Original Article

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Comparison of Incidence and Clinical Outcomes of COVID-19 among Healthcare Workers in the Pre-vaccination and Post-vaccination Periods: A Real-world Impact Study

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Abstract

Aim: Real-life data on the effect of coronavirus disease-2019 (COVID-19) vaccination is limited. We aimed to compare the incidence of COVID-19 among healthcare workers (HCWs) in the pre-vaccination and post-vaccination periods during the COVID-19 pandemic and identify associated factors for COVID-19 development.

Methods: In this single-center and cross-sectional study, HCWs employed in a tertiary care hospital were included. Pre-vaccination (14 October, 2020 and 14 January, 2021) and post-vaccination periods (1 March, 2021 and 1 June, 2021) were compared. A subgroup analysis was performed on HCWs without a previous history of COVID-19. Additionally, univariate regression analysis of COVID-19 development in the post-vaccination period was performed.

Results: Of 2,922 HCWs, 2,096 (71.7%) were vaccinated. The incidence of COVID-19 was higher in the pre-vaccination period (16.3%) than in the post-vaccination (6.6%) (p<0.01). In the subgroup analysis, the incidence of COVID-19 was 16.6% in the pre-vaccination period and 8.1% in the post-vaccination period (p<0.01). Previous history of COVID-19 (p<0.01) and double-dose vaccination (p<0.01) were associated with a decreased risk of COVID-19 development.

Conclusion: This study demonstrates the real-life impact of COVID-19 vaccination in reducing disease development and preventing poor clinical outcomes in a setting where the vaccination rate among HCWs was fairly low.

Keywords: COVID-19, vaccination, incidence, healthcare workers

Introduction

The coronavirus diseases-2019 (COVID-19) pandemic had a magnificent impact on global health, especially on healthcare workers (HCWs). Researchers from Turkey and all around the world made a great effort to better understand the epidemiology, clinical features, risk factors, and predictors of poor clinical outcomes, including the need for hospital admission, intensive care unit (ICU) transfer, and in-hospital death (1-3).

Nevertheless, treatment of and prevention against COVID-19 are still under research (4,5). Vaccination is one of the most effective methods of preventing infectious

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diseases and the poor clinical outcomes that accompany them. Also, there is evidence that CoronaVac, which is an inactivated whole-virion severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) vaccine, is safe and effective against COVID-19 (6). A randomized clinical efficacy trial has demonstrated that COVID-19 vaccination decreased the risk of COVID-19 development and COVID-19 related poor outcomes (7). However, there are a limited number of vaccine studies on the real-life experiences of preventing COVID-19 development, related hospitalization, and mortality among HCWs.

Therefore, we compared the incidence and clinical outcomes of COVID-19 among HCWs in the pre-vaccination and post-vaccination periods during the COVID-19 pandemic. Additionally, factors affecting the development of COVID-19 in the post-vaccination period were analyzed.

Materials and Methods

Compliance with Ethical Standards

All procedures performed in this study were in accordance with the ethical standards of the Declaration of Helsinki. This study was approved by the University of Health Sciences Turkey, Istanbul Haseki Training and Research Hospital Clinical Research Ethics Committee (approval number: 96-2022, date: 11.05.2022) and the Advisory Board on Coronavirus Research of the Republic of Turkey Ministry of Health Written informed consent was waived because of the retrospective nature of this study.

Study Design

In this single-center and cross-sectional study, HCWs employed in a tertiary care hospital were enrolled. Demographic features, clinical characteristics, and outcomes of HCWs with COVID-19 were recorded via data-sheets from follow-up forms. The vaccination status of all HCWs was collected via the hospital electronic medical record system.

The pre-vaccination period was defined as the 3-month period before the first vaccination was started (between October 14, 2020 and January 14, 2021). The post-vaccination period was defined as the 3-month period from 15 days after the second dose of vaccination (between 1 March, 2021 and 1 June, 2021).

