

Research Article

Overview of S-RBD Antibody Levels After Covid-19 Vaccination in Premenopausal and Menopausal Women

Gambaran Kadar Antibodi S-RBD Pascavaksinasi COVID-19 pada Perempuan Premenopause dan Menopause

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Abstract

Objective: To determine the levels of S-RBD antibodies in premenopausal and postmenopausal women who received the COVID-19 vaccine.

Methods: This study involved 21 premenopausal and postmenopausal women who received two doses of CoronaVac at 28 days intervals. The duration of vaccination was 4-24 weeks. This study was conducted on May–October 2021 in Kendari City, Indonesia. Blood samples were taken at a health care facility and examined at the Prodia Clinical Laboratory. Participants were healthy women, willing to participate, and signed informed consent. Participants were excluded if they had a history of COVID-19, had taken antibiotics or immunomodulators in the last 24 hours, had a history of acute/chronic inflammatory disease and malignancy, were traumatized and received monoclonal antibody therapy.

Results: Participants were 52.95±7.61 years old. The duration of the second vaccination was 13.67±5.26 weeks. The lowest level of S-RBD antibody was menopause with vaccination duration ≤12 weeks (185.59±112.34 U/mL), and the highest was premenopause with vaccination duration >12 weeks (257.5±3.54 U/mL). The S-RBD antibody level in premenopausal women was higher than in menopausal women at the duration of vaccination ≤12 weeks (223.37±63.45 vs 185.59±112.34 U/mL) and >12 weeks (257.5±3.54 vs 225.55±91.14 U/mL). There was no significant difference in S-RBD antibody levels between two or more groups ($p>0.05$).

Conclusion: S-RBD antibody levels in postmenopausal women after receiving two doses of COVID-19 vaccine were lower than in premenopausal women, but the difference was not significant. S-RBD antibody levels in postmenopausal women increased with increasing duration of vaccine administration.

Keywords: COVID-19 vaccine, immune response, menopause, S-RBD antibody.

Abstrak

Tujuan: Mengetahui gambaran antibodi S-RBD pada perempuan premenopause dan menopause yang mendapat vaksin COVID-19.

Metode: Penelitian ini melibatkan 21 perempuan premenopause dan menopause yang telah melakukan vaksinasi sebanyak dua dosis (interval 28 hari) dengan CoronaVac dalam kurun waktu 4-24 minggu pasca vaksinasi. Penelitian telah dilaksanakan pada bulan Mei–Oktober 2021 di Kendari, Indonesia. Pengambilan sampel darah dilakukan di fasilitas pelayanan vaksinasi COVID-19 dan pemeriksaannya dilakukan di Laboratorium Klinik Prodia. Partisipan adalah perempuan yang sehat, bersedia ikut dan menandatangani informed consent. Partisipan akan dikeluarkan dari kelompok sampel bila memiliki riwayat COVID-19, mengkonsumsi antibiotik atau immunomodulator dalam 24 jam terakhir, memiliki riwayat penyakit inflamasi akut/kronik dan penyakit keganasan, dalam kondisi trauma, dan mendapat terapi antibodi monoklonal.

Hasil: Umur partisipan adalah 52,95±7,61 tahun. Durasi waktu vaksinasi kedua adalah 13,67±5,26 minggu. Kadar antibodi S-RBD yang terendah adalah kelompok menopause dengan durasi waktu vaksinasi ≤12 minggu (185,59±112,34 U/mL) dan yang tertinggi pada premenopause dengan durasi vaksinasi >12 minggu (257,5±3,54 U/mL). Kadar antibodi S-RBD pada premenopause dengan durasi vaksinasi ≤12 minggu lebih tinggi dibanding pada menopause (223,37±63,45 U/mL vs 185,59±112,34 U/mL). Kadar antibodi S-RBD pada premenopause dengan durasi vaksinasi >12 minggu lebih tinggi dibanding pada menopause (257,5±3,54 U/mL vs 225,55±91,14 U/mL). Tidak ada perbedaan yang signifikan kadar antibodi S-RBD antara dua atau lebih kelompok ($p>0,05$).

Kesimpulan: Kadar antibodi S-RBD perempuan menopause setelah mendapat dua dosis vaksin CoronaVac lebih rendah daripada premenopause, namun perbedaannya tidak signifikan. Kadar antibodi S-RBD pada perempuan menopause meningkat dengan bertambahnya durasi pemberian vaksin.

Kata kunci: antibodi S-RBD, menopause, respon imunitas, vaksin COVID-19.

