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Comparison of Antibody Responses Following Vaccination with AstraZeneca and Sinopharm

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ABSTRACT

Background: Vaccines are the most effective way to prevent Coronavirus 2 severe acute respiratory syndrome (SARS-CoV-2).

Objectives: To compare the antibody response of healthy individuals vaccinated with either the AstraZeneca (ChAdOx1 nCoV-19) or the Sinopharm (BBIBP-CorV) vaccine, in those who had no prior infection with SARS-CoV-2.

Methods: Thirty seven participants were included, of which 17 were administered the AstraZeneca (ChAdOx1 nCoV-19) vaccine, while 20 were given the Sinopharm (BBIBP-CorV) vaccine. SARS-CoV-2 neutralizing antibody and anti-receptor-binding domain (RBD) IgG levels were checked 4 weeks after giving the first and the second dose of either vaccine using the enzyme-linked immunosorbent assay (ELISA) technique.

Results: The AstraZeneca (ChAdOx1 nCoV-19) vaccine exhibited a higher levels of anti-(RBD) IgG compared with the Sinopharm (BBIBP-CorV) in both the first (14.51 µg/ml vs. 1.160 µg/ml) and the second (46.68 µg/ml vs. 11.43 µg/ml) doses. About neutralizing Abs, the titer of the antibody was higher in the AstraZeneca (ChAdOx1 nCoV-19) recipients than in the Sinopharm (BBIBP-CorV) subjects after the first (7.77 µg/ml vs. 1.79 µg/ml, P<0.0001) and the second dose (10.36 µg/ml vs. 4.88 µg/ml, P<0.0001).

Conclusions: Recipients vaccinated with two doses of the AstraZeneca (ChAdOx1 nCoV-19) had superior quantitative antibody levels than Sinopharm (BBIBP-CorV)-vaccinated subjects. These data suggest that a booster dose may be needed for the Sinopharm (BBIBP-CorV) recipients, to control the COVID-19 pandemic.

Keywords: COVID-19, Vaccine, Neutralizing antibody, Oxford-AstraZeneca, Sinopharm

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INTRODUCTION

Three novel coronaviruses, Coronavirus-Associated Severe Acute Respiratory Syndrome (SARS-CoV), Middle East Respiratory Syndrome Coronavirus (MERS-CoV), and Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), belong to β coronaviruses which cause human-to-human transmission and global pandemic (1). SARS-CoV-2 is an enveloped single-stranded positive-sense RNA virus that causes the pandemic of coronavirus disease 2019 (COVID-19) and results in millions of deaths across the globe (2). The genome of SARS-CoV-2 is almost 30 kb which encodes major structural proteins, including spike (S) protein, envelope (E) protein, membrane (M) protein, nucleocapsid (N) protein, and accessory proteins (ORF 3a, 6, 7a, 7b, 8, and 10) (3). The S protein is essential for the life cycle of SARS-COV-2 and is considered a major target antigen for vaccines against the virus. In the host cells, the spike protein is cleaved into S1 (receptor-binding domain (RBD)-containing) and S2 (non-RBD-containing) subunits (4). Neutralizing antibodies against S1RBD hinder interaction with angiotensin-converting enzyme 2 (ACE2) receptors, while those against S2 block membrane fusion between the viral envelope and the host cell membrane (5). Our information about SARS-COV-2 genome structure, the available clinical and pre-clinical data about SARS-CoV and also the results of MERS-CoV vaccination trials promise solutions for designing efficacious COVID-19 vaccines and SARS-CoV-2 vaccinations. Various forms of vaccine candidates targeting SARS-CoV-2 are classified as inactivated virus vaccines (Sinovac Biotech, Beijing, China; Sinopharm Beijing Institute of Biotechnology, Beijing, China; Bharat Biotech, Hyderabad, India), adenovirus type 5 (Ad5) vector vaccine (Cansino Biologics, Tianjin, China), Ad26-based vector vaccine (Janssen/Johnson & Johnson, Titusville, NJ, USA), the chimpanzee adenovirus vector vaccine (AstraZeneca, Cambridge, UK/Oxford University, Oxford, UK), Ad5 and Ad26-based vector vaccine (Gamaleya, Moscow, Russia), protein subunit based vaccines (Novavax, Gaithersburg, USA; Anhui Zhifei Longcom Biopharmaceutical, Ahui Zhifei, Longcom Biopharmaceutical, Hefei, China), mRNA vaccines (Moderna, Cambridge, US/NIAID, MA, USA; Pfizer, New York, NY, USA/BioNTech, Mainz, Germany), and DNA vaccines (Inovio Pharma, Missouri, MO, USA/International Vaccine Institute, Seoul, Korea) (6, 7).

