



## Perspective

### SARS-CoV-2 Infection after Vaccination in Health Care Workers: Case Series

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#### Abstract

**Introduction:** COVID-19 vaccine was given to Health Care Workers (HCW) during the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) pandemic. The vaccine effectiveness in reducing hospitalization and death is documented, but reducing transmission is less known. We report two clusters of HCW with COVID-19 following vaccination.

**Methods:** Data was retrieved from the hospital HCW Covid-19 tracing database from March 2021 to May 2021 in tertiary teaching and referral hospital.

**Results:** Two clusters were identified. The first cluster had three subjects with two fully vaccinated subjects and one unvaccinated subject. All had mild symptoms, and the unvaccinated subject was positive with SARS-CoV-2 longer than the other subjects. The second cluster had four vaccinated subjects and one unvaccinated subject. The unvaccinated subject developed severe symptoms and was admitted to critical care. One vaccinated subject in the second cluster was infected with SARS-CoV-2 four months before vaccination and was infected the second time. Only one subject from both clusters could return to work within 14 days after their positive tests.

**Discussion:** Covid-19 vaccination effectiveness can be measured by measuring outcomes such as preventing infection, reducing hospitalization, and preventing deaths. Although most HCW symptoms were mild, SARS-CoV-2 infection caused loss of human resources and extended sick leave to add more burden to an already straining health system.

**Conclusion:** SARS-CoV-2 infection after vaccination in health care workers as possible. Social distancing, usage of masks and hand washing is still currently a reasonable practice even after vaccination.

**Keywords:** Cluster; COVID-19; Immunity; Infection prevention; Vaccination

#### Introduction

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection and its disease (Covid-19) has afflicted millions of people in a worldwide pandemic and on its path changed the lives of billions of people. Vaccines that are safe and effective for Covid-19 are needed urgently as part of a plan to solve the pandemic. An array of modalities including novel techniques are being utilized as vaccine platforms such as mRNA (manufactured by Moderna and BioNTech/Pfizer), inactivated virus (Sinovac,

Sinopharm), viral vector (Oxford/AstraZeneca, Gamaleya, Janssen/Johnson&Johnson, CanSino), and protein subunit (Novavax) with each reporting a 63-95% protection against Covid-19 after a two-dose regimen in persons 16 years of age or older [1-3]. Health care workers (HCW) were the first group to be vaccinated as HCW was considered a high-risk group. By March 2021, 1,436,994 Indonesian healthcare workers, or 97,84 % of the workforce, have received their second dose of the vaccine [1,4]. Our hospital was a tertiary referral and teaching hospital also complied to our national regulation by vaccinating our staff. Studies identified that Covid-19 vaccines generally prevented hospitalization and death, but its ability to prevent transmission is less reported [1-3]. We aim

to report two clusters of COVID-19 among HCW post-vaccination.

**Method**

The study was a retrospective case series of two consecutive clusters in a government-owned tertiary referral and teaching hospital in Indonesia from March 15th to May 31st, 2021. Institutional ethical clearance and patient publication consent were obtained number LB.02.01/X.6.5/189.A/2021, and data was gathered from the hospital staff Covid-19 tracing database. The database included all HCW such as consultants, residents, nurses and non-HCW such as administration staff and security staff. No intervention was done on the subjects, and observation was done after the hospital has conducted its mandatory COVID-19 vaccination program in January 2021.

**Results**

The hospital had 5115 HCW consisting of 3688 hospital staff and 1427 students such as residents, sub-specialistic trainees

and medical students. The vaccination program started on January 20th, 2021. The first cluster started when two anesthesia residents complained of fever and cough at the end of March 2021. They were put on mandatory self-isolation, and Polymerase Chain Reaction (PCR) testing concluded that both doctors were positive for SARS-CoV-2 (Figure 1). The first doctor, a male (P1), had received his second Covid-19 vaccination on February 15th, 2021. However, the second doctor, a female (P2), was a volunteer on the Covid-19 double-blinded vaccination trial in our local affiliated University in December 2020 and, after confirmation, had received a placebo. Contact tracing revealed that P1’s wife (P3) was also symptomatic and tested positive for SARS-CoV-2 later that week. The wife was a doctor who also had received two doses of the Covid-19 vaccine on February 10th, 2021. The Covid-19 vaccine they received was Corona-vac ( Sinovac Ltd, China). These patients represented the first cluster of HCW with Covid-19 infection after two doses of vaccination in our hospital.

