Short communication

Antibody responses induced by inactivated SARS-CoV-2 virus in healthcare workers at a rural hospital in Indonesia

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ABSTRACT

Introduction and Aim: Vaccines from various manufacturers have shown their efficacy against COVID-19 globally. In this study, the aim was to evaluate the immune response in subjects after the second vaccination with inactivated SARS-CoV-2 virus at Mamami Hospital located in a rural area in Indonesia.

Materials and Methods: The study employed a cross-sectional research design. The research took place at Mamami Hospital, Kupang City, East Nusa Tenggara, Indonesia, from April 5 to August 8, 2021. The research comprised a total of 30 health workers who served as the participants in this study.

Results: Immunoserology results show that 1 respondent was non-reactive and 2 had antibody results < 10. There were 7 respondents with antibody results > 10 - 40. Serological antibodies > 40 - 80 were found in 3 respondents. Serological antibodies > 80 - 120 were not found. Serological antibodies > 120 - 160 were found in 3 respondents. One respondent had serological antibodies ranging from 160 to 200, while 13 respondents had antibodies ranging from 200 to 400.

Conclusion: In the present study, inactivated SARS COV-2 virus vaccine significantly contributed to the acquisition of anti-SARS-CoV-2S antibodies of 30 health workers.

Keywords: COVID-19; immunological; health workers; vaccination.

INTRODUCTION

The SARS-CoV-2 coronavirus has been in circulation for years by now. Indonesia reported its first case of COVID-19 on 2nd March in 2020, and the disease has rapidly spread, affecting various aspects of life, including healthcare, due to limited medical services (1,2). In addition to an increased SARS-CoV-2 infection rate, there is a high prevalence of long COVID-19. Multiple treatment options have been explored to manage COVID-19 patients and reduce mortality rates (3). To combat SARS-CoV-2, the Indonesian government initiated a COVID-19 Vaccination Program on January 13, 2021, divided into four phases. The initial phase targeted healthcare workers and utilized the CoronaVac vaccine, produced by Sinovac Life Sciences in Beijing, China (4). Given their high exposure risk to SARS-CoV-2 and the need to protect the healthcare system, healthcare workers received priority for vaccination, with most of them already having received the Sinovac vaccine. However, limited data are available on how different factors, such as gender and prior COVID-19 infection, impact the antibody levels induced by this vaccine, especially in an Indonesian context. Previous studies have suggested that males face a higher risk of severe COVID-19 outcomes, and prior SARS-CoV-2 infections may offer some protection against reinfection (5, 6).

Sinovac's CoronaVac, created in Beijing, China, utilizes a traditional inactivation process to stimulate an immune response against different elements of the SARS-CoV-2 virus, such as the matrix, envelope, nucleoprotein structures, and spike protein. In a phase 2 clinical trial, 97% of participants seroconverted 28 days after receiving CoronaVac, which was administered with a 3 mg dosage on both day 0 and day 28. Nonetheless, phase 3 trials conducted in different countries reported varying levels of effectiveness, with efficacy rates ranging from 51% to 84%. Nevertheless, the real-world effectiveness of current vaccines in preventing initial infection and reinfection, as well as the duration of this protection, remains uncertain. The primary aim of this study is to quantitatively measure the antibody levels in blood samples taken from healthcare workers after they receive the initial and follow-up doses of the inactivated SARS-CoV-2 vaccine (7-9).

MATERIALS AND METHODS

It is a descriptive observational study made up of a cross-sectional design which is a study that examines the relationship between the independent variable and the dependent variable, where observations are made of the independent and dependent variables using the perspective method. This study has been granted ethical approval by the Health Research Ethics Commission at the Faculty of Medicine, University of Nusa Cendana. The research took place at Mamami Hospital, Kupang City, East Nusa Tenggara, Indonesia, from April 5 to August 8, 2021. Health workers at Mamami Hospital were the participants in

this study. As of February 2021, 30 health workers have been vaccinated.