COVID-19 vaccinations induce protective adaptive immunity, including specific T cell and B cell antibody responses (8). Specific antibodies such as IgM, IgG1, IgG3, and IgA mainly bind to the spike protein and can neutralize the fusion and entry of SARS-CoV-2 to the host cell. Therefore, these antibodies form the 'immunological memory' and could aid in preventing potential the COVID-19 virus (9). The serum concentrations of these antibodies can be analyzed to assess the efficiency of different types of vaccines. Therefore, in this research, we examined the concentrations of specific antibodies in participants who have been vaccinated with the AstraZeneca (ChAdOx1 nCoV-19) vaccine versus those who were vaccinated with the Sinopharm (BBIBP-CorV).

MATERIALS AND METHODS

Study Participants

The Sinopharm vaccine was given to 20 adults in two doses (BBIBP-CorV) (10 females and 10 males, mean±SD age of 35.15±5.79 years) and 17 individuals who had been vaccinated with the two doses of the AstraZeneca (ChAdOx1 nCoV-19) (10 females and 7 males, mean±SD age of 35.47±5.56 years) were enrolled in this study. Fresh blood (5 ml) was obtained from each participant 4 weeks after the administration of the first and the second doses of either COVID-19 vaccine. Before the trial, participants' informed permission was obtained.

Inclusion and Exclusion Criteria

We included individuals who had received two doses of the Sinopharm vaccine (BBIBP-CorV) or the AstraZeneca (ChAdOx1 nCoV-19) COVID-19 vaccines. A history of COVID-19 infection that was confirmed, as well as present COVID-19 infection were both exclusion criteria, in addition to a history of alcohol usage and smoking, infections with hepatitis viruses and HIV, people with autoimmune disorders and malignancies, those with a history of allergies or anaphylaxis, those immunocompromised, those taking corticosteroids, and the ones taking immunosuppressing drugs.

Laboratory Testing

Following the collection of venous blood samples from the people, SARS-CoV-2 neutralizing antibody and SARS-COV-2 anti-RBD IgG levels (Pishtaz Teb Diagnostic, Iran) were evaluated in serum using the enzyme-linked immunosorbent assay (ELISA) technique according to the company's specifications. The measurement of SARS-CoV-2 anti-RBD IgG and SARS-CoV-2 blocking antibody levels were performed by indirect and competitive ELISA, and the results were expressed in relative unit RU/ml and μg/ml, respectively.

Statistical Analysis

The data were represented as median and every statistical analysis was completed utilizing SPSS version 22 and Graphpad Prism version 8 software. We looked at the normality of the distribution of antibody concentrations using the Kolmogorov-Smirnov test, after which to compare variables between the two vaccine groups the Mann–Whitney U test was used. The potential for correlation between variables was assessed using the Spearman's rho method and linear regression analysis. Statistics were considered significant for the P values under 0.05. The following symbols were used to denote results that were statistically significant: *P<0.05, **P<0.01, ***P<0.001 and ****P<0.0001.

RESULTS

The SARS-COV-2 Anti-RBD IgG Antibody Level

The comparison of SARS-COV-2 anti-RBD IgG after the first and the second dose of vaccines showed that the median serum levels of anti-RBD IgG increased after the second dose of the Sinopharm (BBIBP-CorV) (11.43 μg/ml vs. 1.160 μg/ml, P<0.001) and the AstraZeneca (ChAdOx1 nCoV-19) (46.68 μg/ml vs. 14.51 μg/ml, P<0.001, Figure 1). Based on the type of the vaccine, the median serum levels of anti-RBD IgG were higher in the AstraZeneca (ChAdOx1 nCoV-19) recipients than in the Sinopharm (BBIBP-CorV) subjects after both the first and the next dose of vaccine (P<0.0001 and P=0.020, respectively, Figure 1).

