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ORIGINAL ARTICLE

# Comparison of Antibody Responses Following COVID-19 Vaccination Between Individuals With and Without Comorbidities

## Perbandingan Respons Antibodi setelah Vaksinasi COVID-19 antara Individu dengan dan tanpa Komorbiditas

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## ABSTRACT

**Background**

Vaccination is a Crucial public health strategy for reducing the transmission of viral infections and protecting populations from severe illness. COVID-19 vaccines have played a significant role in decreasing the incidence and mortality rates linked to the virus. However, immune responses to vaccination may differ among individuals, especially those with comorbidies that could alter immune function. This study aimed to compare antibody responses in adults with and without comorbidities, 18 months after receiving the COVID-19 vaccine.

**Methods**

This was a cohort study with two sampling time points: before vaccination and 18 months after vaccination. The study was conducted in Yogyakarta, Indonesia. Data were collected through self-administered questionnaires and venous blood sampling. Antibody titers were measured to evaluate the humoral immune response in participants with and without comorbidities.

**Results**

Before vaccination, the highest proportion of positive antibody titers was found among females (40.2%), individuals aged 18–44 years (44.7%), those with a senior high school education (48.1%), and individuals with normal body weight (44.3%). A Comparison of antibody levels at baseline and 18 months after vaccination between groups with and without comorbidities showed no statistically significant difference, with a p-value of 0.992.

**Conclusions**

Although no significant difference was found in antibody responses between individuals with and without comorbidities, comorbid conditions may still influence immune response depending on their type and severity. These findings suggest the need for further research to examine the specific effects of various comorbidities on long-term vaccine-induced immunity.

**Keywords:** Antibody response; Aomorbidities; COVID-19 Vaccine.

## ABSTRAK

**Latar Belakang**

Vaksinasi merupakan strategi penting dalam kesehatan masyarakat untuk mengurangi penularan infeksi virus dan melindungi populasi dari dampak berat suatu penyakit. Vaksin COVID-19 telah berkontribusi signifikan dalam menurunkan angka kejadian dan kematian akibat virus tersebut. Namun, respons imun terhadap vaksinasi dapat bervariasi antar individu, terutama pada mereka yang memiliki kondisi komorbid yang berpotensi memengaruhi fungsi sistem imun. Penelitian ini bertujuan untuk membandingkan respons antibodi pada orang dewasa dengan dan tanpa komorbiditas, 18 bulan setelah menerima vaksin COVID-19.

**Metode**

Penelitian ini merupakan studi kohort dengan dua titik waktu pengambilan sampel: sebelum vaksinasi dan 18 bulan setelah vaksinasi. Studi dilakukan di Yogyakarta, Indonesia. Pengumpulan data dilakukan melalui pengisian kuesioner mandiri dan pengambilan darah vena. Titer antibodi diukur untuk menilai respons imun humoral pada partisipan dengan dan tanpa komorbiditas.

**Hasil**

Sebelum vaksinasi, proporsi tertinggi individu dengan titer antibodi positif ditemukan pada kelompok perempuan (40,2%), usia 18–44 tahun (44,7%), tingkat pendidikan sekolah menengah atas (48,1%), dan kelompok dengan berat badan normal (44,3%). Perbandingan kadar antibodi pada saat baseline dan 18 bulan setelah vaksinasi antara kelompok dengan dan tanpa komorbiditas menunjukkan tidak ada perbedaan yang bermakna secara statistik, dengan nilai p sebesar 0,992.

**Kesimpulan**

Meskipun tidak ditemukan perbedaan signifikan dalam respons antibodi antara individu dengan dan tanpa komorbiditas, kondisi komorbid tetap dapat memengaruhi respons imun tergantung pada jenis dan tingkat keparahannya. Temuan ini menunjukkan perlunya penelitian lanjutan untuk mengeksplorasi efek spesifik dari berbagai jenis komorbiditas terhadap kekebalan jangka panjang yang diinduksi oleh vaksin.


