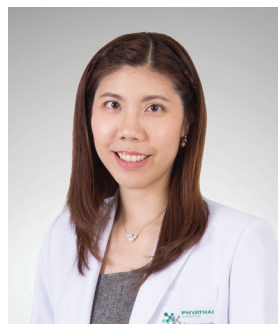


# SARS-CoV-2 IgG Antibody Response after Immunization of Healthcare Workers with Inactivated COVID-19 Vaccine (CoronaVac) at Phyathai 3 Hospital

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## Abstract

**OBJECTIVES:** To evaluate the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) anti-spike Immunoglobulin G (IgG) antibody response after CoronaVac immunization of healthcare workers at Phyathai 3 Hospital.

**MATERIALS AND METHODS:** The descriptive study was performed at Phyathai 3 Hospital between March 2021 and May 2021. Healthcare workers who received two doses (three weeks apart) of the CoronaVac vaccine were included. Blood samples for anti-spike IgG antibodies were taken from each healthcare worker before getting vaccinated and four weeks after completing two doses of the vaccine.

**RESULT:** A total of 88 healthcare workers were enrolled in our study. Fifty-three (60%) of them were female, 84(95%) were physicians, 46(52%) were obese and 33(37.5%) had at least one coexisting condition. The mean age was  $45.8 \pm 9.3$  years. Seven (8%) of participants were older than 60 years of age. All participants did not have IgG antibodies at baseline. Eighty-seven (98.9%) healthcare workers had seroconversion of anti-spike IgG antibodies four weeks after completing two doses of the CoronaVac vaccine. The mean level of anti-spike IgG at four weeks after completing vaccination was  $115 \pm 85$  unit/ml (range, 1.77-297.3 unit/ml). Anti-spike IgG levels were significantly higher in females than males ( $p = 0.02$ ). Normal-weight participants showed higher anti-spike IgG levels than obese individuals ( $p = 0.01$ ). IgG antibody responses tended to decrease with age. The highest IgG levels were observed in the ages of 30-40 years.

**CONCLUSION:** Two doses of the CoronaVac vaccine could induce a 98.9% rate of seroconversion in healthcare workers. Female and normal-weight participants were significantly associated with a higher level of IgG response. Younger adults had a higher immune response than older adults in our setting.

**Keywords:** SARS-CoV-2 IgG, Anti-spike IgG, CoronaVac, Sinovac, health care workers, COVID-19 vaccine

COVID-19 disease is an emerging disease caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), an enveloped, single-stranded RNA Betacoronavirus. This virus has been rapidly spreading, resulting in a pandemic and clusters of pneumonia cases around the world. The pandemic first broke out in Wuhan, a city in the Hubei Province of China, and has been spreading throughout the globe.<sup>1-3</sup>

The SARS-CoV-2 virus is mainly transmitted via respiratory droplets and contact with infected secretions. Airborne transmission of SARS-CoV-2 can occur during medical aerosol-generating procedures, such as endotracheal intubation, extubation, respiratory tract suctioning, bronchoscopy, or non-invasive ventilation,<sup>4-6</sup> which contributes to an increased risk of infection to healthcare workers. Infection control interventions to reduce transmission include hand hygiene, the use of appropriate protective personal equipment (PPE), early identification and isolation of patients, environmental disinfection, and vaccination.

CoronaVac is an inactivated coronavirus vaccine developed by Sinovac, a Chinese pharmaceutical company. From the phase 2 study, it showed good seroconversion in the vaccinated group compared to the placebo group.<sup>7</sup> In Brazilian clinical trials, the efficacy rate in preventing any symptomatic disease of Coronavac is 50.4%.<sup>8</sup>

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CoronaVac is the first COVID-19 vaccine that was approved and shipped to Thailand in March 2021. This vaccine is recommended for use in adults between the ages of 18 and 59 years. Medical workers and frontline health workers will be the first group of people to be vaccinated. The primary objective of this study is to evaluate the SARS-CoV-2 anti-spike IgG antibody response after CoronaVac immunization of healthcare workers at Phyathai 3 Hospital.