The SARS-CoV-2 Neutralizing Antibody Level

Anti-SARS-CoV-2 blocking antibody concentrations were analyzed in both vaccinated groups in the study (Figure 2). As demonstrated, the median serum levels of an antibody that blocks SARS-CoV-2 were higher among those who received the two doses of the Sinopharm (BBIBP-CorV) and the AstraZeneca (ChAdOx1 nCoV-19) as compared with those who received one dose of either COVID-19 vaccines (10. 36 μg/ml vs. 7.77 μg/ml, P<0.001 and 4.88 μg/ml vs. 1.79 μg/ml, P=0.029, respectively, Figure 2). The amount of anti-SARS-CoV-2 neutralizing antibody in those who had received the first dose of the AstraZeneca (ChAdOx1 nCoV-19) was higher than in those who had received the first dose of the Sinopharm (BBIBP-CorV) (P<0.0001). In addition, increased anti-SARS-CoV-2 neutralizing antibody amount was shown in those cases who had received the second dose of the AstraZeneca (ChAdOx1 nCoV-19) as compared with the Sinopharm (BBIBP-CorV) subjects (P<0.0001).

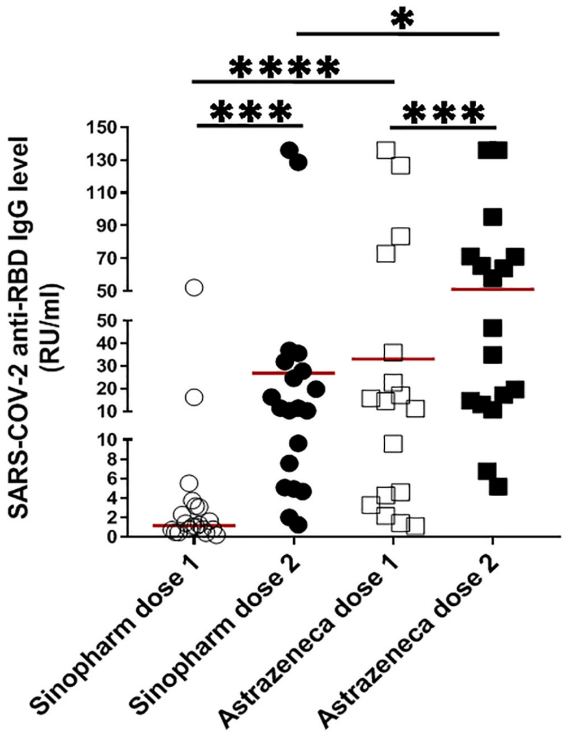

Figure 1. SARS-COV-2 anti-RBD IgG antibody level post AstraZeneca (ChAdOx1 nCoV-19) or Sinopharm (BBIBP-CorV) vaccination. Each symbol represents an individual; the median is represented by horizontal lines. *P<0.05, **P<0.01, ***P<0.001 and ****P<0.0001; Data analysis used the Mann–Whitney U test.

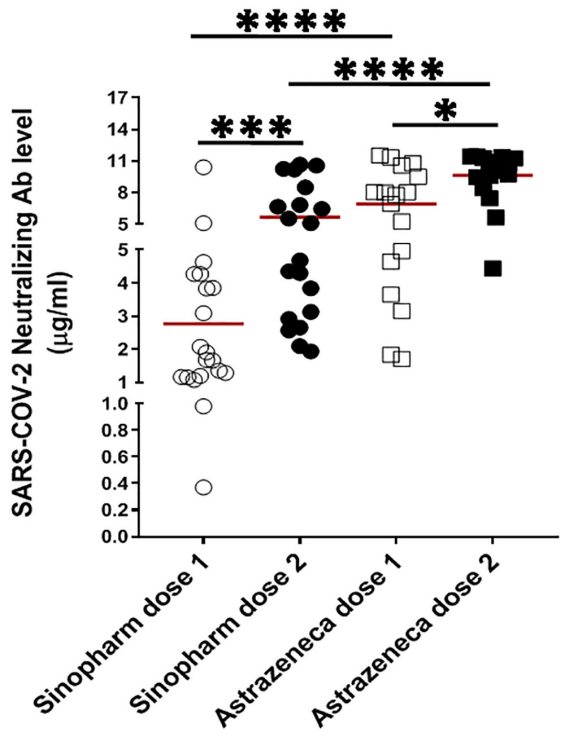

Figure 2. SARS-COV-2 neutralizing antibody level post-AstraZeneca (ChAdOx1 nCoV-19) or Sinopharm (BBIBP-CorV) vaccination. Each symbol represents an individual; the median is represented by horizontal lines. *P<0.05, **P<0.01, ***P<0.001 and ****P<0.0001; Data analysis used the Mann–Whitney U test.

