Epidemiology and Infection

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Original Paper

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Cite this article: Mansour Ghanaie R *et al* (2023). Assessment of early and post COVID-19 vaccination antibody response in healthcare workers: a multicentre cross-sectional study on inactivated, mRNA and vector-based vaccines. *Epidemiology and Infection* **151**, e12, 1–7. https://doi.org/10.1017/S0950268822001984

Received: 24 May 2022
Revised: 11 December 2022
Accepted: 15 December 2022

Key words:
Anti-spike IgG; COVID-19 vaccines; healthcare personnel; immunity; Iran; SARS-CoV-2

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Assessment of early and post COVID-19 vaccination antibody response in healthcare workers: a multicentre cross-sectional study on inactivated, mRNA and vector-based vaccines

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Abstract

In this multicentre study, we compared the status of antibody production in healthcare personnel (HCP) before and after vaccination using different brands of COVID-19 vaccines between March 2021 and September 2021. Out of a total of 962 HCP enrolled in our study, the antibody against the S1 domain of SARS-CoV-2 was detected in 48.3%, 95.5% and 96.2% of them before, after the first and the second doses of the vaccines, respectively. Our results showed post-vaccination infection in 3.7% and 5.9% of the individuals after the first and second doses of vaccines, respectively. The infection was significantly lower in HCP who presented higher antibody titres before the vaccination. Although types of vaccines did not show a significant difference in the infection rate, a lower infection rate was recorded for AstraZeneca after the second vaccination course. This rate was equal among individuals receiving a second dose of Sinopharm and Sputnik. Vaccine-related side effects were more frequent among AstraZeneca recipients after the first dose and among Sputnik recipients after the second dose. In conclusion, our results showed diversity among different brands of COVID-19 vaccines; however, it seems that two doses of the vaccines could induce an antibody response in most of HCP. The induced immunity could persist for 3–5 months after the second vaccination course.

Introduction

The humoral immune response plays a prominent role in fighting against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and protection against re-infection [1]. Antibodies to SARS-CoV-2 are detectable approximately 2 weeks after the onset of symptoms and can persist for at least 6 months [2]. Evaluation of the immune response following a SARS-CoV-2 infection and vaccination can provide a valuable tool in determining the nature of the unprecedented pandemic we are facing and can indicate the rate of disease transmission over time [3].

COVID-19, first detected in December 2019 in Wuhan, China, has rapidly become a global pandemic affecting 498 704 919 people as on 10 April 2022, and claiming the life of 6 202 473 people worldwide [4]. Among other entities, healthcare workers (HCWs) are potentially at

high risk for SARS-CoV-2 infection due to the direct contact with COVID-19-positive patients and also due to community exposure.

The clinical manifestations of COVID-19 range widely from asymptomatic infection to severe life-threatening multi-organ failure [5]. There are concerns that, compared to the general population, many HCWs seem to acquire SARS-CoV-2 infection in an asymptomatic or mildly symptomatic manner. As a result, the infection may not be detected early in the course of the disease, making them act as silent spreaders [6, 7]. There is currently a paucity of information on the pre- and post-vaccination COVID-19 seroprevalence among HCWs. The prevalence of antibody seropositivity in the pre-vaccination era among Iranian general and high-risk populations was estimated as 17.1% and 20.0%, respectively [8]. Although the vaccination for Iranian HCWs began around March 2021, the seroprevalence after receiving vaccination among HCWs has not been yet investigated. In addition, the impact of COVID-19 onset and/or administration of available vaccines on protection against re-infection and the so effects of different types and dosages of vaccines on the induction of neutralising antibodies and conferring alleviation of symptom severity in case of re-infection are not completely clear.

To investigate the effect of protective proceedings, such as vaccinations, on the induction of antibodies and the occurrence of the disease, HCWs can be the optimal population, as they were the first population to receive vaccines and are encountering the SARS-CoV-2-infected patients. In this regard, we aim to evaluate the prevalence of and factors associated with SARS-CoV-2 infection among frontline and non-frontline HCWs regarding the induced antibodies after natural infection and SARS-CoV-2 vaccination with different brands. A possible correlation between antibody response to different brands of the vaccines with age, body mass index (BMI), gender and history of infection was also analysed in this population.