The primary outcome was the development of COVID-19. The secondary outcome was a composite endpoint including hospital admission, ICU transfer, and in-hospital death. To detect the differences in the primary and secondary outcomes between the two periods, pre-vaccinated and post-vaccinated periods were compared. Additionally, a subgroup analysis was performed on HCWs without a previous history of COVID-19. The incidence rates of COVID-19 in the community and in HCWs in our study group were compared. Community-related data were obtained from the Republic of Turkey Ministry of Health's Coronavirus Information Platform (8). Prior to November 25, 2020, data were determined by proportioning patient data based on the symptomatic COVID-19 incidence rate. Moreover, HCWs with and without COVID-19 in the post-vaccination periods were compared to identify protective factors for developing COVID-19.

Statistical Analysis

Categorical parameters were represented as frequencies (n) and percentages (%), whereas quantitative parameters were represented as median and interquartile ranges. The chi-square test or Fisher's exact test were used to compare categorical data. The Kolmogorov-Smirnov test was used for normal distribution analysis. The Independent sample t-test was applied for normally distributed variables, while the Mann-Whitney U test was performed for variables without normal distribution. A univariate regression analysis for developing COVID-19 was performed. A p-value less than 0.05 was considered significant. Odds ratios (OR) with 95% confidence intervals (CI) were determined. The analyses were performed using IBM SPSS-21 (Statistical Package for Social Sciences, IL, USA).

Results

A total of 2922 HCWs were enrolled in this study. Of these, 1,179 (40.3%) were males. The mean age was 33.3±9.5 years. Overall, the vaccination rate in the study group during the first 3 months of the vaccination program was 71.7%. The single-dose and double-dose vaccination rates were 22.9% (n=668) and 48.9% (n=1428), respectively. Demographic characteristics of HCWs according to vaccination status are represented in Table 1.

Of 2,922 HCWs, 476 (16.3%) had COVID-19 in the pre-vaccination period, whereas 193 (6.6%) had COVID-19 in the post-vaccination period ($p<0.01$). Clinical deterioration as a secondary outcome occurred in 22 (0.8%) HCWs in the pre-vaccination period, whereas 11 (0.4%) HCWs had poor clinical outcomes in the post-vaccination period ($p=0.06$) (Table 2).

In the subgroup analysis, after excluding HCWs with a previous history of COVID-19 in the last 3 months, the incidence of COVID-19 was 16.6% in the pre-vaccination period and 8.1% in the post-vaccination period ($p<0.01$) (Table 3).

The weekly and cumulative incidence rates showed the positive impact of the COVID-19 vaccination program in preventing COVID-19 development among HCWs in our study group. While the concurrent lockdown might have influenced our results, these same trends did not occur either during the previous lockdown among HCWs in our hospital or during the current lockdown at the community level. The weekly incidence rates of COVID-19 in the community and HCWs in our study group are demonstrated in Figure 1. The cumulative incidence rates of COVID-19 in the community and HCWs in our study group are demonstrated in Figure 2.

When we evaluated the factors affecting the development of COVID-19 in the post-vaccination period, previous history of COVID-19 (OR: 0.01, CI: 0.00-0.17,

Table 1. Demographic characteristics of healthcare workers according to the vaccination status in the first 3-month period

Parameters	Total (n=2,922)	Unvaccinated (n=826)	Single-dose vaccinated (n=668)	Double-dose vaccinated (n=1,428)
Age (mean ± SD)	33.3±9.5	33.5±10.1	32.3±9.0	33.6±9.4
Sex				
Male, n (%)	1,179 (40.3)	338 (40.9)	271 (40.6)	570 (39.9)
Female, n (%)	1,743 (59.7)	488 (59.1)	397 (59.4)	858 (60.1)
Comorbid diseases, n (%)	758 (25.9)	176 (21.3)	154 (23.1)	428 (30.0)
HT, n (%)	442 (15.1)	101 (12.2)	92 (13.8)	249 (17.4)
DM, n (%)	270 (9.2)	65 (7.9)	49 (7.3)	156 (10.9)
CAD, n (%)	137 (4.7)	34 (4.1)	27 (4.0)	76 (5.3)
Asthma/COPD, n (%)	32 (1.1)	5 (0.6)	8 (1.2)	19 (1.3)
Pre-vaccination COVID-19 history, n (%)	534 (83.7)	326 (63.7)	47 (94.9)	161 (90.1)
Pre-vaccination COVID-19 history (last 3 months), n (%)	58 (2.0)	26 (3.1)	13 (1.9)	19 (1.3)
Pre-vaccination COVID-19 history before the last 3-month, n (%)	476 (16.3)	300 (36.3)	34 (5.1)	142 (9.9)

