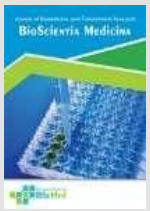
eISSN (Online): 2598-0580



Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscmed.com

Comparison of Post Vaccination Antibody Levels for Coronavirus Disease 2019 (COVID-19) between Survivors and Non-Survivors of COVID-19

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ARTICLE INFO

Keywords:
IgG levels
Anti-SARS-CoV-2
COVID-19
Survivors of COVID-19

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All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/bsm.v6i17.729

A B S T R A C T

Background: The COVID-19 vaccine is useful for protecting the body by causing or stimulating specific immunity in the body. COVID-19 survivors are a group of individuals who have been exposed to COVID-19 and have successfully recovered from COVID-19 infection. Exposure to COVID-19 causes the activation of memory cells and anti-SARS-CoV-2 IgG antibodies. In contrast to individuals who have never been exposed to COVID-19, the bodies of individuals who are not COVID-19 survivors have not had the experience of exposure to COVID-19, which causes the absence of memory cells and anti-SARS-CoV-2 IgG antibodies. This study is one of the first studies to explore differences in anti-SARS-CoV-2 IgG antibody levels in survivors and non-survivors of COVID-19 at Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia. **Methods:** This was an analytic observational study with a cohort approach. A total of 136 research subjects participated in this study. Observation of anti-SARS-CoV-2 IgG levels was carried out before vaccination, weeks 2, 12, and 24. Data analysis was carried out using SPSS univariate and bivariate. **Results:** The COVID-19 survivors group consistently from the time they were vaccinated, weeks 2, 12, and 24 showed a relatively higher average anti-SARS-CoV-2 IgG level than the non-COVID-19 survivors' group. The group of survivors of COVID-19 shows a trend of decreasing average anti-SARS-CoV-2 IgG levels over time. In contrast to the non-survivor group of COVID-19, which showed a trend of increasing anti-SARS-CoV-2 IgG levels. **Conclusion:** There were differences in anti-SARS-CoV-2 IgG levels between the COVID-19 survivor group and non-survivor COVID-19 group at Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia.

1. Introduction

Coronavirus disease 19 (COVID-19) is an infectious disease that causes acute respiratory syndrome caused by the SARS-CoV-2 virus. This disease was first documented in humans in China in December 2019 and was declared a global pandemic by the World Health Organization (WHO) in March 2020. SARS-Cov-2 infection can cause a wide range of clinical manifestations. Infected patients can be asymptomatic (asymptomatic), have mild symptoms, or develop severe pneumonia, acute respiratory distress syndrome (ARDS), sepsis, to septic shock. The COVID-19 pandemic, which has spread very quickly, has created crises in all aspects of life worldwide. WHO has implemented various health protocols to control the spread of COVID-19. Primary prevention efforts that are thought to be more effective are through the

establishment of herd immunity, which can be safely achieved through vaccination.[1-3]

The COVID-19 vaccination aims to break the chain of disease transmission and stop the COVID-19 outbreak. The COVID-19 vaccine is useful for protecting the body by causing or stimulating specific immunity in the body. COVID-19 survivors are a group of individuals who have been exposed to COVID-19 and have successfully recovered from COVID-19 infection. Exposure to COVID-19 causes the activation of memory cells and anti-SARS-CoV-2 IgG antibodies. In contrast to individuals who have never been exposed to COVID-19, the bodies of individuals who are not survivors of COVID-19 have not had the experience of exposure to COVID-19, which causes the absence of memory cells and anti-SARS-CoV-2 IgG antibodies. The vaccinations are given still provide benefits for both survivors and non-survivors. For survivors, vaccination is believed to be able to strengthen the immune system by increasing anti-SARS-CoV-2 IgG antibody levels. Meanwhile, for non-survivors, the COVID-19 vaccination provides an initial exposure to COVID-19, which is expected to stimulate the body to produce anti-SARS-CoV-2 IgG antibodies.[4,5] This study is one of the first studies to explore differences in anti-SARS-CoV-2 IgG antibody levels in survivors and non-survivors of COVID-19 at Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia.

2. Methods

This study was an analytic observational study with a cohort approach and used primary data at Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia. A total of 136 research subjects participated in this study. The research subjects met the inclusion criteria in the form of individuals aged 18 years, individuals who had been declared fit for vaccination, individuals who had received 2 times the Sinovac vaccine and 1 Moderna booster vaccine, and individuals who had signed informed consent as a form of willingness to participate in this study. This study was approved by the medical and health research ethics committee at Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia (Number: 82/kepkrsmh/2021).

