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Seroprevalence Study of Post-Pandemic COVID-19: Post-Vaccination Antibody Protects Over a Year in Young Adult

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Abstract

The COVID-19 epidemic spread worldwide for three years before the WHO eventually declared it over in 2023. It is because of the massive COVID-19 vaccination program. Nonetheless, persons who have received vaccinations against COVID-19 are still at risk for contracting new strains of SARS-CoV-2. Determining the levels of anti-SARS-CoV-2 IgG antibodies in young adults following vaccination necessitates conducting a seroprevalence study of antibodies during the COVID-19 pandemic. This study used a cross-sectional descriptive design method. Antibody IgG anti-SARS-Cov-2 was examined using the chemiluminescent microparticle immunoassay (CMIA) method, also carried out at the Prodia Laboratory. Statistical analysis used the Mann-Whitney and Kruskal-Wallis Test to know the difference between two or more variables that might influence IgG concentration. This study showed that all blood samples from this research subject (100%) still had reactive anti-SARS-Cov-2 IgG antibodies, even though most of the research subjects (82.35%) had received their last vaccination for over one year. Several variables were tested statistically; the influence of gender, ethnic group, blood type, body mass index, vaccine type, vaccine dose, last vaccination time, and COVID-19 disease history on anti-SARS-Cov-2 IgG levels show that there is no significant influence from all of these factors. As many as 100% of subjects had antibodies that were reactive to COVID-19. Anti-SARS-CoV-2 IgG antibodies can persist for more than one-year post-vaccination.

Keywords: COVID-19, SARS-CoV-2, IgG Antibody, Pandemic, Vaccination

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1. Introduction

The SARS-Cov-2 virus, also known as COVID-19 or the 2019 novel coronavirus (nCov-2019), which is what causes COVID-19, first produced an outbreak in Wuhan, Hubei Province, China, in December 2019[1]–[3]. By attaching the Spike glycoprotein component to the ACE receptor, which is also the receptor for the SARS-Cov-1 virus that previously caused outbreaks, this virus infects people [4][6]. The clinical symptoms of COVID-19 infection are almost the same as those of other respiratory diseases, such as fever, cough, myalgia, dyspnoea, and pneumonia [7], [8]. Blood tests revealed T-cell and B-cell responses to SARS-Cov-2 around a week after COVID-19 symptoms first appeared. IgG and IgM seroconversion can occur simultaneously or sequentially, reaching a plateau within six days after seroconversion [9]. IgM seroconversion generally increases from day nine, while IgG increases on day 11 after symptoms appear [10]. The wave of new COVID-19 cases that emerged due to the emergence of new variants, such as the delta and omicron variants, turned the pandemic that had subsided into a crisis again. This incident gave rise to the global community's need for vaccine boosters [11][14]. The most sensible course of action under pandemic circumstances is to get vaccinated against COVID-19, which offers hope for reducing the spread of SARS-CoV-2 [15].

Vaccination is an essential breakthrough in the world of medicine. Since the introduction of vaccination, several infectious diseases can be prevented, and the impact

has been to reduce the mortality rate due to several infectious diseases, some of which have even been successful to the point of non-existence [16] [17]. Vaccines are a very effective therapy for dealing with infectious diseases and even eradication, such as the smallpox virus [18]. The SARS-Cov-2 virus interacts with angiotensin converting enzyme-2 (ACE2) on the surface of lung alveolar cells to employ the Spike protein as a means of entry. Researchers worldwide target this Spike protein for potential vaccine development [19]. Many vaccinations against SARS-CoV-2 were developed in record time. These types of vaccines include conventional vaccines (Sinovac, Sinopharm)[20], adenovirus (Ad) vectors (Gamaleya, J&J Janssen, AstraZeneca) [21], [22], and mRNA (Pfizer, Moderna)[23]–[25]. Clinical trials showed that it was more effective against severe disease (59 to >95%) than against mild or asymptomatic disease (47 to 94%) [11], [26]. At six months after immunization, those who were 70 years old had lower neutralizing antibody (NAb) titers from mRNA vaccines, which consistently had greater effectiveness rates (30 % without NAb) [26]. Lower IgG Ab levels, particularly in those over 60, were associated with future infections in the Pfizer mRNA vaccine 6-month cohort in Israel [27]. Indonesia itself has at least three types of vaccines used, namely inactivated vaccines (Sinovac, Sinofarm), viral vector vaccines (AstraZeneca), and m-RNA vaccines (Pfizer, Moderna). These vaccines have been shown to elicit an immune response by producing neutralizing antibodies; however, multiple investigations have revealed that the longevity of the antibody response is uncertain. Thus, the purpose of this study was to measure the post-vaccination IgG antibody titers and the seroprevalence of anti-SARS-Cov-2 IgG antibodies following the COVID-19 pandemic. The research subjects included were in the 18-25-year age group because, generally, at this age, their immune system is still optimal.