HT: Hypertension, DM: Diabetes mellitus, CAD: Chronic artery disease, COPD: Chronic obstructive pulmonary disease, SD: Standard deviation, COVID-19: Coronavirus disease-2019

Table 2. Comparison of pre-vaccination and post-vaccination periods in terms of COVID-19 development and the clinical deterioration

Parameters	Pre-vaccination period (n=2922)	Post-vaccination period (n=2922)	
	n (%)	n (%)	p-value
COVID-19			
Yes	476 (16.3)	193 (6.6)	**<0.01***
No	2,446 (83.7)	2,729 (93.4)	
COVID-related hospitalization			
Yes	22 (0.8)	11 (0.4)	0.06*
No	2,900 (99.2)	2,911 (99.6)	
Need for ICU admission			
Yes	1 (0.03)	1 (0.03)	1.00†
No	2,921 (99.97)	2,921 (99.97)	
In-hospital death			
Yes	0 (0)	1 (0.03)	0.09†
No	2,922 (100)	2,921 (99.97)	
Composite end-point[a]			
Yes	22 (0.8)	11 (0.4)	0.06*
No	2,920 (99.2)	2,911 (99.6)	

[a]: Composite end-point includes COVID-19 related hospitalization, need for ICU admission, and in-hospital death, *: Chi-square test, †: Fisher's exact test. Bold values represent statistical significance at the level of p<0.05. The incidence of COVID-19 was significantly higher in the pre-vaccination period (16.3%) than in the post-vaccination period (6.6%).
ICU: Intensive care unit, COVID-19: Coronavirus disease-2019

p<0.01) and double-dose vaccination against COVID-19 (OR: 0.37, CI: 0.27-0.52, p<0.01) as well as comorbid diseases, including diabetes mellitus (OR: 0.30, CI: 0.13-0.68, p=0.01) and chronic artery disease (OR: 0.31, CI: 0.10-0.97, p=0.03) were associated with a decreased risk of the disease development (Table 4).

Discussion

In this study, we presented a detailed analysis of vaccination profiles in 2,922 HCWs employed in a tertiary care teaching hospital, which is one of the pandemic epicenters in Istanbul, Turkey, and compared pre-vaccination and post-vaccination periods in terms of

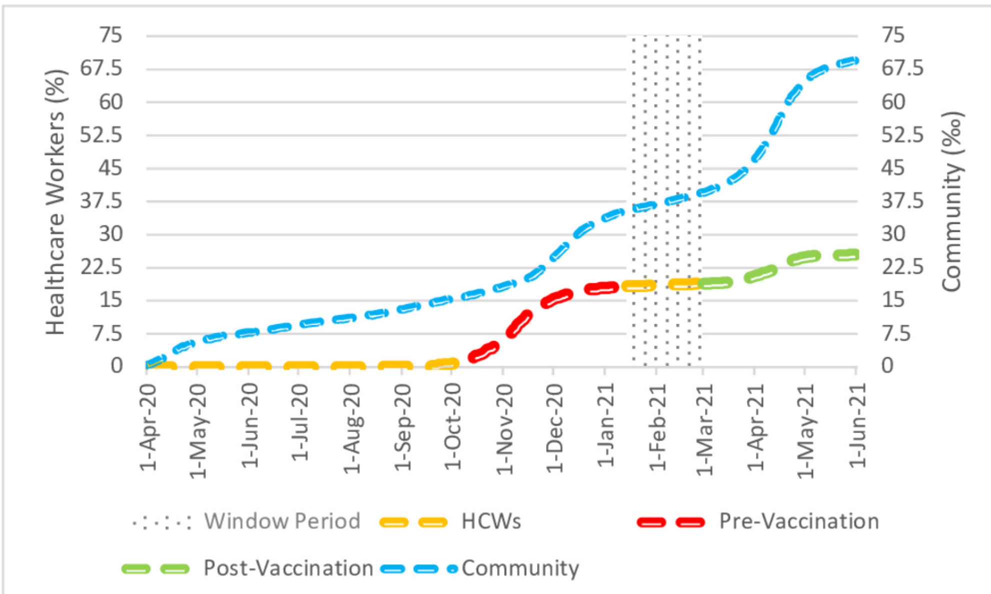

Figure 1. The cumulative incidence rates of COVID-19 in the community and HCWs

COVID-19: Coronavirus disease-2019, HCW: Healthcare workers

Table 3. Subgroup analysis of pre-vaccination and post-vaccination periods in terms of COVID-19 development and the clinical deterioration after exluding healthcare workers with previous history of COVID-19

