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Antibody Response to Inactive SARS-CoV-2 Vaccination in a Cohort of Elderly Patients Living with Obesity

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Elderly patients · Obesity · Antibody response

Abstract

Introduction: Obesity and aging negatively affect the immune system and host defense mechanisms, increasing vulnerability to and worsening prognosis of infectious diseases, leading to vaccine failure. Our aim was to investigate the antibody response against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike antigens and the risk factors affecting antibody levels in elderly patients living with obesity (PwO) after inactive SARS-CoV-2 vaccine (CoronaVac) administration. ***Methods:*** One hundred twenty-three consecutive elderly patients with obesity (age ≥65 years, body mass index [BMI] ≥30 kg/m^2) and 47 adults with obesity (age 18–64 years, BMI ≥30 kg/m^2) admitted between August and November 2021 were enrolled. Seventy-five nonobese elderly people (age ≥65 years, BMI 18.5–29.9 kg/m^2) and 105 nonobese adults (age 18–64 years, BMI 18.5–29.9 kg/m^2) were recruited from subjects who visited the Vaccination Unit. SARS-CoV-2 spike protein antibody titers were measured in patients with obesity and nonobese controls who received two doses of CoronaVac. ***Results:*** SARS-CoV-2 levels of patients with obesity were found to be significantly lower than those of nonobese elderly individuals who had non-prior infection. There was no difference in SARS-CoV-2 levels between patients with obesity and nonobese individuals with prior infection. Age and SARS-CoV-2 level were found to be highly correlated in the correlation analysis in the group of elderly individuals (*r*: −0.184). In multivariate regression analysis, when SARS-CoV-2 immunoglobulin class G (IgG) was regressed on age, sex, BMI, type 2 diabetes mellitus, and hypertension (HT), HT was found to be an independent factor of the SARS-CoV-2 level (β: −2,730). ***Conclusion:*** In the non-prior infection group, elderly patients with obesity generated significantly reduced antibody titers against SARS-CoV-2 spike antigen after CoronaVac vaccine compared to nonobese people. It is anticipated that the results obtained will provide invaluable information about SARS-CoV-2 vaccination strategies in this vulnerable population. Antibody titers may be measured, and booster doses should be delivered accordingly in elderly PwO for optimal protection.

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Introduction

The novel SARS-CoV-2 epidemic, which emerged in Wuhan, China, at the end of 2019, spread to the whole world in a short time and caused a pandemic [1]. COVID-19 was first reported to the World Health Organization (WHO) on December 31, 2019, and on March 11, 2020, the WHO declared a COVID-19 pandemic [2].

As of November 28, 2021, 194 vaccines are in preclinical and 132 vaccines in clinical stages of development, 7 of which have been approved for emergency use [3]. The vaccines for emergency use are Comirnaty (Pfizer/BioNTech), AZD1222/ChAdOx1 (AstraZeneca/Oxford University), Ad26.COV2.S (Johnsson & Johnsson/Janssen), CoronaVac AKO domain (Sinovac Life Sciences), mRNA-1273 (Moderna/NIAID), Sputnik V (Gamaleya Research Institute), and BBV152/Covaxin (Bharat Biotech) [3].

CoronaVac, an inactivated virus vaccine, manufactured by Sinovac Life Sciences (Beijing, China), was the first vaccine to be administered in Turkey in line with the recommendations of the Ministry of Health. This vaccine received emergency use approval from the Turkish Medicines and Medical Devices Agency after a 14-day safety test [4]. As a result of this emergency use approval, CoronaVac vaccine was administered to health care professionals followed by public at high risk: elderly and chronic diseases, immunosuppression [4]. The CoronaVac vaccine is administered in two doses according to the manufacturer's instructions. In our country, this dose interval has been determined as 28 days. As of November 28, 2021, a total of 120,100,914 vaccines have been administered in Turkey so far [4].

Obesity, a chronic relapsing multifactorial disease, is now shown as the second most important cause of preventable death after smoking. Obesity develops with excessive fat accumulation in the body due to genetic, epigenetic, environmental, biologic, behavioral, and sociocultural factors. According to the WHO, it is estimated that there were over 650 million obese adults worldwide in 2016 [5]. The WHO reported 16 million patients living with obesity (PwO) in Turkey in 2016, placing Turkey among those countries with the highest prevalences in Europe [6].

