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Comparison of Antibody Responses at 18 Months after COVID-19 Vaccination in Adults With and Without Comorbidities

Background. The COVID-19 pandemic has ravaged the world and altered the foundations of public health and healthcare systems. Vaccination is the most important step in controlling the spread of the virus and protecting the general public from the harmful effects of COVID-19 infection. This study aims to analyze the antibody response formed after 18 months of COVID-19 vaccination in adults, both with and without comorbidities. **Methods**. This study is a cohort study with two sampling points, namely before vaccination and 18 months after the second dose of the COVID-19 vaccine. The sampling location is Sleman Regency, Special Region of Yogyakarta, Indonesia. Interviews and blood sampling were used for data collection. **Results**. The results of the antibody titer tests conducted before vaccination 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%). A significance value of 0.992 was obtained from the analysis findings that compared the group with and without comorbidities at baseline and 18 months after a second dose. **Conclusions**. Depending on the type of comorbity and how it affects the immune system, certain conditions may have an impact on the intensity and efficacy of the immune response to a vaccine.

KEYWORDS: antibody response; vaccines; CoronaVac; SARS-CoV-2

Introduction

The Coronavirus Disease 2019 (COVID-19) pandemic has disrupted lives around the world, making it one of the greatest disasters in human history. At the end of December 2019, this disease first emerged in Wuhan, China. Because the symptoms are similar to pneumonia, this disease was initially known as Wuhan pneumonia. According to genomic sequencing results, the cause is a new coronavirus. (1) On January 12, 2020, the World Health Organization (WHO) named the new virus 2019 novel coronavirus (2019-nCoV) and officially changed it to coronavirus disease 2019 (COVID-19) on February 12, 2020. As cases of COVID-19 have emerged on various continents, the WHO declared COVID-19 a pandemic on March 11, 2020. (2,3) One of the most effective and efficient methods to combat the COVID-19 pandemic is vaccination. Vaccination stimulates the immune system and generates an immune response consisting of antibodies and T cells, which can recognize and combat the SARS-CoV-2 virus when exposed. (4,5).

The goal of the vaccination program is to reduce the number of SARS-CoV-2 viruses 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. (6,7) The percentage of the population that needs to be immune to achieve herd immunity varies depending on the disease. For COVID-19, it is estimated that around 70–90% of the population needs to be immune, although this figure varies depending on the circulating virus variant. (8,9)

Vaccination aims to generate an adaptive and specific immune response to the source of infection and provide effective protection against infectious disease. 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. Giving COVID-19 vaccination can trigger the body's immunity which will react to the antigens contained in the COVID-19 vaccine. (10,11)

In phase III trials and real-world data, the vaccination has reassuringly shown efficacy and safety in preventing severe COVID-19. (12-14) 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. (12) Nonetheless, there is proof that diabetes mellitus patients have a variety of immunodeficiencies that impact both the innate and acquired immune systems. (15) 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. (16) A Japanese study revealed no significant correlation between vaccine efficacy and diabetes mellitus (17,18), however numerous subsequent studies using real-world data found that vaccine efficacy was lower in diabetes mellitus patients than in the general population, (19,20)
This study aims to compare antibody responses in adults with and without comorbidities after receiving the COVID-19 vaccine over a period of 18 months. By examining the differences in responses over a longer timeframe, this research can provide important insights into the effectiveness of the vaccine in populations with various health conditions and assist in the development of more targeted vaccination policies for high-risk groups.

Methods

Study Design and Participants

As a follow-up to earlier cross-sectional surveys carried out in the Sleman District in 2021 and 2022, this research is being done in this manner. The National Research and Innovation Agency's health ethics commission granted the ethical permission (number 032/KE.03/SK /04/2023). Eighteen months after the second immunization dose, interviews and blood samples were used for data gathering. Three milliliters of blood were drawn aseptically by skilled phlebotomists. The study participants were those who satisfied the inclusion requirements, which included being at least eighteen years old, having taken part in two prior studies (2021 and 2022), having received two doses of the COVID-19 vaccine in the 2021 study, being able to have blood drawn based on a medical examination, and being willing to sign an informed consent form in order to participate in the research. There were 150 individuals in the original study.

Laboratory Examination

The obtained blood was centrifuged for 10 minutes at 8000 rpm in order to separate the serum. The next step was testing the serum for antibodies (IgG) against SARS Co-2 using the SARS-CoV-2 IgG II Quant reagent Kit (Abbott, Diagnostics Division, Sligo, Ireland) and the Chemiluminescent Microparticle Immunoassay (CMIA) method. The Enzyme-Linked Immuno Sorbent Assay (ELISA) has been enhanced using the Chemiluminescent Microparticle Immuno Sp. Assay. Bound achridinylated conjugates were utilized in the final procedure to provide chemiluminescent signals for anti-SARS Cov-2 detection. The chemiluminescent signals from the sample's reaction product were then compared to the signal of the cutoff value that had previously been established via Anti SARS-Cov2 calibration, and this is how the software automatically generated the results. Every step of the antibody testing process follows the instructions that come with the kit. A positive antibody titer against SARS CoV-2 was defined as 50 AU/mL or higher.

Statistical Analysis

Data analysis was conducted using SPSS software v25.0 (SPSS Inc., Chicago, IL) and Microsoft Excel package applications. The results were presented using the mean and standard deviation, depending on the distribution. Numbers and percentages were used to express categorical variables. The Fisher's exact or chi-squared tests were used to analyze categorical variables. The independent t test was statistically analyzed to compare the antibody responses of the two groups.