Correlation of the Antibody Titer with Age and Sex

The correlation between the concentration of SARS-CoV-2 neutralizing antibody, SARS-COV-2 anti-RBD IgG, and the age and the gender of the participants were analyzed. The concentrations of SARS-CoV-2 neutralizing antibody negatively correlated with the age of the subjects who had received one dose and two doses of the AstraZeneca (ChAdOx1 nCoV-19) (P=0.031; r=−0.8149, Figure 3A and P=0.04; r=−0.5196, Figure 3B, respectively). Furthermore, there was a significant negative association between the levels of SARS-COV-2 anti-RBD IgG and the age of those who had received one dose and two doses of the AstraZeneca (ChAdOx1 nCoV-19) (P=0.01; r=−0.9011, Figure 3C and P=0.04; r=−0.5971, Figure 3D, respectively). There were no significant correlations between the concentrations of antibodies and the age of subjects who had received one dose or two doses of the Sinopharm (BBIBP-CorV) COVID-19 vaccine (Figure 4A-D). Furthermore, in both vaccinated groups, the levels of SARS-CoV-2 neutralizing antibody and SARS-COV-2 anti-RBD IgG were not associated with the gender of the participants, and no significant correlation was observed (Table 1).

DISCUSSION

COVID-19 is still an ongoing global pandemic and the world needs to be immunized against the virus with a vaccine to bring this pandemic to an end (10). Following SARS-COV-2 infection, adaptive immunity generates the receptor binding domain-neutralizing antibodies of the spike protein as well as nucleocapsid protein. In addition, most COVID-19 vaccines trigger neutralizing antibodies specific to the spike protein (11).