2. Methods

2.1. Research design

The research method was carried out in a descriptive cross-sectional manner using sequential sampling with a target of 50 samples. The population of this research is medical students at the University of Bengkulu. This research was carried out from Aug 1 - Sept 15, 2023. The location for taking blood samples from research subjects was at the Bengkulu City Branch Prodia Laboratory, while the anti-SARS-Cov-2 IgG examination was carried out at the Central Prodia Laboratory in Jakarta. The study's inclusion requirements include being between the ages of 18 and 25 years, having received at least the second dose of the COVID-19 immunization, and having had their last vaccination at least six months prior. The exclusion criteria are having a disease related to immunodeficiency. The sample size for this research is 51 subjects. This research has ethics committee approval letter No. 22/UN30.14.9/LT/2023 from the Faculty of Medicine and Health Education University of Bengkulu Ethics Committee.

2.2. Antibody Detection

Serum samples were taken after filling out informed consent and questionnaires related to this research. Blood collection from research subjects was carried out at the Prodia Bengkulu Laboratory. After that, the subject's antibody levels were checked using the chemiluminescent microparticle immunoassay (CMIA) method, also carried out at the Prodia Laboratory. To measure anti-SARS-CoV-2 IgG titers, serum was collected from subjects. The serum was inactivated at 56 ℃ for 30 minutes and stored at -20 ℃ before the examination. Anti SARS-CoV-2 IgM and IgG antibodies were examined using the SARS-CoV-2 IgG II Quant assay kit (Abbott®). The CMIA inspection procedure follows the guidelines of the kit. Arbitrary units (AU) per milliliter were used to express the results (positive threshold: 50 AU/mL; maximum limit: 40 000 AU/mL) (Abbott Diagnostics).

2.3. Data analysis

SPSS software was used to do the statistical analysis. The independent T-test is used to find differences between two groups of independent variables if the data is normally distributed; if not, the Mann-Whitney Test is utilized. The Kruskal-Wallis test for data that was not regularly distributed or the One-way ANOVA test for normally distributed data were used to evaluate independent variables from three or more groups. Kolmogorov-Smirnov and Shapiro-Wilk tests are used in the normalcy test. The Spearman Correlation Test was used to assess the correlation between the variables. Significant statistically is a P value less than 0.05.

3. Results

3.1. Characteristics of Research Subject

This research was carried out with a total of 53 subjects; however, two subjects dropped out because the quality of the subjects' blood samples was low, so their antibody levels could not be checked. The characteristics of the 51 subjects who participated in this study are described in detail in Table 1. The gender of the subjects in this study was dominated by females (80.39%). The ethnic origins of the research subjects vary, such as Malay, Rejang, Minangkabau, Javanese, Sundanese, Serawai, Semendo, Komering, Ogan and Batak. Malays are the most ethnic subjects. We also found a variety of blood types in research subjects. Blood type A (41.18%) was the most among others. We also classified the body mass index (BMI) of the research subjects into underweight (24.49%), normal (39.22%), overweight (9.80%) and obesity (25.49%) based on classification of weight by BMI in adult Asians [28]. Most subjects received only two vaccine doses (60.78%); the most recent vaccination was more than one year (82.35%). Subjects used different types of vaccines in COVID-19 vaccination. Some use two doses of a single type vaccine (Two doses of Sinovac or Pfizer), two doses of a combination type (Sinovac-Moderna, Sinovac-Pfizer or Sinovac-Astrazeneca), three doses of a single type (Three doses of Sinovac or AstraZeneca), three doses of a combination type (Sinovac-Sinovac-Moderna, Sinovac-Sinovac-Pfizer or Sinovac-Sinovac-Astrazeneca). Most subjects received the single type two-dose vaccine (50.98%). Most subjects who participated had no history of being confirmed positive for COVID-19 (60.78%). Several subjects had a confirmed positive history of COVID-19 before vaccination (13.73%), after vaccination (13.73%), and before and after vaccination (11.76%).

