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Clinical Application of Chemiluminescence Microparticle Immunoassay (CMIA) to Measure Antibody Responses After 18 Months of Covid-19 Vaccination and Comparison with Enzyme-Linked Immunosorbent Assay (ELISA)

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Antibody Response, Chemiluminescence Cicroparticle Immunoassay, COVID-19, Enzyme-Linked Immunosorbent Assay, Vaccine.

ABSTRACT:

Background/Aim: This study aims to compare the clinical application of the CMIA and ELISA methods in measuring antibody responses after 18 months of COVID-19 vaccination with Sinovac and AstraZeneca. By comparing the sensitivity, specificity, and accuracy of the two methods, it is hoped that we can gain a better understanding of their effectiveness in monitoring the immune response to COVID-19 vaccination over an extended period.

Materials and Methods: The study design is longitudinal. Participants were individuals vaccinated against COVID-19 with Sinovac and AstraZeneca in the previous 18 months. Data collection involved interviews and blood sampling. Antibody response measurements were conducted using the CMIA method, with some samples measured using ELISA for comparison. Data analysis was performed using SPSS software v25.0 and the Microsoft Excel package. An independent t-test was used to compare antibody responses between baseline and 18 months after vaccination. Additionally, a paired sample t-test was used to compare the CMIA and ELISA methods.

Results: The majority of research subjects were women (67.2%), aged 18 to 44 years (9.2%), with an average age of 41.45 years; 58% had completed high school education, and 48% had a normal body mass index. AstraZeneca vaccine recipients outnumbered Sinovac recipients. Before vaccination, 65.4% had SARS-CoV-2 antibodies, with the highest proportion of positive antibodies among females (69.6%), those aged 18–44 years (59.2%), those with a high school education (45.7%), those with a normal weight (55.6%), and those who received the AstraZeneca vaccine (72.3%). After 18 months, all research subjects still showed positive antibody results, with the average antibody titer for AstraZeneca higher than for Sinovac. The analysis revealed no significant difference between results obtained using the CMIA and ELISA methods ($p = 0.992$).

Conclusion: The majority of participants showed a positive antibody response at baseline, which persisted at 18 months after vaccination. The average antibody response was higher in participants given AstraZeneca compared to Sinovac. There were no significant differences in measuring antibody responses with CMIA and ELISA.

1. Introduction

On December 31, 2019, the coronavirus illness 2019 (COVID-19) was first discovered [1]. The virus was identified as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the World Health Organization on February 11, 2020, and the illness was

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dubbed Coronavirus Disease 2019 (COVID-19) [2]. The SARS-CoV-2 virus is responsible for the COVID-19 pandemic, which has spread worldwide and has fundamentally changed public health and healthcare systems.

The development of a COVID-19 vaccine has been a pivotal strategy in combating the pandemic since its declaration by the World Health Organization (WHO) in the early months of 2020. Vaccination has been deemed one of the most crucial strategies for halting the transmission of the virus and protecting the public from the adverse effects of COVID-19 infection [3,4].

Early in the pandemic, assessing antibody responses following COVID-19 vaccination became a primary focus in understanding vaccination efficacy and the durability of immunity conferred by the vaccine. The development of accurate and reliable techniques for measuring antibody responses to SARS-CoV-2 is critical in this context. Two widely adopted techniques proven effective in identifying antibodies to the SARS-CoV-2 virus are Enzyme-Linked Immunosorbent Assay (ELISA) and Chemiluminescence Microparticle Immunoassay (CMIA) [5,6].

As the pandemic progresses, it becomes crucial to understand the effectiveness of vaccination over longer timeframes, particularly beyond 18 months. Antibody responses may change or diminish over this period, potentially impacting the longevity of individual immunity to viral infections and the efficacy of vaccination. Thus, further investigation is warranted to evaluate the relative superiority of CMIA and ELISA in this context and to assess methods for assessing antibody responses following 18 months of COVID-19 vaccination [7,8].

