Iranian Journal of Microbiology
Volume 15 Number 2 (April 2023) 196-200

ORIGINAL ARTICLE

Severity of SARS-CoV-2 reinfection in vaccinated healthcare workers

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Received: January 2023**, Accepted:** March 2023

ABSTRACT

Background and Objectives: The most appropriate approach to control the SARS-CoV-2 epidemic is the widespread adoption of vaccination. Several vaccines against SARS-CoV-2 have been developed and authorized for use in various geographical regions. The aim of this study is to evaluate the efficacy of the vaccination agents presently utilized by healthcare workers (HCWs), and to investigate whether different COVID-19 vaccines would result in the alleviation of symptoms and the severity of clinical presentation.

Materials and Methods: This multi-center survey was conducted on 329 vaccinated HCWs who were reinfected with COVID-19 between January 8, 2021 and April 8, 2021, in Tehran, Iran.

Results: Overall, 92.1% and 70.8% of the participants had received 2 and 3 cumulative doses of COVID-19 vaccines, respectively. There were no differences between first/second and third-dose vaccines with the severity of SARS-CoV-2 infection. Expectedly, vaccination resulted in a less severe clinical presentation of SARS-CoV-2 infection, as reported by the participants.

Conclusion: The results suggest that the efficacy of the vaccination agents presently utilized by HCWs was acceptable with no significant difference in vaccine type. Participants receiving at least two doses of vaccines in this survey exceeded 90%, which is comparably higher than studies conducted in other countries.

Keywords: Vaccination hesitancy; Health personnel; COVID-19; SARS-CoV-2; Immunization

INTRODUCTION

COVID-19, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has been spreading globally since late 2019, with at least 80 million confirmed cases and 1.8 million deaths per year (1). In the absence of highly efficacious specialized therapy for SARS-CoV-2 infection, isolation and quarantine of confirmed patients and suspected individuals, as well as adhering to nationwide immunization programs are currently the optimal approach to combat viral transmission (2).

COVID-19 vaccines induce innate and adaptive immunity through different mechanisms. Adaptive immunity involves an antibody response caused by B cells, which multiply and increase proportionally, leading to the production of specific antibodies that bind to the spike protein to neutralize the viral entry

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into the cells, thus conferring immunity to SARS-CoV-2 infection. These antibodies form the 'immunological memory', which is a major factor in vaccination efficacy (3).

Serological diagnostic tests are based on the detection of antibodies against nucleocapsid (N) and spike (S) antigens of SARS-CoV-2 (3). To prevent the dissemination of COVID-19, several types of vaccines are currently in use, including but not limited to mRNA vaccines such as Tozinameran from Pfizer-BioNTech, and classic inactivated vaccines such as BBIBP-CorV from Sinopharm (4).

Several vaccines have been developed and approved for clinical use worldwide. Specifically, Pfizer-BioNTech (BNT162b2, Tozinameran), Moderna (mRNA-1273, Elasomeran), AstraZeneca (ChAdOx1-S, Covishield), and Janssen (Ad26.COV2.S, Jcovden) COVID-19 vaccines have all been authorized in the majority of Europe. The design of all of the aforementioned immunizing agents is based on the spike (S) glycoprotein from SARS-CoV-2 strains observed in the early stages of the pandemic. However, they differ in their level of efficacy against COVID-19. As with other RNA viruses, SARS-CoV-2 undergoes mutation at a high rate. Genome sequencing analysis demonstrates a nucleotide substitution rate of about $1 \times 10\text{-}3$ substitutions per year that leads to the emergence of variants through point mutations, insertions, deletions, and recombination (5).

In order to achieve herd immunity against COVID-19, a significant proportion of the population must be vaccinated. However, reluctance towards vaccination across different occupations and individuals has surfaced as a major issue in achieving this goal. In the management of the COVID-19 epidemic on a national and worldwide scale, vaccine hesitancy and acceptance have been known as key challenges (6).

Healthcare workers (HCWs) have greater contact with COVID-19 patients in the course of their everyday diagnosis and treatment activities, and so are at a significantly higher risk than other groups for contracting the virus. In the United Kingdom and the United States, previous findings revealed that front-line HCWs have 11 times higher positive rates for SARS-CoV-2 than the overall population. Therefore, prevention and management of infection HCWs are protective for both the patients and health center staff (7).

Among fully vaccinated HCWs, the occurrence of breakthrough infections with COVID-19 was correlated with neutralizing antibody titers during the infection period. Most breakthrough infections were mild or asymptomatic, although persistent symptoms did occur (8).

Thus, the role of HCWs becomes particularly important in advising patients and communities, as well as through role modeling behavior. HCWs are prioritized among the high-risk groups who are considered candidates for early vaccination (9).