## Materials and Methods

This descriptive study was performed at Phyathai 3 Hospital between March 2021 and May 2021. Healthcare workers who received two doses (three weeks apart) of the Coronavac vaccine were included.

Exclusion criteria were healthcare workers who were diagnosed with COVID-19 infection before the first dose of CoronaVac vaccination and between the first and second dose of the vaccine. Written informed consent was obtained from all participants. The study was approved by our institutional review board.

### Study design and data collection

Blood samples for anti-spike IgG antibodies were taken from each healthcare worker before getting vaccinated and four weeks after completing two doses of the vaccine. Data from each individual subject were collected. These include baseline demographic data, evidence of infection within the past three months, and the date of vaccination. The level of anti-spike IgG was analyzed.

Between two weeks prior to the vaccination and the second blood collection, the participants needed to monitor their body temperatures every day and check any upper respiratory infection (URI) symptoms. As per the current patient under investigation (PUI) criteria and guideline for COVID-19 in Thailand, if any of them had a temperature  $> 37.5^{\circ}\text{C}$  and URI symptoms, they would be sent for a nasopharyngeal and throat swab for SARS-CoV-2 reverse transcription polymerase chain reaction (RT-PCR). If the result turned out to be positive, that participant would be excluded.

### Anti-Spike IgG antibodies

The Elecsys Anti-SARS-CoV-2 S assay for use on the Cobas e analyzers (Roche Diagnostics International Ltd, Rotkreuz, Switzerland) is an electrochemiluminescence immunoassay, or ECLIA, intended for qualitative and semiquantitative detection of antibodies to SARS-CoV-2 in human serum and plasma. This assay uses a recombinant protein representing the receptor-binding domain (RBD) of the spike antigen in a double-antigen sandwich assay format. The Elecsys Anti-SARS-CoV-2 S assay detects antibodies to SARS-CoV-2 spike protein RBD. According to the manufacturer, the cut-off values are as follows,  $< 0.8$  U/ml, negative;  $\geq 0.8$  U/ml was positive for anti-SARS-CoV-2 S.

### Statistical analysis

The sample size was calculated using goodness-of-fit tests by chi-square test, 2-sided  $\alpha$  equals 0.05, degree of freedom 1 with a power of 80%. We required 88 participants for this study. Continuous variables were compared using the student chi-square test, Mann-Whiney U test, and reported with a standard deviation, means, minimum and maximum. Fisher's exact test and chi-square were used to compare categorical variables and reported with percentage. A  $p$ -value less than 0.05 was considered statistically significant. All statistical analyses were performed using SPSS version 18.0.

## Results

Eighty-eight healthcare workers, 60% were female, 95% were physicians, 52% were overweight (body mass index [the weight in kilograms divided by the square of the height in meters] of at least 23.0), and 37.5% had at least one coexisting condition. The mean age was  $45.8 \pm 9.3$  years, and 8% of participants were older than 60 years of age (Table 1).

At baseline, none of the participants had any detectable anti-spike IgG antibody. At four weeks after completing two doses of the CoronaVac vaccine, the seroconversion rates of anti-spike IgG antibodies were 98.9% (87 of 88 participants). Only one case without seroconversion was

