ORIGINAL ARTICLE

Level of Anti-SARS-CoV-2 Spike Protein amongst Frontline Health Personnel of a Supra-Tertiary Hospital

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Background: COVID-19 has become a global pandemic, leading to the development of various vaccines to protect against infection. Sinovac-CoronaVac COVID-19 vaccine, an inactivated virus vaccine developed by Sinovac Biotech, has been approved for use. However, limited information is available regarding the immunity level provided by Sinovac-CoronaVac.

Objective: To determine the level of anti-SARS-CoV-2 spike protein antibodies 28 and 90 days after the administration of the second dose of CoronaVac.

Materials and Methods: A descriptive study was conducted, involving 132 healthcare personnel. The antibody levels were measured using the Roche Elecsys anti-SARS-CoV-2 spike protein immunoassay, both at 28 and 90 days after the second dose of CoronaVac.

Results: The majority of participants were female registered nurses. The geometric mean antibody levels on day 28 and 90 were 138.1±2.2 and 66.9±0.3, respectively. By day 90, the antibody levels had declined to 45.3% compared to day 28. Nearly all participants had immunity levels on day 90 lower than those resulting from natural infection.

Conclusion: The present study findings indicated that the immunity level, as measured by anti-SARS-CoV-2 spike protein antibodies, declined below the level observed with natural infection by day 90. Additional vaccine doses are suggested for healthcare personnel to provide rapid protection of the infection.

Keywords: Antibody level; COVID-19; Health care personnel; Immunity

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A newly discovered SARS-CoV-2 virus infection causes COVID-19 disease. Most clinical manifestations are mild to moderate respiratory symptoms that could be self-limited, but in a vulnerable group like elderly or comorbid patients, could get severe symptoms. COVID-19 transmission is done by droplet-like respiratory secretion transmitted by coughing[1]. In November 2021, about 260 million people were infected, and five million people died[2]. There were about two million people infected in Thailand, and 20 thousand people died[3].

The first response policy was to lock-down society, and countries, such as the United States, the United Kingdom, and Thailand, did just that[4-6]. The number of infected people seemed to decline but later rose again in mid-2021[3], then vaccines were discovered. The first available COVID-19 vaccines were the mRNA type, BNT162b2 (Pfizer) and mRNA-1273 (Moderna)[7,8]. Then came AstraZeneca's viral vector vaccine, ChAdOx1, the most commonly used[9]. Other viral vaccines approved by the World Health Organization (WHO) were Ad26.COV2.S from Johnson & Johnson, and rAd26 and rAd5 from the Gamaleya National Center of Epidemiology and Microbiology. Then, there were the inactivated virus vaccines such as the inactivated SARS-CoV-2 vaccines (Vero cell) from Sinopharm and CoronaVac from Sinovac Research and Development in China. CoronaVac is the leading vaccine used in Thailand[10]. This was the situation until the delta variant, after

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which the incidence of infection again surged, and the effectiveness of the COVID-19 vaccination was uncertain.

Research on the infection protection effectiveness of COVID-19 vaccines indicated that mRNA vaccines had the greatest effectiveness, at about 91.0%[11], followed by ChAdOx1 at 60.0%[15]. Data on CoronaVac was insufficient although every vaccine provided more than 90.0% in-hospital admission prevention[11-14].

Another essential method for estimating vaccination protection effectiveness is antibody level studies. For example, two doses of BNT162b2, 28 days apart, results in an average antibody level of 244.1 U/mL[16]. The antibody level three weeks after one dose of either mRNA vaccine (BNT162b2 and mRNA-1273) was greater than after natural infection[17]. Fourteen days after the second dose of ChAdOx1 yields an antibody level of 435.0 AU/mL[17]. By comparison, the antibody level 28 days after the second dose of CoronaVac immunity is 196.0 U/mL[16]. The delta variant was both more infectious and virulent than the alpha, resulting in a greater need for more effective vaccines, so many countries developed a cross-type vaccination plan. For example, Germany launched a vaccination plan crossing ChAdOx1 with BNT162b2[18]. In Thailand, the vaccination guideline was updated crossing CoronaVac with ChAdOx1 plus a booster dose[10]. The current study aimed to determine the level of immunity of people with two doses of CoronaVac.

