

Effectiveness of COVID-19 Vaccine on Augmenting Antibody Level in People in the Special Region of Yogyakarta, Indonesia

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ABSTRACT

Background: Immunity against SARS-CoV-2 is needed to prevent infection so vaccines are indeed humanity's great hope as a weapon to control COVID-19. Seroprevalence data is needed using an antibody test that estimates the percentage of DIY residents who have antibodies against SARS-CoV-2. This study aimed to determine the effectiveness of COVID-19 vaccination on enhancing antibody titers.

Subjects and Method: This was a retrospective cohort study conducted in Yogyakarta, Indonesia, from 19 to 30 November 2021. The study population was people aged ≥ 1 year. A total of 563 study subjects was selected randomly. The dependent variable was the SARS-CoV-2 antibody titer level. The independent variables were COVID-19 vaccination status, gender, age, smoking, outdoor activities, and alcohol consumption. SARS-CoV-2 antibody level was measured using Roche's Elecsys anti-SARS-CoV-2. Other variables were collected using questionnaires. Data were analyzed using a multiple linear regression run on STATA 14.

Results: The initial vaccination led to an elevation in -19 antibody titers, but it was statistically non-significant ($b = 697.82$; 95% CI = -720.90 to 1241.24; $p = 0.603$). The second vaccination resulted in a notable and statistically significant elevation of COVID-19 antibody titers ($b = 1331.38$; 95% CI = 802.30 to 1860.46; $p < 0.001$).

Conclusion: The second dose of the COVID-19 vaccination demonstrated significant effectiveness in boosting COVID-19 antibody titers.

Keywords: COVID-19, vaccination, antibody

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BACKGROUND

Coronavirus disease 2019 (COVID-19) is a disease caused by the coronavirus, which causes severe acute respiratory syndrome and spreads rapidly. The World Health

Organization declared the COVID-19 outbreak a global pandemic on March 11, 2020 (Tatsukawa et al., 2022). To date, the number of confirmed COVID-19 cases as of November 2022 is 6,502,659 cases in Indo-

nesia, and 43,450 cases in the Special Region of Yogyakarta. The recovery rate in the Special Region of Yogyakarta is 94.6%. The death rate was 1.3% in the Special Region of Yogyakarta. Meanwhile, for vaccination, 41 percent of the total of around 352,000 DIY residents aged 12 years and over have been vaccinated. (Yogyakarta Responds to COVID-19, 2022)

Vaccination has been adopted as the main public health strategy to combat the COVID-19 pandemic (Bello et al., 2023). Immunity against SARS-CoV-2 is needed to prevent infection, especially in high-risk groups, namely the elderly, health workers and people with comorbidities. Infection in humans by pathogens results in a history of infection by the immune system called immunological memory, immunological memory protects individuals from infection.

The antibody response formed after vaccination varies. In the inactivated virus vaccine model the antibody response occurs in 14-21 days, for the mRNA vaccine model the anti-body response occurs in 21-28 days, for the viral vector vaccine model the antibody response occurs in 28 days, and for the protein subunit vaccine model it occurs in 21 days. Several demographic characteristics, including age, gender, and body mass index (BMI), play an important role in the development of immunity after vaccination (Pellini et al., 2021).

Until now no seroprevalence data is using an antibody test that estimates the percentage of DIY residents who have antibodies to SARS-CoV-2. This research aimed to determine the seroprevalence of COVID-19 in the DIY area with antibody testing and the effectiveness of giving COVID-19 vaccination on increasing antibody titers formed in the people of the DIY area. The results of the research are expected to help the government in the COVID-19 serosurvey to find out the percentage of the

DIY people who have antibodies against SARS-CoV-2 which can then be used as a basis or reference in creating programs and evaluating COVID-19 vaccination.

SUBJECTS AND METHOD

1. Study Design

This was a retrospective cohort study conducted in the Special Region of Yogyakarta, Indonesia, in November 2021.

2. Population and Sample

The study population was people living in Yogyakarta aged ≥ 1 year old. Total sample of 563 people was selected randomly.

3. Study Variables

The dependent variable was the SARS-CoV-2 antibody level. The independent variables were COVID-19 vaccination status, gender, age, smoking, outside activities, and alcohol consumption.

