

Basic Characteristics of Patients Infected with SARS-CoV-2 after COVID-19 Vaccine: A Cross-Sectional Study in Iran

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ABSTRACT

Introduction: This study aimed to evaluate the baseline characteristics of patients infected with SARS-CoV-2, after receiving first or second doses of COVID-19 vaccine. **Methods:** In this cross-sectional study, we examined 100 patients with SARS-CoV-2 infection after vaccination and collected demographic characteristics and history of underlying diseases, lung involvement, and severity of the disease, as well as the type of vaccine received and the duration of onset of the diseases symptoms after vaccination. The relationship between the disease severity and variables was evaluated by the bivariate analysis. Multiple logistic regression model was performed to predict the severity of the disease by calculating the odds ratios and 95% confidence intervals (CIs). **Results:** The mean±SD age of COVID-19 patients was 62.54±14.93 years. 59% of patients were male. The mean interval between vaccination and onset of symptom disease was 4.95 days. In bivariable analysis, there was a difference between the mean of the lung involvement in CT scan, O₂ saturation, hypertension (HTN), and Severity of the disease ($p < 0.001$). In multiple logistic regression analysis, HTN (OR: 5.6, 95CI:1.07-25.5, $p = 0.04$), O₂ saturation $< 90%$ (OR:1.53, 95% CI: 1.39-2.92, $p = 0.003$) and lung involvement $\geq 30%$ in CT scan were predictors of disease severity. **Conclusion:** Due to the short time interval between COVID-19 vaccination and the disease symptoms in this study, it is recommended all people with any symptom of disease to avoid the vaccination.

INTRODUCTION

COVID-19 is an infectious disease caused by SARS-CoV-2 virus. Most mild to moderate infected patients would recover without special treatment and significant complications (1). Generally, older people with underlying diseases like cardiovascular disease, diabetes, hypertension (HTN), chronic respiratory disease, or cancer are more likely to develop a more serious form of the illness (1-2). Globally, as of 20 September 2022, there have been 609,848,852 confirmed cases of COVID-19, including 6,507,002 deaths, reported to WHO (3). At this time, the United States ranks first in terms of the number of infected people with more than 94 million, followed by India, Brazil, and France. In September 2022, Iran with approximately 7.5 million people infected and 144,344 victims was the seventeenth in terms of the number of COVID-19 patients (3-4). Many strategies were used to control COVID-19 in Iran and other countries, including wearing masks, observing social distance and avoiding gatherings, washing hands frequently, and generally observing personal and social hygiene (4). The most common drug agents for treatment of COVID-19 included

Remdesivir and convalescent plasma. Widely-used Chloroquine, Hydroxychloroquine and Azithromycin combinations as well as Lopinavir-ritonavir were shown to have less efficient treatment effects.

The patients with more severe cases of pneumonia and dyspnea, or uncontrollable fever are admitted in hospital, and nearly 10% are treated in intensive care units. Oxygen supplementation is administered to maintain peripheral blood oxygenation over 90%-96%(5).The COVID-19 vaccine stimulates the immune system to produce antibodies and other proteins to fight the virus in order to achieve milder symptoms and faster recovery (4-5). With the increase in the speed of vaccination in all countries, especially Iran, the incidence and mortality rates have decreased dramatically (6). To date, about 51% of the world and 63% of the Iranian population have received both doses of a COVID-19 vaccine (4).

Many reports suggest only a few people have SARS-CoV-2 infection following the two doses of COVID-19 vaccination (7-8). The Indian Council of Medical Research (ICMR) has reported 0.13% and 0.07% have been found to have COVID-19

infection following the two doses of Covaxin and Covishield vaccines, respectively (9). Similarly, a hospital-based observational study from Apollo hospital, India has stated that 97.8% of vaccinated health care workers (HCW) are protected from SARS-CoV-2 infection, and for only 0.06% of the patients, hospitalization was required (10). Since complete immunity to the virus develop approximately 2 weeks after the second dose of the vaccine, it is believed that in people who develop symptoms during this period and test positive, the virus was probably present in their bodies at the time of vaccination which showed up a few days later (11). In this study, we examined the characteristics of COVID-19 patients, after receiving the available vaccines in Iran.