Materials and Methods

A descriptive study was conducted. Electronic medical records from Health Objects (HO: Srinagarind Hospital's health information system) were reviewed. The present study encompassed 2,124 healthcare personnel vaccinated with two doses of CoronaVac, between March 23, 2021, and July 23, 2021. Based on a preliminary study, a sample size of 120 volunteers was calculated using Winpepi version 11.65, with a confidence interval of 95, assuming a population standard deviation (SD) of 227.0 and an acceptable error of 40.0 U/mL. The study enrolled 132 frontline personnel who had a history of two doses of CoronaVac.

Measuring of anti-SARS-CoV-2 spike protein level

The immunity level of all participants was measured using Roche Elecsys anti-SARS-CoV-2 spike protein, an immunoassay for measuring antibody to SARS-CoV-2 spike protein receptor-binding protein (RBD) in unit U/mL. Measurements were done 28 and 90 days after the second dose of CoronaVac to determine the trend in immunity decline.

Table 1. Personal characteristics of participants

Characteristic	Day anti-SARs-CoV-2 spike protein measured; n (%)	
	28 days after second dose (n=132)	90 days after second dose (n=122)
Sex		
Female	116 (87.8)	107 (87.7)
Male	16 (12.2)	15 (12.3)
Age group (years); mean±SD	36.3±10.4	36.3±10.3
20 to 29	48 (36.4)	44 (36.1)
30 to 39	48 (36.4)	45 (36.9)
40 to 49	16 (12.1)	15 (12.2)
>49	20 (15.1)	18 (14.8)
Job title		
Registered nurse	112 (84.8)	103 (84.4)
• Emergency room	32 (24.2)	31 (26.2)
• Intensive care unit	24 (18.2)	24 (19.7)
• Semi-intensive care unit	9 (6.8)	6 (4.9)
• COVID-19 infection ward	27 (20.5)	25 (20.5)
• Anesthesia room	15 (11.4)	13 (11.5)
• Field hospital	5 (3.7)	4 (3.3)
Physician	4 (3.0)	3 (2.5)
Laboratory technician	6 (4.5)	6 (4.9)
Radiology technician	10 (7.7)	10 (8.2)

SD=standard deviation

Statistical analysis

Data were analyzed using IBM SPSS Statistics, version 28.0 (IBM Corp., Armonk, NY, USA). Personal characteristics, age, sex, and occupation, were described as proportions, means, and standard deviations. The anti-SARS-CoV-2 spike protein was described in terms of geometric means, geometric standard deviations, and statistical significance using the Mann-Whitney U test and the Wilcoxon Signed Ranks test.

Ethical consideration

The Khon Kaen University Ethics Committee reviewed and approved the present study for Human Research based on the Declaration of Helsinki and the ICH Good Clinical Practice Guidelines. Ethical reference number: HE641588.

Results

One hundred thirty-two participants were

Table 2. Level of anti-SARs-CoV-2 spike protein (U/mL)

Factor	28 days after second dose (n=132)		90 days after second dose (n=122)	
	GMT±GSD	p-value	GMT±GSD	p-value
Overall	138.1±2.2		66.9±0.3	<0.001
Sex		0.655		0.737
Male	150.8±2.1		71.1±2.2	
Female	136.5±2.2		67.4±2.4	
Age group		0.561		0.467
20 to 29 years	154.7±2.0		70.8±2.0	
30 to 39 years	130.8±2.3		65.5±2.7	
40 to 49 years	106.5±2.7		53.8±2.7	
More than 49 years	149.0±1.9		80.6±1.8	
Job title		0.791		0.460
Registered nurses	137.0±3.1		67.0±2.4	
• Emergency room	120.4±2.3		54.0±2.1	
• Intensive care unit	169.1±2.1		77.5±2.4	
• Semi-intensive care unit	157.8±2.4		94.8±3.4	
• COVID-19 infection ward	135.7±1.9		72.4±1.9	
• Anesthesia room	114.0±2.4		61.6±3.8	
• Field hospital	162.3±1.3		70.1±1.6	
Physicians	166.0±2.6		83.0±2.7	
Laboratory officers	107.8±3.7		51.0±2.7	
Radiological officers	162.9±2.2		86.5±1.7	
Range (min-max)	15.8 to 908.9		6.7 to 1,041.0	
Mean difference ± SD			86.7±94.2	
Percent of difference			45.3	
Median (min-max)			85.4 (–585.9 to 341.5)	
Percent of median			53.1	
Number of participants with increased anti-SARs-CoV-2 spike protein			2	
Number of participants with decreased anti-SARs-CoV-2 spike protein			120	

