

## COVID-19 infection after vaccination

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**Abstract**

**Background:** Although vaccination is the most effective and specific approach for prevention of infectious diseases, but in a small percentage of vaccinated person's breakthrough infections can occur. This study aimed to determine the effectiveness of different common *coronavirus* vaccines in this area.

**Methods:** 109 COVID-19 vaccinated patients were enrolled, with different types of vaccines (Sinopharm, AstraZeneca, Sputnik, Bharath, CovIran Barkat and Pasto-CoV) and time of administration in 2021 in Babol, Iran. Patients after 14 days of administration of the final dose of corona vaccines with positive COVID-19 RT-PCR test entered to study. Patients' data such as RT-PCR, type of vaccine, age, sex and outcome were collected using electronic medical records.

**Results:** 47 patients were not fully vaccinated, 62 had two vaccine doses and 51 were fully vaccinated and considered to a breakthrough infection. Although, most of the patients with *SARS-CoV-2* infection were either mild (n=18 [16.56%]), or moderate (n=86 [78.9%]), 5 (4.6%) patients had severe or critical illness, of whom 3 admitted in intensive care unit, 3 intubated, and 4 died. The average age of the participants with COVID-19 infections was 61.23 ± 19.91 years.

**Conclusion:** Based on our results, the *COVID-19* breakthrough occurring with two doses of current vaccines were mild and moderate.

**Keywords:** SARS-CoV-2; COVID-19; Vaccine; Breakthrough.

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Vaccination is the most effective and specific way for the prevention of infectious diseases. In spite of the *coronavirus* disease-19 (*COVID-19*) pandemic, the use of vaccines against severe acute respiratory syndrome coronavirus 2 (*SARS-CoV-2*) with wide-ranging of the world's population is the approach to overcome the present health crisis faced by humanity (1).

Several approaches to *COVID-19* vaccine developed concurrently, including mRNA vaccines, vector-based, recombinant protein, inactivated, and live attenuated vaccines. The improvement of the corona vaccine is the key innovation to the probable termination of the pandemic. On the other hand, the mutating nature of the virus and evolutionary events have raised worries about vaccine efficacy due to viral genomic changes (2). Vaccine safety is not a revelation that someone who gets vaccine will definitely not get the disease. A person may be infected again after vaccination. However, in the *COVID-19* epidemic, vaccines reduce the risk of infection in many people, and that is the value of vaccines. On the other hand, many patients who have already been vaccinated develop a mild or moderate form with no symptoms and no severe side effects (3). The vaccine can reduce the incidence of asymptomatic cases as well as the related infectivity (4, 5). As described in other countries and health care institutions, breakthrough infections can occur in a small percentage of vaccinated persons (6-8). Most vaccines that have been approved worldwide considerably reduced the chances of hospitalization, severity and death (9).



Many studies describe the outcomes of vaccinated of COVID-19 infections (10). The six main vaccines were used for mass vaccination against COVID-19 in Babol, including Sinopharm, AstraZeneca, Sputnik, Bharath, CovIran Barkat and Pasto-CoV vaccines. According to the announcement of the Vice Chancellery of Health in Babol University of Medical Sciences, until 17 July 2021, a total of 73,497 vaccine doses have been administered in Babol. Babol is one of the largest cities in northern Iran with a population of about 530,000 and among them, 402530 (75.9%) is the population over 18 years. The total number of second dose vaccines distributed in Babol until July 17, 2021, was 16,503 for Sinopharm, 1,218 for AstraZeneca, 2,931 for Sputnik, 2,287 for Pasto CoVac, 362 for Bharath

and 3 for CoV Iran (table 1) (Unpublished data). Despite the reduction in mortality with COVID-19 vaccines, some factors are important in breakthrough COVID-19 infections after vaccination, such as new variants and the time since vaccination (11). After 22 days of the first dose of COVID vaccine, its efficacy against severe COVID-19 was 100% (12). Although, the breakthrough cases have so far been rare, they are possible (13). We define the efficacy of vaccination against admission to hospital in COVID-19 patients in Babol University of Medical Sciences and Health System. Other studies have described the different safety profiles and efficacy of many types of vaccines (14). So, we studied the safety profile and the rate of breakthrough infection in fully vaccinated patients.

