

Relationship between age, gender, BMI, comorbidity and AEFI Variables with S-RBD antibody levels post covid-19 vaccination

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ABSTRACT

The coronavirus disease 2019 (COVID-19) pandemic is a global problem caused by the SARS CoV-2 virus. Covid-19 vaccination, which is believed to be a solution, started after almost a year of the pandemic. The vaccination program in Indonesia initially used the Sinovac vaccine, a vaccine made from killed or inactivated viruses. This platform has been used in making vaccines for a long time. Vaccination at the UIN Syarif Hidayatullah Jakarta campus uses a vaccine made by PT Bio Farma, COVID-19 Vaccine, with the same raw materials as Sinovac. Cross-sectional research and research subjects were 53 lecturers and teaching staff who had received 2 doses of the COVID-19 Vaccine. Characteristics of age, gender, body mass index, comorbidities and adverse events after immunization (AEFI) were obtained from interviews, questionnaires and physical examination. It was found that there were no significant differences in S-RBD IgG antibody levels in young and elderly adults ($p=0.85$), male and female groups ($p=0.74$), groups with comorbidities ($p=0.93$), history of AEFI ($p=0.78$). However, there was a significant difference between normal BMI and abnormal BMI ($p=0.03$). The variable that had a significantly different relationship in this study was the mean level of IgG S-RBD antibodies in the overweight and obese groups with normal weight.

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INTRODUCTION

In December 2019, a case with severe respiratory symptoms (pneumonia) was reported in Hubei Province, China, which was caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS CoV-2)(Hairunisa & Amalia, 2020)(Zendrato, 2020)(Susilo et al., 2020). This disease spread throughout the world quickly so that WHO declared it a Public Health Emergency of International Concern (PHEIC) and then on March 11 2020 WHO declared it a pandemic of coronavirus disease

2019 (COVID-19)(Muslimah, n.d.)(Simak, 2020)(Hidayah, 2020).

To date, there have been more than 775 million recorded cases of COVID-19 from WHO data throughout the world (data up to May 2024), while the number of cases in Indonesia as of June 1 2024 was 6.8 million positive confirmed cases and as many as 162 thousand people. On August 4 2023, Indonesia declared the end of the COVID-19 pandemic status through Presidential Regulation no. 48 of 2023.(Solikah & Ismiatun, 2023)

The SARS CoV-2 virus is a strain of □-coronavirus which has an envelope with single-stranded RNA genetic material measuring around 30 kb(Muderawan et al., 2021)(Gunardi, 2022)(Al Fajri, 2022). The pathogenesis of COVID-19 infection begins when the SARS CoV-2 virus enters through the upper respiratory tract and then binds to the Angiotensin Converting Enzyme 2 (ACE2) receptor, enters body cells and then replicates within the cells which then enters other cells to re-infect(Fitriani, 2020)(Alkautsar, 2021)(Fatoni & Rakhmatullah, 2021).

The morbidity and mortality of COVID-19 is mainly associated with an excessive inflammatory response that attacks several organs such as the lungs, heart, kidneys and others(SURYANI et al., 2020)(Cahyati et al., 2021)(Pangandaheng et al., 2023)(Liberty et al., 2023). The SARS CoV-2 vaccine is one of the efforts to overcome the COVID-19 pandemic which aims to trigger a humoral immune response by forming neutralizing antibodies which can bind to the S-RBD protein on the virus thereby preventing binding to the ACE2 receptor. Apart from that, it also recognizes CD4 T lymphocytes, CD8 T lymphocytes and macrophages which can increase the ability to eliminate viruses(Prakoeswa, 2020)(Rosyanti & Hadi, 2020)(Apriyanto & Rasak, 2024).

The first clinical trials for the vaccine began in March 2020 just 60 days after the virus genome sequencing was published and accelerated vaccine development(Lamani, n.d.)(Yanuhar & Caesar, 2021)(Ghiffari, 2023). And more than 200 vaccines for SARS CoV-2 have been developed throughout the world and according to the target the COVID-19 vaccine program will start in January 2021. There are several types of vaccine platforms for COVID-19 such as attenuated viruses, killed/inactivated viruses, subunit protein (protein based), recombinant virus vectors (Recombinant viral vectors), and Nucleic acid-based (DNA or RNA).