GMT=geometric mean titer; GSD=geometric standard deviation; SD=standard deviation

enrolled in the first measure at 28 days after their second dose, and 122 participants remained in the second measure at 90 days after their second dose. Most participants were female at 87.7% to 87.8%, and most were between 20 to 29 and 30 to 39 years of age. Nearly all were registered nurses at 84.4% to 84.8% (Table 1).

The geometric mean for the anti-SARs-CoV-2 spike protein level 28 days after the second dose was 138.1 U/mL and dropped significantly to 66.9 U/mL (p<0.001) at 90 days. At 28 days after the second dose, the lowest level was 15.8, and the highest level was 908.9. By comparison, at 90 days after the second dose, the lowest level was 6.7, and the highest level was 1,041.0. The distribution of the level of anti-SARs-CoV-2 spike protein is shown in Figure 1. There was no significant difference between gender, age groups, and occupations. The average difference between 28 and 90 days after the second dose was 86.7 U/mL or a 45.3% drop. There were only two participants who had increased immunity (Table 2). Compared with immunity from natural infection, 55.3% of participants had a greater immunity at 28 days after

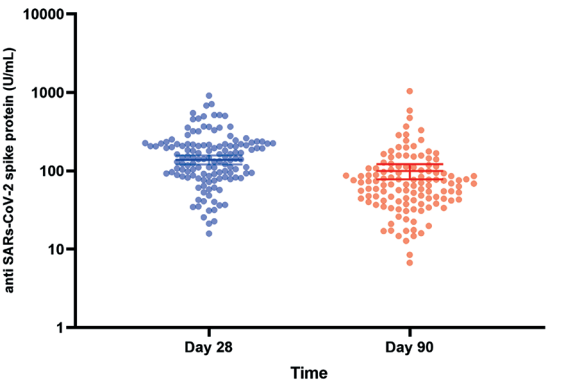

Figure 1. Level of the anti-SARs-CoV-2 spike protein.

Table 3. Number of participants who have immunity level more than natural infection (132 U/mL)

Factors	28 days after second dose (n=132)		90 days after second dose (n=122)	
	n (%)	p-value	n (%)	p-value
Overall	73 (55.3)		23 (18.9)	
Age group		0.685		0.605
20 to 29 years	29 (60.4)		9 (20.5)	
30 to 39 years	24 (50.0)		9 (20.0)	
40 to 49 years	9 (56.3)		2 (13.3)	
More than 49 years	11 (55.0)		3 (16.7)	

the second dose than the cut-off point at 132.0 U/mL. By contrast, the healthcare personnel with superior immunity at 90 days after the second dose compared to natural infection decreased to only 18.9% (Table 3).

Discussion

The antibody levels in the current study resulted from the inactivated viral vaccine, which differs from other vaccines such as mRNA or adenoviral vector COVID-19 vaccines. The benefit of the inactivated viral vaccine is that there is no living or virulent particle that can cause disease[19]; however, the immunity level might be lower than other types of vaccines, and as such additional doses are usually required[20].

In the current study, the participants were examined for immunity two times, once at 28 days after the second vaccination dose and again at 90 days. From prior guidelines, Ireland's Health and Safety Executive (HSE) has defined significant vaccine protection that equals 28 days after the second doses after ChAdOx1[21]. There is insufficient data regarding CoronaVac, so the authors examined immunity as per the same date as ChAdOx1. In general, most vaccines require a booster six months after complete vaccination such as hepatitis B vaccination[22]; however, during the SARS-CoV-2 pandemic, the number of variants of concern, especially the delta variant, raised concern that six months may be too long, and that immunity would drop below a protective level. Thus, a three-month interval is being used for early detection of any decline in immunity.