**Table 1. The frequency of first and second doses of corona vaccines in the population over 18 years of age in the North of Iran**

Vaccine Status	Number (%)
<b>Unvaccinated</b>	329033 (81.7)
<b>Vaccinated (the first dose)*</b>	73497 (18.3)
Sinopharm	42108
Sputnik v	7042
AstraZeneca	17922
Bharath, or	751
CovIran Barkat	1055
Pasto-CoV	4619
<b>Vaccinated (two weeks after the second dose)</b>	23304
Sinopharm	16503
Sputnik v	2931
AstraZeneca	1218
Bharath, or	362
CovIran Barkat	3
Pasto-CoV	2287

## Methods

**Patients and study design:** At a referral medical center for COVID-19 patients in the North of Iran, we studied the hospitalized patients with COVID-19 (confirmed by Real time-polymerase chain reaction [RT-PCR] method at the time of admission) between July 17 and December 2, 2021. Status of Coronavirus vaccination including injection date and type of vaccines (Sinopharm, AstraZeneca, Sputnik, Bharath, CovIran Barkat and Pasto-CoV) were recorded. If the final dose of vaccine was administered at least 14 days before the beginning of symptom or a positive RT-PCR test for SARS-CoV-2, it

was considered as a fully vaccinated patient. Totally, 1552 cases were admitted to Ayatollah Rouhani Hospital with a confirmed COVID-19 and severity of disease was recognized (15). 109 (7.02%) of 1552 cases received at least one dose of a corona vaccine at the time of hospitalization. We entered the patients to study with the following inclusion criteria: more than 18 years of age, the primary care took place at Ayatollah Rouhani Hospital based on home address inside the region of referral hospital, positive of RT-PCR and injected for one or two doses of the current vaccine.

**Data collection:** Approach of diagnosis for SARS-CoV-2 infection was to evaluate all patients who were referred to a hospital as of *COVID-19* patients by RT-PCR reaction. Data collection was done by interviewing the patient or whoever accompanies the patient and retrospective search of the electronic medical records. The information of patient was collected by electronic hospital medical records comprising demographic, medical history and symptoms, comorbidities, and the results of RT-PCR test. Also, we collected the date of administration and type of vaccine, dose number (first or second dose), clinical outcomes and date of dead.

**Statistical analysis:** The SPSS software v. 16.0 (IBM, Chicago, IL, USA) was used for the statistical analysis. The *SARS-CoV-2* prevalence in the stated stratification factors was analyzed using the chi-square test. The *p*-values less than 0.05 were considered statistically significant.

## Results

Of the 109 patients, 47 received a partial vaccine course (one dose of Sinopharm, AstraZeneca, Sputnik, Bharath, CovIran Barkat or Pastro-CoV), 62 were fully vaccinated of whom 51 of them were considered as a breakthrough infection. Although the majority of patients who had a *SARS-CoV-2* infection were either mild ( $n = 18$  [16.56%]), or moderate ( $n = 86$  [78.9%]), 5 (4.6%) patients had severe or critical illness, of whom 3 needed for admission to intensive care unit, 3 for intubation, and 4 died. The number of *SARS-CoV-2* infected cases according to the vaccination status and demographics data was shown in table 2. The median age of cases with severe or critical disease was 73.2 years (range 60–83). The most prevalent underlying diseases in 5 patients with severe or critical disease included cardiovascular disease ( $n = 4$ ). We also noticed that all of these 5 patients had received the Sinopharm vaccine.

**Table 2. Characteristics of COVID-19 patients according to the vaccination status**

	One Dose vaccinated (n=58)	Breakthrough (n=51)	Total (n=109)	<i>P</i> -Value
<b>Sex</b>				
Male	22 (37.9)	24 (47.1)	46 (42.2)	0.437
Female	36 (62.1)	27 (52.9)	63 (57.8)	
<b>Age group</b>				
≤ 50	20 (35.1)	13 (25.5)	33 (30.3)	0.303
>50	38 (64.9)	38 (74.5)	76 (69.7)	
<b>Job</b>				
HCW*	4 (6.9)	11 (21.6)	15 (13.8)	0.085
Freelance	22 (37.9)	16 (31.4)	38 (34.9)	
Housewife	32 (55.2)	24 (47.1)	56 (51.4)	
<b>Patient Statuses; n (%)</b>				
Hospitalized	5 (8.6)	16 (31.4)	21 (19.3)	0.010
Outpatients	52 (89.7)	34 (66.7)	86 (78.9)	
ICU	1 (1.7)	1 (2)	2 (1.8)	
<b>Hospital duration</b>	8.15±6.48	6.60±4.16	6.38±5.91	0.075
<b>Symptoms</b>				
Fever	31 (53.6)	24 (47.1)	55 (50.5)	0.567
Chills	30 (51.7)	26 (51)	56 (51.4)	0.546
Cough	28 (48.3)	14 (27.5)	42 (38.5)	0.031
Weakness	45 (77.6)	38 (74.5)	83 (76.1)	0.823
Sputum	5 (8.6)	4 (7.8)	9 (8.3)	1.000
Myalgia	17 (29.3)	14 (27.5)	31 (28.4)	1.000
Headache	5 (8.6)	8 (15.7)	13 (11.9)	0.375
Breathlessness	26 (44.8)	19 (37.3)	45 (41.3)	0.443
Nausea and Vomiting	6 (10.3)	0 (0.0)	7 (5.5)	0.029