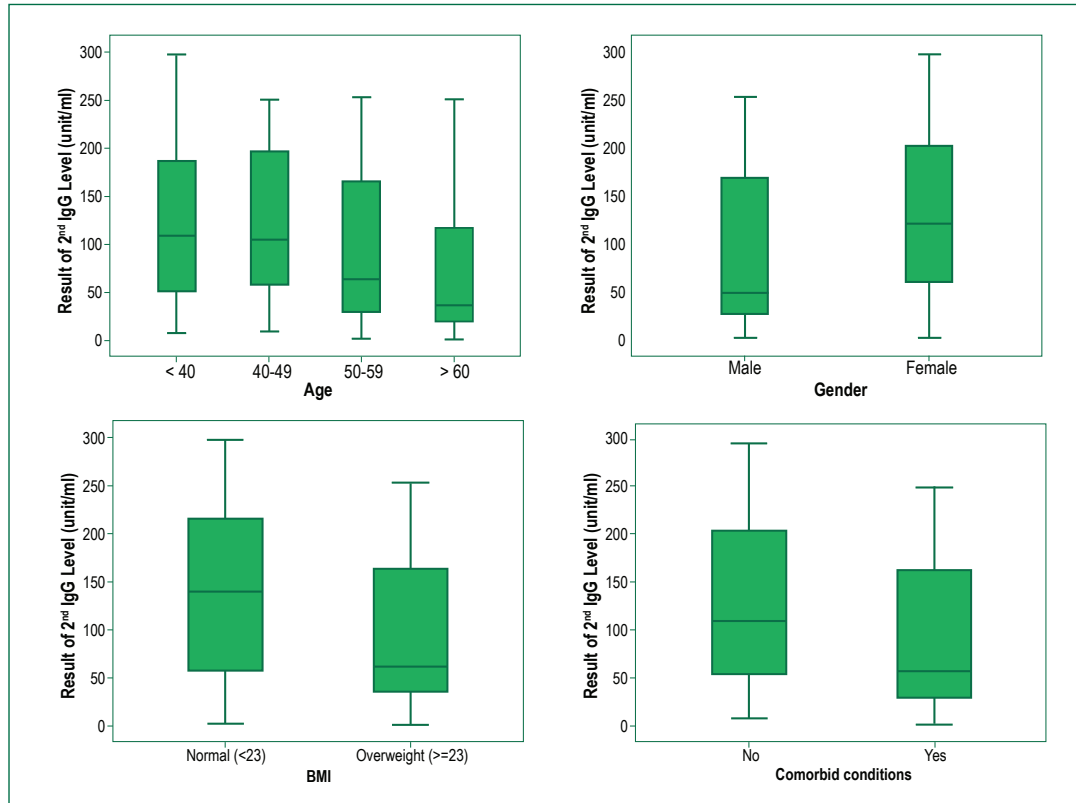
**Table 1:** Baseline Clinical and demographic characteristics of the subjects (n = 88)

Characteristics	n (%)
<b>Age (years)</b>	
30-39	25 (28.4)
40-49	29 (33.0)
50-59	27 (30.7)
60-70	7 (8.0)
<b>Gender</b>	
Male	35 (39.8)
Female	53 (60.2)
<b>Occupation</b>	
Physician	84 (95.5)
Nurse	4 (4.5)
<b>Body Mass Index</b>	
Underweight ( $< 18.5$ )	3 (3.4)
Normal	39 (44.3)
Overweight ( $\geq 23$ )	46 (52.3)
<b>Comorbid conditions</b>	
No comorbid condition	55 (62.5)
Dyslipidemia	24 (27.3)
Hypertension	10 (11.4)
Cerebrovascular disease	4 (4.5)
Autoimmune disease	4 (4.5)
Diabetes mellitus	3 (3.4)
Immunosuppressive drug use	2 (2.3)
Solid organ tumors	2 (2.3)
Cardiovascular disease	1 (1.1)

male with age > 60. He was diagnosed with cutaneous vasculitis and had been consuming oral hydroxychloroquine and 7.5 mg/day of prednisolone. The mean level of anti-spike IgG at four weeks after completing vaccination was  $115.33 \pm 85.44$  unit/ml (range, 1.77-297.3 unit/ml).

Anti-spike IgG levels tended to decrease with age. The highest IgG levels were observed in the ages of 30-40 years.

In contrast, the older group (60-70 years) had the lowest level of anti-spike IgG (Figure 1). Anti-spike IgG levels were higher in females than males ( $p = 0.02$ ). Normal-weight individuals showed higher anti-spike IgG levels than overweight individuals ( $p=0.01$ ). Healthcare workers who had at least one comorbid condition had lower serum IgG levels than persons without comorbidity. (Table 2).



**Figure 1:** Relationship between level of SARS-CoV-2 anti-spike IgG at 4 weeks after completing two doses of the CoronaVac vaccine and demographic characteristics

Note: Solid lines mark the mean.