MATERIALS AND METHODS

Ethics Statement

This study was approved by the Research Ethics Committees of Islamic Azad Tehran Medical Sciences University - Pharmacy and Pharmaceutical Branches (IR.IAU.PS.REC.1400.438).

Study Design

This cross-sectional descriptive study was performed on 100 COVID-19 patients, after receiving one or two vaccine doses (Sino pharm, AstraZeneca, Bharat (COVAXIN)) at Amir Al-Momenin University Hospital in South of Tehran in 2021. The demographic information of the patients, including age, gender as well as the underlying disease of diabetes and hypertension, were collected. The severity of the disease was assessed based on the degree of lung involvement in the CT scan result and the percentage of blood oxygen saturation based

on the latest version of the national COVID-19 diagnosis (12). Mild: lung involvement < 25% and O₂ saturation >93%, moderate: lung involvement: 25-50% and O₂ saturation: 90-93 and severe disease: lung involvement >50% and O₂ saturation <90%. In addition, the time interval between SARS-CoV-2 infection and vaccination was assessed. Also, the dose of the vaccine for each patient was recorded. Data are presented as numbers and proportions for categorical variables and mean (standard deviation) for continuous variables. Association between severity of disease and demographic as well as patients disease basic characteristics were evaluated by chi-square and independent t-test binary analysis. Finally, multivariable logistic regression analysis to predict the severity of the infection after vaccination was used. Odds ratios (ORs) and 95% confidence intervals (CIs) were obtained. A two-sided p-value less than 0.05 was considered statistically significant. All analyses were conducted through SPSS software (IBM spss 23, USA) version 23.

RESULTS

Descriptive Analysis of COVID-19 Patients

The mean±SD age of the patients was 62.54±14.93 years. 59(59%) of the patients were male. The interval between the vaccine injection and COVID-19 infection diagnosis was 4.95±3.08 days. 92% of patients had received Sinopharm vaccine, 6% AstraZenka vaccine, and 2% Bharat vaccine. 91% of the infected cases were after the first dose of the vaccine. Moreover, 22% and 21% of the patients had a past medical history with diabetes and HTN, respectively. The severity of the disease was mild in 34%, moderate in 62%, and severe in 4%. All the results of the descriptive analysis are given in Table 1.

Table1: Descriptive analysis data of COVID-19 patients.

Variables	Number (Percent%) Or Mean±SD
Age	62.54±14.93
Gender	
Male	59(59%)
Female	41(41%)
The interval between vaccination and infection(days)	4.95 ± 3.08
Mean of the lung involvement in CT	30.21% ± 18.56%
O₂ saturation	89.87% ± 6.30%
Vaccine type	
Sinopharm	92(92)
AstraZeneca	6(6)
Bharat(COVAXIN)	2(2)
Infection after	
First dose	91(91)
Second dose	9(9)
DM	
Yes	22(22)
No	78(78)
HTN	
Yes	21(21)
No	79(79)
Severity	
Mild	34(34)
Moderate	62(62)
Severe	4(4)

Factors affecting the Severity of the Disease

There was no statistically significant difference between the severity of the disease and age ($p = 0.3$), sex ($p = 0.6$), the time interval between vaccination and SARS-CoV-2 infection ($p = 0.2$), type of vaccine ($p = 0.5$), first or second dose of injection ($p = 0.4$), as well as the underlying disease of diabetes

($p = 0.4$). However, in the same analysis, we found a statistically-significant difference between the severity of the disease and the mean of the lung involvement in CT scan ($p < 0.001$), O₂ saturation ($p < 0.001$), and HTN ($p = 0.03$; Table 2).

Table 2. The difference between SARS-CoV-2 infection severity based on the patients' characteristics.