Materials and methods

Study design

This prospective multicentre cross-sectional study was designed to determine the proportion of SARS-CoV-2 infection in healthcare personnel (HCP) of three hospitals in Iran from 2020 to 2021. In this study, the WHO COVID-19 protocol was followed (WHO/2019-nCoV/HCW_Surveillance_Protocol/2020.1). A questionnaire was used based on the WHO protocol regarding the general demographic information and questions for COVID-19 infection, such as brands and time of vaccination, exposure history with COVID-19 patients and confirmed infection using polymerase chain reaction (PCR) tests. HCW from different disciplines, including those in the patients' room and those who were indirectly in contact with contaminated materials and the environment, were included in the study in these hospitals. Blood samples were obtained from all HCWs who signed the consent form, and the specimens were sent to the central laboratory for processing and storage. All the serum samples were stored at −70 °C until use for serological assay. The study was approved by the ethical committee of Shahid Beheshti University of Medical Sciences, Tehran, Iran (Code: IR.SBMU.RICH.REC.1399.066).

Sampling and enzyme-linked immunosorbent assay (ELISA)

The blood samples were obtained by venepuncture and transferred into serum separator gel tubes. To separate sera in microcentrifugation tube, centrifugation on 80 000 rpm for 10 min was done. The separated sera were pour into 1.5 ml microtubes and stored them at −70 °C until used for ELISA. To measure infection with SARS-CoV-2, immunoglobulin G (IgG) antibody against the S1 domain of SARS-CoV-2 spike protein was measured using an anti-SARS-CoV-2 IgG antibody kit (Euroimmun, Germany). To calculate the ratio of the antibody in each sample, absorbance on 450/620 nm compared with the calibrator was measured. Interpretation of results was done according to the manufacturer's instructions. Accordingly, ratios equal to and over 1.1 were considered positive, those ≥0.8≤1.1 as borderline and those lower than 0.8 as negative. The collected samples with either positive or borderline results were rechecked with the WANTAI SARS-CoV-2 Ab ELISA kit according to the manufacturer's instructions (WANTAI BioPharm, China).

Statistical analysis

SPSS software was used for statistical analysis. Accordingly, logistic regression analysis was performed to evaluate the effect of factors, such as age groups, BMI and number of household members, and underlying diseases, on SARS-CoV-2 infection and to compare the effect of vaccines on the infection occurrence. The linear regression method was used to analyse the effect of vaccines on the level of antibody-induced after each shot of vaccination.

Results

Overall, 962 HCWs including 663 females and 299 males were enrolled in the study. The demographic characteristics of the study population are summarised in Table 1. In all hospitals,

Table 1. Correlation of SARS-CoV-2 infection with vaccination, gender, job and history of the infection among HCWs

COVID-19 symptoms	Pre-vaccination IgG-positive	Pre-vaccination IgG-negative	*P* value
Fever	110/334, 32.9%	62/333, 18.6%	**0.0001**
Cough	85/334, 25.4%	50/333, 15%	**0.001**
Sore throat	58/334, 17.3%	44/333, 13.2%	0.16
Myalgia	109/334, 32.6%	58/333, 17.4%	**0.0001**
Shortness of breath	51/334, 15.2%	26/333, 7.8%	**0.0034**
Chills	57/334, 17%	35/333, 10.5%	**0.018**
Anosmia	57/334, 17%	34/333, 10.2%	**0.012**
Stomach ache	21/334, 6.3%	16/333, 4.8%	0.5
Diarrhoea	33/334, 9.8%	20/333, 6%	0.08
Vomiting	16/334, 4.8%	15/333, 4.5%	1
Headache	87/334, 26%	58/333, 17.4%	**0.008**
Underlying diseases			
Cardiovascular	8/15, 53.3%	7/15, 46.6%	1
Pregnancy	2/7, 28.5%	5/7, 71.4%	0.28
Diabetes	10/15, 66.6%	5/15, 33.3%	0.14
Hypertension	10/18, 55.5%	8/18, 44.4%	0.74

Significant p values are shown in bold.