**Kata Kunci:** Respons antibodi; Komorbid; Vaksin COVID-19.

## INTRODUCTION

Vaccination is a highly effective and efficient method for combating viral pandemics. Vaccination stimulates the immune system, generating an immune response that includes antibodies and T cells, which can recognize and fight the same virus upon exposure.[1,2] The goal of the vaccination program is to reduce the number of viral infections spreading in the community. By increasing the number of immune individuals through vaccination, the transmission of the virus can be suppressed, creating a herd immunity effect. This occurs when the majority of the population is already immune, thereby protecting those who have not been vaccinated or cannot be vaccinated due to medical reasons.[3,4] Depending on the disease, different populations require different percentages of people to be immune to achieve herd immunity. For coronavirus, especially Sars-Cov-2, it is estimated that around 70–90% of the population needs to be immune, although this figure varies depending on the circulating virus variant.[5,6]

Vaccination aims to generate an adaptive and specific immune response to the source of infection, providing adequate protection against infectious diseases. The success of a vaccine depends on the process of antigen recognition, activation, expansion, the production of memory cells, and the functioning of lymphocytes, which have their respective specialties. Administering a vaccination can trigger the body's immune response, which will react to the antigens contained in the vaccine.[7,8]

In Phase III trials and real-world data, the vaccination has reassuringly demonstrated efficacy and safety in preventing severe SARS-CoV-2 infections.[9,10,11] Additionally, individuals with comorbidities, such as diabetes, and other vulnerable populations linked to an elevated risk of

morbidity and mortality are particularly well-protected by the vaccine.[8] Nonetheless, there is proof that diabetes mellitus patients have a variety of immunodeficiencies that impact both the innate and acquired immune systems.[12] As a result, it is reasonable to assume that, in comparison to the general population, the vaccination's protective impact may be less pronounced. Patients with diabetes mellitus have demonstrated decreased immunogenicity to the hepatitis B vaccine in prior investigations, but the evidence for influenza, pneumococcal, and varicella-zoster vaccines is less certain.[13] A Japanese study revealed no significant correlation between vaccine efficacy and diabetes mellitus[14,15], however, numerous subsequent studies using real-world data found that vaccine efficacy was lower in diabetes mellitus patients than in the general population.[16,17]

This study aims to compare antibody responses in adults with and without comorbidities after receiving the SARS-CoV-2 vaccine over an 18-month period. By examining the differences in responses over a longer timeframe, this research can provide valuable insights into the effectiveness of the vaccine in populations with diverse health conditions and inform the development of more targeted vaccination policies for high-risk groups.

## METHODS

This study was a prospective cohort study conducted in Yogyakarta, Indonesia, involving two sampling time points: the first at baseline, before COVID-19 vaccination, and the second 18 months after receiving the second vaccine dose. The study was conducted between March 2021 and October 2022. Ethical clearance was granted by the Health Research Ethics Committee of the Faculty of Medicine, Universitas Indonesia (No. KET-1039/UN2.F1/ETIK/PPM.00.02/2022).

Participants were adults aged 18 years or older who met the inclusion criteria: being physically eligible for blood withdrawal based on a clinical assessment, having no contraindications for vaccination, and providing signed informed consent. Blood specimens (3 mL each) were collected by trained phlebotomists at both time points, and demographic data were collected through structured, self-administered questionnaires.

Participants were stratified by age group into three categories: 18–44 years, 45–59 years, and 60 years or older. Comorbidities were recorded based on participant self-report and confirmed with available medical documentation when possible. The types of comorbidities included: tuberculosis, asthma, chronic obstructive pulmonary disease, blood disorder, coronary heart disease, car suction, chronic digestive diseases, diabetes mellitus, hypertension, and stroke. Participants were then categorized into two main groups: those with at least one comorbid condition and those without any comorbidities.

The study's flow included recruitment, baseline data and sample collection, follow-up sample collection at 18 months, laboratory analysis of antibody titers, and statistical comparison between groups. Antibody titers were quantified using validated immunoassay methods to evaluate the humoral immune response against SARS-CoV-2. Descriptive statistics were used to characterize the study population. Differences in antibody titers between groups with and without comorbidities were analyzed using the independent t-test or Mann–Whitney U test, based on the data distribution. A p-value of $<0.05$ was considered statistically significant.