	One Dose vaccinated (n=58)	Breakthrough (n=51)	Total (n=109)	P-Value
≥ 3 symptoms	41 (70.7)	33 (64.7)	83 (76.1)	0.542
<b>Comorbidity</b>				
Heart diseases	10 (17.2)	16 (31.4)	26 (23.9)	0.115
Diabetics	18 (31)	7 (13.7)	25 (23.4)	0.040
Hypertension	11 (19)	4 (7.8)	15 (13.8)	0.104
Cholesterol	8 (13.8)	3 (5.9)	11 (10.1)	0.213
Thyroid diseases	4 (6.9)	4 (7.8)	8 (7.3)	1.000
Asthma	3 (5.2)	2 (3.9)	5 (4.6)	1.000
Kidney diseases	1 (1.7)	1 (2)	2 (1.8)	1.000
Liver diseases	1 (1.7)	0 (0.0)	1 (0.9)	1.000
≥ 1 comorbidity	35 (60.3)	25 (49)	61 (56)	0.253
No comorbidity	23 (39.7)	25 (49)	48 (44)	0.243
<b>Severity of Disease</b>				
Mild	6 (10.3)	12 (23.5)	18 (16.5)	0.132
Moderate	50 (86.2)	36 (70.6)	86 (78.9)	
Severe	2 (3.4)	3 (5.9)	5 (4.6)	
<b>Outcome</b>				
Full recovery	26 (44.8)	17 (33.3)	43 (39.4)	0.471
Partial recovery	30 (51.7)	32 (62.7)	62 (56.9)	
Discharge	2 (3.4)	2 (3.9)	4 (3.7)	

\*Health Care Workers

Fifty one cases (0.21%; 51/23304) had condition for breakthrough infection. The mean age of these patients was 61.23 ± 19.91 years (range of 22 to 96 years) and 27 (52.9%) were females. The median duration between the first and second dose of vaccine was 29 days (with the range of 22 -83 days). The common comorbidities included heart diseases (16 cases), diabetes mellitus (7 cases), hypertension (4 cases), and thyroid (4 cases). Weakness was the most common symptom (74.5% cases), and then the chills (51%) and fever (47.1%) (figure 1). There is not any asymptomatic patient. 35 (62.7%) patients

need hospitalization for mild to moderate symptoms and three (5.9%) cases were severe. The mean of hospitalization duration in mild, moderate and severe patients were 5.50 ± 1.00, 7.14 ± 5.23 and 16.5 ± 9.32, respectively ( $P=0.004$ ) (table 3).

With regard to the type of vaccine received among these 51 breakthrough infections, 31 (60.8%) patients received Sinopharm, 10 (19.6%) Sputnik, 4 (7.8%) Bharath, 3 (5.9%) the CoV Iran, 2 (3.9%) AstraZeneca, and 1 (2%) received Pasto CoVac vaccines. The median time of final vaccine to infection was 54 days.

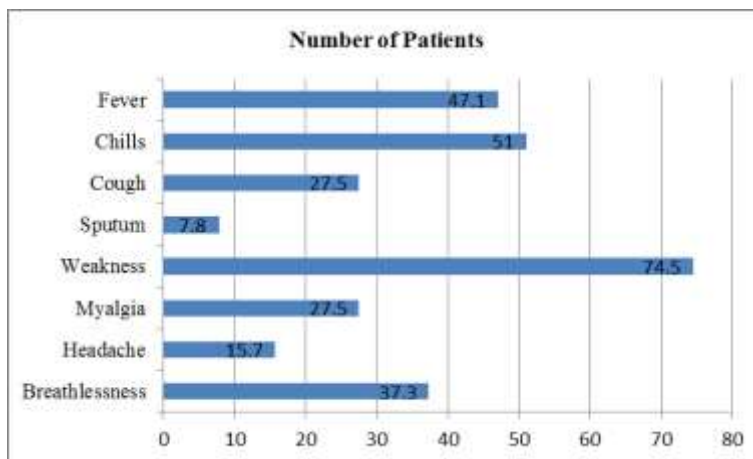


Figure 1. Symptoms of patients with COVID-19 breakthrough

**Table 3. The mean of hospital duration in SARS-CoV-2 infected patients after vaccination**

Characteristics	Mean $\pm$ SD	P- Value
<b>Age</b>		
< 50 Years	4.00 $\pm$ 2.64	0.263
$\geq$ 50 Years	6.88 $\pm$ 4.23	
<b>Severity of Disease</b>		
Mild	5.50 $\pm$ 1.00	<b>0.004</b>
Moderate	7.14 $\pm$ 5.23	
Severe	16.5 $\pm$ 9.32	
<b>Vaccine Situation</b>		
One dose (n=58)	55.25 $\pm$ 14.11	0.075
14 days after two dose (n=51)	61.29 $\pm$ 19.91	
All patients (n=109)	58.10 $\pm$ 17.28	