Table 2. Demographic data related to the participated HCP in this study

	Mofid Children's hospital	Nikan hospital	Bandar Abbas hospital
No. of family members			
1–3	207/415, 49.8%	54/109, 49.5%	63/190, 33.1%
4–6	196/415, 47.2%	52/109, 47.7%	121/190, 63.6%
≥7	12/415, 2.9%	3/109, 2.7%	6/190, 3.1%
Missing	182	29	37
Gender			
Male	215	61	23
Female	382	77	204
Job			
Physician	32	19	0
Nurse	81	14	1
Laboratory staff	21	3	7
Others	263	4	40
Unreported	200	48	179
Ward of activity			
COVID-19 ward	29	1	2
NICU	30	7	15
PICU	27	11	3
Surgery	59	13	5
Other wards/units	452	106	202
History of the previous infection	24/574	6/135	7/216
History of close contact with COVID-19 patients	212/529	55/96	82/195
Vaccine types-first dose			
Sinopharm ($N = 99$)	60	2	37
AstraZeneca ($N = 83$)	192	2	57
Sputnik ($N = 461$)	410	34	105
Others (40)	10	6	24
Infection-post vaccination			
First dose	22/411	0/3	1/205
Second dose	16/263	0/5	Not reported

most personnel were within the two ends of the age spectrum (very young, <25 years, or middle-aged, >45 years) and mostly had up to three family members. According to reported job titles, based on the available records of the participants, 51 physicians, 96 nurses and 31 laboratory staff were included and 307 HCWs were reported working in other entities. Regarding the ward of activity, only 32 individuals worked in the COVID-19 ward, while others reported working in NICU ($n = 52$), PICU ($n = 41$), surgery ($n = 77$) and other units ($n = 760$). Thirty-three HCWs (4%) had a positive history of COVID-19 infection before receiving a vaccination. Moreover, a history of close contact with COVID-19 patients was recorded in 42.5% of HCWs (349/820). The vaccine type distribution among HCWs was as follows: 461 Sputnik, 99 Sinopharm, 83 AstraZeneca and 40 other less common vaccinations. Our results showed post-vaccination infection in 3.7% and 5.9% of the individuals after the first and second doses of vaccines, respectively. HCWs with positive serology for COVID-19 compared with negative ones reported more frequently COVID-19 symptoms, including fever (32.9% *vs.* 18.6%), myalgia (32.6% *vs.* 17.4%), chills (17% *vs.* 10.5%), anosmia (17% *vs.* 10.2%), and headache (26% *vs.* 17.4%). In the same order, the infected HCWs recorded underlying conditions in higher frequency, including diabetes mellitus (66.6% *vs.* 33.3%), hypertension (55.5% *vs.* 44.4%) and cardiovascular disorders (53.3% *vs.* 46.6%), compared with the non-infected personnel (Table 2).

As demonstrated in Table 3, the highest levels of anti-spike antibody ratio 3 weeks or more after first and second doses of vaccines were observed among those receiving AstraZeneca (14 ± 91) and Sputnik (14.5 ± 112). Similarly, vaccine-related side effects were more frequent among AstraZeneca recipients after the first dose and among Sputnik recipients after the second dose (mainly

Table 3. Comparison of COVID-19 vaccines in induction of IgG antibody against SARS-CoV-2 spike protein and their side effects in HCWs

