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DIFFERENCES IN S-RBD ANTIBODY TITERS OF SARS-CoV-2 POST-VACCINATION AND POST-COVID-19 IN UMY EMPLOYEES THAT DO GENERAL MEDICAL CHECK UP AT AMC MUHAMMADIYAH HOSPITAL YOGYAKARTA

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Abstrak

COVID-19 is a global health problem today. Prevention is the best effort, including vaccination. The earliest evidence of the effectiveness of vaccination was marked by an increase in antibody levels. Research is needed to prove the effectiveness of vaccination by measuring levels of SARS-CoV-2 S-RBD antibodies and comparing them with individuals infected with COVID-19. This study aims to determine and prove differences in the levels of SARS-CoV-2 S-RBD antibodies in individuals with a history of COVID-19 vaccination in subjects who have been infected and who have not been infected with COVID-19. The type of research to be conducted is an analytic observational study with a cross sectional design. The variables studied were the levels of SARS-CoV-2 S-RBD antibodies in individuals who received the COVID-19 vaccination. Subjects consist of groups who have experienced infection and who have never been infected with COVID-19. The subjects used in this study were UMY employees who did general post-vaccination check-ups. The sampling technique used purposive sampling method with the inclusion criteria: (i) employees who are actively working (ii) Age 20-56 years (iii) There is a history of infection evidenced by PCR examination evidence (iv) getting vaccinated for more than 2 weeks. Exclusion criteria for employees who have a history of immune or autoimmune deficiency. This research was conducted at AMC Muhammadiyah Hospital. Examination of antibody levels of S-RBD SARS-CoV-2 was carried out using the Elisa method. Data analysis used descriptive method. The research subjects were 90, consisting of 45 subjects who had been exposed and 45 subjects who were not exposed to COVID-19. Subjects exposed to COVID-19 consisted of 25 men and 15 women, while subjects who were not exposed to COVID-19 consisted of 19 men and 26 women. The research subjects were 23 to 64 years old. From the results of the examination of S-RBD SARS-CoV-2 antibody levels, the results showed that the exposed group had a minimum level of 45.16 AU/mL while the maximum level was more than 1,000 AU/mL. In the unexposed group, 12 subjects had levels <3 AU/mL, while the rest had a

minimum level of 3.01 AU/mL and a maximum level of 39.6 AU/mL. From this study, it can be concluded that there are differences in the levels of SARS-CoV-2 S-RBD antibodies which are higher in individuals who have been exposed to COVID-19 than individuals who have not been exposed. There are subjects who have not responded to the COVID-19 vaccination.

Keyword: History of COVID-19 infection, Vaccination, SARS-CoV-2 S-RBD antibodies

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INTRODUCTION

Since it first broke out in Wuhan, Hubei, China in December 2019, COVID-19 has spread massively in many countries, with a total world case of 223,022,538 with a mortality of 2.06% as of September 11, 2021 (WHO, 2021). Compared to other countries, Indonesia is one with the most troubling situation. Based on data from the COVID-19 Task Force, Indonesia has faced more than 4 million confirmed cases with a mortality of 3.3%. In the Province of the Special Region of Yogyakarta, there were 152,722 positive cases with a cure rate of 92.66%, a death rate of 3.3%, and a hospital admission rate of 4.04% as of September 11, 2021(Dinas Kesehatan DIY, 2021).

Diagnosis of COVID-19 with laboratory parameters relies on Reverse Transcription-Polymerase Chain Reaction (RT-PCR) or an antigen test that indicates the presence of the SARS-CoV-2 virus in the sample material; for example, in the nasopharyngeal swab. (Patel dkk., 2020).

The RT-PCR diagnostic test is the gold standard for COVID-19 diagnosis. The results of the RT-PCR test are shown in the cycle threshold value (CT-value), which indicates the number of test cycles carried out to detect the presence of virus in the sample. A high CT-value indicates a low viral load in the tested sample, and vice versa (RS Universitas Udayana, 2020).

Among the target genes in the RT-PCR method, the N gene (nucleocapsid) is one of the targets with the highest analytical sensitivity. The N gene also has the highest number of mRNA copies compared to other genes, making it the target gene for diagnostic tests recommended by *Balitbangkes* (PAMKI, 2021).