By analyzing the relative clinical performance of CMIA and ELISA in assessing antibody responses over an extended duration, we can enhance our understanding of the effectiveness of COVID-19 vaccination and develop more efficient monitoring approaches to sustain long-term community immunity. This study aims to investigate the clinical application of CMIA and ELISA in monitoring antibody responses after 18 months of COVID-19 vaccination, with the intention of assisting healthcare professionals and researchers in selecting the most suitable techniques for tracking antibody responses in mass vaccination scenarios [9,10].

2. Material and Method

2.1. Study design and participants

The design of this research is a longitudinal study. The population of this study is a group of people who were given the COVID-19 Sinovac and AstraZeneca vaccines, live in Bogor City and Sleman Regency, meet the inclusion criteria, and are willing to be involved in research with informed consent. Participants were individuals who had been vaccinated against COVID-19 by Sinovac and AstraZeneca in the previous 18 months. Data and antibody measurements before vaccination were collected shortly before the vaccination dose was given. Participants were randomly selected from a population representing various age groups and demographic backgrounds. Ethical approval was obtained from Ethics Committee of National Institute of Health Research and Development, Ministry of Health No.: LB.02.01/2/KE. 431/2021.

2.2. Data collection

Data collection was carried out by interviewing and taking blood. Before starting the interview, the officer explained the aims and objectives of the research in language that was easily understood by the participants. After that, the officer asked for approval from the research subjects by signing an informed consent. After the interview, officers took blood samples. Blood samples were taken from each participant using standard sampling procedures. A total of 211 serum samples were collected from subjects who had received the Sinovac and AstraZeneca COVID-19 vaccinations in the previous 18 months. Antibody response measurements were carried out using the CMIA method. The CMIA method is carried out using special equipment available in accredited clinical laboratories. The test was carried out in accordance with the instructions for using the tool. Antibody examination was carried out using the SARS CoV-2 IgG II Quant Assay method. This method is an automatic two-step immunoassay test to determine IgG antibodies against SARS CoV-2 quantitatively and qualitatively using chemiluminescent microparticle immunoassay (CMIA) technology. The SARS CoV-2 IgG II Assay is designed to detect Class G immunoglobulin antibodies (IgG), including neutralizing antibodies, against the receptor binding domain (RBD) of the S1 subunit of the SARS-CoV-2 spike protein in serum and plasma. For comparison, some samples were

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measured using the enzyme-linked immunosorbent assay (ELISA) method using the Human SARS-CoV-2 Spike (Trimer) IgG ELISA Kit. This kit is used to detect and measure specific immunoglobulin G (IgG) antibodies against the SARS-CoV-2 spike protein in human blood samples.

2.3. Statistical analysis

Data analysis was conducted using SPSS software v25.0 (SPSS Inc, Chicago, IL) and Microsoft Excel package programs. The mean plus standard deviation was used to report the results, depending on the distribution. Numbers and percentages were used to express categorical variables. Fisher's exact or chi-squared tests were used for categorical variable analyses. A statistical analysis of the independent t test was used to compare antibody responses between baseline and 18 months after vaccination. Meanwhile, statistical analysis of the paired sample t test is used to compare the CMIA and ELISA methods.

3. Results

The characteristics of the research subjects observed in the study included the variables gender, age, education, body mass index, and type of vaccine. Most of the research subjects were women (67.2%), and almost all of the research subjects were aged between 18 and 44 years (9.2%), with an average age of 41.45 years. In terms of education, most of the research subjects had an educational background of completing high school (58%). Meanwhile, based on body mass index, the majority of research subjects had a normal body mass index (48%). Based on the brand of vaccine given, the number of Astra Zeneca vaccine recipients is greater than that of Sinovac.