The Indonesian government has started a COVID-19 vaccination program since January 2021 starting with health workers and those working in health facilities. In the second stage, the target population is public service officers and the elderly community group aged 60 years and over. Using vaccines that have been inactivated by radiation or the addition of chemicals such as formaldehyde or □-propiolakyon which can damage the virus components so that their immunogenicity is reduced. This vaccine is given simultaneously with the adjuvant aluminum hydroxide which helps strengthen the effects of the immune response. There are no live components in this vaccine so there is no risk of causing disease, but it cannot always induce an immune response with the first dose(TAMITA, 2023)(NUR AZIZAH, 2023). The immune response that is formed sometimes does not last long so a booster is needed. 5,6

The vaccination program carried out on lecturers and teaching staff at the UIN Syarif Hidayatullah Jakarta campus uses a vaccine with an inactivated virus platform whose fill and finish process is carried out by Biofarma. This is different from the Sinovac vaccine given to health workers, which is a finished product from Sinovac and one vial for one single dose. The vaccine processed at Biofarma is named COVID-19 Vaccine in multidose form where one vial contains 10 doses(IFANA, n.d.)(Noviana et al., 2021).

There are several factors associated with the risk of SARS CoV-2 infection, including age, gender, comorbidities (diabetes mellitus (DM), hypertension), BMI and post-immunization adverse events (AEFI). This research wants to find out the relationship between the factors above and the levels of IgG S-RBD antibodies that are formed after vaccination.

RESEARCH METHOD

The research design is cross-sectional. Blood specimen collection, qualitative antibody examination

was carried out at the UIN Jakarta Faculty of Medicine and quantitative S-RBD IgG antibody level examination was carried out at the Prodia laboratory. Research ethics were submitted to the Ethics Committee of the Faculty of Medicine, UIN Jakarta. Research subjects were obtained from consecutive sampling involving 53 lecturers and teaching staff at UIN Syarif Hidayatullah Jakarta who met the input criteria. Input criteria include having received two doses of the COVID-19 Vaccine from Biofarma, being willing to take part in the research by signing an informed consent and the research subject has never been infected with SARS CoV-2. Before taking blood, the patient fills out a Google form regarding the required data and is confirmed by the officer when taking blood.

Venous blood research specimens were prepared into serum, then a quantitative IgG antibody examination was carried out using the SARS CoV-2 IgG Quant reagent from PT. Abbott using the chemiluminescent microparticle immunoassay (CMIA) method. This examination detects immunoglobulin class G (IgG) antibodies against the RBD of the S1 subunit of the SARS-CoV-2 Spike protein. Automatic examination to determine qualitative and quantitative IgG antibodies to SARS-CoV-2. The way it works is that the sample, paramagnetic microparticles coated with SARS-CoV-2 antigen, and diluent are mixed and incubated. IgG antibodies against SARS-CoV-2 present in the sample bind to SARS-CoV-2 antigen-coated microparticles. Next, the mixture is washed. And then the antihuman conjugate labeled with acridinium IgG was added and incubated. The resulting chemiluminescent reaction is measured as relative light units (RLU). For interpretation of examination results, levels < 50 AU/ml are Non Reactive (NR) and levels > 50 AU/ml are Reactive.

RESULTS AND DISCUSSIONS

3.1. S-RBD Quantitative IgG Examination Results

The results of the quantitative IgG antibody examination after 1 month after vaccination with 2 doses of the COVID-19 Vaccine showed that all research subjects had S-RBD IgG antibodies with a fairly large range of highest and lowest antibody levels. The total research subjects who took part in the research were 53 people. The results are shown in Table 3.1.

Table 1. S-RBD quantitative IgG examination results

Variable	Median	Min	Max	<i>p</i>
IgG S-RBD	437.9	68.1	1674	0.00

These results were grouped based on individual characteristics such as age, gender, BMI, comorbidities and AEFI and then looked at the comparative relationship between these characteristics and the levels of IgG S-RBD antibodies formed.