Variable	Patient 1 (P1)	Patient 2 (P2)	Patient 3 (P3)
<b>Basic Epidemiology</b>			
Sex	Male	Female	Female
Occupation	Anesthesia Resident	Anesthesia Resident	General Practitioner
Height(Cm)/Weight (Kg)	175/75	160/63	155/50
History of Co-existing Disease	None	None	None
<b>Vaccination Status</b>			
Date of first dose	30/01/2021	09/10/2020*	27/01/2021
Date of second dose	15/02/2021	26/10/2020*	10/02/2021
Covid-19 Vaccine brand	Sinovac	Placebo on trial	Sinovac
<b>Infection Status</b>			
Date of first symptoms	22/03/2021	24/03/2021	27/03/2021
Symptoms experienced	Fever, cough, anosmia, sore throat, joint pain	Fever, cough, anosmia, sore throat, joint pain, nausea and diarrhea	Fever, cough, anosmia, sore throat, joint pain, nausea and diarrhea
Disease Severity	Moderate	Mild	Moderate
Hospital Admission	Yes	No	Yes
Date of Positive PCR	25/03/2021	26/03/2021	29/03/2021
PCR CT-value	22.36	19.69	16.54
Date of Negative PCR	05/04/2021	24/04/2021	09/04/2021
Antibody testing	16.730/AU/ml	Negative	Negative

**Figure 1:** HCW infected post-vaccination.

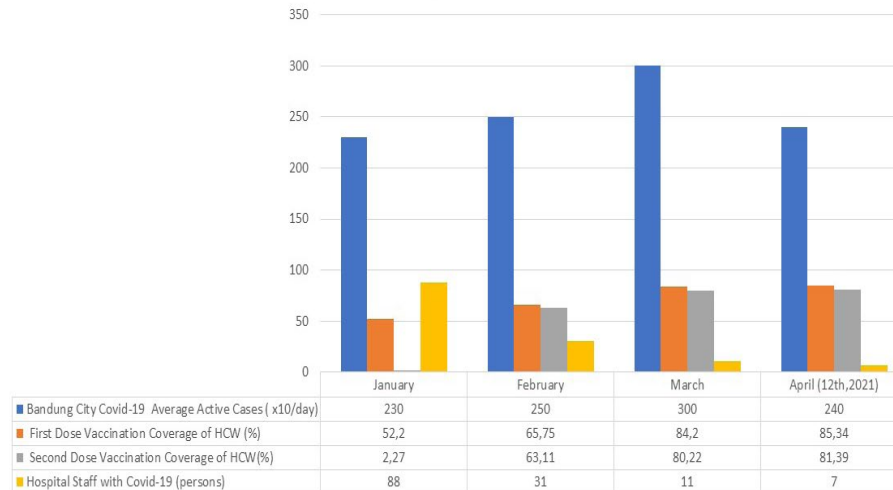
All three patients had an antibody test carried out, and only P1 had a positive IgG for SARS-CoV-2 with a titer of 16.730 AU/ml. P1 and P3 were hospitalized in a district hospital because they were unable to self-isolate in their homes. During hospitalization, they received remdesivir for five days, although their symptoms were relatively mild. P1 tested negative after eleven days, P3 tested negative after eleven days, and P2 tested negative after 29 days, in which all staff was able to return to work afterward. The second cluster consisted of five anesthesia residents who complained of fever with upper respiratory tract symptoms on the third week of May 2021. (Figure 2) Four subjects in the second cluster were vaccinated, and one subject (S4) was not vaccinated because S4 had uncontrolled hypertension. The vaccine they received was Corona-vac (Sinovac Ltd, China). All vaccinated subjects in the second cluster showed mild symptoms that did not require any hospitalization, but S4's symptoms progressed, and he was admitted to critical care on the 5<sup>th</sup> day of his symptom. During his stay, S4 received high flow oxygenation and plasma convalescence therapy. The first subject (S1) was previously infected with SARS-CoV-2 in November 2020 and was vaccinated in March 2021. Until early June 2021, all members of the second cluster remained positive with SARS-CoV-2 and could not provide medical service.