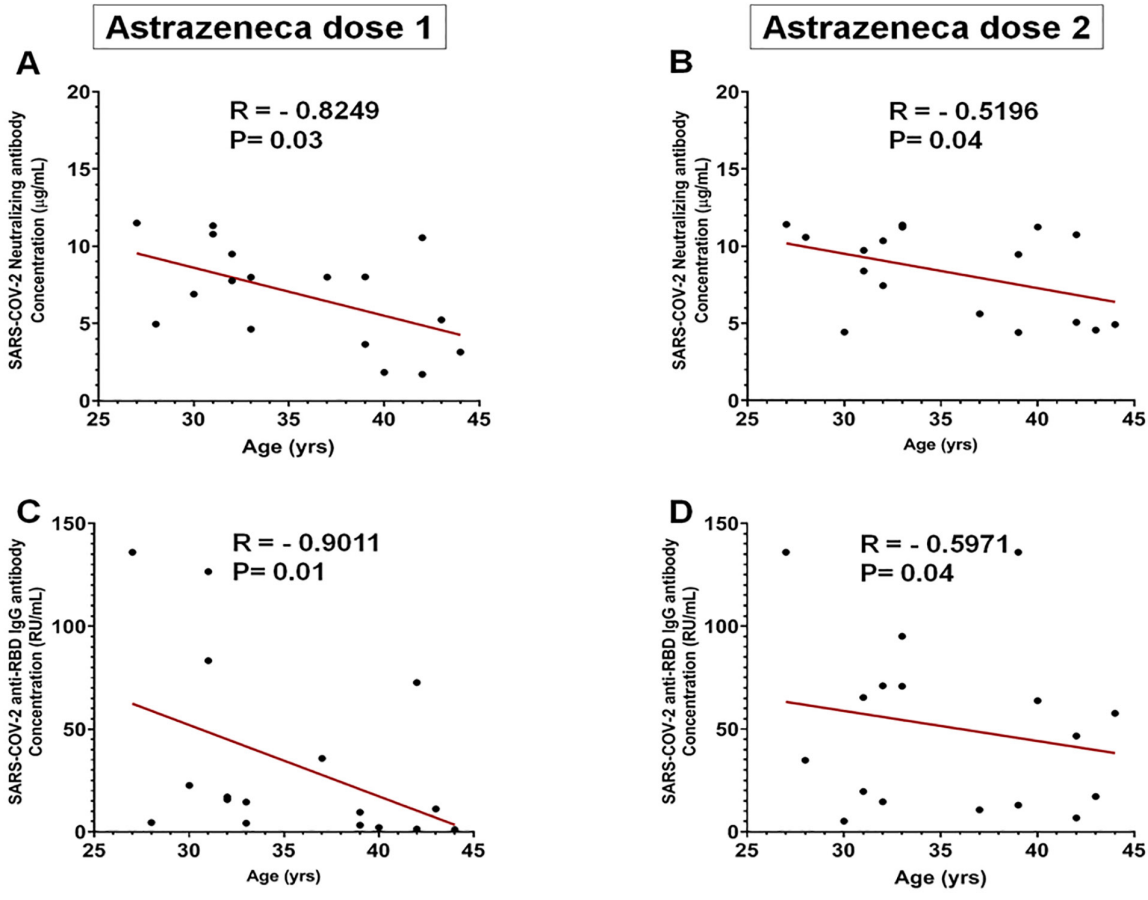

Figure 3. Correlation analysis. Correlation between the SARS-COV-2 neutralizing antibody level (A and B), and SARS-COV-2 anti-RBD IgG antibody level (C and D) with age in AstraZeneca (ChAdOx1 nCoV-19) vaccinated group (Spearman's rank correlation).

Table 1. Correlation of the Antibody Titer with the gender of participants

	Sinopharm dose 1		Sinopharm dose 2		Astrazeneca dose 1		Astrazeneca dose 2	
	r	P	r	P	r	P	r	P
Gender×SARS-CoV-2 neutralizing antibody level (µg/ml)	0.20	0.255	0.35	0.209	0.240	0. 27	0.220	0.33
Gender×SARS-COV-2 anti-RBD IgG antibody level (RU/ml)	0.054	0.166	0.35	0.209	0.241	0.26	0.054	0.186

The quality, quantity, and duration of the neutralizing antibodies following COVID-19 vaccination would be essential for the vaccine monitoring and design (12). The observation of the two studies on the inactivated vaccine and vector-based vaccine have revealed the mechanisms of these two types of vaccine to provoke humoral immunity. Their findings showed that after the vaccination an extreme expansion of long-lasting, isotype G switched IgG¶ memory B cells is detectable that lasts for at least 6 to 8 weeks. The dynamic pattern of memory B cells is similar to the subjects who were infected with SARS-CoV-2 (13, 14).

It is now well-known that the RBD within S1 is responsible for the SARS-COV-2 entry into the cells. Hence, antibodies directed against the RBD domain could inhibit the pathogen entry into target cells (15). In our study, we observed higher titers of SARS-COV-2 anti-RBD IgG antibody in those who had received one or two doses