3.2. Influence Factors of Antibody IgG Anti-SARS-CoV-2 concentration

Several factors that might influence anti-SARS-CoV-2 IgG antibody levels were tested statistically using the IBM

SPSS Statistics 27 application. Before testing differences in variables, all data were tested for normality using the Kormogorov-Smirnov test with the condition that the data is normally distributed if the p value>0 .05. The normality test results showed that the subject data obtained was not normally distributed, so all different tests were carried out using non-parametric statistical tests. To determine the difference between two variables, the Mann-Whitney Test is used, while to determine the difference between three or more variables, the Kruskal-Wallis Test is used. Variables are said to be significantly different if the p-value <0.05. In the gender effect test, the test results showed no significant difference in anti-SARS-CoV-2 IgG levels between men and women. The average anti-SARS-CoV-2 IgG level in women (4668.4 AU/mL) was higher than in men (3763.2 AU/mL). Likewise, the median value in women (2870.0 AU/mL) was higher than in men (1847.5 AU/mL). Likewise, the test of different ethnic group influences showed no significant difference between the levels of anti-SARS-CoV-2 IgG antibodies in the Malay, Rejang, Minangkabau, and Javanese tribes. The highest mean and median IgG levels were in the Java tribe, with 6951.1 AU/mL values and 9483.0 AU/mL, respectively. The lowest mean IgG level was the Malay tribe (4237.2 AU/mL), while the lowest median IgG value was the Rejang tribe (2116.7 AU/mL).

The subject's blood type also did not significantly affect anti-SARS-Cov-2 IgG levels. Subjects with blood type O tend to have the highest mean and median compared to blood groups A, B, and AB, with 5552.2 AU/mL values and 3599.8 AU/mL, respectively. Meanwhile, subjects with blood type A had the lowest average and median IgG levels, with 3495.3 AU/mL values and 2223.1 AU/mL, respectively. Differences in the BMI group also did not significantly influence anti-SARS-CoV-2 IgG antibody levels. The group of subjects classified as obese had the highest mean (6256.3 AU/mL) and median (3671.2 AU/mL) antibody levels compared to the other groups. The lowest mean value of IgG antibody levels was in the normal group (3739.1 AU/mL), while the lowest median value was in the overweight group (1962.2 AU/mL). Vaccine type also did not significantly influence differences in anti-SARS-CoV-2 IgG levels. However, the results of statistical calculations show that the average for subjects who used combination vaccines (5106.1 AU/mL) was higher than single-type vaccines (4024.0 AU/mL). The median value for subjects who used the combination vaccine (2973.6 AU/mL) was also higher than the single-type vaccine (2973.6 AU/mL). Then, the analysis of differences in vaccine doses was also carried out, with the results that there were no significant differences in IgG levels in subjects who had received two or three doses. Interestingly, the results of this statistical analysis show that subjects who received two doses of vaccine (4902.6 AU/mL) had a higher average IgG level than subjects who received three doses of vaccine (3443.0 AU/mL). Likewise, the median value for subjects with a two-dose vaccine (3197.3 AU/mL) was higher than with three doses (2368.7 AU/mL).