The aim of this study was to evaluate the efficacy of the vaccination agents presently utilized by HCWs, as well as to investigate whether different COVID-19 vaccines would result in the alleviation of symptoms and the severity of clinical presentation.

MATERIALS AND METHODS

This multi-center observational study compares the efficacy of vaccination on COVID-19 reinfection in administrative and medical staff between January 8, 2021 and April 8, 2021, in Tehran, Iran. This study included Yas, Farabi, and Ziyayian hospital staff who were above 18 years old and were reinfected with COVID-19.

After obtaining informed consent data collection started. Reinfection was confirmed by positive nasopharyngeal swab PCR for COVID-19 using nucleic acid amplification testing. The nasopharyngeal swab specimen was tested using kit-based (Modular Dx-Kit, Wuhan CoV E & RdRP genes) real-time reverse transcription PCR (RT- PCR) and conventional RT-PCR (for the N region using N1F and N3R primers). The sensitivity of the assay was 95% (10).

In the next step data collection was continued using a pre-designed questionnaire. The questionnaire contained information about working location and position, vaccine types and dosage, medical comorbidities, reinfection severity, and principles of personal hygiene like hand washing and using surgical masks.

This study was done in compliance with the Helsinki Declaration and was approved by the Tehran University of Medical Sciences ethics committee (IR. TUMS. MEDICINE.REC. 1400.1225). All of the included participants provided written informed consent.

The statistical analyses were done with the use of a statistical package for the social sciences (SPSS) version 24.0. A P-value of less than 0.05 was considered as the cut-off for statistical significance. We used Independent T-test and Non-parametric Mann–Whitney U-test to assess differences in means. A Chi-

square and Fisher's exact test were applied to evaluate differences in proportions.

RESULTS

In this study, 329 HCWs were enrolled. About 90% of participants were medical staff and 10% were the administrative staff. The study population age ranged from 20 to 70 years old. About 79% of the participants were females and of them, 5.8% were pregnant, or in the breastfeeding/ postpartum period.

Cardiovascular diseases were the most common chronic disorders (6.61%) followed by hypertension (5.2%). There were no underlying diseases in the remaining 81.2% of the study population. Baseline characteristics of the patients with mild or hospitalized were not different significantly (p-value>0.05) (Table 1).

Overall, 92.1% and 70.8% of the participants had received 2 and 3 cumulative doses of COVID-19 vaccines, respectively. Furthermore, the severity of COVID-19 disease was not affected by the type of first/ second (p-value=0.724), or third (p-value=0.731) dose of vaccines (Table 1).

Four ICU admissions were documented before immunization, while none were reported after that. In addition, ten instances were admitted to the hospital before immunization, but only one case was hospitalized after vaccination. Prior to vaccination, 55 patients required intravenous therapy, compared to 35 subjects after vaccination. There was a significant (p-value<0.001) decrease in regards severity of the illness among hospital employees after immunization. The severity of the prior infection and reinfection with COVID-19 is displayed in Table 2.

In addition to the differences in COVID-19 severity, some complaints including dry cough (p-value=0.010), sore throat (p-value<0.001), headache (p-value<0.001), and fatigue/lethargy (p-value=0.008) were significantly more frequent in post-immunity infection while some symptoms including chest

Table 1. Baseline characteristics of the participants and vaccination history

Variable		Outcome		P-value
		Mild	Hospitalized	
Age	Less than 40	207 (70.6)	27 (75)	0.698
	More than 40	86 (29.4)	9 (25)	
Sex	Female	232 (79.2)	28 (77.8)	0.830
	Male	61 (20.8)	8 (22.2)	
Hospital division	Administrative	28 (9.6)	7 (19.4)	0.084
	Medical	265 (90.4)	29 (80.6)	
Time interval since last vaccine dose	Less than a month	27 (9.2)	2 (5.6)	0.872
	1 to 3 month	119 (40.6)	15 (41.7)	
	3 to 6 month	107 (36.5)	13 (36.1)	
	More than 6 month	40 (13.7)	6 (16.7)	
Cumulative vaccine doses	1/2	84 (28.7)	14 (38.9)	0.246
	3	209 (71.3)	22 (61.1)	
First/second dose vaccine type	Sputnik V (Gam-COVID-Vac)	111 (37.9)	15 (41.7)	0.724
	BBIBP-CorV (Sinopharm)	74 (25.3)	7 (19.4)	
	ChAdOx1-S (Covishield)	57 (19.5)	10 (27.8)	
	BBV152 (Covaxin)	44 (15.0)	4 (11.1)	
	BIV1-CovIran (COVIran Barekat)	6 (2.0)	0	
	FINLAY-FR-2 (Soberana 02)	1 (0.3)	0	
Third dose vaccine type*	Not received	82 (28)	14 (38.9)	0.731
	Sputnik V	2 (0.7)	0	
	BBIBP-CorV	58 (19.8)	5 (13.9)	
	ChAdOx1-S	137 (46.8)	16 (44.4)	
	FINLAY-FR-2	9 (3.1)	1 (2.8)	
	COVAX-19 (SpikoGen)	5 (1.7)	0	

pain (p-value=0.001), and anosmia/hyposmia (p-value=0.001) were significantly higher before vaccination (Table 3).