Variable	Subject 1 (S1)	Subject 2 (S2)	Subject 3(S3)	Subject 4 (S4)	Subject 5 (S5)
<b>Basic Epidemiology</b>					
Sex	Male	Male	Male	Male	Male
Occupation	Anesthesiology Resident	Anesthesiology Resident	Anesthesiology Resident	Anesthesiology Resident	
History of Co-existing Disease	None	None	None	Hypertension	None
Previous COVID-19 infection	yes	no	no	no	No
<b>Vaccination Status</b>					
Date of first dose	11/03/2021	28/01/2021	28/01/2021	Not given	29/01/2021
Date of second dose	23/03/2021	12/02/2021	15/02/2021	Not given	13/02/2021
Covid-19 Vaccine brand	Sinovac	Sinovac	Sinovac	None	Sinovac
<b>Infection Status</b>					
Date of first symptoms	14/05/2021	18/05/2021	20/05/2021	22/05/2021	22/05/2021
Symptoms experienced	Cold and sore throat	Fever and cough	Fever and cough	Fever,cough, dyspnea	Cold and cough
Disease Severity	Mild	Mild	Mild	Mild	Mild
Hospital Admission	No	No	No	Critical Care	No
Date of Positive PCR	18/05/2021	22/05/2021	22/05/2021	23/05/2021	24/05/2021
PCR CT-value	19.01	19.12	18.86	20.01	32.21
Antibody testing	None	None	None	None	None

**Figure 2:** Cluster 2 HCW infected post-vaccination.

We also presented data gathered from the general picture of active infection in our city, vaccination status, and positive HCW in our hospital as a tool for further analysis. (Figure 3) Between January to April 2021, there was a sharp increase of active cases in our city, and while the vaccination process is being carried out, an 60% second dose rate coverage of our HCW was achieved at the end of February 2021 by means that a 14-28 days to positive protective antibody would have been detected by the second week of March. Our data suggest a trend of decreasing infection rates among HCW after vaccination.

Figure 3. Description of Bandung City Active Cases, Hospital Vaccination Coverage and Health Care Worker (HCW) with Covid-19 January- April 2021



## Discussion

Several studies have identified viruses from aerosols and surfaces after inoculation during the early times of the pandemic. However, real-world studies have shown that the environmental SARS-CoV-2 virus is deficient, and few have isolated viable viruses; thus, infection from this source is unlikely. Reports of clusters, which are very commonly present in Covid-19, such as our case, indicated that respiratory transmission is dominant, with proximity and ventilation being critical determinants of transmission risk [5]. Our cluster members' proximity is frequently close since they all worked together in anesthesia. Anesthesiologists are a high-risk HCW group since they routinely perform aerosol-generating procedures that potentially transmit SARS-CoV-2. The clusters also shared many personal activities such as eating, scrubbing up, sharing locker time or sharing sleeping quarters during night shifts. The Centre for Disease Control (CDC) has issued a statement that fully vaccinated people can gather on indoor conditions without masks, but our reports suggest that liberal practice may not be viable enough [6]. We also need to consider that the CDC statement was clarified to only three mRNA vaccines (Pfizer, Johnson & Johnson and Moderna). Further studies regarding the effectiveness of Corona-vac in preventing infection are needed.

P1 in the first cluster had an active antibody during testing, providing partial protection from the virus and a shorter period of positive antigen test. Although HCW was asymptomatic, persistent positive results caused long sick leaves among HCW, as in our hospital [7,8]. Interestingly, P3 was vaccinated but had a negative antibody test and a shorter positive antigen test than P2, who received a placebo. Possibly, a slight titer of antibody undetected

on a rapid antibody test still has a protective effect. Note that for S4, both previous infection and vaccination did not protect from a second infection. Some studies show a general concern about the possibility that a previous infection does not provide immunity, and vaccines will only reduce symptoms during a second infection rather than prevent that infection altogether. This phenomenon could effectively turn vaccinated people into asymptomatic carriers and putting vulnerable populations at risk [5-9].

