG antibodies (Quantivac-Euroimmun/Germany) by ELISA. The antibody response was found to be 91.6% in the study. Factors reducing antibody response are male gender (p=0.007), advanced age (p<0.005), no history of COVID-19 (p=0.015), and previous H1N1 vaccination (p=0.044)[11]. Additionally, the antibody response was higher in this study because 27% of the participants had a history of COVID-19 before they were vaccinated. In our study, all volunteer HCWs did not have COVID-19 disease, and our findings are similar in terms of male gender and age.

In a retrospective study of 75 HCWs who had negative IgM and IgG results before vaccination, IgM and IgG were measured 14-21 days after two doses of the CoronaVac® vaccine. It was observed that 100% of the HCWs developed IgG, but IgM was negative[12].

Preliminary results of a study conducted in Turkey among volunteer HCWs who were administered CoronaVac® vaccine to investigate neutralizing antibodies formed against the region in the SARS-CoV-2 spike protein that binds to human cells were obtained using two different tests: quantitative and qualitative. Immunity was determined as 25.3% at least 28 days after the 1st dose and 97% at least 28 days after the 2nd dose. In

addition, similar to our study, although both sexes had adequate immunity, a significantly higher vaccine immune response was obtained in women than in men[13].

In the CoronaVac® vaccine phase 1 study, a maximum of 38% of adverse events were recorded[14]. In our study, the rate of side effects was slightly higher at 45%. In the phase 3 trial conducted in Turkey, side effects after the CoronaVac vaccine were reported as fatigue, headache, myalgia, fever, chills, and pain at the injection site. Our study shows that the rates of side effects such as local side effects, muscle pain, and headache are higher than in the phase 3 study[11].

It has been reported that immune response and vaccine response decrease with age, and stronger immune response development and increasing functional antibody development are seen in women compared to men[15-17]. Our study's differences in antibody response according to age and gender seem to be expected.

Different antibody response rates in studies may be related to the test being studied measuring different antibodies or using varied kits/methods. Again, the features mentioned above, such as age, gender, and previous history of COVID-19, can also be considered factors affecting the antibody response. In general, most people appear to have an antibody response with the CoronaVac® vaccine. A study of HCWs showed that neutralizing antibody levels decreased significantly within two months[18].

Study Limitations

There are some limitations of our study. First of all, our study was conducted in a single center with a limited number of people in fifteen days. Secondly, the inability to follow-up on the presence of antibodies in disease development is a limitation of our study. Third, using a qualitative method in antibody measurement is another limitation of our study.

Conclusion

This study provides data on antibody levels and side effects obtained with the CoronaVac® vaccine among HCWs. The antibody levels offered by the vaccine and the clinical efficacy of the vaccine; will be clearer with further study.

Ethics

Ethics Committee Approval: The Kayseri City Hospital Ethics Committee approved this study (approval no: 140121/500, date: 14.01.2021).

