

Antibody Response to Sars-CoV-2 in Adults After 18 Months of Second Dose Vaccination of Astra Zeneca

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Abstract. Vaccination is one of the methods of preventing SARS-Cov-2 infection. Although the efficacy of several vaccines has been observed, it is unknown how long the antibodies remain in the body. The purpose of this study was to examine the antibody titers in adults, 18 months after receiving two doses of the Astra Zeneca vaccine. This is a cross-sectional study with adult subjects who received two doses of the Astra Zeneca vaccine in the Bogor area, conducted in 2023. To evaluate antibody titers (IgG) in serum specimens, the Chemiluminescent Microparticle Immunoassay (CMIA) method was utilized. The antibody titer ≥ 50.0 AU/mL was considered positive. The characteristics 122 subjects were mostly: female (63,1%), 36-45 years old, senior high school graduate (45.9%), unemployed (62,3%), had hypertension history (44.7%), and had no COVID-19 infection during the last six months. The results demonstrate that all the subjects had a positive SARS Cov-2 antibody titer, with a range titer of 87 - 80260 AU/mL and a geometric mean titer of 3246.4 AU/mL. In conclusion, this study found that the two doses of the Astra Zeneca vaccine made a significant contribution to the acquisition of anti-SARS-CoV-2S antibodies in adults. Keywords: antibody response, SARS-CoV-2; vaccination, Astra Zeneca

1 Introduction

A cluster of pneumonia patients with an unknown cause emerged in Wuhan, Hubei Province, China, at the end of 2019. Since then, more than 80,000 laboratory-confirmed cases (as of March 23, 2020) have been reported across mainland China as a result of outbreaks and sporadic human infections [1]. Then the World Health Organization (WHO) declared a Public Health Emergency of International Concern (PHEIC) on January 30, 2020, and characterized the outbreak as a pandemic on March 11, 2020, following an outbreak of emerging severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) disease (COVID-19) in China [2].

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In Indonesia, the first two confirmed cases of COVID-19 infection were announced on March 2nd 2020. As of March 27, 2020, the government reported 893 confirmed cases, 78 deaths, and 35 recoveries from 27 provinces [3]. Recently, a steady decrease in the number of COVID-19 patients was reported by the WHO. As of February 4, 2024, there were 774 million confirmed cases of COVID-19, with a global death toll of seven million. The number of cases declined among patients who were hospitalized at the hospital and required intensive care unit (ICU) treatment [4]. The majority of patients have decreased risks of serious illness and death since the current COVID-19 virus variants tend to induce less severe disease and boost immune levels as a result of vaccination.

The antiviral of nirmatrelvir/ ritonavir (brand name Paxlovid) was first recommended by the WHO in April 2022. This antiviral is not only given its therapeutic benefits but also ease of administration and fewer concerns about potential harms [5]. The ongoing development of new treatments for COVID-19, despite the introduction of various therapeutic strategies, faces a significant challenge due to the increasing number of SARS-CoV-2 mutations and new variants [6].

However, in clinical practice, symptomatic treatment strategies are advised and vaccination is likely the most effective method to prevent and control COVID-19 infection. This is because the spread of COVID-19 is very fast, therefore an effective and safe vaccine is needed [7]. Until 2022, the Indonesian Food and Drug Administration has granted emergency use permits for 13 types of COVID-19 vaccines, 10 of them are Sinovac, AstraZeneca, Sinopharm, Moderna, Pfizer, Novavax, Sputnik-V, Janssen, Convidencia, and Zifivax. However, due to vaccine availability at the start of the pandemic in Indonesia, the two first vaccines (Sinovac and Astra Zeneca) were used for the community [8].

AstraZeneca is one of the COVID-19 vaccines with a viral vector (adenovirus) type [9]. The University of Oxford and AstraZeneca, a British Swedish pharmaceutical corporation, collaborated to develop ChAdOx 1nCoV19, a nonreplicating chimp AstraZeneca vaccine known as AZD1222 [10]. The WHO reported a vaccine efficacy of 63.09 % for the AstraZeneca/Oxford vaccine, ChAdOx 1S (recombinant) [9].