Data for this study were collected through the screening of healthcare workers who had been vaccinated in February. After their vaccinations, RT-Ab and immunoserology tests were carried out to establish the presence or absence of antibodies. Following these tests, participants who were to be included in the study were observed, and interviews were conducted using data collection tools. The primary data for this research were gathered from healthcare workers who had undergone vaccination. One month after receiving the vaccine, healthcare workers were subjected to a rapid antibody test to assess the production of IgG and IgM. A further immunoserological examination was conducted two months later to confirm the presence of antibodies.

RESULTS

This study involved a total of 30 health workers, who were employed at Mamami Hospital Kupang, with 22 of them being women, constituting 76.6% of all respondents, and 8 of them being men, accounting for 23.3% of all respondents. These health workers ranged in age from 24 to 60 years. The primary objective of this study was to assess the distribution of patients with positive and negative results among the respondents who worked at Mamami Hospital Kupang from July to August 2021. The characteristics of the respondents are detailed in Table 1.

Table 1: Research respondent variables

Variable	Male respondents	Female respondents
Negative for antibody	8	19
Positive for antibody	0	3
Total	8	22

Before undergoing the examination, the health workers were administered a Rapid Antibody test, specifically testing for IgG and IgM antibodies, to determine if antibodies had developed following their vaccination in February. Among the 30 health workers who received the Sinovac vaccine, 3 of them showed a positive response in their Rapid Antibody test, indicating the presence of immunity in their bodies. For the remaining 27 health workers, their Rapid Antibody tests produced negative results. It is suspected that these 27 individuals did not develop antibodies to either IgG or IgM. As demonstrated in Table 2, a positive outcome in the Rapid Antibody test was observed among health workers who had received their initial vaccination.This study involved thirty health workers. Twenty-two women, or 76.6% of all respondents, and eight men, or 23.3% of all respondents, work at Mamami Hospital Kupang. They are between the ages of 24 and 60. Based on an analysis performa to see the distribution of patients with positive and negative results among the respondents who work at Mamami Hospital Kupang from July to August 2021, a description of the respondent variables can be seen in table 1. Prior to the examination, health workers were given Rapid antibodies, in general, to determine if antibodies had been formed after the vaccination in February. Rapid Antibodies, namely IgG and IgM, are tested in the first month for health workers who have been vaccinated. Out of 30 health workers who have been vaccinated against Sinovac, 3 respondents had a Rapid antibody reactive/positive examination. In the case of 3 of 30 health workers who were vaccinated with the Sinovac vaccine, immunity had developed in their bodies, based on a positive result on the Rapid antibody test. The remaining 27 respondents on the Rapid Antibody test had negative results, but it is suspected that in these 27 health workers no antibodies were formed to both IgG and IgM. As shown in Table 2, a positive result of the Rapid Antibody test was found in health workers who had been vaccinated for the first time.

The health workers at Mamami Hospital received a second vaccine injection 14 days after the first injection. At the Prodia Laboratory, an immunoserological examination was conducted 2 months after the second vaccine. Immunoserological results varied greatly, ranging from non-reactive to antibody values >250. One respondent did not form serological antibodies based on immunoserology results.

Table 2: Serological antibody test (immunoserology) results

Variables	Male	Female
Non reactive	-	1
<10	0	2
>10 -40	0	7
>40-80	2	0
>80-120	0	0
>120- 160	0	2
>160 – 200	1	0
>200	3	12
Total	6	24

There were two respondents with antibody results of 10. Additionally, 7 respondents had antibodies between > 10 and 40. In the serologic antibody range > 40 - 80, 3 respondents were found, in the serologic antibody range > 80 - 120, 0 respondents were found, and in the serologic antibody range > 120 - 160, 3 respondents were found. One respondent had serological antibodies in the range of 160 - 200, while 13 respondents had antibodies between 200 - 400. Thirty health workers were tested for serological antibodies. During the immunoserological examination, various antibody values were found in the health workers who had been examined, as shown in Table 2.

