



# Investigation of the Neutralizing Antibody Response of Healthcare Workers at a Korean University Hospital Six Months After the Introduction of the COVID-19 Vaccine

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Dear Editor,

The coronavirus disease (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which originated in Wuhan, China in December 2019, continues after 22 months [1]. As of late February 2021, Korea began to participate in the global COVID-19 vaccination program [2]. Healthcare workers (HCWs), the elderly, and employees of nursing homes or nursing hospitals were designated as the first individuals to be vaccinated in Korea [2]. HCWs were vaccinated with two different COVID-19 vaccines: those caring for COVID-19 patients were administered BNT162b2, while other HCWs were administered ChAdOx1 nCoV-19 [2]. As it had been six months since the vaccines were introduced, we investigated the neutralizing antibody (NAb) response against SARS-CoV-2, which is highly predictive of protection against COVID-19, using sera obtained from vaccinated HCWs [3].

The GenScript SARS-CoV-2 surrogate virus neutralization test (SVNT) kit (GenScript Biotech Corporation, Piscataway, NJ, USA) and Euroimmun anti-SARS-CoV-2 IgG ELISA (Euroimmun Med-

ical Laboratory Diagnostics AG, Lübeck, Germany) were used. The result readings have been described in a recent study by our group [4]. The Institutional Review Board of Chung-Ang University Hospital (Seoul, Korea) approved this study (2051-001-415).

At Chung-Ang University Hospital, 259 HCWs were vaccinated with BNT162b2 and 1,356 HCWs with ChAdOx1 nCoV-19. Fifty-one HCWs vaccinated with BNT162b2 participated in this study. We previously reported NAb responses one month after the first dose of ChAdOx1 nCoV-19 in 182 HCWs, 115 of whom participated also in the current study [4]. The dates of vaccination and serum sample collection are listed in Table 1. Additionally, sera of four patients two months after COVID-19 diagnosis were tested.

COVID-19 patients showed higher median IgG (interquartile range [IQR], 8.206 [7.448–8.420] vs. 4.726 [3.749–5.367],  $P<0.0001$ ) and SVNT (97.94 [97.63–98.02] vs. 89.19 [79.63–93.24],  $P=0.0379$ ) values than HCWs vaccinated with BNT162b2. HCWs six months after the first dose of BNT162b2 showed higher median IgG and SVNT values than HCWs six months after the

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**Table 1.** Dates of vaccination and sampling, demographic data, and antibody responses of HCWs vaccinated with BNT162b2 or ChAdOx1 nCoV-19 at a university hospital in Korea

Variables	HCWs vaccinated with BNT162b2 (six months after first dose) [A] (N=51)	HCWs vaccinated with ChAdOx1 nCoV-19 (six months after first dose) [B] (N=115)	<i>P</i> [A] vs. [B]	HCWs vaccinated with ChAdOx1 nCoV-19 (one month after first dose) [C] (N=182)	<i>P</i> [A] vs. [C]
Date of vaccination					
First dose	March 11–12, 2021	March 4–10, 2021		March 4–10, 2021	
Second dose	April 1–2, 2021	May 20–25, 2021			
Date of sampling	September 9–14, 2021	September 9–14, 2021		April 12–16, 2021	
Male sex	16 (31.4%)	36 (31.3%)	0.99	65 (35.7%)	0.57
Median age (SD)	39.5 (9.8)	40.0 (10.5)	0.76	39.0 (10.5)	0.76
Age group (yr)			0.75		0.72
20–29	11 (21.6%)	21 (18.3%)		44 (24.2%)	
30–39	14 (27.5%)	39 (33.9%)		56 (30.8%)	
40–49	17 (33.3%)	30 (26.1%)		43 (23.6%)	
50–59	8 (15.7%)	20 (17.4%)		33 (18.1%)	
60–69	1 (2.0%)	5 (4.3%)		6 (3.3%)	
Euroimmun IgG					
Positive	50/50 (100%)	109 (94.8%)	0.18	162/180 (90.0%)	0.015
Median (IQR)	4.73 (3.75–5.37)	2.68 (1.92–3.92)	<0.0001	2.79 (1.72–4.14)	<0.0001
SVNT					
Positive	51 (100%)	112 (97.4%)	0.55	148 (81.3%)	0.001
Median (IQR)	89.2 (79.6–93.2)	72.0 (51.5–87.2)	<0.0001	51.3 (35.9–64.7)	<0.0001