Parameters	Pre-vaccination period (n=2,864)	Post-vaccination period (n=2,370)	
	n (%)	n (%)	p-value
COVID-19			
Yes	476 (16.6)	193 (8.1)	**<0.01***
No	2,388 (83.4)	2,177 (91.9)	
COVID-19 related hospitalization			
Yes	22 (0.8)	11 (0.5)	0.17*
No	2,842 (99.2)	2,359 (99.5)	
Need for ICU admission			
Yes	1 (0.03)	1 (0.04)	1.00†
No	2,863 (99.97)	2,369 (99.6)	
In-hospital death			
Yes	0 (0)	1 (0.04)	0.45†
No	2,864 (100)	2,369 (99.6)	
Composite end-point*			
Yes	22 (0.8)	11 (0.5)	0.17*
No	2,842 (99.2)	2,359 (99.5)	

*: Composite end-point includes COVID-19 related hospitalization, need for ICU admission, and in-hospital death, *: Chi-square test, †: Fisher's Exact test. Bold values represent statistical significance at the level of p<0.05. In the subgroup analysis after excluding HCWs with a previous history of COVID-19 in the last 3 months, the incidence of COVID-19 was significantly higher in the pre-vaccination period (16.6%) than in the post-vaccination period (8.1%).
ICU: Intensive care unit, COVID-19: Coronavirus disease-2019, HCW: Healthcore workers

the incidence and clinical outcomes of COVID-19. We analyzed the early impact (first 3 months) of the COVID-19 vaccination among HCWs. Therefore, the effect of COVID-19 vaccination on the risk of infection and clinical deterioration among HCWs was determined. Additionally, protective factors for the risk of COVID-19 development in the post-vaccination period were identified.

In a phase-3 efficacy trial, the efficacy of CoronaVac against SARS-CoV-2 infection was 50.7% (9). One retrospective study including HCWs in Brazil demonstrated

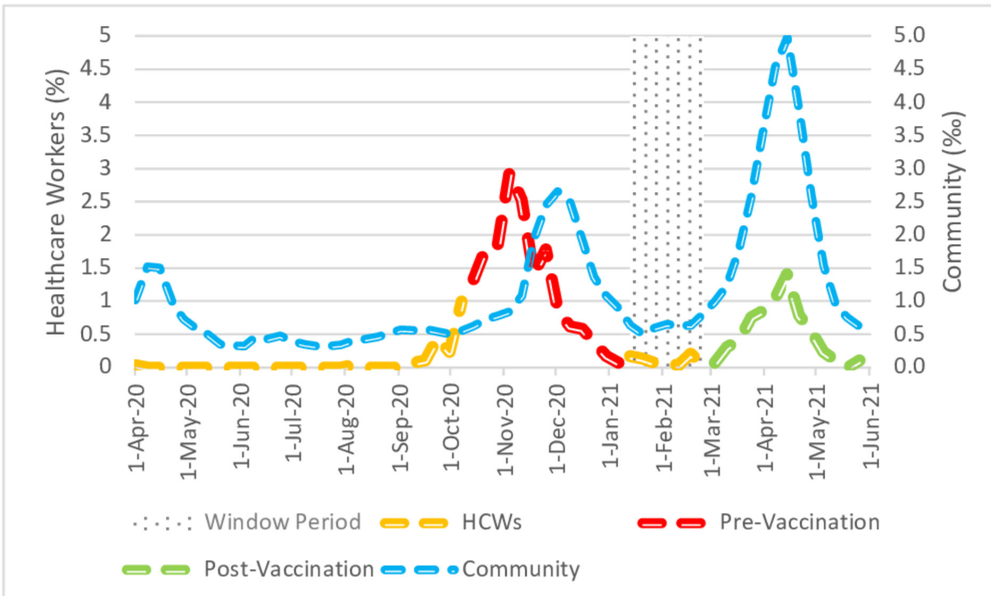

Figure 2. The weekly incidence rates of COVID-19 in the community and HCWs

COVID-19: Coronavirus disease-2019, HCW: Healthcare workers

Table 4. Univariate regression analysis for COVID-19 development in the post-vaccination period