Further studies must understand how the immune system responds to natural infection and vaccination. Local community infection was high from March to April 2021, translating to a higher HCW infection probability. Interestingly, our HCW infection rate was low compared to January to February 2021. Consistent with our findings, a study in California at the end of March 2021 reported that from 28.184 HCW who received the second dose of the Covid-19 vaccine, 37 HCW tested positive, with only 7 of them tested positive 15 days or more from the second vaccination [9,10].

Another vital variable to discuss is the spread of the delta variant in Indonesia. The B.1.617.2(delta) variant of the SARS-CoV-2, first detected in India. By May 19th, 2021, this variant was detected in 43 countries and caused an unprecedented peak in infection rates in speed, number and severity [11]. Laboratory data indicated that the delta variant was characterized by the spike in protein mutations  $\Delta 157-158$ , L452R, T478K, D614G, P681R, and D950N.1 Several of these mutations may affect immune responses directed toward the key antigenic regions of the receptor-binding protein (452 and 478) and deletion of part of the N-terminal domain.23 P681R is at the S1-S2 cleavage site, and it appears that

strains with mutations at that site may have increased replication, which leads to higher viral loads and increased transmission [12]. Delta variant was resistant to neutralization by some drugs, including bamlanivimab, which impaired the drug's ability to bind to the virus's mutated spike. Sera from convalescent patients collected up to 12 months post symptoms were fourfold less potent against variant Delta than variant Alpha (B.1.1.7). Sera from individuals having received one dose of Pfizer or AstraZeneca vaccines barely inhibited variant Delta. Administration of two doses generated a neutralizing response in 95% of individuals, with titers 3 to 5 fold lower against Delta than Alpha. Thus, variant Delta spread is associated with an escape to antibodies targeting non-RBD and RBD Spike epitopes. These findings are concerning since natural infection and vaccination may not protect against the delta variant [12-13].

However, "real world" findings in countries with increasing delta variant cases, such as the United Kingdom and the United States, shows promising results where a high positive case is not accompanied by the increase in mortality which suggests a potential success of their vaccination programs with at least 50% of the population being vaccinated once. This report suggests that mRNA vaccines used in the UK and US, mainly Pfizer and Moderna, effectively reduce mortality due to the delta variant, and a close study should be done on the Sinovac/Sinopharm/Coronavirus vaccines, which relies on the weakened live virus [14].

The cluster of cases in our hospital must be approached carefully, and vaccination must not be considered a failure yet. Our report only shows a small group of patients, and a more extensive observational study is needed to conclude. It is imperative to understand that the vaccines against SARS-CoV-2 might act against infection, disease, or transmission of the virus, and a vaccine capable of any of these elements could contribute to disease control. Studies have also shown that the time and concentration of antibody is not equal in some patients. A booster may be needed to amplify immunity in several cases; thus, evaluating blood immunity levels may be needed to understand the vaccine's effectiveness [1,8-10]. Although the most critical end-point clinically is not to stop infection but to protect a person against severe disease and death caused by SARS-CoV-2, sick leaves burden the health system for the health care workers. Studies have shown that many Covid-19 patients may still test positive for up to 90 days after the first test. However, the World Health Organization (WHO) and CDC recommended that HCW go back to work after 14 days of isolation and symptoms free, but our hospital still required a negative PCR test result. Sick leaves add a burden to the remaining staff and reduce hospital effectiveness in giving health services, especially in higher infection times when

all workforce is needed. Maintenance of basic health protocols such as masks, handwashing, and social distancing is still essential since a sick HCW, although not severe, still needs sick leaves. It will be interesting to observe how the Indonesian government plans to give their HCW with the third booster of m-RNA vaccine will provide a better outcome. Thus, basic health protocol is essential for the time being, vaccinated or not.

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