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**RESEARCH** **Open Access**

# Persistence of Antibody Response Against SARS-CoV-2 After Vaccination

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**Abstract**
SARS-CoV-2 is the causative agent of the disease known as COVID-19. COVID-19 is spreading very fast around the world. One of the immune responses that play a role in against SARS-CoV-2 infection is the production of antibodies, which is 3 weeks after infection. Where within 3 weeks after infection, antibodies will be produced against RBD and the S1 and S2 domains in glycoprotein S and nucleocapsid protein N. The ability of an antibody to inhibit viral infection is determined by its level or titer. This study aims to determine the description of antibody levels against SARS-CoV-2 after vaccination. This type of research is descriptive research. Measurement of antibody levels for SRBD SARS-CoV-2 was carried out using the CLIA method using the MAGLUMI tool. Of the 30 respondents, 23 people had received the third vaccine. The results of this study showed that the average level of SRBD antibodies against SARS-CoV-2 in respondents with 2 doses of vaccine (1.063,786 BAU/mL) was higher than in respondents with 3 doses of vaccine (535.651 BAU/mL). Vaccine intervals of more than 6 months (908.338 BAU/mL) have higher antibody levels than respondents with vaccine intervals of 1-6 months (228.006 BAU/mL). The conclusion of this study is the highest antibody titers are produced >6 months after vaccination, antibody titers are still detectable after 12 months of vaccination, and for further research, it can be measured antibody levels against SARS-CoV-2 from people who have got vaccination for a duration of 2 years or more.

**Keywords:** COVID-19, Immune Response, SARS-CoV-2, SRBD SARS-CoV-2, Vaccines.

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## 1. INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic is caused by severe acute respiratory-syndrome-coronavirus-2 (SARS-CoV-2) (Hou et al., 2020). The first case of SARS-CoV-2 infection in humans was reported from the Chinese city of Wuhan in December 2019 (Alsagaby et al., 2021; Rauf et al., 2020). Within three months of the first case report, global human COVID-19 infection spread rapidly (Ejemel et al., 2020), and was declared a global health problem by WHO on 11 March 2020 (Gao et al., 2020). Data as of October 18, 2022, the number of COVID-19 cases worldwide reach 622 million cases of COVID-19 with 6 million deaths reported to WHO (WHO, 2022a). While in Indonesia there is a total of 6 million more confirmed cases with a death toll of 158,345 cases (WHO, 2022b).

COVID-19 is transmitted through droplets that come out when coughing and sneezing so that the transmission of SARS-CoV-2 can occur very quickly (Han & Yang, 2020). When SARS-CoV-2 enters human cells for infection, it will bind to the angiotensin-converting enzyme 2 (ACE-2) receptor molecule on target cells, where the part of the virus that attaches is spike protein (S). This attachment occurs in the receptor binding domain (RBD) in the S1 domain. After that, it is followed by the formation of the S2 domain pathway of the virus which aims to release nucleic acid (RNA) in the target cell for replication. At this stage the body's immune system will begin to actively work to fight the virus that causes infection, which consist of a cellular immune response and an immune response humoral (Li, 2020). The immune system is the best defense because it provides the body's natural ability to fight virus and infections that occur (Chowdhury, Hossain, Kashem, Shahid, & Alam, 2020).

One of the immune responses that play a role against SARS-CoV-2 infection is the production of antibodies. Three weeks after infection the body will produce antibodies against RBD, S1 and S2 domain of the spike glycoprotein (S) and nucleocapsid protein (N) (L'Huillier et al., 2021). Characteristics of a persistent humoral response over a long period of time play a role in defense against SARS-CoV-2 infection. The humoral immune response, main role by antibody production, where are the antibodies play inhibits the adhesion of SARS-CoV-2 to target cells and helps in neutralizing the virus (Syahniar et al, 2020).