**Table 2:** SARS-CoV-2 anti-spike IgG levels in relation to age, gender, body mass index, and comorbid conditions (n = 88)

	n	Mean $\pm$ SD	Range
<b>Age (years)</b>			
< 40	25	126.97 $\pm$ 89.31	7.42-297.30
40-49	29	125.34 $\pm$ 81.46	9.44-251.00
50-59	27	102.86 $\pm$ 84.10	1.77-252.80
$\geq 60$	7	80.39 $\pm$ 95.67	0.72-251.00
F-test = 0.865, $p = 0.462$			
<b>Gender</b>			
Male	35	89.91 $\pm$ 83.50	0.72-252.80
Female	53	132.11 $\pm$ 83.26	1.77-297.30
T-test = -2.324, $p = 0.022^*$			
<b>Body Mass Index</b>			
Normal (< 23)	42	138.57 $\pm$ 85.85	1.77-297.30
Overweight ( $\geq 23$ )	46	94.11 $\pm$ 80.20	0.72-252.80
T-test = -2.512, $p = 0.014^*$			
<b>Comorbid conditions</b>			
No	55	127.90 $\pm$ 84.59	7.42-297.30
Yes	33	94.39 $\pm$ 83.95	0.72-251.00
T-test = 1.808, $p = 0.075$			

\*Significant differences were observed ( $p < 0.05$ )

## Discussion

This study showed that at four weeks after completing two doses of the CoronaVac vaccine, healthcare workers had 98.9% seroconversion rates of antibodies. According to our results, anti-spike IgG was significantly higher in female than male and normal-weight participants than overweight participants. The immune responses were higher in younger adults (aged 30–40 years) than older adults (aged 60–70 years). This rate of seroconversion is similar to the rates reported previously from phase 1/2 clinical trials of CoronaVac (Sinovac Life Sciences, Beijing, China).<sup>7</sup> In those trials, which enrolled healthy volunteers aged 18–59 years, neutralizing antibody responses were significantly higher in younger adults (aged 18–39 years) than in older adults (aged 40–59 years).

The use of the CoronaVac vaccine is recommended for adults between the ages of 18 and 59 years. However, in our study, some (8% of participants) senior healthcare workers (aged 60–70 years) decided to receive the vaccine. One of them had no seroconversion after completing the vaccination. We are reporting the seroconversion in older participants. The mean of IgG antibodies was  $80.39 \pm 95.67$  unit/ml in the ages of 60–70 years. Compared to the ages of 30–40 years, that had higher IgG antibodies ( $126.97 \pm 89.31$  unit/ml). Further research is needed to estimate the effectiveness of CoronaVac among people over 60 years of age.

There are many methods to test for immunity after vaccination. Pfizer and BioNtech have developed mRNA-based COVID-19 vaccines (BNT162b1 and BNT162b2), which measured geometric mean titers of RBD-specific IgG and geometric mean titers of neutralizing antibody.<sup>9</sup>

Moderna and the National Institutes of Health have also developed an mRNA-based vaccine (mRNA-1273), which induced both spike glycoprotein binding and virus-neutralizing antibody responses.<sup>10</sup> Oxford University and AstraZeneca studied for anti-spike glycoprotein IgG and neutralizing antibodies, and IFN $\gamma$  T-cell responses after chimpanzee adenovirus-vectored vaccination (ChAdOx1/AZD1222).<sup>11</sup> Our study used the level of antibodies to SARS-CoV-2 spike protein RBD for representing seroconversion. The mean of IgG antibodies was  $115.33 \pm 85.44$  unit/ml. However, to our knowledge, no previous studies examined IgG level in protective efficacy. Further studies are also needed to determine the protective level and effectiveness at preventing COVID-19 disease.

Our study had several limitations. First, the sample size is too small. Second, serum IgG levels were collected from each subject before getting vaccinated and only four weeks after vaccination completion. Measuring at three and six months after the second dose of the vaccine may lead to an increase in more information about the immune response. Third, our study examined anti-spike IgG antibodies. Further investigation for neutralizing antibody test is need.

## Conclusion

Two doses of the CoronaVac vaccine could induce a seroconversion rate of 98.9% in healthcare workers. Female and normal-weight participants were significantly associated with a higher level of IgG responses. Younger adults had a higher immune response than the older group.

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