## Discussion

In this study, we described 109 *COVID-19* patients who received at least one dose, and we observed that many patients were not fully vaccinated. Among the 51 breakthrough infections, all were symptomatic and 16 (31.4%) cases were hospitalized, 5.9% need supplemental oxygen or mechanical ventilation. Further, 3.9% patients died. Also, according to the data, there is a significant association between the mean lengths of hospital stay and the severity of the disease and vaccinated hospitalized patients had better prognosis than unvaccinated hospitalized patients, as other studies showed. For example, in Bernal's study, they found that the first dose of the vaccine after 7 to 13 days is 70% effective and 14 days after the second dose is 89% effective and also vaccination with one dose reduces hospitalization to 80% and prevention of mortality with *COVID-19* is 19 to 85% (16).

In one study on 152 Israeli cases, poor outcome was noted in 38 hospitalized fully vaccinated patients by Pfizer/BioNTech's and mortality rate reached 22%. (17). Lower mortality in this study maybe due to lower comorbidities than our study (4% compared with 44%). In Nawfal's study in Iraq, of the 265 participants, after the second dose of AstraZeneca vaccine, 18 (6.8%) participants were infected to SARS-CoV-2. The delta variant was responsible for all infections but none of them need hospitalization (18). According to the time of our study, similar to Nawfal's study in Iraq, the delta variant is responsible for causing this infection.

Generally, while vaccines have uncertain effects on protection against *COVID-19*, more studies are needed to find the factors related to inadequate vaccine response in patients with breakthrough infections. In Pollock's study,

out of 106,349 primary care patients, there were 69 (0.7%) breakthroughs *COVID-19* hospitalization. They reported that vaccination caused low incidence rates of hospitalization due to breakthrough infection (10). This study also showed the role of underlying diseases including cardiovascular diseases, hypertension, diabetes, risk of infection and clinical severity. Another study showed a significant reduction in vaccine efficacy with age and underlying diseases such as diabetes, chronic obstructive pulmonary disease, immunosuppression, and cardiovascular disease (19).

In our study, 51 (0.21%; 51/23304) cases had breakthrough infection. Although the incidence of severe or critical *COVID-19* illness remains low in those who are fully vaccinated, all vaccinated patients with severe or critical illness received Sinopharm vaccine compared to other vaccines. In a study reported by Hellewell et al., vaccination with different vaccines against covid-19 decreases new cases and mortality from the disease (20).

In Haas et al.'s study, vaccination at all ages has been shown to be very effective in preventing symptomatic and asymptomatic infections, hospitalization, severe illness and death. (21). The finding that more than third of the fully vaccinated cases were admitted to a hospital with SARS-CoV-2 and 5 patients were severely or critically ill, could be related to several factors, comprising long distance between the first and second dose or distance of the second vaccine and hospitalization, the new variants of SARS-CoV-2 that might confer decreased vaccine effectiveness.

In Uschner's study, among the 15,808 cases, 638 (4.03%) were positive of *COVID-19* RT-PCR after vaccination. Lower risk of breakthrough can be the reasons of older age, high percentage of face mask use, prior

SARS-CoV-2 infection, and receiving a booster vaccination. Also, the higher rates of breakthrough were reported by applicants vaccinated with BNT162b2 or Ad26.COV2. S compared to mRNA-1273, especially during circulation of the Delta and Omicron variants (22). The findings of this report have two limitations. First, recommend studying design of case-control, matched-based on age, sex, date of initial infection, Type of vaccine and other unknown confounders might be present. Secondly, this is a retrospective study design using data from a single center during an about 4-month period; therefore, these findings cannot be used to conclude causality. Our study shows that most breakthrough COVID-19 infections occurring after vaccination were mild or moderate, although a few patients had severe symptoms and required supplemental oxygen or even intensive care. More studies with larger number of patients are necessary to support these results.

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**Authors' contribution:** Mana Baziboroun and Yousef Yahyapour: Conceived the study, data analysis, coordination and manuscript preparation. Hemmat Gholinia: Statistical and epidemiological analysis, data analysis. Sayyareh Hosseinzadeh: Carried out data gathering. Farzin Sadeghi: Molecular detection and assisted in drafting the manuscript. Also, all authors read and approved the final manuscript.

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