## RESULTS

The characteristics of the research participants observed in the study included variables such as gender, age, education, body mass index, and type of vaccine. Most of the research participants were female (64.7%), and almost all of the research participants were aged between 18 and 44 years (64.0%), with an average age of 40.02 years. In terms of education, most research participants had a high school education (70.7%). Meanwhile, based on body mass index, the

majority of research participants had a normal body mass index (52.7%). Based on the brand of comorbidity, the number of participants with comorbid conditions is 31.0% including tuberculosis, asthma, chronic obstructive pulmonary disease, blood disorder, coronary heart disease, chronic digestive diseases, diabetes mellitus, hypertension, and stroke.

**Table 1.** Characteristics of study participants

| Variable | N | % |
|---|---|---|
| Sex | | |
| Male | 53 | 35.3 |
| Female | 97 | 64.7 |
| Age group (years) | | |
| 18-44 | 96 | 64.0 |
| 45-59 | 45 | 30.0 |
| 60+ | 9 | 6,0 |
| Education | | |
| Elementary School | 11 | 7.3 |
| Junior High School | 14 | 9.3 |
| Senior High School | 106 | 70.7 |
| University | 19 | 12.7 |
| Body Mass Index (BMI) | | |
| Underweight | 13 | 8.7 |
| Normal weight | 79 | 52.7 |
| Overweight | 42 | 28.0 |
| Obesity | 16 | 10.7 |
| Comorbidity | | |
| Yes | 47 | 31.0 |
| No | 103 | 69.0 |

Based on the results of the interviews documented in the questionnaire, it was found that 31.0% of the subjects have comorbidities with various conditions as outlined in Table 2.

**Table 2.** Types of comorbidities experienced by the participants

| Comorbidity | N | % |
|---|---|---|
| Tuberculosis | 3 | 6.3 |
| Asthma | 3 | 6.3 |
| chronic obstructive pulmonary disease | 1 | 2.1 |
| Blood diorder | 1 | 2.1 |
| Coronary heart disease | 2 | 4.2 |
| Car suction | 1 | 2.1 |
| Chronic digestive tract. | 11 | 23.4 |
| diabetes mellitus | 3 | 6.3 |
| Hypertention | 21 | 44.6 |
| Stroke | 1 | 2.1 |

A blood sample is used to evaluate the baseline binding antibody titers. The results indicate that 42.0% of the population has antibodies to SARS-CoV-2, with an average titer value of 752.55, as determined by antibody titer tests conducted before vaccination. Participants in this study who had antibodies against SARS-CoV-2 suggest that exposure to the virus is quite common in the community where the data were collected. The results of the antibody titer measurements at baseline showed that the highest proportion of positive antibodies was found in the female group (40.2%), the age group of 18-44 years (44.7%), those with a senior high school education (48.1%), and the normal weight group (44.3%).

Eighteen months after the second dose, antibody titers were measured. The results showed that all participants from the population had SARS-CoV-2 antibodies with an average titer value of 4530.79. Meanwhile, the comparison of antibody titers between participants with and without comorbidities at baseline and 18 months after the second dose is presented in Table 3. A significance value of 0.992 was obtained from the analysis findings, which compared the groups with and without comorbidities at baseline and 18 months after the second dose. This value is higher than the significance level of 0.05.

**Table 3.** Comparison between participants with and without comorbidities

| Variable | With Comorbidity | | Without Comorbidity | |
|---|---|---|---|---|
| | Baseline | 18 months post vaccination | Baseline | 18 months post vaccination |
| Positive (%) | 42.6 | 100.0 | 41.7 | 100.0 |
| Mean | 1047.4511 | 3846.3484 | 617.9951 | 4896.6224 |
| Median | 6.6000 | 1764.1000 | 7.6000 | 3115.3000 |
| SD | 4096.78779 | 4823.12604 | 1543.39977 | 6702.39589 |
| Minimum | 0.20 | 17.60 | 0.00 | 32.40 |
| Maximum | 1727092.60 | 23854.20 | 12060.70 | 42752.60 |