Comparing COVID-19 vaccine types: BNT162b2 immunity at 28 days after the second dose averages 244.1 U/mL[16]; ChAdOx1 antibody at 14 days after the second dose averages 435.0 AU/mL[17]; and CoronaVac at 28 days after the second dose averages 196.0 U/mL[16]. The authors found that the antibody level of CoronaVac was lower than the mRNAs like BNT162b2 and mRNA-1273. There are limitations due to differences in immunoassays regarding the units of anti-SARS-CoV-2 spike protein, so the authors cannot compare antibody levels among studies. Nevertheless, the immunity level from the current study exceeded the immunity after natural infection; thus, the authors can assume that immunity at 28 days after complete CoronaVac vaccination was higher than the protection level of natural infection. Moreover, at 90 days after vaccination, the level of immunity declined from 28 days, similar to BNT162b2 but different from mRNA-1273[23]. Almost all participants had immunity levels at 90 days lower than natural infection (81.1%). This finding corresponds with the increasing number of infected health personnel who had complete CoronaVac vaccination for at least six weeks. The infections are mostly caused by social activity and family members (pers. comm. Dr. Naesinee Chaiear, 27 Nov 2021). Therefore, social distancing and minimizing social activities remain important along with complete vaccination. Moreover, a recent study shows that the immunity level is rising after an additional dose[24] and due to various types of variants especially the latest Omicron that reduced vaccine effectiveness, suggesting an additional dose of mRNA vaccine may be required for health personnel before 90 days[25].

The present study result showed a declining trend of immunity in participants between the age groups 20 to 29 and 40 to 49. The probable cause is that the humeral immune response dropped with age[26] or it might be because of an inadequate sample size.

The present study had strengths. First, the authors collected immunity data on CoronaVac, the leading COVID-19 vaccine in Thailand. Every participant had a history of complete CoronaVac vaccination without any other COVID-19 vaccines. Secondly, the authors followed the immunity level at 90 days in the same participants to detect any trend in changed immunity.

The present study had limitations. First, the authors did not have sufficient data on the participants such as underlying disease, history of COVID-19 infection, or high-risk contact. Secondly, the present study included only healthy people, which might ignore health and age effects on immunity. The last thing was that the current SARS-CoV-2 antibody tests have not been specifically evaluated to determine the level of protection provided by the immune response to COVID-19 vaccination. Rapid antibody tests primarily indicate the presence or absence of

antibodies that can interfere with viral entry into human cells. However, it is important to note that an antibody level test alone cannot definitively confirm protection against severe COVID-19. Moreover, routine antibody tests do not measure the neutralizing capacity of antibodies, which is a crucial aspect in determining their ability to effectively combat the virus. It is also worth mentioning that antibodies are not the sole components of immune protection against future threats. Various types of white blood cells, including those that retain a memory of the pathogen, play an important role in triggering a response upon re-exposure.

Conclusion

The mean anti-SARs-CoV-2 spike protein 28 days after two doses of CoronaVac was 138.1 U/mL and declines to 66.9 U/mL after 90 days ($p<0.001$). Importantly, the level was lower than the antibody level after natural infection; thus, additional doses are needed before 90 days.

What is already known on this topic?

CoronaVac was the leading vaccine used in Thailand. The antibody level three weeks after one dose of either mRNA vaccine (BNT162b2 or mRNA-1273) was greater than after natural infection. Fourteen days after the second dose of ChAdOx1, an antibody level of 435.0 AU/mL can be seen. By comparison, the antibody level 28 days after the second dose of CoronaVac immunity is 196.0 U/mL.

In Thailand, the vaccination guideline was updated crossing CoronaVac with ChAdOx1 plus a booster dose.

What this study adds?

The findings of this study confirmed the decline of immunity level 90 days after the second doses of CoronaVac and it is below immunity level of natural infection. This evidence drives recommendations for improving guidelines for vaccination in Thailand to choose time for booster doses that should be before day 90 after the second dose of CoronaVac. We also recommend emphasizing the importance of wearing PPE and decreasing social activities to reduce COVID-19 infection rate.

Recommendation

1. CoronaVac is beneficial for healthcare workers in terms of humoral immunity in countries with insufficient vaccines, although the antibody level is not as high as other vaccine types.

2. Additional vaccine doses would be necessary within three months after the second dose.

3. A larger sample size and immunity level after additional doses of vaccination would benefit from further study.

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Conflicts of interest

The authors declare no conflict of interest.

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