	Anti-spike antibody								
	Pre-vaccination	≥3 weeks post first vaccination				≥3 weeks post second vaccination			
	Mean ± S.D.	Sputnik	AstraZeneca	Sinopharm	*P*-value	Sputnik	AstraZeneca	Sinopharm	*P*-value
Antibody ratio	2.14 ± 2.8	7.1 ± (−3.5)	14 ± 91	5.3 ± 2.5		14.5 ± 112	4.2 ± 2.5	3.7 ± 2	
Confirmed infection	352/799 (44%)	5/175 (2.8%)	17/180 (9.4%)	0/45 (0)	**0.005**	12/241 (5%)	2/16 (12.5%)	1/6 (16.6%)	0.2
BMI									
ELISA positive	43 ± 8.5								
ELISA negative	41.4 ± 8.3								
Vaccine side effects									
Fever		61/174, 35%	108/181, 59.6%	1/45, 2.2%	**0.001**	34/97, 35%	11/19, 57.8%	1/8, 12.5%	**0.056**
Myalgia/arthralgia		92/174, 52.8%	131/180, 72.7%	5/45, 11.1%	**0.0001**	123/242, 86.6%	2/13, 15.3%	0/6, 0	**0.002**
Malaise		92/174, 52.8%	123/181, 67.9%	3/45, 6.6%	**0.0001**	117/242, 48.3%	2/13, 15.3%	0/6, 0	**0.005**
Chills		50/174, 28.7%	110/181, 60.7%	1/45, 2.2%	**0.0001**	84/242, 34.7%	3/13, 23%	0/6, 0	0.15
Headache		59/174, 33.9%	82/181, 45.3%	4/45, 8.8%	**0.0001**	75/242, 31%	2/13, 15.3%	0/6, 0	0.13
Hospitalisation		1/269, 0.3%	12/238, 5%	0/78, 0	**0.0006**	8/358, 2.2%	0/64, 0	0/0	0.3
Receiving of COVID-19 drugs		1	2	0		7	0	0	

Significant p values are shown in bold.

Table 4. Multivariate logistic regression analysis for study of the relationship between different independent variables and the occurrence of SARS-CoV-2 infection after administration of the first vaccine dose in HCWs

	OR	s.e.	z	P > z	95% confidence interval	
Positive PCR before vaccination	1.023217	0.166405	0.14	0.888	0.74394	1.407336
Seropositivity before vaccination	0.677493	0.107513	−2.45	**0.014**	0.496393	0.924666
Age	1.015443	0.022407	0.69	0.487	0.972463	1.060323
BMI	1.014778	0.039902	0.37	0.709	0.939509	1.096077
History of COVID-19 in family	0.90869	0.45406	−0.19	0.848	0.341257	2.419633
Number of household members	0.870272	0.162358	−0.74	0.456	0.603747	1.254456

Significant p values are shown in bold.

in the form of myalgia/arthralgia (72.7% and 86.6%, respectively). After vaccination, only 21 HCWs required hospitalisation and 10 HCWs received COVID-19 medications.

In this study, the higher pre-vaccination antibody was correlated with a lower risk of COVID-19 infection after the first vaccination (*P* value: 0.014, odds ratio (OR): 0.68) (Table 4). Furthermore, pre-vaccination antibody level was significantly correlated with lower COVID-19 infection after the second dose of vaccine (*P* value: 0.017, OR: 0.68) (Table 5), meaning that a higher level of antibodies before the first dose of vaccination would decrease the risk of COVID-19 infection after the second dose.

The risk of COVID-19 infection in HCWs receiving AstraZeneca after the first (*P* value: 0.574, OR: 0.72) and second doses (*P* value: 0.659, OR: 0.77) was lower than Sputnik; however, it was not statistically significant. In addition, individuals who underwent Sinopharm dose 1 had lower rates of COVID-19 infection (*P* value: 0.623, OR: 0.57) compared to Sputnik. Nevertheless, this rate was equal among individuals receiving a second dose of Sinopharm and Sputnik (OR: 1) (Supplementary material).

Overall, serum levels of antibodies after the first dose of vaccination were correlated with the forward COVID-19 symptom onset. Results of the linear regression test revealed that the level of antibodies before (*P* value: 0.064) and after (*P* value: 0.034) the first dose of vaccination can affect the risk of COVID-19 infection after the first and second vaccines (Supplementary material).