Obesity negatively affects immune system function and host defense mechanisms. It creates an inflammatory condition associated with chronic activation of the immune system, enabling infectious diseases to become more common and vaccine failure to be higher [7]. Moreover, immunosenescence can lead to decreased vaccine response and susceptibility to infections [8]. In our study, we evaluated the antibody titers against SARS-CoV-2 spike antigen and the risk factors affecting these antibody levels in elderly PwO.

Materials and Methods

Patient Selection

123 consecutive elderly patients with obesity (age ≥65 years, body mass index [BMI] ≥30 kg/m^2) and 47 adults with obesity (age 18–64 years, BMI ≥30 kg/m^2) admitted to the Center for Obesity Management at Istanbul University-Cerrahpaşa, Cerrahpaşa Medical Faculty Hospitals, between August and November 2021 were enrolled. 75 nonobese elderly people (age ≥65 years, BMI 18.5–29.9 kg/m^2) and 105 nonobese adults (age 18–64 years, BMI 18.5–29.9 kg/m^2) were recruited from subjects who visited the Cerrahpaşa Hospitals Vaccination Unit during the same time period. Those enrolled in the study were grouped in alignment with the obesity classification criteria of the WHO. The SARS-CoV-2 immunoglobulin class G (IgG) nucleocapsid (NCP) antibody test was administered to the patients and control subjects to discover those who had prior COVID-19. The study group (BMI ≥30 kg/m^2, $n = 90$) and the nonobese control group (BMI <30 kg/m^2, $n = 61$) have already received two doses of CoronaVac vaccine. Thirty-three patients who had prior COVID-19 and received two doses of vaccine were included in the study as a subgroup. Fourteen individuals who had prior COVID-19 detected among nonobese subjects became controls for this subgroup.

Data Collection

Weight in kilograms and height in meters, gender, age, and clinical characteristics of the patients were recorded. Blood samples were taken on the 3rd to 4th week after the second vaccination. SARS-CoV-2 IgG antibody titers were determined by quantitative serological methods.

Inclusion Criteria

Individuals aged 18–90 years who have 2 doses of CoronaVac vaccine 3–4 weeks apart and BMI >18.5 were included in the study.

Exclusion Criteria

Patients with a diagnosis of immunodeficiency disorders and oncological and hematological malignancies; patients receiving corticosteroids, chemotherapy, and/or immunotherapy; pregnant women; and individuals under 18 years of age were not included in the study.

SARS-CoV-2 IgG NCP Antibody Test

Approximately 3 mL of blood taken from the volunteers participating in the study into tubes containing vacuum separator gel was centrifuged at 5,000 rpm for 5 min, and the serum obtained was transferred to microcentrifuge tubes and stored at −20°C until the study day. On the day of the test, serum samples were first brought to +4°C and then to room temperature (+18°C, +25°C) and made ready for use. The SARS-CoV-2 IgG test (ARCHITECT IgG test, Abbott, USA), which semiquantitatively detects IgG antibodies against the NCP protein of SARS-CoV-2, using the chemiluminescent microparticle immunoassay method was used. The results obtained from all sera studied were given as index signal/cutoff (S/C) units and were evaluated as <1.4 S/C negative and ≥1.4 S/C positive [9].

In a previous study conducted in our microbiology laboratory at Cerrahpaşa Medical Faculty in order to determine the diagnostic performance of antibody tests, the mean NCP IgG (2.03 S/Co) in the acute period of COVID-19 was considered as the cutoff index [8]. Those with a concentration above 2.03 S/Co were considered to have previously contacted SARS-CoV-2, and concentrations between 1.4 and 2.03 S/Co were labeled as inactive vaccine-induced [10].

SARS-CoV-2 IgG II Quant Antibody Test

In the study, the SARS-CoV-2 IgG test, which can quantitatively detect IgG antibodies, including neutralizing antibodies against the receptor binding region of the spike protein S1 subunit of SARS-CoV-2, using the chemiluminescent microparticle immunoassay method (ARCHITECT IgG II Quant test, Abbott, USA) was used. The results obtained from all serums studied were evaluated as arbitrary unit/mL (AU/mL). The concentrations obtained in AU/mL were multiplied by the correlation coefficient of 0.142 and converted to the "binding antibody unit/mL" in the WHO's international standard [10] on anti-SARS-CoV-2 immunoglobulin. Accordingly, concentrations of 50 AU/mL or 7.1 binding antibody unit/mL and above were considered positive. In addition, it was reported that this test was close to 100% compatible with the plaque reduction neutralization test (PRNT), and a concentration of 1,050 AU/mL was associated with a 1:80 dilution of the PRNT [10].