People who have been infected with COVID-19 then successfully recovered (survivors) and who have received vaccinations have immunity or antibodies against future attacks of the SARS-CoV-2 Virus. To find out how much immunity is, there is a method that can detect it, namely the Quantitative SARS-CoV-2 Antibody Examination (Spike-Receptor Binding Domain/S-RBD). Serological analysis of SARS_CoV-2 antibodies can help clarify whether these people have been infected with SARS-CoV-2 in the past (Ghaffari dkk., 2020). Currently, there is uncertainty as to whether the presence of SARS-CoV-2 antibodies provides protection against reinfection, and there is conflicting evidence as to whether antibodies to SARS-CoV-2 can persist for a longer period of time (Ibarrondo dkk., 2020).

The COVID-19 Vaccine Procurement Program and the Implementation of COVID-19 Vaccination are principally part of the Government's efforts to tackle COVID-19 with the aim of establishing herd immunity to reduce morbidity and mortality due to COVID-19. This goal can be achieved with the synergy and roles of all parties, especially the community.

METHOD

This was an analytic observational study with a cross sectional design. The variables studied were SARS-CoV-2 S-RBD antibody titers in two population groups, namely UMY employees who received COVID-19 vaccination and employees who had experienced COVID-19 illness. The research was conducted from January to June 2022. This research has obtained an Ethics Permit and a previous Institutional Permit. The subjects used in this study were UMY employees who underwent general check-up at AMC Muhammadiyah. All subjects have been given an explanation of the purpose and benefits of the study, and have given informed consent. The number of research subjects used in this study was calculated using the Slovin formula. The sampling technique used in this research is non-probability sampling with purposive sampling. Inclusion criteria in this study include: (i) employees who are actively working (ii) Age 20-56 years (iii) A history of infection evidenced by PCR examination evidence (iv) getting vaccinated for more than 2 weeks. For employees who have an infection proven by a positive PCR history. Meanwhile, the exclusion criteria used in this study were employees who had a history of immunodeficiency or autoimmune deficiency.

Subjects were taken whole blood without anticoagulant, then centrifuged to get serum. From the serum samples, the SARS-CoV-2 S-RBD antibody titer was examined. Examination of the SARS-CoV-2 S-RBD antibody titer was carried out in the MMT laboratory of AMC Hospital Yogyakarta using the Elisa method. Data analysis using descriptive method.

RESULTS AND DISCUSSION

Respondents' characteristic

The research subjects were 90, consisting of 45 subjects who had been exposed and 45 subjects who were not exposed to COVID-19. Subjects exposed to COVID-19 consisted of 25 men and 15 women, while subjects who were not exposed to COVID-19 consisted of 19 men and 26 women. The lowest age of the research subject is 23 years old and the highest is 64 years old. Based on age group, 3 subjects exposed to COVID-19 in the 26-35 year age group, 14 subjects in the 36-45 year age group, 24 subjects in the 46-55 year age group and 4 subjects in the 56-65 year age group. Meanwhile, 3 subjects who were not exposed to COVID-19 in the 17–25-year age group, 7 subjects in the 26–35-year age group, 6 subjects in the 36-45 year age group, 24 subjects in the 46-55 year age group and age 56-65 years as many as 5 subjects (see table 1)

Table 1. Respondents' characteristic

Respondents' characteristic	Illness group	Healthy group
	Frequency	Frequency
Gender		
Male	25	19
Female	15	26
Total	45	45
Age		
17-25 year	0	3
26-35 year	3	7
36-45 year	14	6
46-55 year	24	24
56-65 year	4	5
Total	45	45
Lowest age	30	23
Highest age	59	64

a. SARS-CoV-2 S-RBD Antibody Examination Results

The results of the examination of S-RBD SARS-CoV-2 antibody levels showed that the exposed group had a minimum level of 45.16 AU/mL while the maximum level was more than 1,000 AU/mL. In the unexposed group, 12 subjects had levels <3 AU/mL, while the rest had a minimum level of 3.01 AU/mL and a maximum level of 39.6 AU/mL as shown in table 2 below:

	History	
	Exposed	Did not expose
Min	45.16	<3
Max	>1000	39.6

b. Discussion

In this study, there were significant differences in the levels of SARS-CoV-2 S-RBD antibodies after vaccination in the group exposed to COVID-19 compared to the group not exposed. The main goal of vaccination is to achieve immunogenicity, namely the ability of a vaccine to stimulate the emergence of neutralizing antibodies. The vaccine given is expected to reduce the risk of being infected or reduce the risk of having an infection with severe symptoms, when compared to the unvaccinated group. Vaccines are expected to be able to induce the body's immune system and stimulate T lymphocytes and B lymphocytes to form a defense against microorganisms that cause the disease. Vaccines must be able to trigger the synthesis of specific antibodies against certain pathogens at a certain concentration (titer), and then these antibodies can provide a protective effect for a certain period of time. The expected reaction from the COVID-19 vaccination is an increase in the production of neutralizing antibody (NAB), which is an antibody that has a natural virus neutralization effect by the body, so as to prevent the occurrence of COVID-19 infection (Barnes et al., 2020).

Virus components that enter the body through vaccination will be captured by APC, namely dendritic cells or macrophages. Antigen processing in dendritic cells causes small peptides to be displayed on the cell surface in class I and class II Major Histocompatibility Complex (MHC) grooves. Cytotoxic T cells (CD8+) recognize the MHC class I peptide complex and differentiate into cytotoxic effector cells which then produce perforin, lymphotoxin and TNF- which are able to kill infected cells or pathogens, apart from differentiating into effector cells, cytotoxic T cells will also partially become cytotoxic T cells. T memory. Helper T cells (CD4+) recognize the MHC class II peptide complex which will then activate B cells which will then proliferate and differentiate into plasma cells (which will produce antibodies) and memory B cells. Antibodies produced by plasma cells in response to vaccines can be in the form of neutralizing antibodies (S-specific antibodies), and can also be non-neutralizing antibodies such as N-specific antibodies, M-specific antibodies, ORF antibodies and other S-specific antibodies. S-specific antibodies can bind to the specific spike protein S-RBD of the SARS CoV-2 virus, thereby preventing the binding between the spike protein and the ACE-2 receptor which affects the clearance of the virus. The memory B cells that are formed can accelerate the formation of antibodies in the event of further exposure (Colbert et al., 2020).

The SARS-Cov-2 virus infects cells via the ACE2 receptor, as in SARS. Viral RNA, as pathogen associated molecular patterns (PAMPs), will be recognized by pattern recognition receptors (PRRs). Toll-like receptors (TLR) 3, TLR7, TLR8, and TLR9 will detect the presence of viral RNA and DNA in endosomes. While viral RNA receptor retinoic acid inducible gene I (RIG-I), RIG-I), and cytosolic receptor melanoma differentiation-associated gene 5 (MDA5) play a role in recognizing viral RNA in the cytoplasm. (Shi et al., 2020,Li et al., 2020,He et al., 2020)

These results are in line with the research conducted by DuaaW. Al-Sadeq et al which found significant differences in the levels of sRBD antibodies (IgG and IgA) (Al-Sadeq et al., 2021). Research conducted by Steensels et al., 2021 also yielded results that were in accordance with this study (Steensels et al., 2021). sRBD antibody levels in groups of individuals who have been exposed to have higher antibody levels because they already have memory B cells that can accelerate antibody formation in the event of subsequent exposure (vaccination).(Colbert et al., 2020).

CONCLUSION

From this study, it can be concluded that there are differences in the levels of SARS-CoV-2 S-RBD antibodies which are higher in individuals who have been exposed to COVID-19 than individuals who have not been exposed. There are subjects who have not responded to the COVID-19 vaccination.

Ideal conditions are needed to carry out further research. The author would like to thank for the cooperation of this research Faculty of Medicine and Health Sciences UMY, PKU Muhammadiyah Gamping Hospital Yogyakarta, Laboratory of MMT Hospital AMC Yogyakarta.

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