Interesting results were also obtained in the analysis of differences in IgG levels in subjects whose last vaccination was less than one year and subjects whose last vaccination was more than one year. With a much larger number of subjects (42 subjects), subjects vaccinated for more than one year had higher mean and median IgG levels, respectively, 4573.7 AU/mL and 2705.7 AU/mL. Finally, an analysis of the influence of COVID-19 disease history shows no significant difference between subjects who have been confirmed positive for COVID-19 and subjects who have never been confirmed positive for COVID-19. However, there are differences in the mean and median values of the two groups. The average IgG level in subjects without a history of COVID-19 (4783.8 AU/mL) was higher than in subjects with a history of COVID-19 (4036.9 AU/mL). In contrast, the median value of IgG levels in subjects with a history of COVID-19 (2808.1 AU/mL) was higher than in subjects without a history of COVID-19 (2541.5 AU/mL).

4. Discussion

This research has shown seroprevalence data in the post-pandemic COVID-19 era in Bengkulu City. The result describes that 100% of subjects still have reactive IgG antibody anti-SARS-Cov-2. It can happen because all the subjects who took part were physically healthy young adults. According to particular research, young people had higher neutralizing titers than older people [29], [30]. As a result, immunizations may considerably lower viral circulation in comparison to naturally acquired immunity, particularly if it transpires that naturally acquired protective immunity requires re-infection to be reinforced [31]. The efficiency of vaccinations varies between individuals and populations; the immunogenicity of the vaccine is affected by a number of factors, including the characteristics of the host [30].

Over the past few years, awareness of sex's important role in regulating vaccine-induced immunity has grown. Notably, following immunization, females more frequently experience unpleasant effects and have more robust antibody responses than males [32]. The generation and reactivity of antibodies are higher in female patients, as are macrophage and neutrophil activity. Additionally, angiotensin-converting enzyme 2 (ACE2) in-vivo investigations revealed increased expression in the kidneys of male patients compared to female patients, which may account for differences in COVID-19 susceptibility and progression between male and female patients [33]. In a different trial, there was no obvious difference in the antibody response to the heterologous mRNA-1273 booster vaccine between males and females [34]. According to ethnicity, Smith et al. (2021) found considerable disparities in the breadth and strength of the humoral immune response, which may be due to variations in genetic and lifestyle factors [35]. Since ethnic groups frequently have lower socioeconomic status and more excellent rates of medical comorbidities, this may enhance their chance of getting COVID-19 through weakened cell-mediated immunity [33]. According to Ray et al., people with type O and Rh-negative blood are shielded against viral infection, life-threatening disease, and mortality [36]. The regulation of infection by blood type has been explained using cellular models.

Table 1. Characteristics of Research Subject

Characteristic	Group	Quantity (n)	Percentage (%)
Gender	Male	10	19.61
	Female	41	80.39
Ethnic group	Malay	11	21.57
	Rejang	6	11.76
	Minangkabau	8	15.69
	Java	5	9.80
	Sundanese	3	5.88
	Serawai	2	3.92
	Semendo	1	1.96
	Komering	1	1.96
	Ogan	1	1.96
	Batak	1	1.96
	Unmentioned	12	23.53
Blood type	A	21	41.18
	B	10	19.61
	AB	6	11.76
	O	14	27.45
Body Mass Index (BMI)	Underweight	13	25.49
	Normal	20	39.22
	Overweight	5	9.80
	Obesity	13	25.49
Vaccination Doses	Two doses	31	60.78
	Three doses	19	37.25
	Four doses	1	1.96
Last time Vaccine	< 1 year	9	17.65
	> 1 year	42	82.35
Vaccines Type	Single type in 2 doses	26	50.98
	Combination type in 2 doses	5	9.80
	Single type in 3 doses	3	5.88
	Combination type in 3 doses	17	33.33
COVID-19 History	Before Vaccination	7	13.73
	After Vaccination	7	13.73
	Before and After Vaccination	6	11.76
	Never	31	60.78

Table 2. Statistical analysis of factors influencing IgG anti-SARS-Cov-2 levels. A P value <0.05 is statistically significant. (Antibody IgG anti-SARS-CoV-2 Concentration: AU/ml; SE: Standard Error; SD: Standard Deviation)