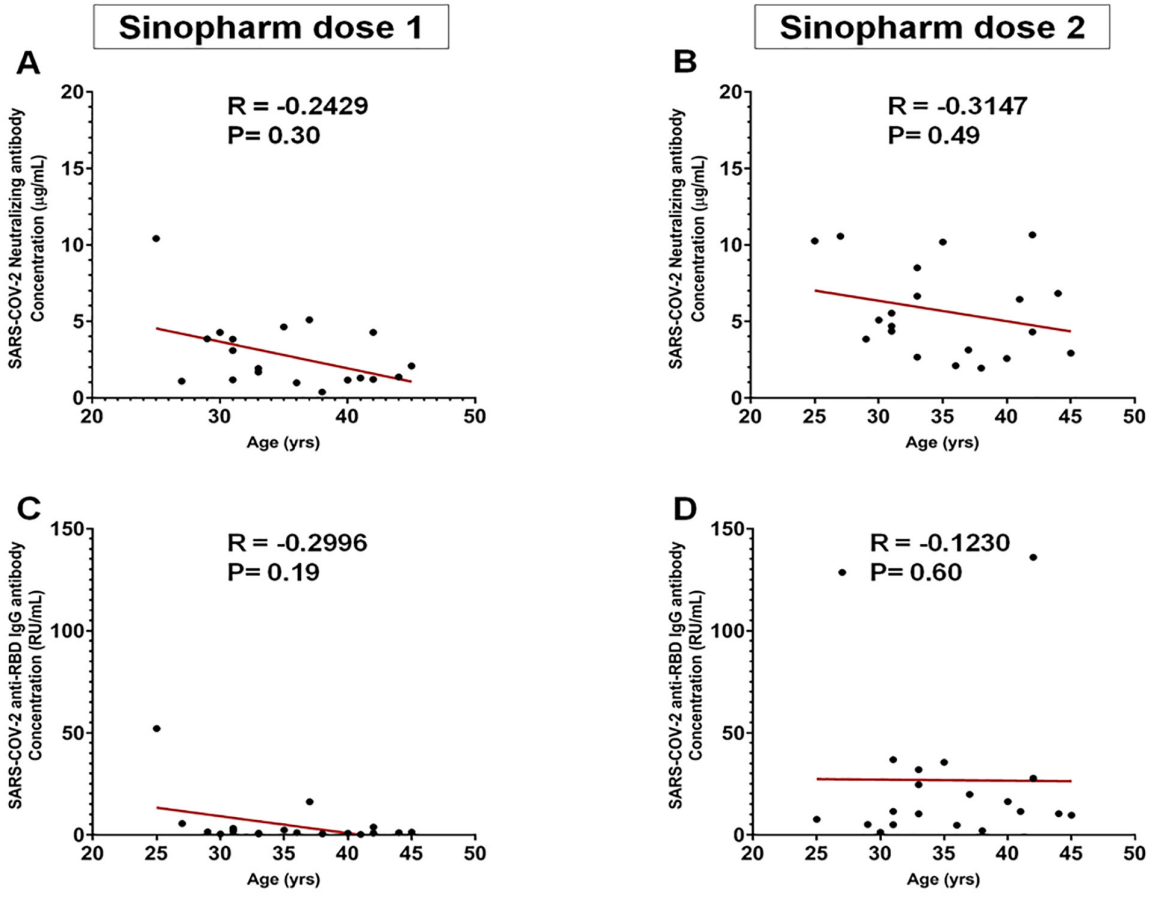

Figure 4. Correlation analysis. Correlation between the SARS-COV-2 neutralizing antibody level (A and B), and SARS-COV-2 anti-RBD IgG antibody level (C and D) with age in Sinopharm (BBIBP-CorV) vaccinated group (Spearman's rank correlation).

of the AstraZeneca (ChAdOx1 nCoV-19) compared with the Sinopharm (BBIBP-CorV) vaccinated participants. Consistent with our results, several previous studies demonstrated that a single dose of the AstraZeneca (ChAdOx1 nCoV-19) or Pfizer/BioNTec vaccine led to high anti-spike IgG antibody levels (16-18). In addition, higher anti-spike antibody response was observed in healthcare workers following the two doses of the AstraZeneca (ChAdOx1 nCoV-19) vaccines (19). In a recent work by Wei et al., the authors showed that two doses of either the AstraZeneca (ChAdOx1 nCoV-19) or the Pfizer SARS-CoV-2 vaccines, achieved high SARS-CoV-2 anti-spike IgG titers in adults who had no prior infection with the virus (20). Moreover, reactions of functional antibodies to a panel of nine antigens SARS-CoV-2 viral variant RBD proteins revealed that the Sinopharm (BBIBP-CorV) and Sputnik V vaccines induced low antibody amounts and RBD-ACE2 blocking activity in comparison with the AstraZeneca (ChAdOx1 nCoV-19) or Pfizer vaccines (21). Another study showed a higher titer of IgG among those who received Pfizer compared with the Sinopharm (BBIBP-CorV) subjects (22). Therefore, our results may indicate that a higher level of neutralizing and SARS-COV-2 anti-RBD IgG antibodies post-AstraZeneca (ChAdOx1 nCoV-19) vaccination can provoke stronger and potent protection against SARSCoV-2 as compared with the Sinopharm (BBIBP-CorV) vaccine.