Informed Consent: A signed informed consent form was obtained from all participants.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: A.K.T., İ.Ç., Design: İ.Ç., Data Collection or Processing: A.K.T., E.E., A.T.Ö., A..K., Analysis or Interpretation: A.K.T., A.T.Ö., İ.T., Literature Search: D.Ç.Ö., İ.T., Writing: A.K.T., D.Ç.Ö.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. World Health Organization (WHO). Weekly epidemiological update on COVID-19; 2021. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports
2. Azap A. COVID-19 Vaccines: Light at the end of the Tunnel. 2020;29(Suppl 1):94-100.
3. World Health Organization (WHO). COVID-19 vaccines; 2021. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/covid-19-vaccines
4. 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 randomised, double-blind, placebo-controlled, phase 1/2 trial. Lancet Infect Dis. 2021;21:39-51.
5. Al Kaabi N, Zhang Y, Xia S, Yang Y, Al Qahtani MM, Abdulrazzaq N, Al Nusair M, Hassany M, Jawad JS, Abdalla J, Hussein SE, Al Mazrouei SK, Al Karam M, Li X, Yang X, Wang W, Lai B, Chen W, Huang S, Wang Q, Yang T, Liu Y, Ma R, Hussain ZM, Khan T, Saifuddin Fasihuddin M, You W, Xie Z, Zhao Y, Jiang Z, Zhao G, Zhang Y, Mahmoud S, ElTantawy I, Xiao P, Koshy A, Zaher WA, Wang H, Duan K, Pan A, Yang X. Effect of 2 Inactivated SARS-CoV-2 Vaccines on Symptomatic COVID-19 Infection in Adults: A Randomized Clinical Trial. JAMA. 2021;326:35-45.
6. Tanriover MD, Doğanay HL, Akova M, Güner HR, Azap A, Akhan S, Köse Ş, Erdinç FŞ, Akalın EH, Tabak ÖF, Pullukçu H, Batum Ö, Şimşek Yavuz S, Turhan Ö, Yıldırmak MT, Köksal İ, Taşova Y, Korten V, Yılmaz G, Çelen MK, Altın S, Çelik İ, Bayındır Y, Karaoğlan İ, Yılmaz A, Özkul A, Gür H, Unal S; CoronaVac Study Group. Efficacy and safety of an inactivated whole-virion SARS-CoV-2 vaccine (CoronaVac): interim results of a double-blind, randomised, placebo-controlled, phase 3 trial in Turkey. Lancet. 2021;398:213-22.
7. Jara A, Undurraga EA, González C, Paredes F, Fontecilla T, Jara G, Pizarro A, Acevedo J, Leo K, Leon F, Sans C, Leighton P, Suárez P, García-Escorza H, Araos R. Effectiveness of an Inactivated SARS-CoV-2 Vaccine in Chile. N Engl J Med. 2021;385:875-84.
8. World Health Organization (WHO). WHO validates Sinovac COVID-19 vaccine for emergency use and issues interim policy recommendations; 2021. Available from: https://www.who.int/news/item/01-06-2021-who-validates-sinovac-covid-19-vaccine-for-emergency-use-and-issues-interim-policy-recommendations
9. Zhang H, Hu Y, Jiang Z, Shi N, Lin H, Liu Y, Wang H, Feng Y, Meng X, Zhang S, Su L, Zheng Z, Dong L, Gao Q, Xia Q. Single-Cell Sequencing and Immune Function Assays of Peripheral Blood Samples Demonstrate Positive Responses of an Inactivated SARS-CoV-2 Vaccine. 2021. Available at SSRN: https://ssrn.com/abstract=3774153
10. Lumley SF, O'Donnell D, Stoesser NE, Matthews PC, Howarth A, Hatch SB, Marsden BD, Cox S, James T, Warren F, Peck LJ, Ritter TG, de Toledo Z, Warren L, Axten D, Cornall RJ, Jones EY, Stuart DI, Screaton G, Ebner D, Hoosdally S, Chand M, Crook DW, O'Donnell AM, Conlon CP, Pouwels KB, Walker AS,

Peto TEA, Hopkins S, Walker TM, Jeffery K, Eyre DW; Oxford University Hospitals Staff Testing Group. Antibody Status and Incidence of SARS-CoV-2 Infection in Health Care Workers. N Engl J Med. 2021;384:533-40.

11. Özdemir HÖ, Tosun S, Coşkuner S, Demir S. Assessment of Factors Affecting Inactivated COVID-19 (CORONAVAC) Vaccine Response and Antibody Response in Healthcare Professionals. Research Square; 2021.
12. Binay U, Karakecili F, Barkay O, Gül Ö, Mertoğlu C. Level of SARS-CoV-2 IgG antibodies after two doses CoronaVac vaccine: Primarily report. Research Square; 2021.
13. Manisa Celal Bayar University. Immune Response to SARS CoV-2 Inactivated (Sinovac-Coronavac) Vaccine [Internet]. Last accessed date: 05.04.2021. Available from: https://www.mcbu.edu.tr/Haber/MCBUTipFakultesiHastanesiSaglikCalisanlarininYuruttugu_SARSCoV2InaktifSinovacCoronavacAsisininBagisiklikYaniti_ArastirmasiSonuclandi_09_20_7
14. Zhang Y, Zeng G, Pan H, Li C, Hu Y, Chu K, Han W, Chen Z, Tang R, Yin W, Chen X, Hu Y, Liu X, Jiang C, Li J, Yang M, Song Y, Wang X, Gao Q, Zhu F. Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine in healthy adults aged 18-59 years: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial. Lancet Infect Dis. 2021;21:181-92.
15. Lord JM. The effect of ageing of the immune system on vaccination responses. Hum Vaccines Immunother. 2013;9:1364-7.
16. Fischinger S, Boudreau CM, Butler AL, Streeck H, Alter G. Sex differences in vaccine-induced humoral immunity. Semin Immunopathol. 2019;41:239-49.
17. Gustafson CE, Kim C, Weyand CM, Goronzy JJ. Influence of immune aging on vaccine responses. J Allergy Clin Immunol. 2020;145:1309-21.
18. Marot S, Malet I, Leducq V, Zafilaza K, Sterlin D, Planas D, Gothland A, Jary A, Dorgham K, Bruel T; Sorbonne Université SARS-CoV-2 Neutralizing Antibodies Study Group, Burrel S, Boutolleau D, Schwartz O, Gorochov G, Calvez V, Marcelin AG. Rapid decline of neutralizing antibodies against SARS-CoV-2 among infected healthcare workers. Nat Commun. 2021;12:844.