No.	Factor	Variable	n	Mean	SE	SD	Median	Minimum	Maximum	p-Value
1	Gender	Male	10	3,763.2	1,190.7	3,765.3	1,847.5	810	11,998.8	0.286 [a]
		Female	41	4,668.4	684.5	4,382.7	2,870.0	737.5	16,261.1	
2	Ethnic Group	Malay	11	4,237.2	1,272.4	4,220.2	3,197.3	1,147.7	16,261.1	
		Rejang	6	4,580.1	2,294.1	5,619.3	2,116.7	1,004.1	15,550.9	0.800 [b]
		Minangkabau	8	5,593.4	1,981.9	5,606.7	2,822.8	1,159.9	16,241.7	
		Java	5	6,951.1	2,229.5	4,985.3	9,483.0	1,229.0	11,635.8	
3	Blood Type	A	21	3,495.3	680.1	3,116.5	2,223.1	737.5	11,635.8	
		B	10	4,974.0	1,655.7	5,235.7	2,394.2	1,004.1	16,261.1	0.463 [b]
		AB	6	4,692.4	2,195.7	5,378.3	2,841.5	1,174.8	15,550.9	
		O	14	5,552.8	1,235.3	4,622.1	3,599.8	1,636.7	16,241.7	
4	Body Mass Index	Underweight (<18,5)	13	3,801.1	982.9	3,543.8	2,088.4	1,174.8	12,493.6	
		Normal (18,5 - 22,9)	20	3,739.4	703.8	3,147.6	2,557.4	737.5	11,998.8	0.393 [b]
		Overweight (23 - 24,9)	5	4,700.1	2,713.5	6,067.5	1,962.2	1,864.7	15,550.9	
		Obesity (>25)	13	6,256.3	1,515.1	5,462.7	3,671.2	810.4	16,261.1	
5	Vaccine Type	Single type Vaccines	29	4,024,0	750.8	4,043.5	2,746.2	737.5	16,261.1	0.594 [a]
		Combination Vaccines	22	5,106.3	964.8	4,525.4	2,973.6	810.4	15,550.9	
6	Vaccine Doses	Two Doses	31	4,902.6	836.5	4,657.5	3,197.3	737.5	16,261.1	0.204 [a]
		Three Doses	19	3,443.0	714.5	3,114.3	2,368.7	810.4	10,516.6	
7	Last Vaccination Time	< 1 year	9	2,480.2	346.7	1,040.2	2,223.1	1,147.7	4,002.3	0.429 [a]
		> 1 year	42	4,573.7	649.9	4,211.8	2,705.7	737.5	16,261.1	
8	COVID-19 Disease History	Positive COVID-19 History	20	4,036.9	835.7	3,737.3	2,808.1	1,004.1	16,241.7	0.743 [a]
		Non-COVID-19 History	31	4,783.8	823.2	4,583.8	2,541.5	737.5	16,261.1	