4. Conceptual Definition

SARS-CoV-2 Antibody Levels. Samples in the form of serum and plasma from participants were identified and analyzed with Elecsys anti-SARS-CoV-2 Roche to quantitatively measure antibodies of SARS-CoV-2 receptor binding and S protein, the measuring tool used by Elecsys anti-SARS-CoV-2 2 Roche, Units 0.40–250 U/mL (can be increased to 2,500 U/mL with 1:10 dilution).

Vaccination Status. The condition of the administration of the COVID-19 vaccine that has been carried out on research subjects as proven by data or certificates through the Care Protect application.

Age. A unit of time that measures the time a person has existed which is calculated from the time of birth to the time of research.

Gender:. Biological differences between men and women since birth.

Alcohol consumption. People consume 1–2 glasses of alcoholic drinks a day.

Smoking. People who smoke cigarettes regularly, even if only 1 cigarette a day.

Outdoor Activities. People go out or do activities outside the home to meet people.

5. Study Instruments

COVID-19 antibody level was measured using Roche's Elecsys anti-SARS-CoV-2 method. Other variables were collected using questionnaire.

6. Data Analysis

Univariate analysis was described using Mean and SD. Data were analyzed using a multiple linear regression.

7. Research Ethics

Ethical approval for this study was granted by the Health Development Policy Agency, Indonesian Ministry of Health. The reference number: LB.02.01/2/KE.640/2021.

RESULTS

1. Univariate Analysis

Table 1 described sample characteristics. Table 1 presents the age-related statistics, indicating a mean age of 39 years (Mean= 39.35; SD= 21.04), with ages ranging from 2 to 93 years.

Table 1. Sample characteristics of continuous data (N=563)

Variables	Mean	SD	Min.	Max.
Age (years)	39.35	21.04	2	93
Antibody titer not yet vaccine	275.34	489.71	0.40	2614
1 st vaccine antibody titer	877.86	1603.86	0.40	8710
2 nd vaccine antibody titer	1591.22	2950.34	4.93	25001

Table 2 indicates that the majority of study subjects have received up to dose 2 (71.76%). The proportion of male and female is equal. More than 50% of participants do not smoke. During the pandemic, 92.54% of

participants were active outside the home. People who did not consume alcohol were 95.56%. Notably, 91.12% of COVID-19 patients tested positive for antibodies.

Table 2. Sample characteristics of categorical data (N=563)

Characteristics	Category	Frequency	Percentages
Vaccine status	Not Vaccinated	125	22.20%
	Vaccine 1	34	6.04%
	Vaccine 2	404	71.76%
Gender	Male	280	49.73%
	Female	283	50.27%
Smoke	Do not smoke	332	58.97%
	Smoker now	139	24.69%
	Former smoker	92	16.34%
Outside activities	Indoor activities	42	7.46%
	Outdoor activities	521	92.54%
Alcohol consumption	No	538	95.56%
	Yes	25	4.44%
Antibody Status	Positive	513	91.12%
	Negative	50	8.88%

2. Multivariate Analysis

2nd dose of COVID-19 vaccine significantly elevated COVID-19 antibody levels (b=

1331.38; CI 95%= 802.30 to 1860.46; p<0.001).

Table 3. Results from multiple linear regression analysis assessing the impact of COVID-19 vaccination on antibody titers.

Independent Variable	b	95% CI		P
		Lower Limit	Upper Limit	
Not vaccinated	260.17	-720.90	1241.24	0.603
1 st dose of COVID-19 vaccine	697.82	-278.05	1673.7	0.161
2 nd dose of COVID-19 vaccine	1331.38	802.30	1860.46	<0.001
Female	-378.58	-906.53	149.38	0.160
Age (years)	2.97	-7.34	13.29	0.572
Current smoking	-324.54	-959.43	310.35	0.316
Former smoker	332.69	-492.84	1158.21	0.429
Outdoor activities	164.51	-651.99	981.00	0.692
Alcohol consumption	-622.69	-1682.07	436.68	0.249
N observation = 563				
Adj R-Squared= 4.20%				
p <0.001				