Table 2. Relationship between individual characteristics and IgG S-RBD antibody levels

Characteristics	n	%	Mean-Median (AU/ml)	<i>p</i>
Age				
Young	26	49.1	437.1 (139.6 - 1674.3)	0.845
Middle - Elderly	27	50.9	500 (68.1 - 1438)	
Gender				
Male	14	26.4	441 (159.1 - 1377.2)	0.747
Female	39	73.6	462 (68.1 - 1674)	
Body Mass Index (BMI)				
Normal	27	50.9	348.2 (71.2 - 1366.2)	0.03
Overweight - Obese	26	49.1	544.9 (68.1 - 1674.3)	
Comorbidities				
Yes	11	20.8	489.5 □ 291.8	0.93
No	42	79.2	449.9 (68.1 - 1674)	
Adverse Events				
Yes	24	45.3	444.1 (68.1 - 1674.3)	0.78

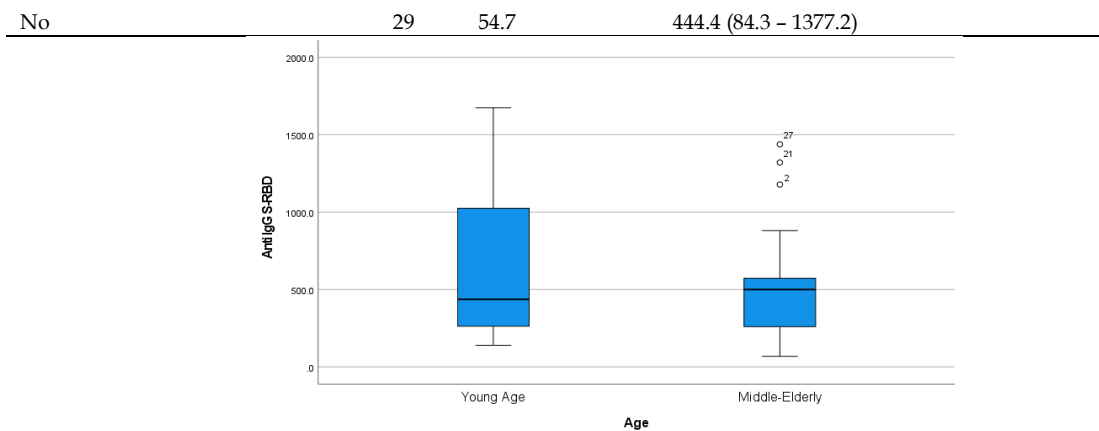


Figure 1. Relationship between average antibody levels in young adults and the elderly