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INTRODUCTION

The government struggles to deal with the COVID-19 pandemic by realizing herd immunity through vaccination.¹ Research with simulation studies shows the controlled spread of SARS-CoV-2 achieved when a large proportion of the population has been vaccinated (70–80%).²

The elderly have a higher risk of suffering severe conditions and mortality caused by COVID-19.³ In a previous study, elderly patients (>65 years) experienced more severe cases of COVID-19 and have a higher mortality rate possibility than survivability.⁴ Of all COVID-19 cases in Indonesia, 11.8% of cases and 46.7% of mortality are the elderly.⁵ Therefore, the elderly are prioritized to receive the COVID-19 vaccine.⁶

The mechanism of the COVID-19 immune response has not been fully understood and is under investigation. The correlation of estradiol with a decrease in vaccine-induced immunity was found during influenza vaccination for women.⁷ However, another study showed antibody response of post-menopausal women who received hormone therapy was similar to that of those who did not.^{8,9}

Quantitative tests for anti-SARS-CoV-2 antibodies could determine the specific antibody response to the vaccine and individual antibody levels and monitor antibody responses.¹⁰ Neutralization test is the gold standard for detecting specific immunity.¹¹ Some standard examinations require a level-3 biosafety laboratory which is difficult to find in developing countries.¹² A substitute assay for the neutralization test is a specific antibody against the Receptor Binding Domain (RBD) of the SARS-CoV-2 virus. The reason is most of the neutralizing antibodies bind to RBD. Each Coronavirus species has a different Sub-unit of RBD due to their bonds with a different receptor. Thus, they are specific.¹³

Today, many researchers investigate COVID-19 to find out various aspects of this virus, including vaccination and the impacts. This study aimed to determine the SRBD antibodies levels in premenopausal and menopausal women after receiving the COVID-19 vaccine. The results of this research are expected to be information for evaluating the COVID-19 vaccine effectiveness.

METHODS

It was a cross-sectional study conducted on May – October 2021 in Kendari City, Indonesia.

Blood samples were taken at the vaccination service facility and examined at the Prodia Clinical Laboratory. Participants were premenopausal and postmenopausal women who had received 2 doses of CoronaVac with an interval of 28 days. The duration of vaccination was 6–24 weeks. Inclusion criteria were healthy, willing to participate, and signed the informed consent. Exclusion criteria were having a history of COVID-19, taking antibiotics or immunomodulators in the last 24 hours, having a history of acute/chronic inflammatory disease and malignancy, traumatic conditions, and receiving monoclonal antibody therapy.

This study used Anti-SARS-CoV-2 S (Roche) reagent, ECLIA method, RBD anti-agent, sensitivity percentage of 98.8%, and sensitivity percentage of 100%. The researchers collected venous blood samples. The plasma or serum of the samples was separated with the centrifugation technique. The applied angular speed was 12.000 rpm within 5 minutes. Plasma or serum was transferred into several 200 L tubes and immediately checked the samples. If it is not possible, so the samples were stored in a freezer at a temperature of 2–8 °C for a maximum of 14 days. Approximately 12–20 µL samples were incubated for 9 minutes with recombinant-specific SARS-CoV-2-S-RBD antigen and ruthenium-labeled recombinant-specific SARS-CoV-2-S-RBD antigen to form a sandwich complex. Add streptavidin-coated microparticles, and a second incubation was carried out. The complex would become a solid phase that reacted with biotin and streptavidin. The reagent mixture was put into a microplate which was magnetically trapped on the surface of the electrode. The unbound substance was rinsed through the washing process. Induction of chemiluminescent emission is carried out by providing an electric current that is measured by a photomultiplier. The results are measured automatically using software by comparing the electrochemiluminescent signal obtained from the sample reaction with the calibration cutoff value signal. The displayed number will describe the antibody titer.

Univariate analysis was carried out to determine the characteristics of the participants and the distribution of the observed variables. Data analysis used SPSS to assess differences with the Kruskal-Wallis test.

This research has received ethical approval from the Health Research Ethics Commission, Faculty of Medicine, Halu Oleo University, number

120/UN29.17.1.3/ETIK/2021.

RESULTS

This report includes 21 participants whose age is 52.95 ± 7.61 years. The second vaccination interval was 13.67 ± 5.26 weeks. The characteristics of the participants are shown in table 1.

Table 1. Characteristics of Participants

Characteristics	n	%
Education		
Middle	5	23.8
High	16	76.2
Occupation		
Housewife	5	23.8
Employess	16	76.2
Parity		
≤ 2	6	28.6
> 2	15	71.4
Age (years)		
≤ 55	10	47.6
> 55	11	52.4

Table 1 shows that the majority of participants are highly educated (76.2%), are employees (76.2%), and have parity > 2 (71.4%).