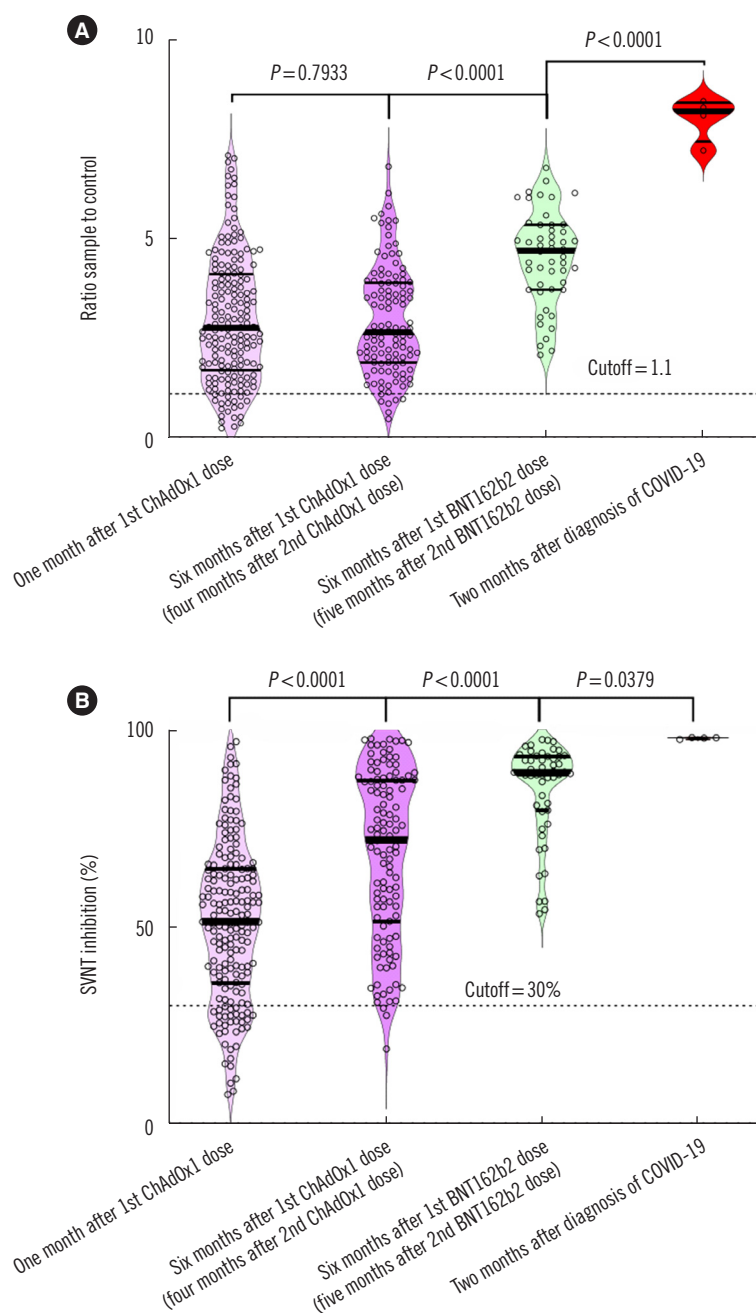
Abbreviations: HCWs, healthcare workers; SD, standard deviation; IQR, interquartile range; SVNT, surrogate virus neutralization test.

first dose of ChAdOx1 nCoV-19. HCWs six months after the first dose of ChAdOx1 nCoV-19 had higher SVNT values than HCWs one month after the first dose (Fig. 1 and Table 1).