Several studies have shown the role of antibodies against SARS-CoV-2 infection, namely: antibodies to protein S persisted for 75 days post-infection in >59% of patients (Iyer et al., 2020); antibody titers did not decrease after 4 months of infection. Intervention in prevention and treatment are important in overcoming current problem (Gudbjartsson et al., 2020) and humoral response persisted during the early 6 months of the pandemic by showing mild clinical symptoms of COVID-19 (L'Huillier et al., 2021). The fact that in COVID-19, sufferers who are symptomatic and have mild can transmit the virus. This is in contrast to SARS-CoV-1 and MERS-CoV, which are transmitted from patients who show clinical symptoms. Several things can be done to prevent this pandemic are implementing hygiene and sanitation as well as maintaining distance, monitoring the virus, and increasing population immunity (Speiser & Bachmann, 2020).

Diagnosis of SARS-CoV-2 infection divided into 2 types, namely: tests for detection infection and tests to detection immunity. Diagnosis infection done by detects genetic material of the virus and detects viral protein (s) from a nasopharynx or saliva swab, or detection of viral antigen proteins. In individuals the results will show positive in a relatively short time after the onset of clinical symptoms, an average of 14 days. However, further positive results of detection of genetic material or viral protein, it cannot be concluded that the infected person has immunity (WHO, 2022a). Diagnosis immunity to Detects antibodies against the virus from prior infection or vaccination. Uses serum/plasma or whole blood specimens to detect antibodies generated by prior SARS-CoV-2 infection or vaccination. SARS-CoV-2 antibodies are usually detectable 1-2 weeks after infection or vaccination. Therefore, serology-based tests

that can detect various antibodies in the blood and are persistent for months or even years are needed (Speiser & Bachmann, 2020; WHO 2023).

The vaccination program against SARS-CoV-2 in Indonesia officially started on January 13, 2021 and by October 9, 2021, 438,885,586 had received the vaccine (WHO, 2022b). The vaccines used in Indonesia are vaccines derived from whole virus, vector viruses, recombinant protein vaccines, and RNA vaccines (Kementerian Kesehatan Republik Indonesia, 2021).

Antibody production in the human body will from on the 7$^{th}$ day after exposure to antigen and it takes about 18 days of the formation of long-lived plasma cells. Research on SARS-CoV-1 in 2003 showed that antibody titers survivors above average over a 2 year period (Jacofsky, Jacofsky, & Jacofsky, 2020).

The ability of antibodies to inhibit viral infection is also determined by the titer. Therefore, a quantitative examination is needed that can measure how much antibody is in the body (Speiser & Bachmann, 2020). One method for examining antibody titers is the Chemiluminescence immunoassay (CLIA) which is a technique for detecting the bonding reaction between antigen and antibody. This examination method has high sensitivity and good specificity (Jacofsky, Jacofsky, & Jacofsky, 2020; Wang, Wu, Zong, Xu, & Ju, 2012). The implementation of the COVID-19 vaccination in Indonesia has not yet measured antibody levels both before and after vaccination. Form the explanation above, the authors are interested to measured of antibody levels against SARS-CoV-2 after vaccination, to provide information on how long and antibody levels after vaccination.

## 2. RESEARCH METHOD

This type of research is a descriptive study, where this study was conducted to determine the description of antibody levels against SARS-CoV-2 after vaccination. The sample size in this study was determined based on a simple random sampling technique, which is based on the number of residents who have received the SARS-CoV-2 vaccine in the city of Denpasar, Bali, and Cimahi Regency, West Java.

This research was conducted by involving research respondents with the following stages: (1) filling out informed consent, here participants receive information regarding the purpose of the research, potential risks, and their rights; (2) filling out questionnaires, here participants fill out a form containing questions, including: name, age, gender, address and history of Covid-19 vaccination.; (3) health examination, here, health examination are carried out, including: checking blood pressure and body temperature. This is done to ensure that participants are healthy and that samples can be taken properly when taken; (4) sampling (in the form of venous blood) then put into a blood tube with clot activator; and (5) After collection of the whole blood, allow the blood to clot by leaving it undisturbed at room temperature. This usually takes 15–30 minutes. Remove the clot by centrifuging at 1,000–2,000 x g at 2-8$^0$C for 10 minutes in a refrigerated centrifuge (Thermo Fisher Scientific, 2023).