Afterward, we evaluated the SARS-CoV-2 neutralizing antibody levels, as a possible indicator of disease immunity in individuals who received the Sinopharm vaccine (BBIBP-CorV) or the AstraZeneca (ChAdOx1 nCoV-19). Our findings demonstrated that the vector-based AstraZeneca had a greater quantitative

efficiency. (ChAdOx1 nCoV-19) COVID-19 vaccine over the classic Sinopharm (BBIBP-CorV). Following the first and the second doses, the AstraZeneca (ChAdOx1 nCoV-19) vaccine resulted in a higher neutralizing antibody concentration than in the Sinopharm (BBIBP-CorV) vaccine in the participants. This result is consistent with the earlier research that indicated people, who had received either the AstraZeneca (ChAdOx1 nCoV-19) or Pfizer vaccine, had developed neutralizing antibodies approximately 30 days after their first dose, and those antibody levels rose more quickly after the second dose of either vaccine (23). Another study revealed a positive rate of neutralizing antibodies among 127 Ad5-nCoV (CanSino) vaccinated participants (24). It is also reported that the mRNA-1273 vaccine stimulates neutralizing antibodies against A.1, B.1, B.1.1.7, and N501Y variants of SARS-COV-2 (25). Individuals with prior COVID-19 have been observed to have a larger percentage of neutralizing antibodies after receiving the Ad5-nCoV vaccine than in those without prior COVID-19. (26). A recent study also indicated that the administration of the two doses of the Corona vaccine or one dose of the BNT162b2 vaccine in individuals without SARS-COV-2 infection elicited neutralizing antibodies similar to individuals with prior infection (27). Khoury et al. illustrated that the mean neutralization level of the Pfizer vaccination was higher than in the mean convalescent level, while the Sinovac vaccine, which is similar to the Sinopharm (BBIBP-CorV), had a mean neutralization level below the convalescent mean. Their findings implied that higher neutralizing antibody titers confer stronger and more durable protection against COVID-19 (11).

On our side, we found a negative correlation between the levels of both antibodies and the age of participants who were vaccinated with the AstraZeneca (ChAdOx1 nCoV-19). A recent study on the correlation of age with SARS-CoV-2 antibody response quantity and quality revealed that the SARS-CoV-2 IgG level negatively correlated with the age in young adults aged between 19 and 24 years (28). Furthermore, lower SARS-CoV-2 anti-spike IgG titers were reported in individuals aged 60 years and vaccinated with the AstraZeneca (ChAdOx1 nCoV-19) (20). Also, it has been found that older people had lower serum IgG or IgA neutralization levels after receiving the first Pfizer vaccination dose, specifically in participants over eighty years old (29). Another study showed a negative association between the age and IgG titers after the second Sinopharm (BBIBP-CorV) vaccine dose among subjects aged 60 years compared with those aged between 40 and 60 years (22). Moreover, a negative relationship was reported between the levels of neutralizing antibodies and the age of uninfected participants who had taken two Pfizer or Moderna dosages (30). Both our results and the previous findings indicated that old age is associated with lower humoral immune response, suggesting the effect of age on vaccine-induced immunity.

Furthermore, we examined the association of SARS-COV-2 anti-RBD IgG antibody as well as neutralizing antibody levels with the gender of individuals who had received one or two doses of the AstraZeneca or the Sinopharm vaccines. Our results did not show any significant correlations between the levels of both antibodies and the gender of participants of the post-vaccination with either the AstraZeneca or the Sinopharm. However, previous studies reported an association between the concentrations of neutralizing antibodies and gender following COVID-19 immunization or spontaneous SARS-COV-2 infection (15, 31-33). This discrepancy may in part be because of the small sample size and thus further large-scale studies are required to determine the association between SARS-COV-2 anti-RBD IgG antibody and, moreover, to neutralize the antibody levels and gender of participants who were vaccinated with the AstraZeneca (ChAdOx1 nCoV-19) or the Sinopharm (BBIBP-CorV) vaccines.

There are a few other restrictions in this study. First, the study only had a small number of participants. Second, just one post-

vaccination sample collection was done (4 weeks). As a result, the study is unable to shed light on antibody degradation.

CONCLUSION

Our findings point to greater quantitative efficiency of the vector-based AstraZeneca (ChAdOx1 nCoV-19) COVID-19 vaccine over the classic inactivated Sinopharm (BBIBP-CorV). We thought this is the first trial to compare SARS-CoV-2 neutralizing antibody and SARS-COV-2 anti-RBD IgG levels between the vector-based vaccine and inactivated virus vaccine in the healthy participants without prior COVID-19 infection. Our study suggests that booster vaccination is needed for subjects who have had the Sinopharm (BBIBP-CorV) vaccine. To get a better knowledge of the protective antibody levels over time, additional large-scale studies are necessary to evaluate the serial titer levels across a wide timeframe.

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Conflict of Interest: None declared.

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