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Original Article

# 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, Sputnic, 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, Sputnic, 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 Sputnic, 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 (%) |
|---|---|
| **Unvaccinated** | 329033 (81.7) |
| **Vaccinated (the first dose)*** | 73497 (18.3) |
| Sinopharm | 42108 |
| Sputnik v | 7042 |
| AstraZeneca | 17922 |
| Bharath, or | 751 |
| CovIran Barkat | 1055 |
| Pasto-CoV | 4619 |
| **Vaccinated (two weeks after the second dose)** | 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, Sputnic, 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, Sputnic, Bharath, CovIran Barkat or Pasto-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) | *P-Value* |
|---|---|---|---|---|
| **Sex** | | | | |
| Male | 22 (37.9) | 24 (47.1) | 46 (42.2) | 0.437 |
| Female | 36 (62.1) | 27 (52.9) | 63 (57.8) | |
| **Age group** | | | | |
| ≤ 50 | 20 (35.1) | 13 (25.5) | 33 (30.3) | 0.303 |
| >50 | 38 (64.9) | 38 (74.5) | 76 (69.7) | |
| **Job** | | | | |
| 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) | |
| **Patient Statues; n (%)** | | | | |
| 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) | |
| **Hospital duration** | 8.15±6.48 | 6.60±4.16 | 6.38±5.91 | 0.075 |
| **Symptoms** | | | | |
| 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 |
| **Comorbidity** | | | | |
| 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 |
| **Severity of Disease** | | | | |
| 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) | |
| **Outcome** | | | | |
| 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%) Sputnic, 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.

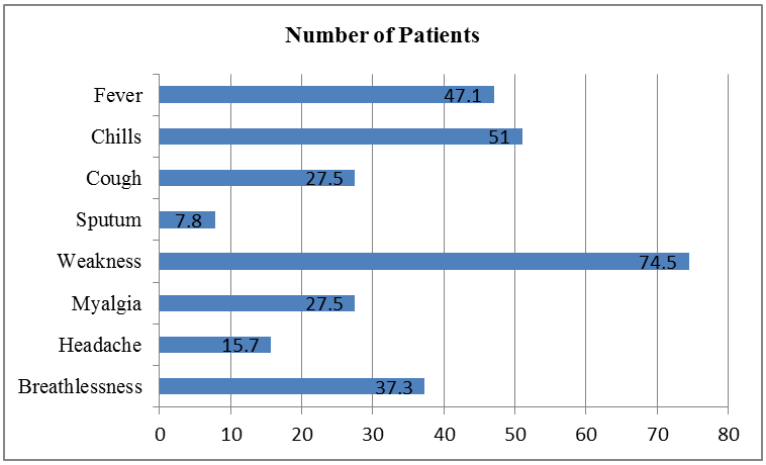


**Figure 1. Symptoms of patients with *COVID-19* breakthrough**

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

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

## Discussion

In this study, we descried 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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**Conflict of Interests:** The authors declare no conflict of interest.

**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.

## References

1. Callaway E. The race for coronavirus vaccines: a graphical guide. Nature 2020; 580: 576-7.
2. Fang E, Liu X, Li M, et al. Advances in COVID-19 mRNA vaccine development. Signal Transduct Target Ther 2022; 7: 94.
3. Machado BAS, Hodel KVS, Fonseca LMDS, et al. The importance of vaccination in the context of the COVID-19 pandemic: A brief update regarding the use of vaccines. Vaccines (Basel) 2022; 10: 591.
4. Regev-Yochay G, Amit S, Bergwerk M, et al. Decreased infectivity following BNT162b2 vaccination: A prospective cohort study in Israel. Lancet Reg Health Eur 2021: 100150.
5. Petter E, Mor O, Zuckerman N, et al. Initial real world evidence for lower viral load of individuals who have been vaccinated by BNT162b2. MedRxiv 2021: 2021-02.
6. Stephenson J. COVID-19 vaccinations in nursing home residents and staff give robust protection, though breakthrough infections still possible. JAMA Health Forum 2021; 2: e211195.
7. Tyagi K, Ghosh A, Nair D, et al. Breakthrough COVID19 infections after vaccinations in healthcare and other workers in a chronic care medical facility in New Delhi, India. Diabetes Metab Syndr 2021; 15: 1007-8.
8. Hacisuleyman E, Hale C, Saito Y, et al. Vaccine breakthrough infections with SARS-CoV-2 variants. N Engl J Med 2021; 384: 2212-8.
9. Huang YZ, Kuan CC. Vaccination to reduce severe COVID-19 and mortality in COVID-19 patients: a systematic review and meta-analysis. Eur Rev Med Pharmacol Sci 2022; 26: 1770-6.
10. Pollock BD, Storlie CB, Tande AJ, Sampathkumar P. Real-World Incidence of Breakthrough Coronavirus Disease 2019 Hospitalization After Vaccination vs Natural Infection in a Large, Local, Empaneled Primary Care Population Using Time-to-Event Analysis. Clin Infect Dis 2022; 75: 1239-41.
11. Moreno-Perez O, Ribes I, Boix V, et al. Hospitalized patients with breakthrough COVID-19: Clinical features and poor outcome predictors. Int J Infect Dis 2022; 118: 89-94.
12. Voysey M, Costa Clemens SA, Madhi SA, et al. Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine: a pooled analysis of four randomised trials. Lancet 2021; 397: 881–91.
13. Keehner J, Horton LE, Pfeffer MA, et al. SARS-CoV-2 infection after vaccination in health care workers in California. N Engl J Med 2021; 384: 1774–75.
14. Ledford H. Six months of COVID vaccines: what 1.7 billion doses have taught scientists. Nature 2021; 594: 164-7.

15. Li Q, Guan X, Wu P, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. N Engl J Med 2020; 382: 1199–1207.
16. Bernal JL, Andrews N, Gower C, et al. Effectiveness of the Pfizer-BioNTech and Oxford-AstraZeneca vaccines on covid-19 related symptoms, hospital admissions, and mortality in older adults in England: test negative case-control study. BMJ 2021; 373: n1088.
17. Brosh-Nissimov T, Orenbuch-Harroch E, Chowers M, et al. BNT162b2 vaccine breakthrough: clinical characteristics of 152 fully vaccinated hospitalized COVID-19 patients in Israel. Clin Microbiol Infect 2021; 27: 1652-7.
18. Hussein NR, Rasheed BN, Naqid IA, et al. A study of SARS-CoV-2 delta variant breakthrough infections and side effects of the Oxford-AstraZeneca vaccine. Public Health Pract (Oxf) 2022; 4: 100303.
19. Yelin I, Katz R, Herzel E, et al. Associations of the BNT162b2 COVID-19 Vaccine Effectiveness with Patient Age and Comorbidities. Available from: https://doi.org/10.1101/2021.03.16.21253686. [Preprint]
20. Hellewell J, Abbott S, Gimma A, et al. Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts. Lancet Glob Health 2020; 8: e488-96.
21. Haas EJ, Angulo FJ, McLaughlin JM, et al. Impact and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID-19 cases, hospitalisations, and deaths following a nationwide vaccination campaign in Israel: an observational study using national surveillance data. Lancet 2021; 397: 1819-29.
22. Uschner D, Bott M, Lagarde WH, et al. Breakthrough SARS-CoV-2 infections after vaccination in North Carolina. Vaccines (Basel) 2022; 10: 1922.