Variables	Severity of disease (COVID-19 infection)		p-value
	Mild 34(34%)	Moderate and Severe 66(66%)	
Age(years)	60.74±17.51	63.55±13.52	0.3
Gender			0.6
Male	19(55.9%)	40(60%)	
Female	15(44.1%)	26(40%)	
BMI	24.66±12.02	25.34±12.6	0.5
The interval between vaccination and infection(days)	4.38±2.44	5.23±3.33	0.2
Mean of the lung involvement in CT scan	13.53%±10.76%	39.51%±15.18%	<0.001*
O₂ saturation	92.65%±3.27	88.44%±6.99%	<0.001*
Vaccine type			0.5
Sinopharm	32(94.1%)	60(90.9%)	
AstraZeneca	2(5.9%)	4(6.1%)	
Bharat(COVAXIN)	0(0)	2(3)	
Infection after			0.4
First dose	30(88.2%)	61(92.4%)	
Second dose	4(11.8%)	5(7.6%)	
DM			0.4
Yes	6(17.6%)	16(24.2%)	
No	28(82.4%)	50(75.8%)	
HTN			0.03*
Yes	3(8.8%)	18(27.3%)	
No	31(91.2%)	48(72.7%)	

Logistic Regression Analysis to Predict Severity of COVID-19

By entering significant variables in the bivariate analysis to the multivariable logistic regression model (forward stepwise method), we evaluated the predictors of a severe type of SARS-CoV-2 infection after COVID-19 vaccination. In this model,

having HTN (OR: 5.6, CI: 1.07-25.5, $p = 0.04$), O₂ saturation < 90% (OR: 1.53, CI: 1.39-2.92, $p < 0.001$) and Lung involvement in the CT scan equal and more than 30% (OR: 1.73, CI: 1.34-2.24, $p < 0.001$) were predictors of severe COVID-19 (Table 3 and Fig. 1).

Table 3: Multivariable logistic regression analysis to predict severity of SARS-CoV-2 infection after COVID-19 vaccination.

Variables	OR(95CI%)	p.value
HTN		0.04*
Yes	5.6(1.07-25.5)	
No(reference)		
The interval between vaccination and infection(days)		0.1
4 ≤	2.17(0.71-6.63)	
4 >(reference)		
O₂ saturation%		0.003*
90 >	1.53(1.39-2.92)	
90 ≤ (reference)		
Lung involvement in CT scan%		<0.001*
30 ≤	1.73(1.34-2.24)	
30 >(reference)		

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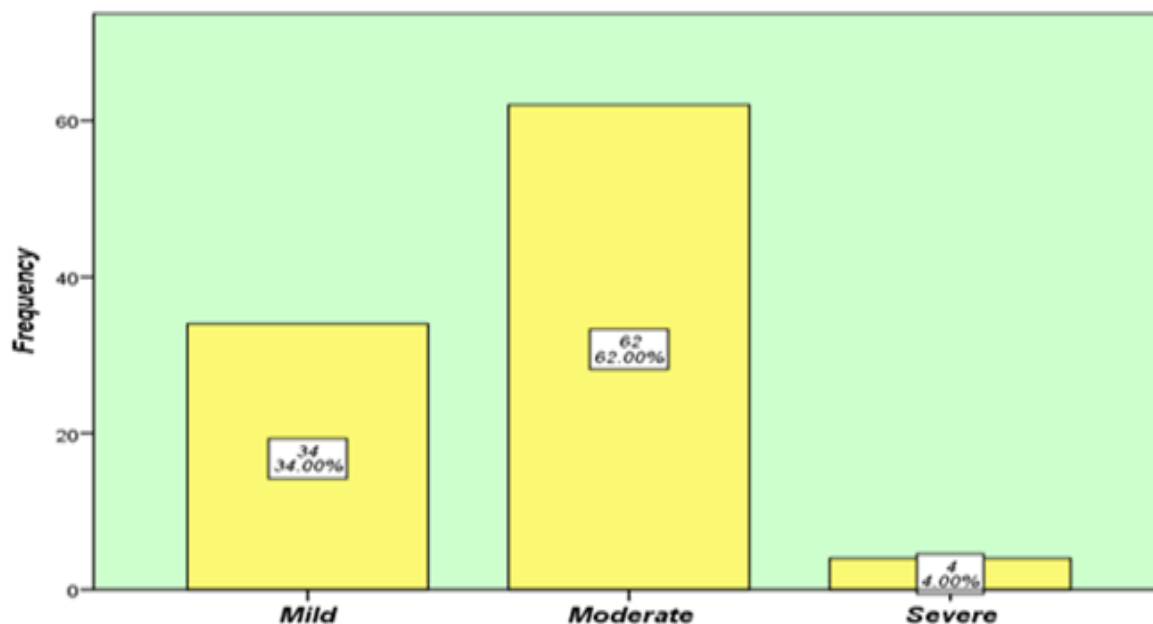


Fig. 1. Severity of COVID-19 infection in the patients after vaccination (Mild: 34%, Moderate: 62%, Severe: 4%).