HCWs vaccinated with ChAdOx1 nCoV-19 showed significantly lower neutralization activity than HCWs vaccinated with BNT162b2 at six months after COVID-19 vaccine introduction. NAb levels are considered correlates of protection against SARS-CoV-2 [5]. Vaccine-induced NAb or adoptive transfer of NAb protected rhesus macaques against SARS-CoV-2 challenge in a dose-dependent manner [6, 7]. Laboratory data from human vaccine trials and real-world outbreaks have shown that the NAb level is an inverse correlate of risk of SARS-CoV-2 or breakthrough infection [3, 5, 8]. Although the appropriate NAb level for protection against breakthrough infection has not been determined yet, the lower neutralization activity in HCWs vaccinated with ChAdOx1 nCoV-19 than in those vaccinated with BNT162b2 suggests that the former are more vulnerable to breakthrough infection than the latter. Booster vaccination is recommended at six months after receiving the primary series of BNT162b2 [9]. Therefore, ChAdOx1 nCoV-19 vaccine recipients with substan-

tially lower NAb levels should receive the booster dose as soon as possible. Given that NAb levels were very low in the relatively young and healthy HCWs, elderly, or individuals with underlying medical conditions may be at greater risk of breakthrough infection. Unlike in the USA and Israel, where mRNA vaccines were administered, ChAdOx1 nCoV-19 was more frequently administered than mRNA vaccines until July 2021 in Korea. Booster vaccination of ChAdOx1 nCoV-19-vaccinated individuals is an important way in controlling COVID-19 spread in Korea.

In this cross-sectional study, individuals in the BNT162b2 group were tested at only one timepoint after vaccination; therefore, it is unknown whether NAb levels decreased six months after vaccination with BNT162b2. In a recent Greek study, the SVNT values of 31 COVID-19 patients 50 days after hospitalization and those of 219 HCWs 50 days after vaccination were nearly similar (median, 96.45% vs. 96.36%) [10]. The significantly lower SVNT values in HCWs six months after BNT162b2 vaccination (89.19%) than those in COVID-19 patients after two months (97.94%) ( $P=0.0379$ ) may indicate that the NAb levels in the BNT162b2 group tended to decrease. Because of insufficient



**Fig. 1.** Antibody responses six months after COVID-19 vaccine introduction at a university hospital in Korea. (A) Nab levels as measured by percentage inhibition in SVNT readings. (B) Antibody levels as measured using Euroimmun IgG ELISA. The violin plots show the distribution of the antibody responses. The thick horizontal line and upper and lower thin lines indicate the median, 25th percentile, and 75th percentile, respectively. Each hollow circle represents a study participant. Abbreviations: Nab, neutralizing antibody; SVNT, surrogate virus neutralization test; Dx, diagnosis.

data in the current study, further research is needed to clarify this.

Considering the neutralizing activity in HCW sera six months after COVID-19 vaccine introduction, booster vaccination should be considered first for individuals who received ChAdOx1 nCoV-

19 at the start of the Korean vaccine program.

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## AUTHOR CONTRIBUTIONS

Conceptualization: Chung JW; Data curation: Choi SH, Park JY; Formal analysis: Choi SH; Funding acquisition: Chung JW; Investigation: Choi SH, Park JY, Chung JW; Methodology: Choi SH, Kweon OJ; Project administration: Chung JW; Resources: Chung JW; Software: Choi SH; Supervision: Chung JW; Validation: Park JY, Park JH, Kim MC, Kweon OJ; Visualization: Choi SH; Writing—original draft: Choi SH, Park JY; Writing—review & editing: Park JH, Kim MC, Kweon OJ, Chung JW.

## CONFLICTS OF INTEREST

None declared.

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