Results

The characteristics of the research partisipants observed in the study included the variables gender, age, education, body mass index, and type of vaccine. Most of the research partisipants were female (64.7%), and almost all of the research partisipants were aged between 18 and 44 years (64.0%), with an average age of 40,02 years. In terms of education, most of the research partisipants had an educational background of completing high school (70.7%). Meanwhile, based on body mass index, the majority of research partisipants had a normal body mass index (52.7%). Based on the brand of comorbidity, the number of partisipants with comorbid is 31.0%.

The initial aim of this study did not focus on comparing immune responses between participants with and without comorbidities, so the sample size of participants with comorbidities is not proportional to the number of participants without comorbidities. 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.

Before adiabetes mellitusinistering the first dose of the COVID-19 vaccine, 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, according to the 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 was 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 between participants with and without comorbidities at baseline and 18 months after the second dose can be seen in Table 3. A significance value of 0.992 was obtained from the analysis findings that compared the group with and without comorbidities at baseline and 18 months after the second dose. This value is higher than the significance level of 0.05.

Discussion

Everybody reacts differently to the vaccine in terms of their immune system. Age, gender, genetics, comorbidities, perinatal factors (birth weight, feeding practices, maternal factors), external factors (pre-existing immunity, infections, antibiotics), environmental factors (geography, season), lifestyle factors (smoking, alcohol consumption, exercise, and length of sleep), and nutritional factors (body mass index (BMI), micronutrients, enteropathy) can all affect humoral and cellular responses following vaccination. Furthermore, the kind of vaccine, the adjuvant utilized, the time of vaccination, the mode of delivery, and the quantity adiabetes mellitusinistered all affect how many antibodies a person develops. (21)

In this investigation, after 18 months post vaccination there was no discernible difference in binding antibody seropositivity between the groups with and without comorbidities ($p > 0.05$). These findings corroborate earlier research by Fonseca et al., which found that healthcare workers with and without comorbidities had comparable seropositivity for anti-spike IgG. However, a significant difference was observed at 1 and 2 days after the first dosage, as well as 6 months after the second dose, when the study compared the median antibody levels after giving the entire virus vaccination to the two groups. (22)

It is commonly known that individuals with comorbidities are high-risk groups for COVID-19. Numerous comorbidities linked to COVID-19 have an impact on immune system function, which directly affects the body's reaction to COVID-19. Moreover, the medications provided to treat these comorbidities have an impact on how COVID-19 advances. (23) Participants with comorbidities had considerably lower antibody titers. After receiving two doses of CoronaVac vaccination, individuals with chronic illnesses also showed low levels of antibodies against the SARS-CoV-2 spike protein, according to Geisen et al. (24) and Bayram et al. (25). These results imply that individuals with long-term medical conditions might require a second dose of the CoronaVac vaccination.

After receiving two doses of CoronaVac, those with concomitant conditions such as diabetes mellitus, hypertension, or dyslipidemia were more likely to test negative for the virus. (22,26,27) Comorbidities have been shown to decrease vaccine immunogenicity and antibody response, much like age-related immunological decline. (28). As a result, people with greater comorbidities were more likely to be seronegative for any COVID-19 immunizations they got. (29). For those who are elderly or have multiple medical conditions, it is advisable to administer a booster dose of the COVID-19 vaccination. (22) This suggestion is based on the current finding that, following one booster dosage of Moderna, all individuals, regardless of age or concomitant disease, were positive for anti-S-IgG antibodies.

Immunization against COVID-19 is not advised in individuals with comorbidities unless directed by their treating physician, as this condition has a negative impact on clinical results. Lymphoma is a common sign of SARS-CoV-2 infection and is linked to serious illness. Multiple studies have reported effects of lymphopenia on natural killer cells, B cells, and CD4+ and CD8+ T cells. The S protein mutation N501Y is one of the most harmful because it affects the Receptor Binding Domain (RBD), the area of the protein that binds directly with the receptor to infect people. Though largely stable, T-cell immunity is likewise largely impacted by the N501Y mutation. (30) People with comorbidities should be especially careful when implementing COVID-19 preventive measures because they are among the most susceptible populations to contracting the virus. Getting the COVID-19 vaccine is one method to accomplish this. As long as the disorders are treated with medical guidance, those with comorbidities are now allowed to receive the COVID-19 vaccine, which is considered safe and useful. Nevertheless, in order to avoid or reduce the likelihood of adverse effects that could jeopardize the patient's health, the COVID-19 vaccination must be administered with extreme caution and careful consideration for medical advice. However, some studies suggest that, as long as the comorbidities are managed, giving the COVID-19 immunization to patients who have them is safe.

Conclusion

The results of the statistical analysis show that there is no difference between the groups with and without comorbidities. Following COVID-19 vaccination, those with comorbidities may have different immune responses than people in good health. Depending on the type of comorbidity and

how it affects the immune system, certain comorbid conditions may have an impact on the intensity and efficacy of the immunological response to the vaccine.

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Authors Contribution

The planning for the research involved all of the authors. IB gathered participants, measured, conducted analysis, and wrote the first draft of the paper. JST oversaw the effort, created the research ideas, and analyzed the findings. IE and AD oversaw the project, evaluated the findings, made revisions, and gave the manuscript final clearance. TR and SC helped with the manuscript revision and result interpretation. M helped to interpret the findings. MDH and KH offered crucial edits to the text and helped explain the findings. Every contributor provided feedback on the text and talked about the findings.

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