Statistics

The SPSS 20 program was used to compare the data. After the normal distribution was determined, the data showing normal distribution were acquired using the independent sample *t* test, and the comparison of the data, not showing normal distribution, was performed with the Mann-Whitney U test. Pearson and Spearman tests were used for correlation according to the distribution of the data. Differences between the groups were evaluated with the Kruskal-Wallis test. The non-normally distributed module of the one-way ANOVA test (Tamhane's T2) was used to compare non-normally distributed data. Linear regression analysis was used for independent factor detection. The results were evaluated at a 95 percent confidence interval (CI), and $p < 0.05$ was considered statistically significant.

Sample Size

Required sample size was calculated as 176 for the 2-tailed *t* test with a 5% significance level to achieve 95% power.

Results

In the study, age and BMI values of 198 elderly and 162 adult individuals were calculated (70 + 5, 31.7 + 6.6, and 41.4 + 10.9, 26.4 + 5.1, respectively). Forty-seven subjects were found to have prior infection after being evaluated with the SARS-CoV-2 IgG NCP antibody test in elderly patients. In the group with no prior infection, SARS-CoV-2 antibody levels of elderly patients with obesity (n = 90) were found to be significantly lower than that of nonobese counterparts (n = 61). There was no statistical difference in SARS-CoV-2 antibody levels in the prior infection group (n = 47) between elderly with and without obesity. In adults, both in the non-prior infection group (n = 124) and the prior infection group (n = 38), antibody levels of people with obesity were significantly lower compared to those in nonobese controls. When we compared the SARS-CoV-2 levels of adults (n = 38) and elderly (n = 47) in prior infection, the antibody levels of adults were found to be significantly higher. In the non-prior infection group, SARS-CoV-2 levels of adults (n = 124) were found to be statistical higher than that of elderly (n = 151) (Table 1).

There was no difference between antibody responses in 90 elderly patients and thirty-nine adults with obesity in the non-prior infection group. Antibody responses of 33 elderly patients with obesity and 9 adult patients with obesity were similar in the group with prior infection (Table 1).

Comparison between Sexes

There was no significant difference between the antibody levels of female (270; 95% CI, 200 to 365 AU/mL) and male (148; 95% CI, 73 to 330 AU/mL) in elderly individuals with obesity and non-prior infection. The result was similar in the nonobese group; there was no difference in antibody levels between females (298; 95% CI, 200 to 445 AU/mL) and males (270; 95% CI, 221 to 365 AU/mL).

In obese and prior infection elderly patients, there was no statistical difference between females' antibody levels (1,808; 95% CI, 897 to 3,640 AU/mL) and males' antibody levels (2,440; 95% CI, 1,096 to 4,916 AU/mL). There was no significant sex difference in antibody levels in nonobese patients: 1,808 (95% CI, 897–3,640) AU/mL in females and 2,440 (95% CI, 1,096–4,914) AU/mL in males.

In adults with obesity and non-prior infection, there was no significant difference between women's antibody levels of 221 (95% CI, 134–330) AU/mL and men's antibody levels of 330 (95% CI, 200–492) AU/mL. In nonobese patients, there was no statistical difference between women's antibody levels of 4,447 (95% CI, 3,640–5,431) AU/mL and men's antibody levels of 4,447 (95% CI, 2,697–7,731) AU/mL.

In obesity and prior infection adults, there was no significant difference between females' antibody levels of 2,208 (601–8,103, 95% CI) AU/mL and males' antibody levels of 1,408 (181–12,088, 95% CI) AU/mL. In nonobese individuals, there was no statistical difference between females' antibody levels of 7,331 (4,914–10,938, 95% CI) AU/mL and males' antibody levels of 5,431 (2,697–10,938, 95% CI).