This study were examined 30 samples. The examination method used to determine the antibody titer of respondents who have been vaccinated is using the CLIA method using the MAGLUMI tool. Chemiluminescent immunoassay (CLIA) is an immunoassay technique where the label, i.e. the true ‘‘indicator’’ of the analytic reaction, is a luminescent molecule. In general, luminescence is the emission of visible or near-visible (k = 300–800 nm) radiation which is generated when an electron transitions from an excited state to ground state. The resultant potential energy in the atom gets released in the form of light (Cinquanta, 2017). The CLIA antibody reagents against SARS-CoV-2 is removed from the box, then the barcode on the reagent is entered into the CLIA tool system, until the lot number of the reagent is detected by the device. The microbead was resuspended and completely homogenized. Then click the calibrate button to run the calibration. Patient serum is placed in the “sample area” and click

the button to run the test. This study has received ethical approval No: LB.02.03/EA/KEPK/ 0138/2022 from Health Research Ethics Committee Poltekkes Kemenkes Denpasar.

## 3. RESULTS AND DISCUSSION

From the research results obtained 30 respondents with a total of 5 male respondents and 25 female respondents. The characteristics of the respondent's data can be seen in Table 1.

**Table 1.** The Characteristics of Respondents Data

| The Characteristics of Respondents | Total | Percentage (%) |
|---|---|---|
| Gender | | |
| Male | 5 | 16,67 |
| Female | 25 | 83,33 |
| Vaccine Dose | | |
| 1st Dose | 30 | 100 |
| 2nd Dose | 30 | 100 |
| 3rd Dose | 23 | 76,67 |
| Long After the Vaccine | | |
| 1-6 months | 11 | 36,67 |
| > 6 months | 19 | 63,33 |
| Vaccine Type | | |
| 1st Vaccine | | |
| Sinovac/Coronavac | 17 | 56,67 |
| Astra Zeneca | 12 | 40,00 |
| Moderna | 1 | 3,33 |
| 2nd Vaccine | | |
| Sinovac/Coronavac | 17 | 56,67 |
| Astra Zeneca | 12 | 40,00 |
| Moderna | 1 | 3,33 |
| 3rd Vaccine | | |
| Sinovac/Coronavac | 1 | 3,33 |
| Astra Zeneca | 10 | 33,33 |
| Moderna | 6 | 20,00 |
| Pfizer | 6 | 20,00 |

Table 1 present that out of 30 respondents, 23 people had received the third dose of vaccine and 7 people had just received the second dose of vaccine. The types of vaccines received by respondents were Sinovac/Coronavac, Astra Zeneca, Moderna, and Pfizer.

**Table 2.** SARS-CoV-2 SRBD Antibody Levels.

| Antibody Levels | BAU/mL |
|---|---|
| Lowest | 25.779 |
| Highest | 3536.086 |
| Average | 658.883 |

Table 2 show that the highest antibody levels was 3536.086 BAU/mL and the lowest was 25.779 BAU/mL with an average of 658.883 BAU/mL.

Of the 30 respondents, 23 people had received the third vaccine dose. The average respondent antibody levels based on the number of vaccines and the duration of the vaccine can be seen in Table 3.

**Table 3.** The Average of SARS-CoV-2 SRBD Antibody Levels.

| | Total Respondents | SARS-CoV-2 SRBD Antibody Levels (BAU/mL) |
|---|---|---|
| Number of Vaccines | | |
| Twice | 7 | 1,063.786 |
| Three times | 23 | 535.651 |
| Vaccine Time | | |
| 1 – 6 months | 11 | 228.006 |
| > 6 months | 19 | 908.338 |

Table 3 shows that 7 people received 2 doses of the vaccine with a SARS-CoV-2 SRBD antibody level of 1,063.786 BAU/mL, and antibody levels in respondents with 3 doses of vaccine were 535.651 BAU/mL. Antibody levels in respondents who received 2 doses of vaccine were higher than those who received 3 doses of vaccine, possibly due to the distance between vaccines in respondents with 2 vaccines does of more than 6 months, namely between 8 – 15 months. In respondents with a vaccine duration of more than 6 months, the average antibody level was 908.338 BAU/mL. The results of antibody levels were higher than respondents with vaccine interval between 1 – 6 months.