## DISCUSSION

Everyone reacts differently to vaccines, depending on their immune system. According to Zimmermann, et al. (2019), humoral and cellular responses following vaccination can be influenced by a variety of factors, including age, gender, genetics, comorbidities, perinatal factors (such as birth weight, feeding practices, and maternal health), external factors (including pre-existing immunity, infections, and antibiotics), environmental factors (like geography and season), lifestyle factors (such as smoking, alcohol consumption, physical activity, and sleep duration), and nutritional status (e.g., body mass index, micronutrient levels, and gut health). Additionally, vaccine type, adjuvant used, time and route of administration, and vaccine dosage all significantly influence antibody production.[18]

In this investigation, after 18 months post-vaccination, there was no statistically significant difference in binding antibody seropositivity between individuals with and without comorbidities ($p>0.05$). These findings are consistent with a study by Fonseca et al. (2022), which found comparable anti-spike IgG seropositivity among healthcare workers with and without comorbidities. However, they reported a significant difference in median antibody levels at certain time points (days 1 and 2 after the first dose and 6 months after the second dose) between these groups after receiving an inactivated virus vaccine.[19]

It is widely recognized that individuals with comorbidities are a high-risk group for SARS-CoV-2 infection. As Callender et al. (2020) explain, many comorbidities associated with COVID-19 affect immune system function and, consequently, the body's response to infection. Additionally, medications used to manage these conditions can influence immune responses.[20] In line with this, Geisen et al. (2021) and Bayram et al. (2021) observed lower antibody titers in individuals with chronic diseases following two doses of the CoronaVac vaccine, suggesting that individuals with long-term health conditions may require booster doses.[21,22]

Similarly, Fonseca et al. (2022), Karamese et al. (2022), and Barin et al. (2022) reported that individuals with underlying conditions, such as diabetes mellitus, hypertension, or dyslipidemia, were more likely to test seronegative after receiving two doses of CoronaVac.[19,23,24] Kwetkat et al. (2020) also emphasized that comorbidities, much like immunosenescence in older people, can impair vaccine immunogenicity.[25] Huang et al. (2023) further supported this, showing that individuals with a higher burden of comorbidities were more likely to be seronegative after SARS-

CoV-2 vaccination.[26] Thus, based on current evidence, including findings from Fonseca et al. (2022), booster doses may be particularly beneficial for elderly or comorbid individuals, as they help enhance and prolong immune protection.[19]

Lymphopenia is a hallmark of SARS-CoV-2 infection and is often associated with severe disease progression. Its effects on B cells, $CD4^+$ and $CD8^+$ T cells, and natural killer cells have been extensively documented. According to Reynolds et al. (2021), mutations in the spike protein, such as N501Y, which affects the receptor-binding domain, may impair viral neutralization and also influence T-cell immunity. However, these responses tend to remain relatively stable.[27]

People with comorbidities should exercise heightened caution during SARS-CoV-2 infection, given their increased vulnerability. Vaccination is one of the most effective preventive strategies. As long as comorbid conditions are well managed, COVID-19 vaccines are considered safe and effective for this population. Nevertheless, vaccination should be administered carefully and under medical supervision to minimize potential adverse effects. Some studies suggest that when managed properly, vaccination of individuals with comorbidities is both safe and beneficial.

## CONCLUSION

This study found no significant difference in antibody responses between individuals with and without comorbidities, 18 months after COVID-19 vaccination. This suggests that comorbidities—particularly those that are mild and well-controlled—do not substantially impair antibody formation against SARS-CoV-2. However, these findings only reflect the humoral aspect of the immune response and do not represent the full spectrum of immunity. Given that individuals with comorbidities remain at higher risk for severe COVID-19 outcomes, complete vaccination and booster doses remain essential. Further studies with larger sample sizes and assessments of cellular immune responses are needed to gain a more comprehensive understanding of vaccine effectiveness in this population.

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## AUTHORS CONTRIBUTION

Study conception and design: IB, K, MDH; Data collection: TR and AD; Analysis and interpretation of results: S, JST, IE; Draft manuscript preparation: IB, K, MDH.

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## CONFLICT OF INTEREST

Competing interests: No relevant disclosures.

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