Table 1. Vaccine response in elderly patients living with obesity

	Non-prior infection (n = 151)		Prior infection (n = 47)	
	BMI ≥30 (n = 90)	BMI <30 (n = 61)	BMI ≥30 (n = 33)	BMI <30 (n = 14)
Demographic, clinical, and laboratory characteristics of elderly (age ≥65 years)				
Age[a]	69±5	70±5[a]	67±4	66±5
Sex (F/M)*	66/24	25/36*	24/9	9/5
BMI*	35±5	25±2*	36±5	25±2
SARS-CoV-2 IgG*, [b]	221	298[a]	3,294	1,998
(95% CI), AU/mL	(164–298)	(221–365)	(2,208–4,447)	(1,211–3,640)
SCV*, n (%)	84 (93)	61 (100)[a]	33 (100)	14 (100)
	Non-prior infection (n = 124)		Prior infection (n = 38)	
	BMI ≥30 (n = 39)	BMI <30 (n = 75)	BMI ≥30 (n = 8)	BMI <30 (n = 30)
Demographic, clinical, and laboratory characteristics of adults (age 18–64 years)				
Age*	46±9	38±11[a]	42±7	42±11
Sex (F/M)*	20/20	68/16[a]	5/3	19/11
BMI*	33±3.5	23±2.7*	31±0.9	24±0.9
SARS-CoV-2 IgG*, [b]	270	4,447*	1,998±2.4	6,634±2.4
(95% CI), AU/mL	(200–365)	(3,640–5,431)	(897–4,023)	(4,914–8,955)
SCR*, n (%)	37 (94)	75 (100)[a]	8 (100)	30 (100)
	Non-prior infection (n = 275)		Prior infection (n = 85)	
	adults (n = 124)	elderly (n = 151)	adults (n = 38)	elderly (n = 47)
Demographic, clinical, and laboratory characteristics of adults (age 18–64 years) and elderly (age ≥65 years)				
Age*	41±11	70±5*	42±10	69±4
Sex (F/M)[a]	88/36	91/60	24/14	33/14
BMI*	26±5	31±6*	25±4	33±6
SARS-CoV-2 IgG*, [b]	1,808	244*	4,914	2,697
(95% CI), AU/mL	(1,480–2,440)	(200–298)	(3,640–7,331)	(1,998–3,640)
HT*, n (%)	8 (6)	36 (23)*	1 (2)	4 (8)
T2DM*, n (%)	5 (4)	49 (32)*	2(5)	15 (31)
SCR*, n (%)	122 (99)	145 (96)[a]	38 (100)	47 (100)

F, female; M, male; BMI, body mass index; SARS-CoV IgG (AU/ml), severe acute respiratory syndrome-coronavirus immunoglobulin G (arbitrary units per milliliter); HT, hypertension; T2DM, type 2 diabetes mellitus; SCR, seroconversion rate. * p <0.05 suggested statistical significance. [a] p >0.05 value, age, and BMI values are given as mean±standard deviation. [b]Geometric mean values are given.

Multivariate Regression and Correlation Analysis

In multivariate regression analysis, when the SARS-CoV-2 IgG level was regressed on age, sex, BMI, type 2 diabetes mellitus, and hypertension (HT), independent risk factors were found for HT on SARS-CoV-2 antibody levels (β = −2,730). Age and SARS-CoV-2 antibody levels were found to be highly correlated in correlation analysis for the group of elderly patients (r = −0.184).

Antibody Response according to BMI

In the non-prior infection group in the elderly, when the 3 groups were compared, no difference was found in terms of antibody levels (BMI 18.5–24.9 [n = 23]: 270 [95% CI, 200–403], BMI 25–29.9 [n = 38]: 270 [95% CI, 200–365], BMI >30 [n = 90]: 244 [95% CI, 181–298] AU/mL). In the non-prior infection group in the adults, when the 3 groups were compared, while no difference was found between normal weight and overweight individuals, a significant difference was found between normal weight individuals and obese patients, overweight and obese patients (BMI 18.5–24.9 [n = 55]: 4,914 [95% CI, 4,023–6,002], BMI 25–29.9 [n = 30]: 3,640 [95% CI, 2,697–4,914], BMI ≥30 [n = 39]: 270 [95% CI, 200–365] AU/mL).

Seroconversion Rates

In the non-prior infection group, the seroconversion rate (SCR) was significantly lower in the elderly population (96%) than in the adult population (99%). In the elderly population, the SCR was statistically lower in the obese (84%) than in the nonobese population (100%). In the adult population, the SCR was statistically lower in the obese (94%) than in the nonobese population (100%). The SCR was 100% in all groups compared with the prior-infection group (Table 1).

Discussion

The current literature has shown that antibody response after COVID-19 vaccination in PwO [11] and antibody response in elderly [12–14] are considerably lower than their nonobese or younger counterparts, respectively. In a study conducted in an adult population, antibody levels were found to be negatively correlated with age and BMI in individuals vaccinated with CoronaVac. In the same study, antibody levels were found to be lower in patients with cardiovascular disease and diabetes mellitus than in those without [15].