In our study, the association between several factors with antibody levels after the first and second vaccines was also assessed. Serum levels of antibodies before the first dose of vaccine affected antibody levels after receiving the first dose, although it was not statistically significant (*P* value: 0.089, coefficient: 5.7). Moreover, when compared to AstraZeneca, Sputnik and Sinopharm produced a lower mean of antibody levels, i.e. 12- (*P* value: 0.186) and 15- (*P* value: 0.430) fold, respectively. BMI was weakly associated with serum antibody level after the second dose of vaccination. Accordingly, HCWs with higher BMI who had a history of pre-vaccination infection mounted higher levels of antibody after the second dose of vaccination (*P* value = 0.054, correlation coefficient: 0.13). No association was observed between the level of pre-vaccination antibody and BMI (*P* value = 0.244) (Supplementary material).

The duration from vaccination to COVID-19 onset in HCWs who were vaccinated with AstraZeneca was longer than that in individuals receiving Sputnik vaccine (*P* value < 0.001), which could be due to diversity in time points of their introduction for HCP (Supplementary material).

Discussion

In this study, we measured antibodies to SARS-CoV-2 spike protein in HCWs of three Iranian major hospitals to detect adaptive immune response to vaccinations with two doses of either AstraZeneca, Sinopharm or Sputnik. Most HCWs were female and within the two ends of the age spectrum. No correlation was observed between age or gender and COVID-19 seropositivity; however, a relative positive correlation was detected between higher BMI values and serum antibody level after the second dose of vaccination. In a study on 88 Thai HCWs between March and May 2021, seroconversion of anti-spike antibodies 4 weeks after the second dose of the CoronaVac vaccine was observed in almost all HCWs (98.9%). In this study, the anti-spike

Table 5. Multivariate logistic regression analysis for study of the relationship between different independent variables and the occurrence of SARS-CoV-2 infection after administration of the second vaccine dose in HCWs

	OR	s.e.	z	P > z	95% confidence interval	
Seropositivity before second vaccination	0.682266	0.109149	−2.39	**0.017**	0.49863	0.93353
Positive PCR before vaccination	0.970964	0.163428	−0.18	0.861	0.698125	1.350434
Age	1.017439	0.022811	0.77	0.441	0.9737	1.063144
Number of household members	0.85812	0.165158	−0.8	0.427	0.588466	1.251338
History of COVID-19 in family	1.013621	0.513175	0.03	0.979	0.375777	2.734141
BMI	1.020345	0.040424	0.51	0.611	0.944113	1.102731
Seropositivity after 1st dose of vaccine	0.90703	0.041756	−2.12	**0.034**	0.828773	0.992676

Significant p values are shown in bold.

IgG level was positively correlated with female gender, lower age and normal-weighting [9]. An Irish study on 5788 HCWs showed that seropositivity is higher among healthcare assistants, nurses, individuals with daily exposure to patients with COVID-19, age 18–29 years and living with other HCWs with Asian background, and male sex [10].

Another study measured the antibodies produced against the receptor-binding domain (RBD) of spike-protein and nucleocapsid protein in 314 Turkish HCWs who received the CoronaVac vaccine. Seropositivity was developed in 99.6% of participants 4 weeks after the second dose of the vaccine. It was also shown that individuals who were smokers and/or obese produced lower titres of RBD antibody [11]. A Greek study evaluated the antibody response of 564 HCWs after two-dose vaccination with BNT162b2 (Comirnaty®; BioNTech and Pfizer) mRNA COVID-19 vaccine. Similar to the Thai study, a greater antibody increase was observed in female and younger age groups [12]. Contrarily to our finding, other studies found no statistically significant difference in the vaccine antibody levels regarding the BMI in HCWs [13, 14].

In the present study, HCWs with pre-vaccination-positive IgG were found to have higher rates of underlying comorbidities, including diabetes mellitus, hypertension and cardiovascular disorders, however, pregnant HCWs were less commonly categorised as IgG-positive group which may pertain to more protection measurement applied before vaccination. We did not assess the correlation between underlying disorders and the level of antibody production. However, a study examined anti-spike antibodies in 515 Indian HCWs in response to AstraZeneca (ChAdOx1-nCOV, Covishield™) and BBV-152 (Covaxin™) vaccines, 21 days or more after taking the first and second doses of both vaccines. In this study less anti-spike antibody was produced in HCWs with age >60 years, male gender, those with any comorbidities and hypertension history. The authors reported a significantly higher seropositivity rate and geometric mean titre for AstraZeneca compared with Covaxin™.