DISCUSSION

The primary challenge over the last year has been to provide broad access to a safe and effective vaccine for the pandemic. Prompt vaccination with the

inactivated SARS-CoV-2 virus is essential for containing the pandemic and steering extensive vaccination campaigns. This study was conducted to evaluate the rates of antibody responses to the inactivated SARS-CoV-2 virus. Following the initial vaccine dose, there were virtually no antibody responses. But a notable increase in antibodies occurred after the administration of the second dose (8,9). An effective and safe vaccine, combined with essential measures such as practicing good hand hygiene, maintaining social distance, and adopting universal mask usage, plays a crucial role in managing the pandemic. Various vaccines, utilizing diverse production methods, have gained emergency use authorization on a global scale. The World Health Organization has granted emergency use approval to a range of vaccines, including AstraZeneca/Oxford, Johnson & Johnson, Moderna, Pfizer/BioNTech, and Sinopharm. These vaccines have reported efficacy rates spanning from 63.09% to 95%. Additionally, CoronaVac (Sinovac), which received WHO emergency use authorization on January 6, 2021, exhibited efficacy rates of 51% in Brazil, 65% in Indonesia, and 84% in Turkey, as determined from Phase 3 studies (10).

A crucial question in the context of COVID-19 vaccination is the duration and level of protection conferred by antibodies produced. Ongoing questions involve ascertaining how long the protective effect lasts and whether a booster dose is necessary. A study involving healthcare professionals who had contracted COVID-19 revealed that IgG antibodies resulting from the infection provided protection against reinfection for a duration of about up to 6 months (11). There is limited information available regarding the protective effectiveness of naturally acquired antibodies after a COVID-19 infection. Hence, it is advisable to receive vaccination regardless of one's prior COVID-19 infection status. A critical question arises concerning whether a single vaccine dose suffices for individuals who have previously had COVID-19. Among a group with prior COVID-19 experience, 96% tested positive for antibodies. After the first vaccine dose, the antibody levels in 75 individuals who had previously experienced COVID-19 at least four months earlier had tripled. Even though there was a slight dip in the average antibody levels following the second dose, these levels remained approximately almost 3 times higher than those observed in individuals without a prior infection. Based on the entirety of available data, it seems reasonable to consider that administering a single vaccine dose 3 to 6 months after a COVID-19 infection may suffice for individuals with confirmed prior infection, thereby enabling the prioritization of vaccine resources to protect vulnerable populations. In case of potential virus re-exposure, the role of memory B and T cell responses becomes pivotal, with T cell responses emerging within 14 days after receiving a single dose of the CoronaVac vaccine, and B cell responses improving after the second dose (12-14).

This study suggests the continued importance of administering COVID-19 vaccines in two doses to individuals without a confirmed SARS-CoV-2 exposure history. Limited research exists on the effectiveness of COVID-19 vaccines in people with chronic conditions or prior COVID-19 infections. The inclusion of participants with and without chronic conditions and those with or without prior infections in this study provides valuable real-world insights. However, this study, conducted at a single facility with a small participant pool, had limitations, such as the inability to assess cellular immune responses. Despite acknowledging the potential for SARS-CoV-2 virus exposure between the collection of blood samples following the first and second vaccine doses, the participants were not routinely subjected to PCR tests for acute COVID-19 diagnosis prior to the study. Furthermore, the study uncovered a notable gender-based difference, with female participants exhibiting significantly higher antibody levels in the three months post-vaccination, aligning with findings from another study. Nevertheless, the exact cause of this gender disparity remains unknown.

CONCLUSION

In the present study, inactivated SARS COV-2 virus vaccine significantly contributed to the acquisition of anti-SARS-CoV-2S antibodies of 30 health workers.

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CONFLICT OF INTEREST

There is no conflict of interest found during this study.