Parameters		**Presence**		**Absence**		**OR**	**CI**	**p-value**
		n	**%**	**n**	**%**			
Sex								
Male		68	5.8	1,111	94.2	0.79	0.58-1.07	0.13
Female		125	7.2	1,618	92.8			
Comorbidity	Yes	38	5.0	720	95.0	0.68	0.48-0.99	**0.04**
	No	155	7.2	2,009	92.8			
DM	Yes	6	2.2	264	97.8	0.30	0.13-0.68	**0.01**
	No	187	7.1	2,465	92.9			
HT	Yes	23	5.2	419	94.8	0.75	0.48-1.17	0.20
	No	170	6.9	2,310	93.1			
COPD	Yes	2	6.3	30	93.8	0.94	0.22-3.97	0.94
	No	191	6.6	2,699	93.4			
CAD	Yes	3	2.2	134	97.8	0.31	0.10-0.97	**0.03**
	No	190	6.8	2,595	93.2			
Double-dose vaccination	Yes	53	3.7	1,375	96.3	0.37	0.27-0.52	**<0.01**
	No	140	9.4	1,354	90.6			
Previous history of COVID-19	Yes	0	0.0	534	100.0	0.01	0.00-0.17	**<0.01**
	No	193	8.1	2,195	91.9			

Bold values represent statistical significance at the level of p<0.05. Previous history of COVID-19 and double-dose vaccination against COVID-19 as well as comorbid diseases including diabetes mellitus and chronic artery disease were associated with decreased risk of the disease development.
HT: Hypertension, DM: Diabetes mellitus, CAD: Chronic artery disease, COPD: Chronic obstructive pulmonary disease, COVID-19: Coronavirus disease-2019, OR: Odds ratio, CI: Confidence interval

that while vaccination with CoronaVac was associated with a 0.5-fold decreased risk, the adjusted effectiveness was 36.8% of the double-dose vaccination against COVID-19 (10). Rovida et al. (11) showed that unvaccinated patients were transferred to the ICU more frequently (29.2%) than vaccinated patients (3.7%) among HCWs. In a community-based observational study, the efficacy of booster doses with various vaccines against the development of symptomatic COVID-19 was between 78.8% and 96.5% (12). In a recent impact-study conducted in Turkey, mortality was observed less frequently in patients who had COVID-19 in the post-vaccination period compared to those with COVID-19 in the pre-vaccination period (13). In a retrospective study in Denmark, the risk of hospitalization and mortality rate were significantly lower in vaccinated patients with solid organ transplants than in unvaccinated patients (14). In an Italian study, vaccinated patients had a less severe disease than unvaccinated patients, although vaccinated patients were older and had higher comorbidities (15). At the same time, McNamara et al. (16) demonstrated that vaccination programs decreased the risk of COVID-19 development, visits to emergency departments, and hospitalization among older adults.

Jara et al. (17) reported that the adjusted vaccine effectiveness was 65.9% for COVID-19 development, 87.5% for COVID-19 related hospitalization, 90.3% for preventing ICU admission, and 86.3% for preventing death. A retrospective real-life Turkish study that included HCWs found waning immunity in HCWs vaccinated with CoronaVac and the researchers reported that the unadjusted and adjusted effectiveness for preventing COVID-19 development was 47% and 39%, respectively (18). In our study, the incidence of COVID-19 was lower in the post-vaccination period compared to the pre-vaccination period. Moreover, COVID-19 vaccination and previous history of COVID-19 were found as protective factors for the disease's development. Additionally, HCWs with comorbid diseases had COVID-19 less frequently. This could be due to the high compliance of the HCWs with comorbid diseases. In this study, poor clinical outcomes occurred less frequently in the post-vaccination period compared to the pre-vaccination period.