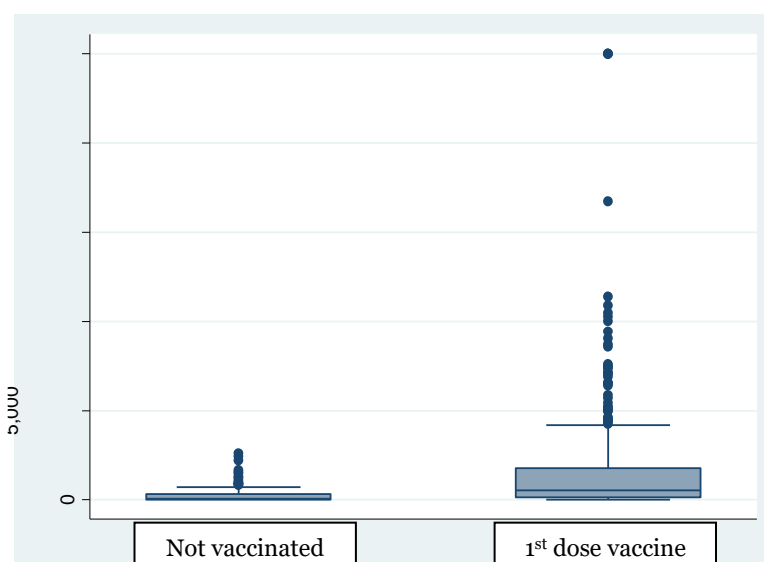


Figure 1. Box plot of differences in COVID-19 antibody titer

DISCUSSION

Table 3 presents the results of multiple linear regression analysis on the effect of COVID-19 vaccination on antibody titers, by controlling for the influence of a number of confounding factors. Table 3 shows that the first vaccination was able to increase COVID-19 antibody titers, but it was not statistically significant. On average, people who had received the first vaccination had an antibody titer 697.82 units higher than those who had not been vaccinated (b= 697.82; 95% CI= -720.90 to 1241.24; p= 0.603). The implication is that although the

first vaccination was able to increase antibody titers, it was not high and significant enough to provide protection against infection with the COVID-19 virus.

Table 3 shows that the second vaccination was able to increase the COVID-19 antibody titer, and it was statistically significant. On average, people who had received the second vaccination had an antibody titer 1331.38 units higher than those who had not been vaccinated (b= 1331.38; 95% CI= 802.30 to 1860.46; p <0.001). The implication is that the second vaccination is able to increase antibody titers quite high and statistically significant, so that it is able to

provide protection against infection with the COVID-19 virus.

Table 3 also shows that various factors that are thought to influence the estimation results of the effectiveness of the COVID-19 vaccine do not confound the estimation results, where none of the potential confounding factors show any influence. Adjusted R squared= 4.20% means that all independent variables in this linear regression model are only able to explain 4.20% of the variation in COVID-19 antibody values. The $p < 0.001$ means that the relationship between the independent variable as a whole and the dependent variable (antibody titer) in this linear regression model shows a relationship that is statistically very significant, which means the relationship is consistent

1. Effect of the first dose of vaccination on COVID-19 antibody titers

The results of this study showed that research subjects who had been vaccinated with dose 1 were able to increase the COVID-19 antibody titer, but it was not statistically significant. On average, people who have received the first vaccination have an antibody titer that is 697.82 units higher than those who have not been vaccinated, so the implication is that, although the first vaccination can increase the antibody titer, it is not high enough and significant enough to protect against infection with the COVID-19 virus.

Vaccination is the administration of a vaccine to actively increase a person's immunity against a disease, so that if one day they are exposed to the disease they will not get sick or will only experience mild illness and will not become a source of infection. The COVID-19 vaccine is given by intramuscular injection in the upper left arm using a disposable syringe (Auto Disable Syringes/ADS) (Ditjen P2P Kemenkes RI, 2021). The last vaccine injection is higher than after the first injection, so it is proven that repeated

vaccine injections in the elderly can increase immunogenicity and increase the effect of the COVID-19 vaccine (Zhang et al., 2022).

The aim of COVID-19 vaccination is to reduce the transmission/transmission of COVID-19, reduce morbidity and death rates due to COVID-19, achieve herd immunity in society and protect society from COVID-19 so that they remain socially and economically productive (Unit Tasks for Handling COVID-19, 2021). Vaccination aims to stimulate the emergence of neutralizing antibodies in order to achieve immunogenicity (Kemenkes RI, 2021). It is hoped that COVID-19 vaccination will be able to reduce the risk of infection or reduce the risk of experiencing infection with severe symptoms when compared to groups who are not vaccinated (Kemenkes RI, 2021).

2. The effect of the second dose of vaccination on COVID-19 antibody titers

The results of this study show that the second vaccination can increase COVID-19 antibody titers, and this is statistically significant. On average, people who have received the second vaccination have an antibody titer that is 1331.38 units higher than those who have not been vaccinated, so the implication is that the second vaccination is able to increase the antibody titer quite high and statistically significant, so it is able to provide protection against infection with the COVID-19 virus.