Several studies reported a decrease in immunity to the COVID-19 vaccines after several periods. Levin E.G. et al. (2021) described a reduction in humoral response in individuals who had received a second dose of the BNT162b2 vaccine (Pfizer-BioNTech) in Israel, especially in males, among people aged 65 years and over and those who were immunosuppressed [11]. Similar results were obtained in a study conducted on 231 health workers in Belgium who also had received two doses of the BNT162b2 vaccine regimen (Pfizer-BioNTech) [12]. Furthermore, a study of the Coronavac vaccine clinical trial conducted in China showed a decrease in neutralizing antibody titers after 6–8 months of administration of two doses of the vaccine [13]. These results are comparable to those reported by a study conducted in Thailand, which showed a decrease in antibody titers 3 months after administration of two doses of Coronavac [14]. The decline in immunity following the COVID-19 vaccination raises the question of whether the government should implement measures connected to the status of immunity in society. Therefore, the study's goal was to assess antibody response 18 months after receiving two doses of the Astra Zeneca vaccine administered in 2021. Figures and tables

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2 Materials and Methods

2.1 Design and sample

This research is a cross-sectional study, a follow-up to the previous studies conducted in the Bogor district in 2021 and 2022. The ethical approval was obtained from the health ethics commission of the National Research and Innovation Agency, no 032/KE.03/SK /04/2023. Data collection was carried out by interviews and blood sampling 18 months after the 2nd dose of vaccination. Blood collection of 3 ml was conducted aseptically by experienced phlebotomists. The research subjects were those who met the inclusion criteria, namely: age 18 years or more, had participated in previous studies (in 2021 and 2022), had received 2 doses of the Astra Zeneca vaccine in the 2021 study, could have blood drawn based on a doctor's examination and were willing to participate in this research by signing the informed consent. The number of initial study subjects (2021) was 150 subjects then it reduced to 122 subjects in 2023. All subjects who met the inclusion criteria were included in the 2023 study regardless of the booster immunization status obtained.

2.2 Sample examination

For serum separation, collected blood was centrifuged at 8000 rpm for 10 minutes. The serum was then tested for antibodies (IgG) against SARS Co-2 using the Chemiluminescent Microparticle Immunoassay (CMIA) method with the SARS-CoV-2 IgG II Quant reagent Kit (Abbott, Diagnostics Division, Sligo, Ireland). Antibody testing was carried out at RSUD Ciawi Bogor due to the equipment's availability. The Chemiluminescent Microparticle Immuno Assay is an improved version of the Enzyme-Linked Immuno Sorbent Assay (ELISA). Anti-SARS Cov-2 detection used bound achridinylated conjugates to generate chemiluminescent signals in the final reaction. The software then generated the results automatically by comparing the chemiluminescent signals obtained from the sample's reaction product with the signal of the cutoff value previously obtained by Anti SARS-Cov2 calibration. All stages of antibody testing adhere to the procedures included in the kit. The antibody titer against SARS CoV-2 of 50 AU/mL and more was considered positive.

2.3 Data analysis

Data were analyzed descriptively using univariate SPSS tools and Excel to determine the antibody titer 18 months after the administration of the second dose of the Astra Zeneca vaccine. The mean antibody titer is expressed by the geometric mean titer (GMT).

3 Results

A total of 122 subjects participated in this study, mostly consisting of: women (63.9%), age range 20-65 years with the highest proportion in the age group 36-45 years (40.2%), graduated from senior high school (45.9%), not working or as a housewife (62.3%), and have a history of hypertension (44.7%). Related to the government's policy for administering vaccine boosters, 67.5% of subjects had received the first dose of the booster vaccine but none had received the second dose. As many as 1.6% did not know the booster status. All subjects claimed not to have been infected with COVID-19 in the last 6 months (Table 1). The results of the antibody examination showed that all subjects had a positive titer against SARS Cov-2 (100%), with a minimum titer of 87 AU/mL, a maximum titer of 80260 AU/mL, and a geometric mean titer of 3246.4 AU/mL (Table 2).