Table 1. Characteristics of Study Participants

Variable	N	%
Sex		
Male	69	32,7
Female	142	67,3
Age (years)		
18-44	125	59,2
45-59	82	38,9
60+	4	1,9
Education		
Elementary School	38	18,0
Junior High School	40	19.0
Senior High School	118	58,0
University	15	7,1
Body Mass Index (BMI)		
Underweight	17	8,1
Normal weight	99	46,9
Over Weight	65	30,8
Obesity	30	14,2
Vaccine		
Sinovac	89	42,2
Astra Zeneca	122	57,8

The measurement of the binding antibody titer at baseline is a blood sample carried out immediately before administering the COVID-19 vaccine dose 1. From the results of measuring the antibody titer before vaccination, it was seen that 65.4% had SARS-CoV-2 antibodies. The presence of SARS-CoV-2 antibodies in participants in this study indicates that there has been quite high exposure in the population where the data was collected. The highest proportion of positive antibodies was found in the female group (69.6%), aged 18–44 years (59.2%), high school education (45.7%), group with normal weight (55.6%), and subjects who were given the AstraZeneca vaccine (72.3%). When measuring SARS-CoV-2 antibodies after 18 vaccinations, the measurement results of all research subjects still showed positive results.

Table 2. Results of measuring the SARS-CoV-2 antibody response at baseline

Variable	Negative (%)	Positive (%)	Total (%)
Sex			
Male	37,0	30,4	32,7
Female	63,0	69,6	67,3
Age group (years)			
18-44	63,0	57,2	59,2
45-59	32,9	42,0	38,9
60+	4,1	0,7	1,9
Education			
Elementary School	15,1	19,6	18,3
Junior High School	11,0	23,2	19.0

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(2), 1077-1082 | ISSN:2251-6727

Senior High School	58,9	54,3	55,9
University	15,1	2,9	7,1
Body Mass Index (BMI)			
Underweight	11,0	6,5	8,1
Normal weight	49,3	45,7	46,9
Over Weight	28,8	31,9	30,8
Obesity	11,0	15,9	14,2
Vaccine			
Sinovac	71,2	26,8	42,2
Astra Zeneca	29,8	73,2	57,8

Figure 1 shows a picture of antibodies from baseline and 18 months after administration of the COVID-19 vaccine. We can see that in research subjects who were given the Sinovac vaccine, the average antibody titer before vaccination was 735.92 AU/mL. Meanwhile, for AstraZeneca, the average antibody titer before vaccination was 2567.39 AU/mL. In measuring the antibody titer after 18 months after vaccination, in research subjects given the Sinovac vaccine, the antibody titer was 4535.79 AU/mL, and for AstraZeneca, it was 5696.47 AU/mL.

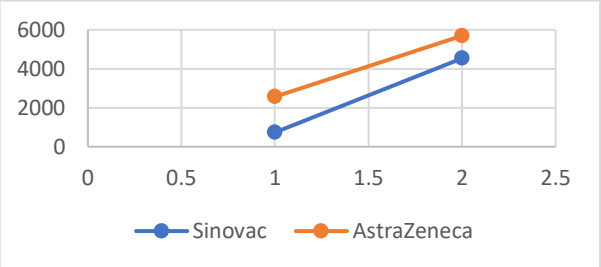

Figure 1. a picture of antibodies from baseline and 18 months after administration of the COVID-19 vaccine.

The results of the analysis comparing the results of measuring the antibody response using the chemiluminescence microparticle immunoassay (CMIA) and enzyme-linked immunosorbent assay (ELISA) methods obtained a significance value of 0.992, which was greater than the significance level of 0.05. So it can be concluded that there is no difference in results between examinations using the CMIA and ELISA methods. This can also be seen from the average value of each method, which is not much different, namely with an average difference of 9.29213 as shown in Table 3.

Table 3. Comparison of Measurement Results Using the CMIA and ELISA Methods

Methods	Mean	Standard Deviation	Mean Standard Error	P
CMIA	4530,7966	6105,81063	647,21463	0,992
ELISA	4540,0888	6105,92636	647,22690	

4. Discussion

One of the vaccines widely used in many countries is Sinovac, which employs an inactivated virus to stimulate the immune system. Preliminary research suggests that the Sinovac vaccine effectively reduces the risk of contracting COVID-19, developing severe disease, and mortality from the virus. However, studies indicate that the level of protection varies based on demographics and vaccination settings. Research across multiple countries shows efficacy rates for preventing severe disease or death ranging from fifty to over eighty percent [11, 12].