COVID-19 vaccination can increase antibodies against SARS-CoV-2. According to (Rokom, 2022), there was an increase in antibody titers formed after COVID-19 vaccination in Indonesia in general by 86.6% in November – December 2021. The increase in antibody titers after the first vaccination had a higher proportion of antibodies at 91.3 %. The passage of time shows that the amount of most antibodies derived from the vaccine, including anti-

bodies that neutralize the virus, decreases because the immune system forms memory cells that can be activated after exposure to the virus and includes cellular immunity. Giving a vaccine booster can help strengthen immunity because the efficacy and effectiveness of vaccination only lasts 6 months. After more than 6 months, antibody titers will decrease. Research subjects who received the second dose of vaccine had more vaccine efficacy and effectiveness when compared to research subjects who only received the vaccine. dose 1 (Hamady et al., 2022).

3. The influence of confounding factors on antibody titers

Various factors that were thought to influence the estimated results of the effectiveness of the COVID-19 vaccine apparently did not confound the estimation results, where none of the potential confounding factors showed a statistically significant influence ($p > 0.05$). The confounding factors include gender, age, smoking, outside activities and alcohol consumption:

a. Gender

The gender of the research subjects was not significantly associated with antibody titer, $p = 0.160$. According to research/studies on the biology of viral infections, it shows that there are differences in the prevalence and severity of COVID-19 disease related to gender. This is associated with smoking habits, where it is known that men tend to smoke when compared to women. One study also said that smoking is associated with higher excretion of the Angiotensin Converting Enzyme 2 (ACE2) receptor for Corona virus (Cai, 2020).

Gender influences various aspects of adaptive immunity. Sex hormones influence the immune system so that women have higher immunoglobulin levels and a stronger immune response after immunization or infection than men. The immune response in women to vaccines and infec-

tions is generally more effective and more aggressive than in men. One reason is the fact that women have two X chromosomes, and men only have one X chromosome.

b. Age

The age of the research subjects was not significantly associated with antibody titer, $p = 0.572$. Aging is a complex process accompanied by functional decline in various physiological systems. In elderly individuals changes in the immune system result in a less sharp adaptive immune response, increased propensity for inflammatory responses, increased susceptibility to infections, and increased production of auto-antibodies (Gudelj et al., 2018). According to research conducted by Sarvati (2020), the elderly are an age group that is vulnerable to various diseases, one of which is COVID-19. This happens because elderly people have experienced physical and mental changes due to the aging process. Aging is the process of slowly losing the ability of tissues to repair the damage they suffer.

The aging process causes the body's response to vaccines to decrease (CNN Indonesia, 2021). In the elderly, immunity as a protector of the human body cannot be as strong as at a young age. This is what makes the elderly vulnerable to various diseases, one of which is the SARS-CoV-2 coronavirus that causes COVID-19. Viral and host factors play a role in SARS-CoV-2 infection. The cytopathic effect of the virus as well as its ability to counteract the immune response determines the severity of the infection. Dysregulation of the immune system then plays a role in tissue damage infected by SARS-CoV-2. Insufficient immune response can lead to viral replication and tissue damage. But on the other hand, an excessive immune response can also result in tissue damage (Sarvasti, 2020).

c. Smoker

The results of this study showed that smoking in research subjects was associated with an insignificant antibody titer of 0.316. Although according to research/studies on the biology of viral infections, it shows that there are differences in the prevalence and severity of COVID-19 disease related to gender. This is associated with smoking habits, where it is known that men tend to smoke, when compared to women. One study also said that smoking was associated with higher excretion of the Angiotensin Converting Enzyme 2 (ACE2) receptor for coronavirus (Cai, 2020). Research by Ferrara et al., (2022) investigated the possible impact of smoking on the humoral response to the BNT162b2 mRNA COVID-19 vaccine also known as the BioNTech-Pfizer COVID-19 vaccine, vaccine-induced antibody titers decreased more rapidly in active smokers compared to non-smokers.

d. Outdoor Activities

The results of this study showed that in research subjects activity outside the home was not significantly associated with antibody titers, $p=0.692$. Regular physical activity outside the home can be associated with preventing various non-communicable and infectious diseases during the Covid-19 pandemic (Lee et al., 2012).