Table 1. Characteristics of subjects who received two doses of the Astra Zeneca vaccine

Characteristics of the subjects	n	%
Sex		
Male	44	36.1
Female	78	63.9
Age groups (years)		
18-25	9	7.4
26-35	7	5.7
36-45	49	40.2
46-55	44	36.1
56-65	13	10.7
Range	20 - 65	
Last Education		
Not Graduating from Elementary School	7	5.7
Elementary School	25	20.5
Junior High School	33	27.0
Senior High School	56	45.9
University	1	0.8
Occupation		
Student	1	0.8
Private sectors	7	5.7
Unemployed/ housewife	76	62.3
laborer	37	30.3
others	1	0.8
Comorbidities history		
Hypertension	54	44.7
Diabetes Mellitus	6	4.7
Chronic Gastrointestinal	5	4.0
Asthma	2	2.0
Obesity	18	14.7
Booster vaccine status		
No booster	40	32.8
first booster	80	65.7
second booster	-	-
unknown	2	1.6
COVID-19 infection in the last 6 months		
Yes	-	-
No	122	100

Table 2. The antibody titers for SARs Cov-2 after 18 months of receiving two doses of the Astra Zeneca vaccine

Variable	Result
Positive titer antibody*	100%
Min titer	87 AU/mL
Max titer	80260 AU/mL
GMT	3246.4 AU/mL
n	122

*Positive titer ≥ 50 AU/mL

The minimum antibody titers in subjects who had not received the first booster dose and those who had received the first booster dose were nearly identical, but the maximum titers in subjects who had received the first booster dose were nearly double (42343.6 AU/mL vs 23459.1 AU/mL). GMT was also higher in subjects who had not received a booster than in those who had (3607.48 AU/mL vs 2984.74 AU/mL). The subjects with unknown booster status had the highest GMT of 11353.66 AU/mL among the three booster statuses, but there were only two of them (Table 3.).

Table 3. The antibody titers for SARs Cov-2 after 18 months of receiving two doses of the Astra Zeneca vaccine based on the booster status

Booster status	Min titer (AU/mL)	Max titer (AU/mL)	GMT AU/mL)	n (%)
No booster	87	23459.1	3607.48	40 (32.8)
First booster	98.9	42343.6	2984.74	80 (65.7)
unknown	1606.1	80260.0	11353.66	2 (1.6)

4 Discussion

The results showed that 18 months after two doses of vaccination with the Astra Zeneca vaccine, all subjects (122 subjects) had positive titers (titers ≥ 50 AU/mL) with a titer range of 87 - 80260 AU/mL and GMT (3246.4 AU/mL). This finding demonstrates that antibodies remain in the body 18 months after the second dose of Astra Zeneca vaccination. However, two subjects had antibody titers of less than 100 AU/m.

The Astra Zeneca vaccine is an adenovirus type, not a live virus vaccine, so it can be used to vaccinate people who have been infected with COVID-19 at intervals of at least 3 months, pregnant or lactating women (by considering the benefits and risks that may arise), and the subjects aged 18 years and over [15]. Considering the availability of the vaccines, the Astra Zeneca vaccine (ChAdOx1-S, recombinant) was used at the beginning of the COVID-19 pandemic in Indonesia.

Although all subjects had positive antibodies, not entirely derived from the primary two doses of the Astra Zeneca vaccine alone, because most of the subjects had received the first booster vaccine dose. Booster vaccinations would boost immunity for the majority of individuals whose humoral response declines or weakens following the second dose of the initial immunization, particularly 28 days following the booster dosage [16]. Vaccination with both vaccines substantially increased T-cell responses, anti-spike IgG responses, and neutralizing antibodies against ten SARS-CoV-2 variants in recovered subjects, and these responses were sustained for 7 months [17]. In addition, the antibody titers were stable after the third vaccination over a one-month follow-up period, while they demonstrated a tendency to drop after the second vaccine [18].