REFERENCES

1. Otsuka, S., Hiraoka, K., Suzuoki, M., Ujiie, H., Kato, T., Yokota, I., *et al.*, Antibody responses induced by the BNT162b2 mRNA COVID-19 vaccine in healthcare workers in a single community hospital in Japan. Journal of Infection and Chemotherapy. 2022;28(4): 539-542.
2. Devendra, S., Vishnu, A. A review on the COVID-19, its history, diagnostic approaches, role of herbs and current world scenario. Biomedicine. 2021 Sep 7;41(2):328-332.
3. Heriyanto, R. S., Kurniawan, A., Wijovi, F., Halim, D. A., Jodhinata, C., Marcella, E., *et al.*, The role of COVID-19 survivor status and gender towards neutralizing antibody titers 1, 2, 3 months after Sinovac vaccine administration on clinical ear medical students in Indonesia. International Journal of Infectious Diseases. 2022; 113: 336-338.
4. Dinc, H. O., Saltoglu, N., Can, G., Balkan, I. I., Budak, B., Ozbey, *et al.*, Inactive SARS-CoV-2 vaccine generates high antibody responses in healthcare workers with and without prior infection. Vaccine. 2022;40(1): 52-58.
5. Bencharattanaphakhi, R., Rerknimitr, P. Sinovac COVID-19 vaccine–induced cutaneous leukocytoclastic vasculitis. JAAD case reports. 2021; 18: 1-3.
6. Cucunawangsih, C., Wijaya, R. S., Lugito, N. P. H., Suriapranata, I. Antibody response to the inactivated SARS-CoV-2 vaccine among healthcare workers, Indonesia. International Journal of Infectious Diseases. 2021; 113:15-17.

7. Souza, W. M., Amorim, M. R., Sesti-Costa, R., Coimbra, L. D., Brunetti, N. S., Toledo-Teixeira, D. A., *et al.*, Neutralisation of SARS-CoV-2 lineage P. 1 by antibodies elicited through natural SARS-CoV-2 infection or vaccination with an inactivated SARS-CoV-2 vaccine: an immunological study. The Lancet Microbe. 2021; 2(10): e527-e535.
8. Liu, J., Yan, W., Liu, Z., Han, Y., Xia, Y., Yu, J. A colloidal gold-based immunochromatographic strip for rapid detection of SARS-CoV-2 antibodies after vaccination. Medicine in Novel Technology and Devices. 2021; 11: 100084.
9. Earle, K. A., Ambrosino, D. M., Fiore-Gartland, A., Goldblatt, D., Gilbert, P. B., Siber, G. *et al.*, Evidence for antibody as a protective correlate for COVID-19 vaccines. Vaccine. 2021; 39(32): 4423-4428.
10. Emel, A. Z. A. K., Karadenizli, A., Uzuner, H., Karakaya, N., Canturk, N. Z., Hulagu, S. Comparison of an inactivated Covid19 vaccine-induced antibody response with concurrent natural Covid19 infection. International Journal of Infectious Diseases. 2021; 113: 58-64.
11. Calil, V. M. L. T., Palmeira, P., Zheng, Y., Krebs, V. L. J., Carvalho, W. B. D., Carneiro-Sampaio, M. CoronaVac can induce the production of anti-SARS-CoV-2 IgA antibodies in human milk. Clinics. 2021;76.
12. Yu, Y. P., Chen, J. T., Jiang, Z. W., Ling, W. A. N. G., Yu, C. K., Yan, X. Y., *et al.*, Modeling the Long-term Antibody Response and Duration of Immune Protection Induced by an Inactivated, Preservative-free Hepatitis A Vaccine (Healive) in Children. Biomedical and Environmental Sciences. 2020; 33(7): 484-492.
13. Kim, J. H., Hotez, P., Batista, C., Ergonul, O., Figueroa, J. P., Gilbert, *et al.*, Operation Warp Speed: implications for global vaccine security. The Lancet Global Health. 2020;9(7): e1017-e1021.
14. Su, Q. D., Zou, Y. N., Yi, Y., Shen, L. P., Ye, X. Z., Zhang, Y., *et al.*, Recombinant SARS-CoV-2 RBD with a built in T helper epitope induces strong neutralization antibody response. Vaccine. 2020; 39(8):1241-1247.