Table 2. Severity of COVID-19 in healthcare workers before and after vaccination.

Severity of infection	Vaccination		p-value
	Before	After	
No sign	122 (37.1)	93 (28.3)	
Mild symptoms without treatment	138 (41.9)	200 (60.8)	
Parenteral antiviral treatment	55 (16.7)	35 (10.6)	<0.001
Admitted to the hospital	10 (3.0)	1 (0.3)	
Admitted to ICU	4 (1.2)	0	

Table 3. Symptoms experienced in the course of SARS-CoV-2 infection prior to and following vaccination

Symptoms	Vaccination		p-value
	Before	After	
Dry cough	85 (25.8)	115 (35)	0.010
Sore throat	70 (21.3)	168 (51.1)	<0.001
Headache	94 (28.6)	135 (41)	<0.001
Fatigue and lethargy	147 (44.7)	168 (51.1)	0.080
Chest pain	59 (17.9)	33 (10)	0.001
Anosmia, Hyposmia	79 (24)	45 (13.7)	0.001
Gastrointestinal symptoms	63 (19.1)	45 (13.7)	0.038
Loss of consciousness	6 (1.8)	3 (0.9)	0.508
Severe back pain	48 (14.6)	58 (17.6)	0.289
Other symptoms*	37 (11.2)	49 (14.9)	0.134

* Such as Muscle or body aches, sneezing, chills, skin changes, and eye problems.

DISCUSSION

With no specific treatments for COVID-19, vaccination is a forefront technique available to a medical practitioner against COVID-19, and HCWs are among the first target group for immunization during the course of epidemics as they are at high risk of infection (11, 12).

Similar to our finding, higher rates of vaccine acceptance were observed in Ecuador (97.0%) (13), Malaysia (94.3%) (14), and China (91.3%) (15), with the majority of studies reporting vaccination acceptance over 70% in general public within various countries (16).

As the World Health Organization has stated that there is an urgent need to evaluate COVID-19 vaccine effectiveness (17), this survey which investigated the real-world effectiveness of COVID-19 vaccines against several major outcomes, including symptomatic COVID-19, severe diseases, and death related to COVID-19, showed that vaccination resulted in a less severe clinical presentation of SARS-CoV-2 infection, as reported by the participants.

The interesting finding should be taken into consideration in the context of this study where participants were inoculated with a variety of inactivated or recombinant vaccines for their first or third dose including Sputnik V (Gam-COVID-Vac), BBIBP-CorV (Sinopharm), ChAdOx1-S (Covishield, Oxford-AstraZeneca), BBV152 (Covaxin), BIV1-CovIran (COVIran Barekat), FINLAY-FR-2 (Soberana 02), COVAX-19 (SpikoGen).

Despite this, the proportion of participants hospitalized for COVID-19 was not statistically different between vaccine types. These results suggest that vaccines may be similarly efficacious in reducing the severity and symptomatic alleviation of reinfections in HCWs. While large observational studies are currently absent for Sputnik V, BBIBP-CorV, Covaxin, SpikoGen, or COVIran Barekat, in line with this study, all of the vaccines confer protection against severe COVID-19 infection as stated in a comprehensive review by Fiolet et al. (18).

In addition, this study showed an incredible decrease in HCWs' compliance with personal hygiene such as hand washing and wearing masks after their vaccination. While evidence suggests that as time pass, vaccine effectiveness is below the WHO's minimal criteria of 50% regards the outcomes of infection or even symptomatic disease (19). This emphasizes the importance of booster vaccination and personal hygiene compliance (20-22).

Despite the strength points, this study has, however, some limitations. Firstly, lack of control group from non-vaccinated HCWs. Secondly, using self-reporting questionnaires. Nevertheless, current findings must be further confirmed by large-scale population-based observational studies.

CONCLUSION

The results of this survey suggest that the efficacy of the vaccination agents presently utilized by HCWs was acceptable with no significant difference in vaccine type. Participants receiving at least two doses

of vaccines in this survey exceeded 90%, which is comparably higher than studies conducted in other countries.

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