Physically active people tend to be more resistant to infections through better immune resistance to pathogenic organisms. Physical activity outside the home has an indirect protective effect against infectious diseases by improving cardiovascular health and body metabolism. Physical activity is also related to the immune response which can increase antibody titers after vaccination so that the body's immunity is greater in physically active populations (Nieman, 2020).

Physical activity outside the home for an average of 30 minutes at moderate to

vigorous intensity can help increase the concentration of CD4 T cells and IgA immunoglobulin in carrying out various functions in the immune system (Swain et al., 2012). Research from Chastin, et al (2021) shows that regular physical activity outside the home can increase resistance to infectious diseases in the general population because it can reduce the risk of infection and death from infectious diseases, and strengthen vaccination programs (herd immunity can be achieved).

e. Alcohol Consumption

The results of this study showed that research subjects who consumed alcohol were associated with non-significant antibody titers ($p=0.249$). Long-term and short-term alcohol consumption can cause a decrease in lymphocytes, and changes in IgA and IgM immunoglobulins have been observed in men and women who consume alcohol (Barr et al., 2016). Epithelial cells, macrophages, and dendritic cells are the first line of immune defense that are most vulnerable to high doses of alcohol. Ethanol weakens the ability of leukocytes to migrate to infected sites, inducing functional abnormalities in T and B lymphocytes (Meadows et al., 2015).

Alcohol has long and short-term effects on every organ in the body, so there is no "safe" limit for consumption, the risk of worsening health increases with every glass of alcohol consumed. In the current context, excessive alcohol consumption weakens the immune system making it more susceptible to contracting the SARS-CoV-2 virus (Calina et al., 2021).

4. Adjusted R square and p

The results of this study showed the value of Adj R-Squared= 4.20%, meaning that all independent variables in this linear regression model were only able to explain 4.20% of the variation in COVID-19 antibody values. R square adjusted can measure the level of confidence in adding independent

variables appropriately in increasing the predictive power of the model, by looking at these values, it can be said that the antibody titer variable in the community in the D.I. Yogyakarta area is influenced by 4.20% by dose 1 and dose 2 vaccination variables, gender, age, smoking status, outdoor activities, and alcohol consumption status.

The results of this study p-value of <0.001 mean that the relationship between the independent variable as a whole and the dependent variable (antibody titer) in this linear regression model shows a statistically very significant relationship, which means that the relationship is consistent. COVID-19 vaccination can increase antibodies against SARS-CoV-2. According to (Rokom, 2022), there was an increase in antibody titers formed after COVID-19 vaccination in Indonesia in general by 86.6% in November to December 2021. The increase in antibody titer after the first vaccination had a higher proportion of antibodies of 91.3%.

This study concluded that COVID-19 vaccination can increase COVID-19 antibody titers after controlling the influence of several confounding factors. But the increase is not statistically significant. On average, people who had received the first vaccination had an antibody titer 697.82 units higher than those who had not been vaccinated ($b = 697.82$; $CI\ 95\% = -720.90$ to 1241.24 ; $p = 0.603$). This study showed that the second vaccination was able to increase COVID-19 antibody titers, and was statistically significant. On average, people who had received a second vaccination had an antibody titer of 1331.38 units higher than those who had not been vaccinated ($b = 1331.38$; $CI\ 95\% = 802.30$ to 1860.46 ; $p < 0.001$). This study also showed that various factors that were thought to influence the estimation of the effectiveness of the COVID-19 vaccine did not confuse the estimates, where none of the potential con-

founding factors (sex, age, smoking status, outdoor activities, and alcohol consumption status) showed a statistically significant effect ($p > 0.050$).

The first vaccination is not high enough and not significant enough to protect against infection with the COVID-19 virus, so it must be followed by subsequent vaccinations. The second vaccination was able to increase antibody titers quite high and statistically significant, so as to provide protection against infection with the COVID-19 virus. Suggestions that can be given in accordance with the results of research and discussions obtained, among others, for the Regional Government, Special Region of Yogyakarta, namely providing vaccinations, carrying out dose 2 or Booster vaccines to the community, for the public it is necessary to educate the public for booster vaccination because antibody titers will increase even more if booster vaccination is carried out, while for further researchers it is expected to add other variables that are in this study was not studied, as was the duration of COVID-19 vaccination against antibody titers.

AUTHOR CONTRIBUTION

Joko Budiyono and Bhisma Murti have collaborated on concept, research design and data analysis; Joko Budiyono wrote the article; Didik Tamtomo reviews the article.

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CONFLICT OF INTEREST

There is no conflict of interest in this study.

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