We found vaccine-related side effects more frequently among AstraZeneca recipients after the first dose and among Sputnik recipients after the second dose, mainly with myalgia/arthralgia presentations. Sputnik was the first vaccine used for the vaccination of most Iranian HCWs and some studies have investigated its side effects among HCWs. In a large Iranian study about the side effect of Sputnik among 13 435 HCWs vaccinated between February and April 2021, 3236 self-declaration reports of adverse effects were reported with a higher frequency among female and young participants. Pain at the injection site, fatigue and body pain were reported in almost half of the individuals, followed by headache, fever, joint pain, chilling and drowsiness. Moreover, a detectable level of RBD and neutralising antibodies were found in more than 90% of 238 participants after the first and second doses of vaccine [15].

In the current study, we found lower antibody levels in HCWs receiving Sputnik and Sinopharm compared with AstraZeneca. Although this finding could not directly support efficacy of AstraZeneca in HCWs, the efficacy of this vaccine was confirmed by earlier studies. In a small study in Sudan in June 2021, 30 out of 40 (75%) individuals were seropositive for anti-spike IgG after the first dose of the Oxford-AstraZenka vaccine. The antibody titre ranged from 1.2 to 2.7 S/CO (sample mean chemiluminescent signals (RLUs)/cut-off RLUs), with a significantly higher mean titre for females. Side effects similar to our study, including arm pain at the site of the injection, headache, fever, fatigue and gastrointestinal tract disturbances were recorded [16].

In our study, the highest levels of anti-spike antibody were measured among HCWs who received AstraZeneca and Sputnik in comparison with Sinopharm, both after the first and second doses of the vaccines. The induced antibody level was significantly increased after the second dose in comparison with the first dose. Consistent with our finding, results of a study on HCWs who received CoronaVac showed a significant increase in anti-spike antibodies after the second dose of vaccination, while an inadequate antibody response was measured after the first dose of the vaccine [13].

In the current study, HCWs who had a history of pre-vaccination infection mounted higher levels of antibody after the second dose of vaccination. The impact of previous COVID-19 infection on post-vaccination antibody production has been shown in a few studies. Parai *et al.* [17] evaluated antibodies against anti-spike and nucleocapsid proteins in 134 Indian HCWs before and 28 days after receiving two dosages of either BBV-152 or AZD1222 vaccines from January 2021 to April 2021. After a single dose, 96% of HCWs with prior COVID-19 infection were found to be seropositive, while only 61.3% of non-infected HCWs developed antibodies, which increased to 82.7% after the second dose [17]. In the Kontou survey [12], HCWs with a positive history of natural COVID-19 and/or those working in COVID-19 clinics produced higher titres of antibody after the first dose. Another study in Israel investigated BNT162b2 mRNA COVID-19 vaccine immunogenicity 21 days after the first dose in 514 HCWs. Similar to other studies, immunogenicity decreased with age. Notably, antibody titres in those with prior infection were higher than naïve individuals regardless of the presence of detectable pre-vaccination IgG antibodies [18]. In a study from Turkey, 1072 HCWs were evaluated after 28 days of the first, and 21 days of the second dose of CoronaVac. After the first and second doses, anti-spike antibodies were detected in 834 (77.8%) and 1008 (99.6%) HCWs, respectively. Seropositivity was considerably higher among females and was found to be highest in participants aged 18–34 years. Antibody titres were significantly higher in those who had COVID-19 infection before vaccination and lower in HCWs with chronic diseases [19]. In a recent study that was performed on 59 HCWs residing in Maryland and receiving Pfizer-BioNTech or Moderna vaccine, participants with previous COVID-19 infection had higher antibody titre in response to a single dose of mRNA vaccine than those who were not previously infected. Furthermore, antibodies achieved higher titres and neutralisation compared with Ab-negative volunteers [20]. Urbanowicz *et al.* followed 45 HCWs serologically and repeated SARS-CoV-2 antigenic exposure, through vaccination or natural infection, and their results showed that multiple exposures to SARS-CoV-2 spike protein could expand reactive spike-specific antibody responses [21].