Until now, SARS-CoV-2 infection is a serious global health threat because of its severity and rapid spread throughout the world. The development of a vaccine to control the spread of SARS-CoV-2 is very rapid. The basis for assessing vaccine efficacy is immune surveillance by measuring antigen-specific antibodies. Although SARS-CoV-2 infection can induce the production of antibodies that recognize different viral antigens, antibodies directed against RBD are the most relevant because of their neutralizing activity. Therefore, most of the SARS-CoV-2 vaccines were developed to induce the production of antibodies against the SARS-CoV-2 spike protein. Thus, measurement of circulating levels of anti-S-RBD can provide valuable information about acquired immunity against SARS-CoV-2 (Lo Sasso et al., 2021).

Different vaccines can cause different levels of antibody response (Alsagaby et al., 2021) The CDC, (2020) compared two mRNA vaccines, namely mRNA-1273 with BNT162b2, where two doses of mRNA-1273 induced higher antibody titers with a Geometric Mean Titer (GMT) of 3.836U/mL. Whereas two doses of BNT162b2 (GMT 1.444 U/mL) (CDC, 2020) Faico-Filho et al., (2020) suggested the possibility that there was a difference in the antibody response produced by BNT162b2 and AZ1222 where both elicited IgM and IgG response (Faíco-Filho, Passarelli, & Bellei, 2020). Alharbi et al., (2022) conducted a study to determine the antibody response induced by the COVID-19 vaccine, namely BNT162b2 and AZD1222 against 432 individuals. Anti-SARS-CoV-2 IgG spikes in most of the subjects after the first vaccine and remains high after 6 months. At 1 year post-vaccination, antibody levels were low then increased again after receiving the third dose. The third dose is given an average of 250 days after the second dose (Alharbi et al., 2022).

Based on the results of the study, the antibody level of the second dose of vaccine was higher than the third dose, possibly due to the duration of the vaccine in the second dose between 8 – 15 months. Recent studies have shown that the humoral response continues to develop long after vaccination, with memory B cells after vaccination showing an increase in both quality and number compared to the start of vaccination (Bates et al., 2021; Turner et al., 2021; Wang et al., 2021)

The reported effectiveness of the Sinovac vaccine against COVID-19 infection was 49.4% at ≥14 days after vaccination (Hitchings et al., 2021). The efficacy of the Astra Zeneca vaccine against infection ranged from 33.5% at ≥14 days after vaccination, 25% to 63.9% at 22 – 90 days after vaccination (Madhi et al., 2021). Vaccine efficacy after 14 days after the second dose was 66.7%. Voysey et al., (2021) noted that differences in the efficacy of the first and second doses of vaccine could be attributed to several factors, such as the intensity of the

COVID-19 pandemic in different countries and the length of the prime-boost interval between the first and second doses. Longer prime-boost intervals (≥12 weeks) indicate higher vaccine efficacy (Voysey et al., 2021)

The efficacy of the first dose of Moderna vaccine against infection was 95.2% at ≥14 days after vaccination (Baden et al., 2021). Studies show that the effectiveness of the Pfizer vaccine increases gradually, starting 14 days after the first dose, and finally reaching a peak of 91% effectiveness on day 21 (Hunter & Brainard, 2021). Mohammed et al., (2022) concluded that a single dose of vaccination with the Pfizer vaccine significantly reduced symptoms of SARS-CoV-2 infection and provided protection against severe infection. This protection is maintained for > 6 weeks (Mohammed et al., 2022).

Different factors influencing antibody response to SARS-CoV-2 vaccination such as age, vaccination regimen, days since vaccination, and previous infection. The number of samples in this study is still small which can cause differences in results with other studies that use different sample sizes.

## 4. CONCLUSION

From the results of this study it can be concluded, among others: (1) The conclusion of this study is the highest antibody titers are produced >6 months after vaccination, antibody titers are still detectable after 12 months of vaccination; and (3) for further research, it can be measured antibody levels against SARS-CoV-2 from people who have got vaccination for a duration of 2 years or more.

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