This study observed individual sociodemographic data, clinical data, and laboratory data of individuals who received the COVID-19 vaccine. This study also observed anti-SARS-CoV2 IgG levels. Anti-SARS-CoV2 IgG levels were assessed using the CMIA method, so anti-SARS-CoV2 IgG levels were obtained. Measurement of anti-SARS-CoV2 IgG levels was carried out before vaccination, 2 weeks, 12 weeks, and 24 weeks after COVID-19 vaccination. This study also observed the history of survivors or non-survivors of COVID-19. Data analysis was performed with the help of SPSS software version 25. Univariate analysis was performed to present the frequency distribution of the research data. Bivariate analysis was carried out to present and compare anti-SARS-CoV2 IgG levels between groups of survivors and non-survivors of COVID-19 using the T-test, with a p-value <0.05.

3. Results

Table 1 shows the baseline characteristics of the research subjects. Each group, both survivors and non-survivors of COVID-19, showed no significant differences in terms of age, gender, body mass index, or history of comorbidities such as autoimmune, asthma, type 2 diabetes mellitus, hypertension, hyperthyroidism, and allergies. These results indicate that each group has fairly good homogeneity.

4. Discussion

In this study, subjects with a history of being infected with COVID-19 already had memory B cells in their bodies through previous Sinovac vaccinations, so there was an increased immune response through memory cells. Memory B cells will secrete antibodies with a higher affinity than primary plasma cells due to hypermutation and somatic selection, so the levels of antibodies produced will be higher. It is the reason for the significant difference in SARS CoV2 IgG levels between groups with a history of infection with COVID-19 and those without a history of infection with

COVID-19 in this study. In week 2, after heterologous vaccination using the Moderna vaccine as a booster for the third dose, there was no significant difference in the quantitative IgG levels of SARS-CoV-2 between the group with a history of infection of COVID-19 and the group without a history of infection with COVID 19 with the quantitative IgG levels of SARS CoV-2 of 72287.5 AU/mL and 54487.7 AU/mL respectively. This is possibly due to the Moderna vaccine, which works effectively in groups without a history of being infected with COVID-19 resulting in humoral immunity levels that are almost the same as the group with a history of being infected with COVID-19. The Moderna vaccine is an m-RNA vaccine type vaccine. This vaccine encodes a viral protein spike (S) from SARS-CoV-2 and has high immunogenicity. The vaccine's M-RNA is modified by two proline mutations so that the vaccine is more stable.[6-9]

Table 1. Baseline characteristics of research subjects.

Variable	Group		Total	P
	Survivor (n= 61)	Non-survivors (n=75)		
Age				0.453*
≥ 60 years	2 (3.3%)	6 (8%)	8 (5.9%)	
56 – 59 years	4 (6.6%)	3 (4%)	7 (5.1%)	
46 – 55 years	6 (9.8%)	11 (14.7%)	17 (12.5%)	
36 – 45 years	20 (32.8%)	17 (22.7%)	37 (27.2%)	
24 – 35 years	29 (47.5%)	38(50.7%)	67 (49.3%)	
Gender				0.522*
Male	18 (29.5%)	26 (34.7%)	44 (32.4%)	
Female	43 (70.5%)	49 (65.3%)	92 (67.6%)	
Body mass index				0.762*
Obesity II	8 (13.1%)	7 (9.3%)	15 (11.0%)	
Obesity I	18 (29.5%)	20 (26.7%)	38 (27.9%)	
Overweight	8 (13.1%)	8 (10.7%)	16 (11.8%)	
Normoweight	23 (37.7%)	31 (41.3%)	54 (39.7%)	
Underweight	4 (6.6%)	9 (12.0%)	13 (9.6%)	
Comorbid autoimmune				1.000**
Yes	2 (3.3%)	2 (2.7%)	4 (2.9%)	
No	59 (96.7%)	73 (97.3%)	132 (97.1%)	
Asthma				0.242**
Yes	5 (8.2%)	2 (2.7%)	7 (5.1%)	
No	56 (91.8%)	73 (97.3%)	129 (94.9%)	
DM type 2				0.379**
Yes	1 (1.6%)	4 (5.3%)	5 (3.7%)	
No	60 (98.4%)	71 (94.7%)	131 (96.3%)	
Hypertension				0.970*
Yes	8 (13.1%)	10 (13.3%)	18 (18.2%)	
No	53 (86.9%)	65 (86.7%)	118 (86.8%)	
Hyperthyroid				1.000**
Yes	2 (3.3%)	2 (2.7%)	4 (2.9%)	
No	59 (96.7%)	73 (97.3%)	132 (97.1%)	
Allergy				0.962*
Yes	12 (19.7%)	15 (20.0%)	27 (19.9%)	
No	49 (80.3%)	60 (80.0%)	109 (80.1%)	

*=Chi-square, **=Fisher's exact, p>0.05 = not significant.