Our results showed post-vaccination infection in 3.7% and 5.9% of the individuals after the first and second doses of vaccines, respectively. The infection was significantly lower in HCWs who presented higher antibody titres before the vaccination. The results also showed low frequency of hospitalisation among the partially and fully vaccinated HCWs. In a case series study in Saudi Arabia, 20 HCWs who experienced the new infection after receiving the Pfizer-BioNTech COVID-19 vaccine were analysed. Most of the HCWs in this study had COVID-19 infection within the first and the second weeks of vaccination, and infection after the third week decreased, as confirmed infection after the second dose of vaccine was reported only in two

HCWs [22]. In a study in India, post-vaccination infection with SARS-CoV-2 was recorded in 2.63% of vaccinated HCWs with AstraZeneca (76.5% and 23.5% of these cases were among the fully vaccinated and partially vaccinated HCWs, respectively). The infection similarly caused a reduced rate of hospitalisation in these HCWs (0.06%) [23].

This study had several limitations. We performed blood sampling at different time points which may affect longitudinal correlation in terms of vaccine-related seropositivity. Furthermore, we could not evaluate vaccine efficacy among participants as all personnel had already received vaccination and we could not make a comparison between HCWs with and without vaccinations. However, this study represents the first study reporting vaccine outcome among HCWs from a developing health setting. Further studies with more sample size on individuals other than HCWs are required to characterise variable aspects of vaccine administration, and besides humoral immunity, molecular studies investigating probable cellular immunity mechanisms are needed.

In conclusion, our results showed a diversity among different brands of COVID-19 vaccines regarding the induced antibody levels and side effects; however, it seems that two doses of the vaccines could induce antibody response in the most of HCWs. History of previous infection with SARS-CoV-2 seems to boost stronger humoral immunity in HCWs, regardless of types of the vaccines. Our findings showed increase in the number of infection after 3–5 months of the second vaccination course. Further follow-up study is needed to show protection of the vaccines against common variants of SARS-CoV-2 circulating among children and HCWs who are in their contact.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0950268822001984.

Acknowledgements. The authors would like to thank all staff of Mofid Children's Hospital, Nikan hospital and counsellors in Clinical Research Development Center of Children Hospital, Hormozgan University of Medical Sciences, Bandar Abbas, Iran for their help.

Financial support. This study was supported by Pediatric Infections Research Center, Research Institute for Children's Health, Shahid Beheshti University of Medical Sciences, Tehran, Iran (Grant numbers 29578 and 27744), Deputy of Research Affairs, Shahid Beheshti University of Medical Sciences, Tehran, Iran, and the Robert Koch Institute (Germany) that supported this study by providing diagnostic material through a special COVID pandemic grant from the German Ministry of Health.

Conflict of interest. None.

Data availability statement. Anonymous data are available upon reasonable request to the corresponding author.