[a] Mann Whitney Test
[b] Kruskal-Wallis Test

These views are supported by the observation that spike protein/Angiotensin-converting enzyme 2 (ACE2)-dependent adhesion to ACE2-expressing cell lines is exclusively inhibited by human anti-A antibodies, whether monoclonal or endogenous. Because O or B blood types develop anti-A antibodies, people with non-A blood types may be less susceptible to SARS-CoV-2 [37]. However, this research showed no significant differences in blood type to IgG antibody. According to the findings of the Allan et al. (2021) and Alessa et al. (2022) investigation, none of the COVID-19 vaccinations was associated with any statistically significant blood type-related side effects [38], [39]. The results of this study show that BMI does not significantly influence anti-SARS-CoV-2 IgG levels. The antibody response was similarly found to have no significant association with BMI, according to Visalli et al. (2023) [40]. Interestingly, subjects with obesity have the highest IgG level. Both young and old obese people have reduced in vivo and in vitro antibody responses, and their peripheral B cell pools exhibit a higher proportion of pro-inflammatory late/exhausted memory B cells and a lower number of anti-inflammatory transitional B cells [41]. Numerous epidemiological results suggest that body weight is connected to the likelihood of infection and the progression of disease [42]. Numerous delivery methods, such as mRNA, DNA vaccines, viral vectors, protein subunits, and virus-inactivated immunization approaches, are used in the COVID-19 vaccines that have been licensed or are being studied [25]. In this study, subjects used one single type and combination type vaccine. The results showed no significant difference in IgG levels in single-type vaccines and combination-type vaccines. According to a study by Ward et al. (2022) that was limited to people who received their second dose between 10 and 12 weeks after the first or who received their first vaccination 12 weeks earlier, antibody positivity was higher in people who received BNT162b2 (Moderna) rather than ChAdOx1 (AstraZeneca) vaccine [43]. The virological diversity and epidemiological distribution of vaccinations impact the efficacy of anti-COVID-19 immunity induced by the present vaccines. The diversity of newly developing SARS-CoV-2 strains has reduced the effectiveness of the vaccination and compromised long-term immunity to the disease [44]. Tartof et al.'s findings from 2021 show that BNT162b2 is highly effective at preventing hospital admissions up to around six months after receiving the vaccination [45]. However, the most exciting result of this study is that the IgG level is still high even though most subjects have had the COVID-19 vaccine for more than a year. It means booster doses of the COVID-19 vaccine could give humoral immunity protection over a year in healthy young adults. These results are in line with the study of Swadźba et al. (2023), which shows that antibodies can persist in vaccinated subjects for more than one year [46].

Another exciting result of this study is that there is no significant difference in subjects with two or three vaccine doses. Although the Centers for Disease Control and Prevention (CDC) recommends a vaccine booster of up to three doses, this must be discussed further. Determining whether the general population needs a third vaccination dose is challenging because it lacks a trustworthy protective correlation and threshold [12]. According to the findings of this study, two doses of the vaccination are more effective than three doses of the vaccine based on the mean and median values of anti-SARS-Cov-2 IgG levels. Additionally, both exhibited IgG antibody reactivity in healthy young people for over a year. As a result, the significance of the third dose, administered six months following the second dose, needs to be reviewed.

This research showed that COVID-19 disease history did not significantly influence IgG anti-SARS-CoV-2 levels. Studies by Painter et al. (2023) showed that vaccinated people experienced more intense spike-specific reactions during infection than did uninfected people [47]. However, the reference viral strain that was first discovered in Wuhan is the basis for the great majority of COVID-19 vaccinations that are currently licensed. At first, the COVID-19 vaccinations successfully provided protection. However, the antibodies produced in the immunized people showed progressively lower virus-neutralizing efficacy against antigenically dissimilar variations, particularly Delta and Omicron, due to the evolution of SARSCoV-2 and the appearance of new variants [48], [49]. Omicron infection appears to be the catalyst for the development of circulating antibodies that bind to both the vaccine strain and novel variations, as evidenced by the identical amount and kinetics of the increase in binding antibody titers against the RBD from D614G and Omicron subvariants [47]. There are still several limitations to this research. First off, the sample size is not too high to have an impact on the outcomes of the statistical analysis that was done. Second, because there were not enough subjects to study all of the groups equally, some of the groups had extremely diverse subjects, reducing the statistical significance of the discrepancies. Third, non-parametric tests are used in all statistical analyses because the data distribution in this study is generally abnormal.

5. Conclusions

According to the seroprevalence of COVID-19 IgG antibodies, every subject still has reactive IgG. Despite receiving the last vaccination more than a year earlier, most participants (82.53%) still maintained significant levels of anti-SARS-CoV-2 IgG antibodies. Several variables, including gender, ethnicity, blood type, body mass index, type of vaccine, dose of vaccine, and history of COVID-19, do not significantly influence anti-SARS-Cov-2 IgG levels. Two doses of the vaccination have a higher mean and median IgG level than three doses in healthy young adults, according to the comparison between giving two and three doses of the vaccine. It is vital to reevaluate the necessity of giving subsequent vaccine boosters in light of their efficacy.

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