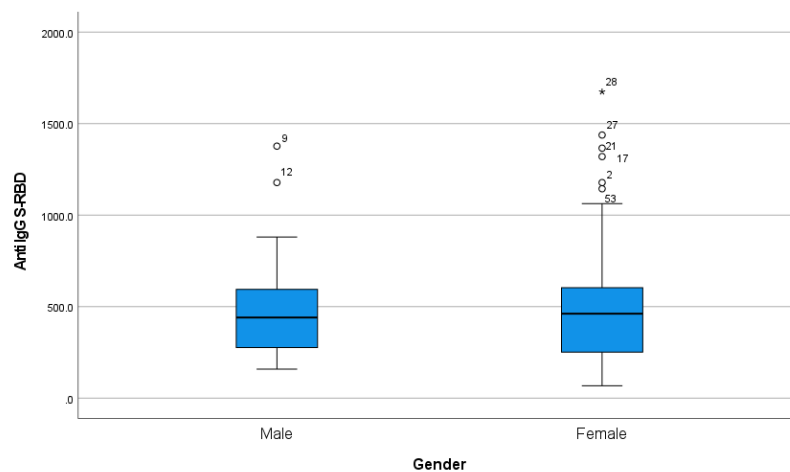


Figure 2. Relationship between average antibody levels in men and women

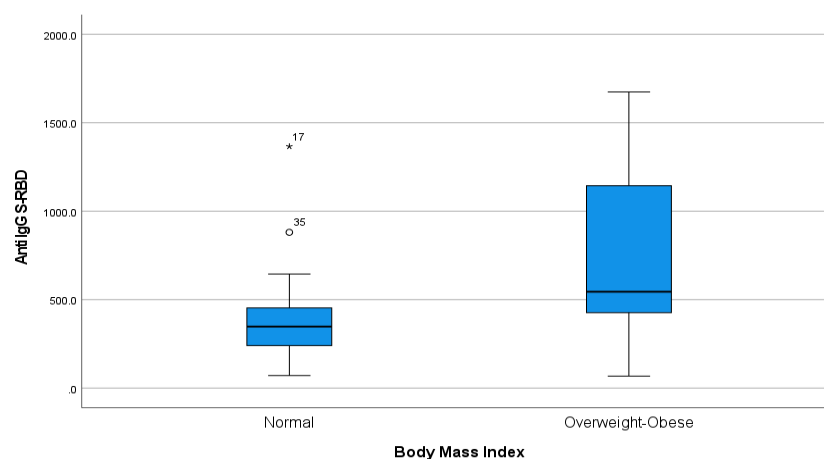


Figure 3. Correlation between average antibody levels in Abnormal and Normal BMI

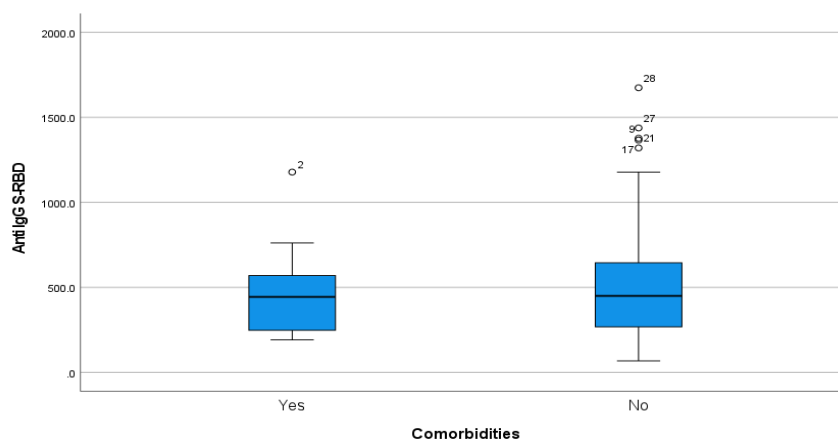


Figure 4. The average relationship between antibodies and comorbidities

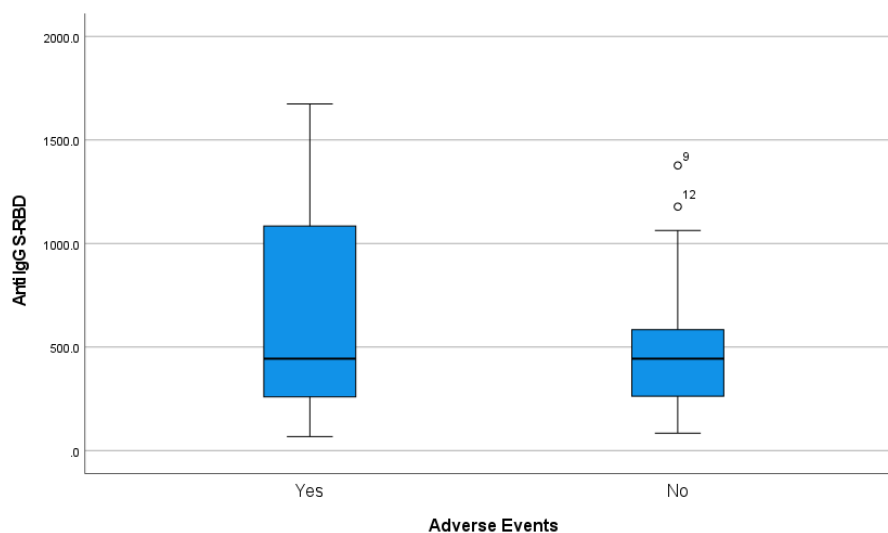


Figure 5. The relationship between the average antibody and the incidence of AEFI

Discussion

The S-RBD IgG antibody examination is useful for detecting the emergence of seroconversion after SARS-CoV-2 infection and detecting the immunogenicity of Covid-19 vaccination. The IgS S-RBD antibody examination detects antibodies against the Spike protein which has a strong correlation with neutralizing antibodies so this examination is quite good for assessing the immune response to SARS CoV-2. In phase 1 and 2 clinical trials of the Sinovac vaccine, it was found that seropositivity appeared after 14 days of vaccination.