A study conducted with health care workers who were vaccinated with a single dose of BNT162b2, the antibody response of individuals under the age of 38 years was found to be higher than in those over the age of 56 years. Another result from this study was that the antibody response of normal weight individuals was higher than that of overweight individuals [16]. In another prospective study, cellular response and IgG levels of patients with severe obesity were found to be lower than other lower BMI categories in individuals vaccinated with two doses of BNT162b2 [17].

Our study is the first to demonstrate the post-vaccine antibody response to SARS-CoV-2 infection in elderly PwO. Elderly people with obesity generated significantly reduced antibody titers against SARS-CoV-2 spike antigen after CoronaVac vaccine compared to nonobese controls. Moreover, HT was shown to be a negative risk factor for antibody levels in elderly with obesity, and this was in alignment with the literature [18]. HT is associated with increased cardiometabolic complication, which negatively affects the immunological response to vaccination [18]. There is a study stating that antihypertensive drugs with sympatholytic effect can positively affect antibody responses after COVID-19 vaccine [19]. We showed that antibody responses of elderly with obesity who had no prior infection were significantly lower than those of nonobese elderly. However, in the prior infection arm, antibody levels in elderly people with obesity had an unprecedented higher antibody response, although insignificant, compared to nonobese controls. This may be attributed to the results being skewed due to small cohort size, the frequency of SARS-CoV-2 infection, and the length of time after infection in this group.

In the literature, it is known that cellular and humoral immunity are affected with aging. There is a decrease in T cell numbers, function, and lymphokine secretion with aging. Decreased cellular immunity increases susceptibility to viral infections. Antibody response to vaccines is also low as the ability to produce antibodies to a specific antigen decreases with age. At the same time, the protection of antibodies produced by B lymphocytes decreases [20]. In the study by Seyahi et al. [12], antibody responses were found to be lower in twenty-two elderly individuals after inactive COVID-19 vaccine compared to healthy adults. In a recent similar study, antibody responses were evaluated in individuals older than 80 years and younger than 60 years of age who received BNT162b2 vaccine. Antibody responses were found to be lower in elderly individuals compared to adults [13]. In a study conducted by Okyar-Baş et al. [21], no difference was found in terms of age in individuals vaccinated with CoronaVac when they compared the seropositive and seronegative groups.

In our study, adults generated a significantly higher antibody response than elderly in both non-prior and prior infection groups. In the study by Hammerman et al. [14], in patients with COVID-19 who were vaccinated with BNT162b2, the effectiveness of the vaccine was 60% in individuals aged 65 years and over, while it was 82% in individuals aged 16–64 years.

In a study by Zhang et al. [22], there was no significant difference in antibody levels between men and women vaccinated with CoronaVac. In another study, no statistical difference between the sexes was found in neutralizing antibody rates after inactivated SARS-CoV-2 vaccine [23]. Our results regarding both sexes were in alignment with both of these studies.

Conclusion

We recommend closer follow-up and additional dose of vaccination against COVID-19 in a population with numerous noncommunicable diseases and whose immune response may be compromised due to obesity and age, making them susceptible to infection and its consequences.

Limitations

A clear cut interpretation would have been made regarding the protection status of vaccines in patients with obesity compared to normal weight controls if the protective neutralizing antibody titers were known. Waist circumference measurement values or HOMA-IR results were not included in our study. The antibody levels of the patients were not checked before the vaccine was administered. The cellular immunity of the patients was not evaluated.

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Statement of Ethics

The study was approved by the local Institutional Review Board, the Ethics Committee of the Cerrahpasa Faculty of Medicine, reference date and number: 05.05.2021-90357, and was in accordance with the 1964 Helsinki Declaration and its later amendments or comparable ethics standards. Written informed consent was obtained from all participants.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

All the authors provided substantial contribution to the design and implementation of this study and to the generation of the manuscript. The contributions of each author are as follows: V.D.Y. and B.K. conceived the design and purpose of the work. Z.K., R.A., and H.Ö.D. analyzed the data. V.D.Y., Z.K., and A.N.D. interpreted the results based on the available literature and drafted the manuscript. V.D.Y. performed critical revisions. V.D.Y. and B.K. provided the final version of the article.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author. The data used and analyzed during the current scoping review are available from the corresponding author on reasonable request.

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