In Indonesia, the government's policy of administering two booster vaccine doses began to be implemented on January 12, 2022. The implementation of booster vaccines is carried out independently with priority at the age of over 18 years and intervals of 6 months or more after the second dose of vaccination. Although none of the subjects received the complete booster dose, most of the subjects had received the first dose of the booster vaccine. The type of booster vaccine given could be homologous or heterologous with the two previous doses of vaccine, the choice of booster vaccine type is adjusted according to established guidelines [19]. There are 5 types of vaccines used as boosters for the COVID-19 vaccine in Indonesia, namely CoronaVac, Pfizer, AstraZeneca, Moderna, and Zifivax.[20].

The subject's confession and/or vaccination support data were used to determine booster status. However, two participants had uncertain booster status since they did not recall and did not provide immunization documents. Similarly, the history of COVID-19 infection in the six months preceding data collection is solely reliant on subject recognition. Subjects who had gotten the initial booster showed higher antibody titers, but lower GMT values than subjects who had not had a booster. This fact could be due to several factors, including the fact that the range of antibody titers in subjects who have received boosters is wider, the distribution of antibody titers may be clustered at a certain value, the proportion of subjects is not the same (80 vs 40), the possibility of subjects having been infected with COVID-19 in the previous six months, and the presence of comorbid diseases. Some COVID-19 disease symptoms mirror the flu disease, consequently, laboratory tests are required to confirm the COVID-19 infection. Hence, all data linked to the history of COVID-19 infection is based on the subject's confession. COVID-19 infection is caused by a coronavirus that takes longer to develop symptoms or is asymptomatic, can be more severe, and is contagious for a longer period [21].

Several studies describe that immune response to vaccines can vary between individuals. However, immune responses can be greatly influenced by vaccination type and personal health. When healthy people are exposed to mRNA vaccines or adenovirus vectors, their B and T cells begin producing antibodies earlier than usual. However, those who were unwell had a higher chance of suffering negative outcomes as a result of relapses in their pre-existing diseases. When combined, matching the appropriate vaccination to a patient's condition can lead to improved results [22]. The age factor is known to be associated with the risk of severity and antibody formation in COVID-19. For example, a study in Japan revealed that among fully vaccinated patients, vaccine effectiveness against death was 88.6% among patients 60–69 years of age. The effectiveness tends to decrease as the patient ages [23]. The highest proportion of seropositivity and antibody titers were found in the 18-30 years age group, and then decreased in the older age, particularly after the first dose of vaccination [24]. In addition, children under 10 years have lower SARS-CoV-2 infection susceptibility compared to younger/middle-aged adults, while adults over 60 years have higher susceptibility and require additional protection measures [25, 26].

The female sex is known to produce higher humoral and cellular immune responses when infected with disease or through vaccination [27]. Based on a study in France in 2020, it was found that young women have higher antibody titers against COVID-19 than older [28]. A history of comorbidities increases the risk of death from COVID-19, such as hypertension or diabetes mellitus, and is more likely to develop a more severe course and progression of the disease [29]. Blood pressure also strongly correlates with an antibody titer after the second vaccination of the Astra Zeneca vaccine [30]. This finding is because most antibodies target receptors and ion channels involved in blood pressure, and there was evidence of a link between increased antibodies and pregnancy-related hypertension [31].

Compared to a similar study of Astra Zeneca vaccination conducted in Indonesia, this study of antibody titers 18 months after two doses of the Astra Zeneca vaccine remains high, even with no booster vaccination (3607.48 AU/mL). A study by Lukas S et al (2023) in

Jakarta reported that a month after the second dose of Astra Zeneca vaccination, the average antibody titer by CLIA method was above 200 U/mL, the highest value in the age group 56-55 years, but then decreased to 188 U/mL in subjects over 55 years old. That study recorded that age and physical exercise are the two factors that influence antibody response [30]. It is supported by another study that factors such as age, gender, and the intensity of physical activity influence the immunological response to COVID-19. It is advisable to follow long-term, moderate protocols for physical exercise since they are regarded as the most recommended. It is important to carefully evaluate these factors when assessing the immune response to COVID-19 [32].

5 Conclusion

In conclusion, the antibody level 18 months after two doses of the Astra Zeneca vaccination remains positive with a fairly high average titer in adults. However, with the emergence of new variants of the COVID-19 virus, protective antibodies are required. Booster with the homolog or heterology vaccines is expected to protect against COVID-19 infection that may occur in the future.

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