This research aims to determine the immunogenicity of the Covid-19 vaccine produced by PT Biofarma in stimulating the emergence of IgG S-RBD antibodies. The examination results showed that all research subjects had antibodies to the S-RBD protein with a fairly high median antibody level, namely 437.9 (68.1 - 1674.3) AU/ml. 54 people participated in this study, but after further history taking, 1 research subject was not included in the study because he was suspected of having been infected with Covid-19 with quite high levels of IgG S-RBD antibodies (2409.1 AU/ml).

Based on age, research subjects were grouped into young adults (26 - 44 years) and elderly (45 - 65 years) based on WHO criteria. In this study, it was found that there was no significant difference in the means between the two groups ($p=0.84$). Advanced age is one factor in weakening

the immune system. In old age, thymus involution is found, which is characterized by decreased production of immune cells from the thymus. In T lymphocytes the number of naive T lymphocytes and CD4 cells is reduced, while in B lymphocytes the number of naive B lymphocytes is reduced and the production of IgM and IgD is reduced as well as changes in the regulation of the inflammatory mediator IL-6.

In this study, gender did not have a significant relationship with S-RBD IgG levels ($p=0.75$). The SARS-CoV-2 virus that enters the body binds to cell surface proteins, namely the ACE2 receptor and the TMPRSS2 serine protease, then enters the cell. These two proteins are more abundant in men than women because they are also targets of the androgen receptor. 11 So men are more susceptible to infection than women. It is also necessary to know further whether the greater number of viruses recognized by the immune system also correlates with the number of antibodies produced by the immune system.

For the variables normal BMI (18.5 - 24.9) and abnormal BMI including overweight, obesity I and obesity II (25 - ≥ 30), a significantly different relationship was found ($p=0.03$). The mean quantitative IgG level in the abnormal BMI group was 544.9 AU/ml and the median in the normal BMI group was 348.2 AU/ml. A study of obese subjects who were given influenza vaccination showed a decrease in CD8 T cell responses which is thought to be due to increased leptin levels which trigger the release of pro-inflammatory cytokines.

Comparison of quantitative IgG antibody levels in the group with comorbidities and those without comorbidities was not significantly different ($p=0.93$). The mean IgG antibody level in the group with comorbidities was 489.5 AU/ml and the median in the group without comorbidities was 449.9 AU/ml. The comorbidities detected in this study were DM and hypertension. In the order of priority for vaccination, groups with comorbidities are in second place. Diabetes mellitus can not only cause damage to the natural immune system such as neuropathy, but also disrupt the cellular immune system such as disruption of cytokine production, inhibition of leukocyte recruitment, dysfunction of neutrophils, macrophages and NK cells as well as disruption of pathogen recognition.

Harrison et al's research concluded that hypertension is related to the activation of pro-inflammatory cytokines. Hypertension can cause T cell activation which ultimately triggers the release of the pro-inflammatory cytokine IL-17 which in chronic conditions can cause damage to organs such as the heart and kidneys which affects the body's immunity. 14 The results of research by Pelleni et al and Watanabe et al reported IgG antibody levels against SARS-CoV-2 post-vaccination is lower in individuals with hypertension.

Comparison of the mean IgG antibodies in groups with AEFI and without AEFI did not have a significant difference ($p=0.78$). The group that reported AEFI had a median IgG antibody level of 444.1 AU/ml and the median in the group without AEFI was 444.4 AU/ml. Levy et al reported that there was a relationship between AEFI and higher levels of IgG S-RBD antibodies. 17 Research by Hwang et al stated that there was no relationship between the incidence of AEFI and humoral immunogenicity after the Covid-19 vaccine.

Several studies that also looked at the relationship between age, gender and BMI with SARS CoV-2 gave varying results. Pellini et al's research on 248 health workers concluded that antibodies were higher in women, young age and normal BMI. 15 Jabbal et al's research on 514 health workers found that antibody levels decreased at older ages and there was no relationship between antibody levels and gender. 19 Ozdemir et al's research on 264 health workers concluded that antibody levels were low in the elderly and male gender.

CONCLUSION

In a study of 53 teaching staff and teaching staff at UIN Syarif Hidayatullah Jakarta, it was found that there was no relationship between the average IgG S-RBD antibody levels and age, gender, comorbidities and AEFI. However, in this study it was also found that there was a relationship

between the average IgG S-RBD level and the BMI variable, where normal BMI had lower IgG S-RBD levels than those who were overweight and obese.

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