Table 2 shows a comparison of anti-SARS-CoV-2 IgG levels in survivors and non-survivors of COVID-19. The COVID-19 survivors group consistently from the time they were vaccinated, weeks 2, 12, and 24 showed a relatively higher average anti-SARS-CoV-2 IgG level than the non-COVID-19 survivors' group. The group of survivors of COVID-19 shows a trend of decreasing average anti-SARS-CoV-2 IgG levels over time. In contrast to the non-survivor group of COVID-19, which showed a trend of increasing anti-SARS-CoV-2 IgG levels.

Table 2. Comparison of anti-SARS-CoV-2 IgG levels in survivors and non-survivors of COVID-19.

Quantitative IgG levels of SARS CoV-2 (AU/mL)	Group		P*
	Survivor of COVID-19	Non-survivors of COVID-19	
When to vaccinate	30555.9 (298.8 – 291387.5)	465.6 (26.7 – 11291.8)	<0.0001
Week 2	72287.5 (19259.5 – 427080)	54487.7 (421.4 – 288521.5)	0.115
Week 12	15539.4 (1059.6 – 65732)	11442.25 (952.4 – 50210)	0.017
Week 24	5298.7 (1093.6 – 21457.7)	4090.8 (69.30 – 29178)	0.123

*Independent T-Test, $p<0.05$ = significant.

Heterologous vaccination using different vaccine platforms in this study has the advantage of being an available two-way mechanism of effector cell production, in which vaccine antigen involves naive CD4 and also memory cells, both humoral and cellular so that the immunogenicity produced by heterologous vaccines is stronger. This is in line with the results of a study that stated that with heterologous vaccination using mRNA vaccines as a booster, Health workers who were previously vaccinated with two doses of CoronaVac (Sinovac) had higher quantitative IgG levels compared to health workers who received the homologous CoronaVac (Sinovac) vaccination as the third booster dose after 14 days after injecting the vaccine. Likewise, other studies stated that after monitoring 14 days after heterologous vaccination, the median IgG titer value was substantially higher in the group that received 2 doses of Sinovac heterologous vaccination and booster with Moderna compared to health workers who received 3 times the Sinovac homolog vaccination with no previous history of being infected with COVID-19.[10-13]

At week 12 after vaccination, there was a significant difference in IgG levels between the group with a history of infection and the group without a history of infection, with IgG levels of 15539.4 AU/ml and 11442.25 AU/ml, respectively. The results of this study were similar to studies that stated that at 3 months post-vaccination mRNA, the average decrease in antibodies was 37.9% in individuals with a history of previous infection and 44.7% in individuals without infection. However, all participants still had a strong antibody response within 3 months. Likewise, in one study, the median IgG value showed an increase from the first 1-2 weeks to the third week, peaking at 4-6 weeks after vaccination. Subsequently, IgG values decreased progressively, with a significant decrease observed past the tenth week of mRNA vaccination, and vaccinated individuals with a history of previous COVID-19 infection showed lower levels of IgG decline than individuals without a history of COVID-19 infection (each percentage decrease of 17.9 and 22.6%).[14-16]

Individuals with a history of infection have antibody levels that are formed naturally and are induced by antibodies from vaccination. This is called hybrid immunity. There is a role for the memory B cell compartment in generating a strong neutralizing humoral response. Antibodies formed with hybrid immunity have a longer half-life, so the reduction rate is relatively more stable than antibodies without hybrid immunity. Therefore natural infection followed by COVID-19 vaccination induced a more durable antibody response than natural SARS-CoV-2 infection or just 2 doses of COVID-19 vaccination. This may be the underlying reason that the group with a history of infection had IgG levels that were still very high compared to the group without a history of infection.[17,18]

At week 24 after vaccination, there was a difference in quantitative IgG levels of SARS CoV-2 between the two groups, but not statistically significant. According to a study, the antibody reduction rate in healthcare workers with a history of being infected with COVID-

19 and without a history of being infected with COVID-19 was 0.1% and 1.3%, respectively, at 24 weeks, with antibody levels at 2 weeks being considered the baseline. That is, infected participants who underwent vaccination had higher antibody titers and maintained effective antibody titers for a longer duration than uninfected participants who underwent vaccination. Another study found that individuals who were previously infected and who had quantitative IgG levels before the vaccine was higher than individuals who had never been infected with COVID-19. After getting one dose of the m-RNA vaccine, the quantitative IgG levels would equally fall at 6-7 months, with a slightly higher reduction rate in patients with no previous infection. The risk of reinfection among individuals who were infected before vaccination is proportional to the proportion of infections among never-infected individuals who received 2 doses of vaccine.[19,20]

5. Conclusion

There were differences in anti-SARS-CoV-2 IgG levels between the COVID-19 survivor group and the non-survivor COVID-19 group at Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia, where the COVID-19 survivor group had a higher average anti-SARS-CoV-2 IgG level than the non-survivor COVID-19 group.

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