Meanwhile, another globally utilized vaccine is the AstraZeneca shot, which introduces the viral spike protein gene into the body through a modified adenovirus vector. Clinical trials suggest that the AstraZeneca vaccine is reasonably effective in lowering the risk of COVID-19-related severe illness, hospitalization, and mortality. Despite the exceedingly low risk, some countries have expressed concerns about the extremely rare possibility of blood clot formation after receiving this vaccine [13, 14].

There are currently limited studies comparing the efficacy of Sinovac and AstraZeneca vaccines, and findings vary depending on study design, the population studied, and the epidemiological context. However, in certain instances, it has been observed that the Sinovac vaccine may be less effective than the AstraZeneca vaccine, particularly in preventing severe infections and symptoms. It's important to note, however, that both vaccines continue to provide robust protection against COVID-19 and have been instrumental in curbing the epidemic in many countries [15, 16].

Earlier investigations have observed different antibody responses following immunization with Sinovac and AstraZeneca vaccines. Several studies suggest that compared to the AstraZeneca vaccine, the Sinovac

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JCHR (2024) 14(2), 1077-1082 | ISSN:2251-6727

vaccine may induce a lower level of antibody response, especially after the first dose. However, individual variations in immune response persist, and antibody response may increase significantly following the second dose [12, 17].

Understanding the duration and longevity of antibody response after Sinovac and AstraZeneca immunization is crucial. While precise information on the duration of protection following COVID-19 vaccination is still limited, some studies suggest that antibody responses may peak several months after vaccination and then decline [18, 19]. Notably, individual differences in antibody responses to COVID-19 vaccination extend to disparities between Sinovac and AstraZeneca vaccines. The degree and duration of an individual's antibody response following vaccination can be influenced by various factors, including age, gender, immunological status, and genetics [20, 21].

A deeper understanding of antibody responses after Sinovac and AstraZeneca immunization can inform vaccination strategies and pandemic control efforts. This enables adjustments to vaccination plans, such as administering booster shots or additional doses, and enhances epidemiological surveillance to identify high-risk demographics [22].

It has become common practice to assess antibody responses to SARS-CoV-2 using CMIA and ELISA methods. The second approach, ELISA, enables the detection and measurement of the SARS-CoV-2 spike protein with high sensitivity and specificity. While the ELISA technique induces color changes in the antigen-antibody complex due to enzyme activity, the CMIA method employs antigen-coated micro particles to elicit an antibody response. Although both methods have proven successful in COVID-19 testing, further research is needed to directly evaluate antibody responses in clinical settings following COVID-19 vaccination [23, 24, 25].

Compared to ELISA, the CMIA approach is recognized for its high sensitivity and faster reaction times. CMIA can detect antibodies in smaller quantities within shorter processing periods, thanks to luminescence technology. This allows for the more rapid and efficient use of CMIA in large-scale monitoring of antibody responses. On the other hand, ELISA offers better stability and lower costs, albeit requiring a longer analysis time. In situations where time is not a critical factor, such as laboratory research, ELISA is frequently utilized. Due to its affordability and ease of use, ELISA remains a popular choice in various settings. A comparison of CMIA and ELISA in the context of post-COVID-19 immunization antibody responses will provide valuable insights into their efficacy in monitoring immune responses over extended periods, such as 18 months following vaccination. By combining data from both approaches, we can gain a more comprehensive understanding of the dynamics of antibody responses, including the longevity of antibody levels over time and their impact on an individual's immunity to infection [23, 24, 25].

5. Conclusion

The results of this study reveal that most individuals had a positive antibody response at baseline, and that all participants continued to have a positive antibody response eighteen months after vaccination. Compared to Sinovac, individuals who received the AstraZeneca vaccination had a higher average antibody response. There were no discernible variations in the antibody response measurements obtained using ELISA and CMIA.

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Journal of Chemical Health Risks

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JCHR (2024) 14(2), 1077-1082 | ISSN:2251-6727

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