DISCUSSION

COVID-19 vaccination does not mean 100% protection against the infection; hence, every vaccinated person has to wear masks and observe the social distance (8). Researchers have concluded that maximum protection could be achieved two weeks after the second dose of COVID-19 vaccine (9). Whilst partial protection against COVID-19 may be achieved as soon as 12 days after the first dose, this protection is likely to be short-lived (9-10). We found that 91% of the patients who contracted the disease after receiving the vaccine had only received the first dose. Despite many efforts to increase the vaccine efficacy and to prolong immunity, it is believed that environmental and host-specific factors such as age, sex, safety history, genetics, and comorbidities, as well as pregnancy, can affect vaccine efficacy (10).

In the current analysis, 27.3% of patients with moderate and severe SARS-CoV-2 infection had HTN, while only 8.8% of the patients with mild COVID-19 had high blood pressure. Priyanka has shown in a study that a severe disease with higher mortality has been reported for the male patients, although the impact of the gender on immune response against SARS-CoV-2 is still unexplored (11). In this study, the mean interval between the vaccination and the infection was 4.95 ± 3.08 days. Considering that many patients became ill after the first dose of the vaccine, it could be assumed that they have not sufficient immunity against the virus and or are in the incubation period of the disease on the day of vaccination. One published study has shown a rate of 0.5 and 0.2 percent of SARS-CoV-2 infection after the first and second dose of the vaccination (12).

In the risk factor analysis, it has been reported that frailty is associated with post-vaccination infection in older adults (≥ 60 years) after their first vaccine dose (odds ratio (OR) 1.93, 95% CI 1.50–2.48; $p < 0.0001$), and individuals living in highly deprived areas have increased odds of post-vaccination infection following their first vaccine dose (OR 1.11, 95% CI

1.01–1.23; $p=0.039$), however, the severity of the disease is reported lower than those who had not been vaccinated. For instance, individuals without obesity (BMI <30 kg/m²) are shown to have lower odds of the infection following their first vaccine dose (OR 0.84, 95% CI 0.75–0.94; $p=0.003$) (12). Although we did not find any association between severity of disease and BMI in patients here, Stefan has reported obesity and impaired metabolic health as important risk factors for severe COVID-19 which also promote vaccine-breakthrough SARS-CoV-2 infections in fully vaccinated people (13). Moreover, evidence suggest BMI >23 kg/m² could increase risk of hospital admission or mortality due to COVID-19 (13). A study published by Gao and colleagues in 2021 has provided support for the role of insulin resistance in promoting severe COVID-19. In addition, increased glycosylated hemoglobin (HbA1c) levels are reported to be associated with a reduced immune response to an influenza A (H1N1) vaccine (14). Another study has also provided support for the role of insulin resistance in promoting severe COVID-19(15). Altogether, these findings indicate COVID-19 vaccine effectiveness might be slightly lower among people with a higher number of coexisting conditions, such as obesity, type 2 diabetes, and hypertension, than people with a low number of coexisting conditions (16). Wang et al. have concluded the risk for breakthrough infection range from 6.8% for tobacco use disorder to 7.8% for cannabis use disorder, all significantly higher than the 3.6% in the non-substance-use disorders population ($p < 0.001$)(17).

Considering the short time between the infection and receiving each type of COVID-19 vaccine in this survey, it is recommended to advice people with feelings and symptoms of flu to avoid vaccination. A rapid COVID-19 test may also help to assess a patient with SARS-CoV-2 infection before the vaccination. Further studies on vaccinated individuals with more population and long-term follow-up are recommended to elucidate the risk-factors associated with COVID-19 vaccination.

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CONFLICT OF INTEREST

The authors declare they have no conflict of interests.

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