Table 2. Mean, Standard Deviation, Minimum and Maximum Values of S-RBD Antibody Levels based on the Duration of Vaccination

Variabel	S-RBD antibody levels (U/mL)				
The duration of vaccination	Minimum	Maximum	Mean	SD	P-value
Premenopause					
(weeks)					
≤ 12	150.1	260.0	223.37	63.45	.855*
> 12	255.0	260.0	257.50	3.54	.686*
Menopause					
(weeks)					
≤ 12	9.42	260.0	185.59	112.34	.962*
> 12	18.82	260.0	225.55	91.14	.444*

Table 2 presents descriptive analysis, namely the minimum, maximum, mean, standard deviation, and normality values of the data distribution in each group. The lowest levels of S-RBD antibodies were menopause with vaccination duration 12 weeks (185.59 ± 112.34 U/mL), and the highest was premenopause with vaccination duration >12 weeks (257.5 ± 3.54 U/mL).

At the duration of vaccination 12 weeks, the mean S-RBD antibody levels in premenopause were higher than in menopause (223.37 ± 63.45 U/mL vs 185.59 ± 112.34 U/mL). S-RBD antibody levels at vaccination duration >12 weeks also found that premenopause was higher than

menopause (257.5 ± 3.54 U/mL vs 225.55 ± 91.14 U/mL).

The Shapiro-Wilk normality test showed that the data was not normally distributed ($p < 0.05$) so that the Kruskal-Wallis difference test was continued. There was no significant difference in S-RBD antibody levels between two or more groups ($p > 0.05$).

DISCUSSION

This study aims to describe the SRBD antibody levels in premenopausal and postmenopausal women who received two doses of the COVID-19 vaccine. Receptor Binding Domain (RBD) is an important target for antiviral compounds and antibodies that can be evaluated post-vaccination.¹⁴ This study showed that there was a difference in S-RBD antibody levels between premenopause and menopause but it was not statistically significant. Menopausal women have a good COVID-19 vaccine-induced immune response. They had lower immunity responses due to COVID-19 vaccine induction than premenopause women.

These findings are in line with Wu et al. that reported in their clinical test that CoronaVac could be properly tolerated and was immunogenic for healthy adults aged older than 60 years old. Responses of neutralizer antibodies on the population toward SARS-CoV-2 did not decrease.¹⁵ Estradiol affects modulated immune cells, namely B cell activation and production of neutralizing antibodies, including S-RBD.^{16,17} In addition, some factors influence the immune response to vaccines, namely intrinsic factors (age, sex, genetic, comorbid), extrinsic factors, lifestyle, nutrition, environment, vaccine administration, and vaccine factors.¹⁸

These results indicate differences in SRBD antibody levels between pre-menopause and menopause based on the duration of vaccination. Statistically, it is not significant. The highest amount of SRBD antibody titer was found on participants with > 12 weeks of vaccination, both in premenopausal and menopausal women. The findings showed menopausal women, after receiving twice doses of vaccine, could improve their antibodies. The same findings were similar with premenopausal women. Thus, menopausal women could take vaccination schedules as younger women did.

It is in line with the study who found that two doses of vaccination with CoronaVac were able

to induce a humoral response in people older than 60 years old. Patients with comorbidity tended to have lower immune responses toward vaccine and infection. These matters resulted in higher vaccination doses or vaccination schedule changes for this group.¹⁹

A study in China found anti-spike antibody responses in health care workers aged 60 years (n=24) after the first dose was relatively low (37.5%). their immunogenicity could reach the level of people aged between 18-59 years old after receiving the second dose (95.7%).¹¹ A study in Chili on CoronaVac found the seroconversion level for people aged 60 years old with a percentage of 18.1% after 14 days of first vaccine administration. Then, the percentage turned into 100% after the second dose received after 28 days.²⁰ The findings were similar to this study, although this is preliminary research. We found an increased antibody titer during <12 weeks after the second dose. This finding would be a consideration to provide vaccination for the susceptible group.

The RBD subunit is an epitope that produces neutralizing antibodies specific to Spike (S) protein.²¹ In this study, participants had varying levels of S-RBD antibodies. Research in identifying the correlation between neutralizing antibodies and CD4+ T cells against S protein found an important role for CD4+ T cell activation in collaborating the activity of B cells and T cells against SARS-CoV-2.²¹ Titer levels of antibodies that are protective against SARS-CoV-2 are still unknown. Memory T cells and B cells triggered by the inactivated vaccine are expected to play an important role in protection against infection by SARS-CoV-2.²²

In this study, some participants have S-RBD antibody titers below <250 U/mL. It could be caused by the low immunogenicity of the inactivated vaccine if compared to the SARS-CoV-2 vaccine using other methods due to the multivalence of antigens from the inactivated vaccine or the decrease in the number of B cells and memory cells due to aging.^{23,24}

CONCLUSION

Based on the results of this study, we conclude that after vaccination, postmenopausal women have lower levels of S-RBD antibodies than premenopausal women. However, the difference is not significant. S-RBD antibody levels in postmenopausal women increased with the

duration of vaccine administration. Two doses of CoronaVac can induce excellent immunity in postmenopausal women, both in terms of and timing of repeated dosing.

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CONFLICT of INTERESTS

The authors declare that there is no conflict of interest.

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