In a study that included HCWs in India, the vaccine effectiveness against COVID-19 development was about 44% and 89% for partially and fully vaccinated HCWs, respectively. Haas et al. (19) demonstrated that the incidence of COVID-19 and related poor outcomes declined with the increased vaccination rate. In a study from the United States, they detected a significant decline (about 50%) in the daily COVID-19 cases in the 21-25 day post-period after the initial doses of vaccination (20). Another study comparing the pre- and post-vaccination periods in the United States found that as the vaccination rate increased, COVID-19 and related-poor clinical outcomes decreased. Additionally, the researchers revealed that older adults had the highest vaccination rate and a greater decline (up to 66%) was observed in the older adults (21). In the study by De Faria et al. (22), the effectiveness two weeks after the second dose of CoronaVac among HCWs was 50.7%. Toniasso et al. (23) reported that the incidence of COVID-19 decreased by 65% in people with a previous history of COVID-19 in the post-vaccination period.

Shoukat et al. (24) reported a 30% decline in COVID-19 cases, a 51% decline in hospitalizations, and a 48% decline in deaths compared with the expected rates between pre-vaccination and post-vaccination periods, although single and double-dose vaccination rates among adults were 64% and 69%, respectively. In a cohort that comprised more than 90% fully vaccinated older adults, the vaccine effectiveness for vaccinated people with no known prior COVID-19 was 81.8% (25). Cavanaugh et al. (26) reported that in a nursing facility, approximately 90% of residents and 52% of HCWs were fully vaccinated and vaccine protection rates for COVID-19 development, hospitalization, and death were 66%, 94%, and 94%, respectively. Additionally, they revealed that the vaccination effectiveness for developing COVID-19 among HCWs was 76%. As a result, studies conducted with different types of vaccines, study protocols including study populations and time frame, viral dynamics including SARS-CoV-2 variants, and COVID-19 measures such as lockdown applications, have different results in preventing COVID-19 and related poor outcomes. However, most studies have confirmed either the efficacy, effectiveness, or positive impact of COVID-19 vaccines.

Study Limitations

Our study had some limitations. First, this study was conducted retrospectively in a single center. Second, given the study design, measuring the efficacy or effectiveness of COVID-19 vaccination could not be possible. We evaluated pre-vaccination and post-vaccination periods and could compare the two periods. Comparing two different periods does not reflect either vaccine efficacy nor vaccine effectiveness. However, this study allowed us to measure the impact of COVID-19 vaccination among HCWs in the real world setting. Third, different pandemic dynamics, such as viral mutations, lockdown applications, and community compliance with COVID-19 measures, may influence the impact of COVID-19 vaccination. However, this study had several strengths. First, we could closely evaluate the possible cases with active surveillance since the study population was comprised of HCWs in our pandemic hospital. Second, we could measure several possible confounding variables, including age, sex, and comorbid conditions. These variables were not found as significant covariates for each outcome in our study setting comprising HCWs. Third, to mitigate the possible effect of the prior SARS-CoV-2 infection on cases, we performed subgroup analysis after excluding HCWs with a previous history of COVID-19 infection in the last 3 months.

Conclusion

This study demonstrates the real-life impact of vaccination against COVID-19 in both reducing disease development and preventing poor clinical outcomes in a setting where the vaccination rate among HCWs is fairly low. Additionally, previous history of COVID-19 and COVID-19 vaccination were detected as protective factors for the disease's development.

Ethics

Ethics Committee Approval: This study was approved by the University of Health Sciences Turkey, Istanbul Haseki Training and Research Hospital Clinical Research Ethics Committee (approval number: 96-2022, date: 11.05.2022)

Informed Consent: Written informed consent was waived because of the retrospective nature of this study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: S.S., B.C., Design: S.S., B.C., O.F.B., Y.E.O. Data Collection or Processing: B.C., G.T., Analysis or Interpretation: S.S., B.C., O.F.B., G.T., Y.E.O., F.P., G.S., Literature Search: S.S., B.C., Y.E.O., Writing: S.S, B.C., O.F.B., G.T., Y.E.O.

Conflict of Interest: No conflict of interest was declared by the authors.

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