References

1. **Sharma O *et al.*** (2020) A review of the progress and challenges of developing a vaccine for COVID-19. *Frontiers in Immunology* **11**, 585354.
2. **Gaebler C *et al.*** (2021) Evolution of antibody immunity to SARS-CoV-2. *Nature* **591**, 639–644.
3. **Jackson-Thompson BM *et al.*** (2021) Prospective assessment of SARS-CoV-2 seroconversion (PASS) study: an observational cohort study of SARS-CoV-2 infection and vaccination in healthcare workers. *BMC Infectious Diseases* **21**, 544.
4. **Worldometers** (2021) https://www.worldometers.info/coronavirus/.
5. **He X *et al.*** (2020) Clinical symptom differences between mild and severe COVID-19 patients in China: a meta-analysis. *Frontiers in Public Health* **8**, 561264.
6. **Self WH *et al.*** (2020) Seroprevalence of SARS-CoV-2 among frontline health care personnel in a multistate hospital network-13 academic medical centers, April–June 2020. *Morbidity and Mortality Weekly Report* **69**, 1221–1226.
7. **Menon V *et al.*** (2021) Longitudinal humoral antibody response to SARS-CoV-2 infection among healthcare workers in a New York City hospital. *BMJ Open* **11**, e051045.
8. **Poustchi H *et al.*** (2021) SARS-CoV-2 antibody seroprevalence in the general population and high-risk occupational groups across 18 cities in Iran: a population-based cross-sectional study. *The Lancet. Infectious Diseases* **21**, 473–481.
9. **Ongkittikul MDS and Rompho RNP** (2021) SARS-CoV-2 IgG antibody response after immunization of healthcare workers with inactivated COVID-19 vaccine (CoronaVac) at Phyathai 3 hospital. *The Bangkok Medical Journal* **17**, 100.
10. **Allen N *et al.*** (2021) Prevalence of antibodies to SARS-CoV-2 in Irish hospital healthcare workers. *Epidemiology and Infection* **149**, e157.
11. **Uysal EB *et al.*** (2021) Evaluation of antibody response after COVID-19 vaccination of healthcare workers. *Journal of Medical Virology* **94**, 1060–1066.
12. **Kontou E *et al.*** (2021) Antibody response following a two-dose mRNA vaccination regimen, in health care workers of a tertiary hospital in Athens, Greece. *Journal of Personalized Medicine* **11**, 576.
13. **Tekol SD *et al.*** (2021) Detection and evaluation of antibodies to SARS CoV-2 spike protein in healthcare workers after inactivated COVID-19 (CoronaVac) vaccination. *Southern Clinics of Istanbul Eurasia* **32**, 217–222.
14. **Herzberg J *et al.*** (2022) SARS-CoV-2-antibody response in health care workers after vaccination or natural infection in a longitudinal observational study. *Vaccine* **40**, 206–212.
15. **Babamahmoodi F *et al.*** (2021) Side effects and immunogenicity following administration of the Sputnik V COVID-19 vaccine in health care workers in Iran. *Scientific Reports* **11**, 21464.
16. **Abdaltam KGS, Hammad MMA and Mohamedahmed MBA** (2021) Determination of SARS-CoV-2 antispike immunoglobulin G level after first dose of Oxford-AstraZeneca vaccine among healthcare workers in Khartoum state. *Journal of Virology Research & Reports* **2**, 1–3.
17. **Parai D *et al.*** (2021) Single-dose of BBV-152 and AZD1222 increases antibodies against spike glycoprotein among healthcare workers recovered from SARS-CoV-2 infection. *Travel Medicine and Infectious Disease* **44**, 102170–102170.
18. **Abu Jabal K *et al.*** (2021) Impact of age, ethnicity, sex and prior infection status on immunogenicity following a single dose of the BNT162b2 mRNA COVID-19 vaccine: real-world evidence from healthcare workers, Israel, December 2020 to January 2021. *EuroSurveillance* **26**, 2100096.
19. **Bayram A *et al.*** (2021) Quantitation of antibodies against SARS-CoV-2 spike protein after two doses of CoronaVac in healthcare workers. *Journal of Medical Virology* **93**, 5560–5567.
20. **Saadat S *et al.*** (2021) Binding and neutralization antibody titers after a single vaccine dose in health care workers previously infected with SARS-CoV-2. *JAMA* **325**, 1467–1469.
21. **Urbanowicz RA *et al.*** (2021) Two doses of the SARS-CoV-2 BNT162b2 vaccine enhance antibody responses to variants in individuals with prior SARS-CoV-2 infection. *Science Translational Medicine* **13**, eabj0847.
22. **Alshamrani MM *et al.*** (2022) Post-vaccination SARS-CoV-2 infection among healthcare workers in tertiary care hospitals in Saudi Arabia: a case series. *Journal of Infection and Public Health* **15**, 10–12.
23. **Vaishya R *et al.*** (2021) SARS-CoV-2 infection after COVID-19 immunization in healthcare workers: a retrospective, pilot study. *The Indian Journal of Medical Research* **153**, 550–554.